

## The Fundamentals of Pemphigoid Patient Education Webinar Transcript

**Becky Strong:** Welcome everyone. This call is now being recorded. I'm Becky Strong, the IPPF Outreach Director and I will be your host for today's webinar. Thank you for joining us. I'd like to thank you for being on the call with us, and for the support provided by Sanofi and Regeneron for making today's call possible. Before we begin. We want to take a quick poll to see who we have on the call with us today. If you wouldn't mind taking a moment to answer the survey in front of you, what disease subtype do you have? Let us know if you have bullous pemphigoid, mucous membrane pemphigoid, ocular cicatricial pemphigoid, or pemphigoid gestationis. And while you do that it is my pleasure to introduce you to our speaker for today. Dr. Janet Fairley is the John S. Strauss Professor and Head of the Department of Dermatology at the University of Iowa. Dr. Fairley completed medical school, residency training and a research fellowship at the University of Michigan. Dr. Fairley's interests include autoimmune skin diseases, complex medical dermatology and skin and cutaneous manifestations of systemic illness. She has published over 140 articles and book chapters. Dr. Fairley is a diplomate of the American Board of Dermatology and a member of the American Academy of Dermatology and the Society for Investigative Dermatology. Dr. Fairley is currently the President of the Dermatology Foundation and of the past-president of the Society for Investigative Dermatology. Dr. Fairley is also an honorary member of the Société Française de Dermatologie and the recipient of a lifetime achievement award from the Medical Dermatology Society. Her work on autoimmune blistering diseases has been funded by the NIH, and the Veterans Administration.

**Becky Strong:** I guess we are going to share the results of our poll. I forgot that, I'm sorry. So it looks like a number of people have bullous pemphigoid and mucous membrane pemphigoid and then a lesser amount with ocular cicatricial pemphigoid and pemphigoid gestationis so welcome to all of you, and we hope today's webinar will be very helpful, and you will learn a lot of information. Just to review some housekeeping items... (Reviews Housekeeping Slides). Now it is my pleasure to hand it over to Dr. Fairley to discuss the Fundamentals of Pemphigoid and then to have a question and answer session afterward. So welcome Dr. Fairley.

**Dr. Fairley:** Thank you. Now I just have to see if I can get this up so everybody can see it. I'm happy to be here. I've done live presentations for the IPPF before, and it's always fun to interact with members of the IPPF because, as a group you all are extremely well-informed I find and are always interested to be even more well-informed. My assignment today was the basics of pemphigoid and the variances of pemphigoid. So we'll get right at and I hope we'll have plenty of time to answer any questions that I don't answer in my presentation.

**Dr. Fairley:** So there are several types of pemphigoid. There's what we call classic bullous pemphigoid, which is by far the most common form. There's also mucous membrane pemphigoid and I'll talk about that in more detail but ocular cicatricial pemphigoid probably comes as a subtype within mucus membrane pemphigoid. Then there's juvenile bullous pemphigoid. We don't have any juvenile folks on the phone, and since they're usually under 6, that's not too surprising and it's extremely rare. I've seen only a handful of these in my entire career. And then pemphigoid gestationis which very much resembles classic bullous pemphigoid but occurs during pregnancy, and tends to be limited to pregnancy. So I'm going to

focus mainly on the top 2, but happy to answer any questions folks have about the other 2 when we get to the question and answer period.

**Dr. Fairley:** I always like to show this as kind of a place to start. If you think about your skin as a big wall, and the purpose of the wall is to keep the good stuff in and the bad stuff out. This is the Great Wall of China. It's pretty, probably no prettier than your skin. But in pemphigoid, what's happening it, you can think about it as if the foundation of this wall has just let go from the ground below. So basically the upper layer of the skin, called the epidermis, has come loose from its moorings to the dermis, and that means your skin barrier is broken, and that leads to all the signs and symptoms that many of you have. One question a lot of people have is, how is this different from pemphigus? Are they the same thing? Are they related? Pemphigus is different. Pemphigus is also an autoimmune disease of the skin but in pemphigus think about if you're looking at this wall, the bricks start to fall apart from each other. It's an autoimmune attack, but it causes a different picture than we see with pemphigoid.

**Dr. Fairley:** Here's pemphigoid. A lot of you know this, this is pretty bad pemphigoid. You can see a lot of times it starts out with these big hive-like lesions that then go on and blister. Here's your wall letting loose from its moorings. That's the upper layer of the skin, the epidermis, and it's coming loose here. That's the blister cavity, and here's the ground it should be attached to, which is, is the lower layer, the skin called the dermis. This picture is just a special test called immunofluorescence testing, and you might hear your doctor talk about that. This bright line you see here is a manifestation of the attack by the immune system on that attachment between the upper and lower layers of the skin. The cartoon here is the specific place, at least in classic bullous pemphigoid, that your immune system is attacking your skin. If you look at this yellow part, it's kind of like a rivet holding your upper layer to the lower layer and this yellow part is the part that kind of anchors down in the ground, and the green part is the portion that's sticking up into those cells up in the epidermis. Right at this area is where a classic bullous pemphigoid attacks this protein. In mucous membrane pemphigoid it's a little farther down, down deeper in the protein buried in the dermis. So that's kind of the nuts and bolts of what's going on with your immune system, and where it's attacking your skin.

**Dr. Fairley:** Classic bullous pemphigoid is the most common of the autoimmune diseases. It's interesting because it has significantly increased in incidence over the past 20 years. Some of the increase can be explained by the aging of the population but there's something else going on we really don't understand yet, because there is a true increase beyond just the aging of the population. But beyond all that, what everybody asks me is why, what the heck is going on doc, why do I have this?

**Dr. Fairley:** There are a couple of risk factors. This is all my favorites, age is a risk factor. So the average age onset is 74 years. As I said, we're having a rising incidence as the population ages, but as I already said, there's more than just that. I show this picture now, because I feel I can show this picture now because one day one of the folks I've worked with for many years now informed me I am a good candidate to be a control for all our studies in bullous pemphigoid. I'm aging right along with all of you BP patients. If any of my patients are out there they will know my line and my line is as we get older, our eyes don't work as well and our ears they'll work as

well, our skin doesn't work as well, neither does our immune system, and that's probably why, as we get older, we're more at risk for things like pemphigoid.

**Dr. Fairley:** There are age associated changes in our immune system and it predisposes you to autoimmune diseases. It also causes a decrease in adaptive immunity. So we don't respond as well as we get older to things like vaccinations but you can get this kind of chronic, low-grade, inflammatory state that puts you at risk for autoimmunity. Actually patients with classical bullous pemphigoid have increased markers on their T cells of immunosenescence. So it seems like if you have pemphigoid you have a little bit more of these changes in your immune system going on that are probably what's put in your risk.

**Dr. Fairley:** The other thing that is a marker, I'm sorry is a risk factor for classic pemphigoid is underlying neurologic disease. But I want to be really clear about this for those of you in the audience, it's preexisting neurologic disease. If you have bullous pemphigoid but you don't have any of these other things like Dementia or Parkinson's, you are at no higher risk than anybody else to develop Dementia, Parkinson's, or Stroke. But if Uncle Fred has Parkinson's disease, he has a higher risk of developing being bullous pemphigoid later on. So that association is only valid when you have the neurologic disease before you get your pemphigoid. So again, if you don't have any of those but you have pemphigoid, don't worry your risk is no higher than anybody else in the population.

**Dr. Fairley:** Why, when people have had long-standing neurologic disease are they more prone to BP? It turns out Col XVII, that little cartoon I showed you where it is attacking the skin is also expressed in the brain. Obviously it is doing something quite different in the brain, because you don't have epidermis in your brain, and we don't know exactly what function is there. But the hypothesis is the deterioration when you have dementia or Parkinson's in the central nervous system may allow your immune system to see that protein and in some patients who may have a tendency to develop bullous pemphigoid, it will bring it out. Interestingly, we've looked at this a bit, and stroke seems to be somewhat different. The risk for stroke seems to be just right around the time of the stroke, and in our patients that have stroke it doesn't seem like they're pemphigoid last quite as long, so that still remains to be studied but it is interesting that different types of neurologic disease seem to maybe have a little different mechanism for how they work.

**Dr. Fairley:** Here's another big question that folks always have, are medications a risk factor? There's been a lot of large studies. If you go looking through the literature, any particular medicine, you'll find one case report of somebody who supposedly got it right after starting a medicine. The only real accurate way to know if that is just happenstance or real, is to look at large numbers of patients and the big what we call epidemiologic studies that look at lots and lots of patients repeatedly show several medications that really do seem to have some association with pemphigoid. One are the loop diuretics, and they're used for hypertension or fluid overload in folks who have heart disease. I put just the common names here. If you're wondering is my diuretic a loop diuretic, Lasix is probably by far the most commonly used also Bumex and Demadex, those are the common loop diuretics you might be on. Thiazides are not related in large epidemiologic studies, and those are probably the very most common for hypertension. Another anti-hypertension that's been associated with is Spironolactones. Phenothiazines make the list but only if they encompass a lot of years in the population they're

looking at. Phenothiazines used to be used for mood disorders and psychiatric disorders but they're almost never used these days. We see almost no patients being put on these currently so it's kind of dropping off. When I talk to my friends who are psychiatrists, they say we have such better therapies these days, there's very few people on these, so I wouldn't worry too much about that. The other new kid on the block are the Gliptins and Gliptins are anti-diabetic agents, you'll see them advertised on TV, and those have a pretty clear association with pemphigoid. But these are the only diabetic medicines that are associated, not other diabetic medications. If somebody's been on these medications for 20 years, I sometimes have patients who've been on Lasix for 20 years, before their pemphigoid shows up, it's probably unlikely that stopping that medicine is going to have much effect on their pemphigoid. But I do think Gliptins have such a strong, oftentimes direct correlation, if you start the Gliptins the disease shows up. I've had a number of patients when we stop the Gliptins the pemphigoid remitted relatively rapidly, so might be worth thinking about with those medicines. The other new kid on the block or the PD1 inhibitors but I won't talk about these too much, but they are anti-cancer drugs. Again, you will see them advertised on TV, and they activate T cells against tumor cells. Unfortunately, they can also induce autoimmune disease, including bullous pemphigoid but that's probably just because they're unleashing all the breaks on the immune system so it makes some sense.

**Dr. Fairley:** The other big question, COVID-19 and COVID-19 vaccination. The no data here is underlined. There's no data to suggest COVID-19 or the vaccine can induce new bullous pemphigoid but let me say the operative piece here is we just don't have enough data yet to know. It may be, it may be not. Just like when I talked about medications, you have to really study a whole population to see if it really is a real association. Approximately 80% of patients in the age range of BP are vaccinated and 50% of patients over the age of 65 have had COVID recently. So it's really hard to suss out would they have developed pemphigoid anyhow during that period of time or is this really triggering it? One thing that to me suggests it's maybe unveiling itself in people who might have been programmed to develop eventually is we're not seeing BP in 20 year olds or 30 year olds or in folks that are all getting COVID and getting the vaccines as well. They aren't in the right age range and in the right population, for we normally see it. There are a number of reports of triggering mild flares, post vaccination, but again not enough to know for sure if this is true. But reported flares were mild and easily controlled, so I think currently the risk from COVID or from the vaccination is greater than the risk of flaring. The fact that folks have an autoimmune disease suggests their immune system isn't working perfectly so you don't want to add the risk of COVID on top of it. But stay tuned because there are some attempts to gather much more data to see what the real effect of COVID or its vaccination is.

**Dr. Fairley:** I'm going to talk about mucous membrane pemphigoid next. Mucous membrane pemphigoid is much rarer than classic bullous pemphigoid. If any of my patients are out there, I bless you all for participating in our database and things, because it lets us track the relative abundance of MMP patients versus BP patients. In my database currently there are about 250 patients with active bullous pemphigoid, but only about 70 with mucous membrane pemphigoid,

so less common. Here's some pictures. The most common place we see it is the oral mucosa. This is an eye with mucous membrane pemphigoid. That's what you're iris should look like normally and you see all this cloudiness and this scarring that is scarring from mucous membrane pemphigoid involving the eye. This is probably part of your body you don't get to see very often. This is down looking towards your vocal cords, and this is involvement way down deep in the throat at what's called the epiglottis and down in the area coming up on your vocal cords. Now ocular cicatricial pemphigoid and cicatricial pemphigoid, pretty much convention has gone to calling everything mucous membrane pemphigoid because some people have more scarring, some people have less scarring. So MMP is kind of the preferred term now. Ocular or OCP was a name given to mucus membrane pemphigoid that only involved the eyes. Now we have a multi-specialty clinic here in Iowa, looking at MMP and taking care of MMP patients and our outspoken ophthalmologist Mark Griner who's a cornea specialist, and sees most of our patients believes that pure ocular involvement without anything else is exceedingly rare. He says we ophthalmologists don't like to look at anything other than the eyes, and in reality, of the 70 patients in our database we really only have 2 that don't have evidence of disease elsewhere. Eyes are particularly problematic, though, because even when you reverse the disease, if you've got a lot of scarring that is much harder to deal with, the scarring can be permanent. Whereas oral mucous membranes tend to replace themselves pretty well. So do areas deep in the throat though we'll talk a little bit more about this in a minute. Here's the distribution of the various areas that can be involved with MMP, this is the study we did with our 70 patients, utilizing our ear, nose and throat specialist eye specialist, someone from the dental school, in addition we used folks from OBGYN or GI as needed. What we found in our study, when we actually had everybody see all the patients we had a much higher incidence of anal/genital involvement than previously recorded and most of this was in woman who, it isn't as easily visible to them. And if they're not having lots and lots of symptoms maybe it goes undetected. But when we examine folks on their first visit we found much higher incidents that were standardly reported. Asked my friend, Mark Griner the ophthalmologist, they're not looking at anybody's genitals in the ophthalmology clinic. So it takes looking. I also would encourage any, don't be embarrassed, please. If you have burning or anything that suggests you might have involvement in this area to let your doctor know, because there are things that can be done to help. The other thing we found is, we had a very high incidence of ocular involvement. It's a little more common in the men than the women. I would tell you, when I see somebody with ocular disease, unless it's flamingly active, I can't tell subtle disease that's why it's so important to have an ophthalmologist you work with, and we just work hands in hand because they can look into the eye and see whether there's actual evidence of inflammation back there that maybe I can't see out on the front part of the eye yet. Oral involvement is the most common. Skin is relatively common but is pretty minor in most. The ones we worry about the most are eye involvement, people with laryngeal involvement. Also, women particularly with genital involvement sometimes can really get strictures which inhibit any sexual activity. So we try to jump right on those.

**Dr. Fairley:** Symptoms that you should report for the eyes are crusting, watering, change in your vision. For laryngeal symptoms, difficulty talking, change in voice, swallowing. Swallowing can either sometimes be affected in the posterior part of the throat and the larynx, or sometimes it's in the esophagus. It's hard to sometimes separate those without having our ENT folks look down there and figure it out. For the nose, a lot of people get bloody noses, or especially in the

morning, they get real crusty stuff out of the nose. The genitals, burning with urination, pain with intercourse, those sorts of symptoms can be symptoms of MMP. I will say this, MMP tends to be pretty true to form. If you have ocular disease but you don't have it any place else, mostly it kind of stays put to where it starts. If I see somebody and they got it in their mouth or nose but have nothing in their eyes it's really quite unusual for people to progress and pull in additional sites. We don't understand that we don't know why that happens that way but pretty much it's true to form. I know a couple of people were sending questions that they were very concerned about it moving on to involve their eyes but if you had a good eye exam and a thorough workup, and you have no eye involvement it's less likely to get it down the road.

**Dr. Fairley:** MMP is not just one disease. There are several subtypes of MMP.

And they are divided up by their subtypes, depending on exactly what part of that area that holds the mucosa to its dermis. BP 180 that we talked about in classic bullous pemphigoid is one of the targets. But remember, I showed you the cartoon, the folks with MMP the body attacks a slightly different portion of the protein than people who have standard classic bullous pemphigoid that's mostly on their skin. The other subtype that is pretty well described is Laminin 332 that is another target. Another one is Collagen VII. Collagen VII is, if any of you are real mavens of autoimmune diseases in the skin, Collagen VII is the target antigen in epidermolysis bullosa acquisita. So sometimes you will here people calling this mucous membrane predominant epidermolysis bullosa acquisita or the other old name for it was Brunsting-Perry disease but basically it is a variant of mucous membrane pemphigoid that is targeting the Collagen VII protein that's another part of that area that holds the skin layers together. The other one that's a little more controversial is this fourth protein called Alpha 6 Beta 4 integrin. We do see antibodies to this in some patients with mucous membrane pemphigoid but they usually show up when folks have other antibody systems too. So they might have BP 180 plus they have this. Or they might have laminin 332 plus they have this. Nobody's ever shown that these antibodies, in and of themselves, can cause mucus membrane pemphigoid. So that's why there's a question mark next to that one. But these 3 subtypes are pretty well characterized.

**Dr. Fairley:** Subtyping MMP is not easy. It's a technical issue and it's not just an easy blood test you can order to separate out which subtype you have. To subtype our 70 patients it took us over a year to do in my research lab. But we really wanted to know, were there important differences between these subtypes and turns out there are. So we divided them into subtypes called spiderman and dermal types. When I showed you that picture of how the skin separates in classic bullous pemphigoid and all the epidermis floats to the top, and then there's the dermal layer down below. So the epidermal type, the BP 180, that would float to the top of that blister and the dermal types would float to the bottom, Collagen VII and Laminin 332. What we found when we divided folks up and we looked and saw what type they had, those that had the epidermal type that reacted with BP 180 were more likely to go into complete remission and tended to have less severe disease. The dermal types, those that targeted Collagen VII or Laminin 332 had more sites of involvement, they were more difficult to control, more likely to need something like Rituximab to control their disease and were less likely to go in remission than those that had the BP 180 type. So hopefully over time, we'll get better tests to allow determination of exactly what type folks have because there may be some real ramifications

and how aggressive we should be in treating their disease. Particularly with laryngeal involvement, ocular involvement, scarring there is what you don't want to see. I had one woman who came to see me, and she basically had a tracheostomy because nobody realized what was going on with her, and she ended up losing her airway for a period of time. We were able to get her treated and get that tracheostomy out, which was great, but we don't want to see it get to that point.

**Dr. Fairley:** The other thing, because you guys know everything, the folks at the IPPF, they've studied their diseases so I'm going to discuss this, which is the cancer risk in the Laminin 332 form of mucus membrane pemphigoid. This was described quite a number of years ago. The patients who have this type of mucus membrane pemphigoid do have an increased risk of cancer, but it's in a very narrow window around the time they develop their disease. In the first group of these patients there were for 35 patients, 10 of them had a solid tumor. But like I said, it's within that range. So if you've had mucous membrane pemphigoid for 3 years you're outside of any window of risk. It really doesn't matter what type you have the risk window is gone. Sadly, it takes so long for most people with MMP to get the right diagnosis, a lot of them are beyond their 14 month window before anybody ever realizes what's wrong. For patients that say, well I have MMP but I don't know what subtype I have, I've only had it 6 months what should I do? Because you're telling me there's not an easy way to measure what type I have. My answer to that is always, everyone should be totally up to date on your routine cancer screening. You should let your primary care physician know that you have this disease, and make sure if you have any risk factors like smoking, that they look at a chest x-ray or things that would be very targeted. But as I said, I'm very hopeful that we're going to have better diagnostic tools soon so we can subtype this.

**Dr. Fairley:** Therapy, I'm going to talk about therapy kind of generally, and I'll tell you which ones are better for MMP versus BP. We always think about it from a physician's perspective, what are we going to do for you right now to make you feel better? And then how are we going to manage this long term? And sometimes those are different questions. For the initial control there aren't a whole lot of things that can give quick control. For initial control, Doxycycline is a tetracycline antibiotic that is used quite a bit and it's used for two reasons. Number one, we published a paper not too long ago that showed that untreated patients with classic bullous pemphigoid have an extremely high rate of colonization by staph aureus. So part of this is getting rid of the staph aureus. But this also has another effect totally outside its ability to get rid of staph and that it helps prevent the enzymes that the immune system activates to chew up that basement membrane, it actually inhibits those. It's got 2 actions. A lot of times folks will be put on that quickly. High potent topical steroids, particularly if you don't have real extensive disease or also for MMP. My friend, the dentist who works with us, Dr. Ellstein makes special trays that'll hold the steroids right up on the gums and help. So if somebody's got limited disease there, sometimes we can get away without using any systemic steroids. But the reason that oftentimes we do go to systemic steroids at the early stages are the fact that it's one of the only things that acts quickly. The half-life of antibodies in your blood, and the antibodies are what your immune system is using to attack your skin or your mucous membranes, that's about 3 weeks. The prednisone is one of the few things that acts quickly and gets rid of the irritation and gets you better quickly. Other immunosuppressants that are classically used are things like

mycophenolate, methotrexate, azathioprine and none of those act real quickly. They can help get that prednisone down to a reasonable level but they don't do that well all by themselves usually, and they're more for the chronic phases of treatment. Other things early on in treatment, and I'm going to get back to this because I think we are at a tipping point of treatment for all these autoimmune diseases. I think things like mycophenolate, methotrexate, and azathioprine are going to be used less and less in the future because I think we have a lot better things coming down the pipeline

**Dr. Fairley:** For vaccination, this used to be more complicated because we had different types of vaccines, but the bottom line is all of these vaccines are safe when you are being treated for one of these disorders. You can get the Shingrix, you can get influenza, and the pneumococcal. It used to be influenza, the inhaled form was a live vaccine, so we didn't want you to get that when you were on these immunosuppressants, but nobody uses that more because it's not as effective. The only vaccination I would tell you if you are traveling internationally, and you're going to a travel clinic to get some unusual vaccinations targeted towards the areas you're visiting in the world make sure they know that you have pemphigoid and you are on whatever medications you are on or you just had a course of Rituximab so that they know because there are some of those vaccines that might not be appropriate for you.

**Dr. Fairley:** Osteoporosis prevention is another thing that comes up, and this is very specifically related to prednisone use. Everybody should be on vitamin D and calcium supplementation if you're on steroids for more than just a very short term. Baseline bone densitometry, if you haven't had it yet, a lot of women who are postmenopausal already had this, for men sometimes they're not so good about checking them, but a baseline bone densitometry is not a bad thing. And then a discussion of potentially using bisphosphonates. Bisphosphonates are medications that can be used to help prevent bone loss triggered by steroids. They are not without complications, and usually, if I am concerned that somebody is being on steroids for a long time I will refer them to an endocrinologist with special expertise and the risks and benefits of bisphosphonates, but something to be aware of.

**Dr. Fairley:** Potential new therapies. This is what makes me happy. For a long time in my career we learned so much about what was causing these diseases, and what the target was in the immune system, and what happened after those antibodies hit the basement membrane but the treatments never changed. But that is changing now. So some of the newer therapies are those that can prevent production of antibodies. The prototypical one that prevents your immune system from making those antibodies that it's using to attack your skin or your mucous membranes is Rituximab. Rituximab was initially developed to treat lymphoma where it was used along with a lot of other chemotherapy agents. It's used in a little different way for autoimmune blistering diseases but it has been very effective with pemphigus and it is actually the only approved medication for pemphigus. It tends to put disease in remission, so you take Rituximab and then for many folks it puts them in remission and allows us to stop prednisone and other immunosuppressants. It is my go to for patients with bad MMP. The lady who had laryngeal involvement, folks with ocular involvement, we tend to use Rituximab. We can get folks under control better. If I start with methotrexate or mycophenolate, and give it time to fail, that leads to increased scarring. And the ophthalmologist is all over my case to be more



aggressive, and get after it with Rituximab and try to put it in real remission to preserve the vision. The other medication that can be used, but more specifically in regular classic bullous pemphigoid is one called Omalizumab. It binds to something called IgE and in classic bullous pemphigoid, that type of antibody is important. It doesn't seem to be quite as important in MMP but this can be very helpful in classic bullous pemphigoid again to get people off the steroids. A newer medicine that's under investigation right now is one called Benralizumab. Benralizumab basically prevents activation of these cells called eosinophils in the skin. Eosinophils are activated by some of those antibodies that are attacking your skin, and they kind of join the fray and make things even worse. So this is being looked at as potentially a therapy for classic bullous pemphigoid. Right now we're not as sure the eosinophils are as important in MMP. So we'll see down the road. If it works well for classic, then maybe we'll see what we can do with MMP. Then finally preventing cytokine activation with a medicine called Dupilumab. You probably heard that on TV because it's approved for use in atopic dermatitis, and there's lots of Dupixent ads on TV. But there's some preliminary evidence that this may work quite well in classic bullous pemphigoid. Again for MMP it's not as clear, it might work. One of the issues, particularly people with ocular involvement, is one of the side effects of Dupixent can be eye irritation so that would probably be the last resort for us in people with MMP. And these are just a few of the ones, there's a lot of other things potentially, that people are interested in looking at the by their mechanism of action, at least in theory, might be helpful for either MMP or classic BP. But these are the ones that people are looking at right now so you're more likely to start hearing things about them.

**Dr. Fairley:** I said I wasn't going to talk about babies, but you know babies bottoms are usually cuter than us adults. This is a child who is treated with Omalizumab that I talked about, and that it works even in childhood form.

**Dr. Fairley:** And I think with that I'm going to open up the floor to questions, and we have at least 20 min to answer any questions that you guys have, and there is a ton of stuff in chat

**Becky Strong:** Dr. Fairley, I have to tell you that was an amazing presentation. I know I learned a lot today, so thank you so much for giving us such a great overview. We did have some questions in the chat, and I think they're good ones. Elaine is asking if she has MMP only in her mouth, which specialty is the best to be able to take care of her?

**Dr. Fairley:** Boy, I will tell you this, MMP is truly an orphan disease. Folks show up to all sorts of physicians and many of them just don't know that much about it. There's such a lag time between when people get symptoms, and when they get the right diagnosis. Usually what I suggest, I think the IPPF is developing a database where you can go look by your location and find people who have expertise in autoimmune blistering diseases. I think that will be very helpful because I will tell you that a lot of dentists aren't aware of it. A lot of ear, nose and throat doctors aren't aware of it. That's one thing that we've talked about with our multi-specialty group is we need our ENT guy to be out and talking to the ear, nose and throat doctors nationally, and we need more ophthalmologists to be talking about it. There are clearly a subset that are very interested in OCP or MMP involving the eye but we really need to raise the knowledge about it,

because that's one of the problems for the delay in diagnosis is physicians just don't know enough about it.

**Becky Strong:** Thank you, Tim says that he has been treating his disease topically, and it seems to work over time, but his disease is moving to another place. If it doesn't get worse, do you continue using a topical only, or when do you know when it's time to move to other medications?

**Dr. Fairley:** To me a lot of it is patient comfort. If somebody tells me I don't mind it, I can keep up with it. I get all healed up here, and then next week I get a little spot on my leg, but it's not much. Then I have that discussion about the risk-benefit if you want to add something else or is this keeping it tolerable for you? When people tell me I can't sleep at night, it itches so much it's keeping me awake, then I'd probably discuss some other alternatives. With MMP it definitely depends on the area of involvement. If people have progressive eye involvement, laryngeal involvement, anything like that then we're probably going to move to something much more aggressive than just topicals.

**Becky Strong:** We've gotten quite a few questions submitted to us before the webinar about the dreaded itch. Brenda asks, is there a reason that so many of the itchy eruptions on her skin are symmetrical on each side of her body? And then kind of combining that, we're getting a lot of questions about what do you recommend for itch and how to help control the itch? People are saying that it's legitimately, making them crazy and interrupting sleep and it's very problematic in their lives is the polite way to put it.

**Dr. Fairley:** Oh, absolutely. I'll tell you, I don't think anybody needs to feel apologetic about complaining about the itch because there was a quality of life study that showed that itch was every bit as disruptive to people's lives as pain. Because it does things like that, it keeps you up at night. If you can't get a good night's sleep, you're miserable. So yes, I think itch needs to be addressed. If people are still itching though, it means their immune system is still active against their skin. And when I have somebody who we are not getting past that itch, it probably means we need to be more aggressive with treatment because the reason you're itching is because the disease is still active. You may not be seeing big blisters on your skin but it means it's still active. That's one thing I always teach my residents, if somebody comes in the BP and they look really good, but they're still itching. I'm saying if you go measure their antibodies, they're still going to be positive, because they still have activity. Or same thing, if somebody looks really good, and then they call up and say, I'm starting to get itchy again, you need to come in, because that means your disease is going to reactivate. So the itch is an indicator your disease is not under great control yet, and it needs more attention.

**Becky Strong:** Great, thank you. You had discussed neurological disease, and its effect with pemphigoid, Carolyn is asking if MS is included with the neurological diseases as well?

**Dr. Fairley:** Those 3 that are based on big population studies, and because dementia, Parkinson's and stroke are so common, they show up as statistically significant. But there are a number of studies that show that folks with MS have a higher incidence of pemphigoid. Likewise, we have quite a number of patients in our database who have autoimmune peripheral

neuropathy and BP. But in all of those like what I said before, the neurologic disease seems to always pretty much predate the onset of the BP. And it is something that we really need to know more about. It's been a very tough nut to crack, to figure out exactly what it is about neurologic disease that's triggering this. And we work for some time with one of our Parkinson's disease experts here and we found that some patients with Parkinson's had very low levels of pemphigoid antibodies but we couldn't ever figure out what tipped some folks over then into actually getting the disease. So there is still work to be done for sure.

**Becky Strong:** Okay. Denise was asking for clarification when you were talking about the Lasix. She said that she's been using Lasix for edema for probably about 12 years but her issues only started about 5 or 6 months ago. Are you saying that stopping it or changing it won't have any effect on the disease?

**Dr. Fairley:** Usually it doesn't. Usually in a situation like that I think the likelihood it's going to change things is low. On the flip side it might be worth having a conversation with your primary care doctor and say, is there an alternative I could take besides the loop diuretic? If they can, it might be worth a try. But usually, when it's somebody who's been on it for years and years the likelihood of having that make your pemphigoid go away is pretty low.

**Becky Strong:** Okay, thank you. Cheryl is asking about ocular involvement, and just for a clarification as well. You had mentioned that ocular involvement with MMP if it spreads to the eyes, it happens relatively quickly. So does that mean that if it doesn't show up relatively soon after diagnosis it won't?

**Dr. Fairley:** Usually it won't. I think that's why some of the folks who are called OCP initially because they showed up with their eyes initially and maybe didn't get a good exam of their mouth or some other place it might be hiding, but it's really quite rare for the eyes to show up 2 years later or 3 years later.

**Becky Strong:** Great! We've gotten a lot of questions about Rituximab. You had mentioned that it was approved for pemphigus but do you know if it will be approved for pemphigoid? This person said that they know that this is sometimes a concern for insurance companies using treatments that are not approved. Then kind of in the same vein of that question, how do you prescribe Rituximab for MMP if it's not approved?

**Dr. Fairley:** So what I can say is, Pascal Joly in France is the one who did a lot of the studies on pemphigus that got it approved for use. Rumor has it, they are doing a similar trial with pemphigoid. So perhaps it will be approved. I have to go to bat with the insurance companies routinely. I mean, there are no approved drugs for pemphigoid, either MMP or the classic kind.

So when they come and tell me I can't give a patient something. I come back and say, do you want me not to treat them then, because there's no approved drugs. We work with a specialty pharmacists, and she's great. But there are articles out there that show that Rituximab can prevent blindness in MMP that involves the eye. So when they start to hassle me if a patient has ocular involvement, I just send them the article and say, do you really want this patient to go blind? It does take some arguing but we've had good luck getting things approved when patients need it.

**Becky Strong:** Thank you. You have covered Rituximab and other monoclonal antibodies. But do you have any information on Ustekinumab?

**Dr. Fairley:** There's not much data out there. Ustekinumab is approved for psoriasis and some other disorders. There was one paper out of Germany that suggested maybe it might be helpful but I don't think there's enough data out there compared to some of the other medications that suggests it's going to be real helpful. But as I showed, MMP is not a monomorphous disease. It's not just one type, there's different subjects. So potentially it's going to work in one of the subtypes but not all.

**Becky Strong:** Great. Thank you. Do you have any idea about the remission data for Rituximab to control moderate to severe MMP? Or are there other medications that need to be used in conjunction with the Rituximab, such as IVIg or another medication?

**Dr. Fairley:** We usually try to use Rituximab as a monotherapy. For quite a number of patients, it will put them into a complete remission, off other therapy. So we can stop the prednisone. I stop mycophenolate or methotrexate as soon as they start the Rituximab because there's pretty good data that if you mix those you're going to have higher instances of infections and things without great improvement in the treatment. So I try to use it alone without adding other things to it. If somebody's got really bad disease, we have sometimes used it along with IVIg but for many patients it will put them into remission for a period of time. I would say with MMP, one thing I can't do is reverse the scarring. So if there is scarring in the eye or the larynx that's kind of back to baseline. But for new inflammation it can oftentimes help control. That doesn't mean it won't come back at some point. So sometimes we are treating people again in a year or two years or whenever it seems to be sneaking back on them.

**Becky Strong:** Great. Thank you. So we've also gotten a few questions submitted before the webinar about scalp lesions. Is there a best way to care for the scalp lesions and are there any techniques to washing the hair that won't make the lesions worse?

**Dr. Fairley:** For most folks, I always suggest a mildly carollytic shampoo nothing too harsh. Even some of the over the counter Head and Shoulders or professional grades sometimes that can be enough to get some of the scale and things out of there. But again, the major way to get improvement is to actually treat the underlying disease, because until you do that you're kind of on a treadmill. We can add a topical sometimes but I think sometimes it's difficult because if your scalp is really raw putting a topical agent on there might make it burn putting a top of legion on there may make it burn even more so sometimes it's just hard to use those those agents

**Becky Strong:** Great. Thank you. Asha is asking, is it helpful to take niacinamide along with doxycycline for MMP?

**Dr. Fairley:** There's one paper that did that based on theory so a lot of doctors still do it. Doxycycline has been tested separately and shown to have a beneficial effect but nobody knows whether niacin helps. It's hard to find, it gives people headaches. I don't usually use it,

but some doctors will still use it based on that old paper. It's not harmful but I don't think we have great data that it's adding a lot.

**Becky Strong:** Great, thank you. Diane is asking a great question, and I guess we should have thought about it earlier so I appreciate her writing this in. What is the difference between mild, moderate, and severe disease?

**Dr. Fairley:** There's consensus groups that have kind of put benchmarks on there

but those benchmarks generally are designed for clinical trials is what I would say. It depends on if you're talking about pemphigoid or MMP. To me any involvement of the eye or larynx that can't be easily controlled, is moderate to moving on to severe disease because we know it puts those organs at risk. There are assignments, but they're designed for clinical trials, they're not very helpful for the average patient. If you're miserable and you're not sleeping at night, you've got moderate severe disease. It's disrupting your life, and I think those sort of quality of life issues are to me what's really important. If somebody comes to me and they've still got lesions, but they say, they don't bother me, I slap a little Clobetasol on them and I'm done, I'm fine. That's good. Somebody comes in with the same amount of disease and says I'm itching at night. It's keeping me up all night. Then we need to address it.

**Becky Strong:** Great. Thank you. This is a question more about remission. What is the definition of remission? And how much time should we treat bullous pemphigoid when there are no signs of the disease? Is there a length of time after the disease or lesions cease that treatment should be continued?

**Dr. Fairley:** Yeah, that's a great question. The average duration of pemphigoid is 2 to 5 years but it's a bell-shaped curve. Some people are on the long end of that, and it goes on for a while, and some people are at the short end. So it's a little bit unpredictable. What I usually will do is taper off medications one by one. I get rid of the most side-effect, producing. Usually prednisone is usually the first one I try to get rid of. Then after that I will try to get rid of the Doxycycline and then after that the topicals. What I do like to do is measure antibodies in classic bullous pemphigoid because those are pretty easily measured and if those antibodies are back to a normal range and we've got you down to really low levels, then I'm pretty comfortable telling people to stop. If you still have pretty high levels of antibodies, oftentimes when we try to stop it will come back because it's just an indicator your immune system hasn't calmed down yet. What I don't like to do is get people on a roller coaster where we get them down, and they're on a really low level of prednisone then we try to stop, and then we got to go way back up to control it. That's really disruptive for folks. So if we've got you down to a menial dose of steroids and it's not a high enough dose to give you side effects from them but you still got antibodies in your blood, then I usually keep going until we see those antibodies disappear. Most people with classic bullous pemphigoid, when they go into a true remission, we can stop their medicines, and they don't have any evidence of antibodies in their blood, it's very rare for their disease to come back later. We don't understand that, either. If we could figure out why your immune system suddenly turns off that reaction maybe we could do that earlier and make it stop right away but we haven't figured out why it goes into that remission eventually.

**Becky Strong:** Great. Well, thank you so much for that. Another question is, after using IVIg how long can remission be, or how long can it be expected?

**Dr. Fairley:** It's very, very individual. Most people say, if you're going to go into remission with it, it's some place between 6 months and a year. But if you look at MMP, I think there's maybe even more data on that out of the Lubeck group. Some people do really require more chronic use, and that's one of the issues because it's kind of a pain to continuously have to go for infusions.

**Becky Strong:** Our last question, Dr. Fairley and I know we're right at time so I hope you'll answer this one for us. We've gotten some questions about thick scarring that has developed from pemphigoid. The questions are, is there anything that can be done to help protect the skin, the new skin, and prevent the thick scarring from occurring with the disease. And if the use of silicone gels, are those effective treatments helping the scarring?

**Dr. Fairley:** Scarring usually occurs when there's been a secondary infection on top of the pemphigoid, that's one of the reasons we try to make sure there is not staph in there. The silicone gel sheetings can help some. Sometimes we can inject steroids directly into the scars to help flatten them out a bit. And I presume you're talking about on the skin rather than other places. When you have active disease, probably the best thing to do is just plain old Vaseline or Aquaphor with some sort of non-stick dressing on top of it, something fairly simple. We don't like to see real thick crusts develop on top of it. So you can shower or bathe and then get a little Vaseline or Aquaphor and then a non-stick dressing. That'll probably minimize the chances of developing with thick scars. But once they're there, there are things that can be done. You should see your dermatologists, because there are some things they can do to help with those.

**Becky Strong:** Great. Thank you. Well, this has been a very quick hour, and I really appreciate everybody who joined us today. I know that there's a lot of questions that we unfortunately couldn't get to. And I really appreciate you, Dr. Fairley for joining us and answering so many questions.

**Dr. Fairley:** Well, I thank you and I thank all the patients, too. I tell my trainees that the best things I've learned I've always learned from my patients, so thank you for sharing with me too.

**Becky Strong:** Great. I'd also like to give a huge shout out to the support provided by sanofi and Regeneron for helping to make today's call possible. Before I go, I do have a few announcements. If you're interested in learning more about pemphigus, please join us next week on February 16th at 11:00 am Pacific, 2:00 PM Eastern, with Dr. Brittany Schultz, to discuss the fundamentals of pemphigus. We'll also be having a patient webinar on Thursday, April 6th with Dr. Annette Czernik to discuss the fundamentals of prednisone, one of the treatments that Dr. Fairley talked about today. Registration for these webinars will be opening soon. We also want to thank all of those who participated in the Externally Led Patient Focused Drug Development meeting that the IPPF hosted on January 25th with the FDA. If you didn't get to speak and share your story we are still looking for people to submit written comments to be

included in our voice of the patient report. Please submit your written comments to [pfdd@pemphigus.org](mailto: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](http://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](http://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](mailto: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 and thank you to sanofi and Regeneron for your generous support to allow these webinars to happen. Thank you.