

Eye Care for Pemphigus and Pemphigoid

Amethyst: Welcome, everyone. I'm Amethyst Yale and I am the Community Engagement Manager here at the IPPF and I will be your host for today's webinar. Thank you for joining us. Today, we are joined by Dr. Praneetha Thulasi from Emory Eye Center for today's Patient Education Webinar. This call is now being recorded.

I would like to thank you for being on the call with us and to our Sponsors Sanofi Regeneron, Genentech, and argenx, and for making today's call possible. "Information is a key factor in treating and living with any condition. However, every patient's situation is unique. The IPPF reminds you that any information found on the internet or during presentations should be discussed with your own doctor or healthcare team to determine if it applies to your specific situation." Let me introduce you to our speaker for today.

Dr. Thulasi is a faculty member at Emory Eye Center, specializing in Cornea, Cataract, External Diseases, and Refractive Surgery. She graduated from Saint Louis University with a Bachelor of Arts degree in biology and a minor in mathematics and computer science. She then earned her MD and completed a one-year transitional program and her ophthalmology residency at Emory. After residency, Dr. Thulasi completed a fellowship in cornea, refractive surgery, and external diseases at the University of Illinois in Chicago. Her clinical focus includes infectious and inflammatory diseases of the ocular surface. She has presented research at numerous conferences, including the American Society of Cataract and Refractive Surgery, the Association for Research in Vision and Ophthalmology, and the North American Neuro-Ophthalmology Society. Her work also has been published in professional journals such as the Journal of Refractive Surgery, Current Opinions in Ophthalmology, and the Annals of Emergency Medicine.

Before we begin I would like to go over a few housekeeping items. Those of you who are on their computer for their webinar, You will see on your screen that you can access the audio of today's Webinar by either using your telephone, to call in, or from the speaker, and Mike on your computer. For those of you who are on their computer for this webinar, you will see on your screen that you can access the audio either by using your telephone to call in or from your speakers and mic on your computer. As you see on my screen right now you have the option to select one or the other. Please be sure to select the method that you will be using. If you would like to ask a question please type your question into the text box under the questions section in your GoToWebinar sidebar. We received many pre submitted questions prior to the webinar as this is a very popular topic. We will try our best to answer as many questions as we can within the hour.

On the webinar today we will be discussing oral care for Pemphigus and Pemphigoid. If you ask a question that does not pertain to the webinar subject I will have to ask you to email me after the webinar. For those of you on the call that aren't on the web, you will not be able to ask a question. So if you would like to ask a question, please click on the link that was provided to you

in your confirmation email. Now, it is my pleasure to introduce Dr. Thulasi to discuss Eye Care for pemphigus and pemphigoid and answer your questions.

Dr. Thulasi: Hello everybody, and thank you for the kind introduction. I work at the Emory Eye Center in Atlanta, Georgia. And I see all kinds of patients, including folks who have Ocular Cicatricial Pemphigoid. I have no financial disclosures. This is a topic that I think a lot of folks in the audience probably know and understand a lot better than anything a clinician can tell you, but as you know Pemphigus and Pemphigoid, while they show up in similar ways they are very different as far as pathophysiology is concerned. Pemphigus as you know is abnormality within cell adhesions. Whereas, Pemphigoid is an abnormality between cells in the underlying basement membrane. Eye involvement in Pemphigus Focus is generally pretty rare, primarily we deal with Pemphigoid patients, so I am going to direct this talk mostly to Pemphigoid but some of these topics should be generalizable.

The underlying cause of all issues with the eye from Pemphigoid is inflammation. And inflammation causes a lot of damage to the ocular surface. But what is the ocular surface? I know sometimes a simple term like that can be confusing. When we talk about the ocular surface, we are talking about the entire external portion of the eyeball, as well as your eyelids. As we know, the eyeball itself is protected by these windshield wipers, which are eyelids. There is a very normal anatomy of eyelids. Which when you blink closes the eye completely. We have oil glands in the eyelids about 30 in the top and 20 in the bottom and the lashes point out and away from the eyeball and help protect the eye from any external events. The surface of the eye and an inflammation that affects the I can be on the eyeball itself as well as on the outside of the eyelid and the inner lining of the eye. So, what we call a cornex is this sort of inner lining of the eyelid. And this is very important to maintain a good, healthy, normal environment. We have both the superior fornix as well as an inferior fornix. Both are very important to make sure that the normal anatomy works well. And the eyelids or the windshield wipers are the barriers that they are meant to be. Another key component to help the surface of the eye is the tears. And tears do get made in the lacrimal glands, which are underneath the eyelid. And although that doesn't seem like an obvious place for inflammation, that can be an early target for inflammation. The way that the eye surface stays healthy is by tears and when we say tears, or aqueous layer, you know, the tear surface there's actually quite a few components to it. So, if this here the epithelium is the tear surface there are just the physical tears themselves would be called aqueous and there are microscopic mucus. That kind of acts as a cushion. So every time the eyelid blinks on top of the eyeball, there isn't any trauma. On top of all these is oil or lipid layer, secreted by the eyelid glands, that keeps the tears from evaporating. All of these have to work really well for somebody to maintain a clean and clear ocular surface, without any inflammation. Of course, inflammation leads to damage of these various portions. And it can be selectively, more uncertain aspects of this tear film than others. I'm not going to go into pathophysiology because there really are hundreds and thousands of papers that address this and it's really hard to simplify everything into, you know, 30 to 40 minute talk here. But we know that there is something about patients who get Ocular Cicatricial Pemphigoid that seems to be genetic. And there is an environmental trigger, we don't know what it is. And that trigger, then, initiates a cascade of inflammation, both the B cell inflammation, and P cell inflammation. That

then causes continuous damage to the surface of the eye, and eventually leads to scarring and damage.

Now, symptoms of Pemphigoid are very gradual. In fact, so gradual that it is almost impossible to get good data on when symptoms actually start or end or when the disease process actually started in a patient. Initially, when eye symptoms start, they can be as simple as redness, irritation, dry, eye sensation. They just look like dry eyes. Overtime again, months to years. They can often lead to scar tissue on the eyeball, so not just the part you see, but also underneath the eyelid. And, as that scar tissue contracts, it can start pulling the eyelids inward, you know, so we see something called intro beyond. These are words basically letting us know that the normal anatomy of the eyelid has been so compromised that the lashes that usually protect the eyeball are now causing active damage. As this damage continues, we can start seeing more substantial scar tissue that can get to be so severe that it causes damage to the stem cells that keep the surface healthy and lead to permanent scarring and blindness. And then this is a process that happens over a course, generally thought of to be months to years. By the time they make it to me, I'm a tertiary care provider. Oftentimes, they are already in this stage, or further stage. The first couple of stages can be very subtle, and oftentimes it's not unusual for patients to go into doctors over and over again, with complaints that, say, minimally or minimally improved with normal therapies. The goal, of course, is to catch it early. Diagnose it early and treat it early before we get to the scar tissue stage. It's easier said than done. Why can't we seem to find patients right there? It's because patients who look like they just have a terrible, dry surface can be from anything, right? Dry eyes can be from a million different things. About 15% of the population have dry eyes. In fact, dry eyes are probably the most common thing I see in all the dry eye patients. A small percent, maybe less than 1%, actually end up having Ocular Cicatricial Pemphigoid. So for a provider to have OCP on their differential early would be rather unusual you know. Zebras are zebras for a reason, because it's not very common that we see them. Of course once they get to that scar tissue stage, of course it'd be great if we caught them there before any further damage happens. Again, scar tissue can happen from about 50 different things. And a lot of these things are pretty common in the general population. So, for a provider to think of Ocular Cicatricial Pemphigoid, again, has to be an extremely high degree of suspicion. Entropy is extremely common as we get older. There's entire textbooks dedicated to them. So OCP is just one of many of them. So again, you know, a great time to diagnose it. But oftentimes, not, you know, OCP is not the first thing or providers thinking about. When they get to the stem cell deficiency stage. You know, the differential starts shrinking, and OCP becomes much higher on the list. But oftentimes, that's a little on the late side. Inflammation, as we talked about, can lead to damage of that lacrimal gland of those goblet cells that make the mucus of the eyelid glands that make oils to really that inflammation causes permanent damage to many of these structures And initiates the damage, and then the damage is can become sort of self propagating. Decreased tears lead to dryness. Dryness then leads to more inflammation and inflammation causes further damage. And it's one of those things where the eye can tolerate a fair amount of stress. But once that critical threshold has been reached when enough oil glands, enough mucus glands, enough meibomian glands have been damaged. They can be irreversible. How do we diagnose this? As I said, Ocular Cicatricial Pemphigoid is notoriously difficult to diagnose. It is not uncommon for patients to come see me after having been followed

by three or four other providers for many different things. For their eyelids, for their dry eyes, for their redness for many, many things. And eventually, they make it to a tertiary care hospital. We don't have good literature on when this starts, or how long it takes for them to get to that scarring stage. We just don't, because it's so hard to catch these patients at an earlier stage. But it is very important as I said, to do without any other concepts, scar tissue on the eyeball can be from many things, and it would be a disservice to a patient to blame it all on Ocular Cicatricial Pemphigoid when he could be something else that is treatable or fixable in an easier way. So, it's very important that we take a good history of all their symptoms, all their previous surgeries, all their drops as well as any other systemic issues. You know, whether they have other rashes, if they have any symptoms in their mouth. If they have any other diagnoses that could look like Ocular Cicatricial Pemphigoid all of those can be very, very critical. It's not uncommon that I've had patients referred to me for Ocular Cicatricial Pemphigoid and they have something completely unrelated. The definitive gold standard way is to take a biopsy. So take a piece of the conjunctiva, that's the layer that covers the eyeball, and look under the microscope to see which layers have been damaged and to make sure nothing else is hiding. By nothing else, I mean other scarring diseases as well as, sometimes even skin cancers can look like scar tissue and they can be very subtle. We can also do serum testing for antibodies in the blood because as we know Pemphigoid is a systemic disease. It's not just often affecting the eyes. It affects tons of other mucous membranes as well. So they often have systemic antibodies that could help us with diagnosis as well.

The tissue biopsy, there's two different kinds of biopsies we do. One is something called anatomic pathology. It just literally looks at the cells under the microscope. And the big thing that they look for when we do these biopsies is just to make sure there isn't anything, that it's not squamous cell carcinoma, that it's not something called sarcoïd or that they don't have granulomas. So, nothing else that could make it seem like this is Ocular Cicatricial Pemphigoid but it's not. The more convincing way to diagnose this is something called immunohistochemistry. There we look for antibodies that cause damage to the layer. That then leads to the scarring in Pemphigoid. Obviously, biopsy is not perfect. If you look at literature, a patient with Cicatricial Pemphigoid having a positive biopsy is actually pretty low. More likely than not, you get a negative biopsy. The bigger the biopsy we take, the higher the chance that we get a positive result, but the larger the biopsy, the more likely that I will worsen the scar tissue. So it's one of those things where we find a fine balance. The other thing is, if the surface is so inflamed that there's nothing but scar tissue, I may not see much scar tissue looks like scar tissue. Sometimes I don't see these antibodies if it's been so severely damaged. So something to keep in mind. I'm often asked by patients, if the dive in a biopsy is negative, why am I still being treated as Ocular Cicatricial Pemphigoid? It's not uncommon that the biopsy is negative.

Now, moving on to the treatment. So there's really four main prongs to treatment. Treat the inflammation systemically because, again, I cannot emphasize enough, this is a systemic disease. This is inflammation that's coming from the rest of the body. So that's really the main thing. Treat the systemic inflammation locally on the eyeball. Prevent any further damage, and restore normal anatomy and vision as much as possible. I will not go into the systemic treatments too much. This is, you know, very complicated, very personalized, and really

depends on a patient's, each their other comorbidities, other medications, their kidney status, liver status, certain genetic disease status. So this can be extremely complicated and best left to our immunologists or rheumatology or dermatology who manage our patients. But I cannot emphasize enough without systemic treatment. There is not much I can do on the eyeball. So very, very, very critical that this is addressed as soon as possible. We then treat the inflammation locally and that is where I can help. There's a few things we can use to treat that inflammation: steroids, medicine, both cyclists foreign, and a medicine called topical. Steroids are probably the most potent therapy I have to stop inflammation. Of course, I can't keep them on steroids long term, just like we can't keep the patients on steroids pills long term. Because they can cause glaucoma, they can make the cataracts worse. They can lead to just very local immunosuppression that can then lead to an inflammation and sometimes steroids and the underlying disease itself can affect the normal recycling of collagen and can lead to a corneal melt. So you know, they're certainly not something we have the luxury of using forever, but sometimes, you know, you are stuck between two terrible choices. So our goal always is to get to the lowest dose necessary.

If I cannot get the patients off steroids with systemic therapy then we can use steroids, sparing agents, cyclosporine is probably the first in line as a steroids sparing agent that targets something called T cells. It's commercially available in a certain low concentration but you can also get them compounded at a much higher concentration and cyclosporine can really help us limit the amount of steroids necessary. These drugs burn, unfortunately, commercial or compounded. These drugs can have a lot of burning. They can also take awhile to kick in. Cyclosporine really takes about three months to see any significant persistent improvement in inflammation. Tacrolimus is another steroid sparing agent that we can use and it targets something called calcineurin and it decreases the cytokine production. It also decreases inflammation. This, unfortunately, has to be compounded. There is a tacrolimus ointment that is commercially available, that can sometimes be used on eyelids. But for the most part these are compounded drops and these burn even worse than cyclosporine but they can help limit the amount of steroids necessary. Now, restoring that normal tear film cannot be emphasized enough to prevent any further damage. And there's a few things we do to prevent further damage from the tear from inflammation. First is artificial tears. We flush away, in artificial tears, again, are available over the counter, their non prescription. And these can help us just flush inflammatory debris from the surface of the eye or decrease the amount of inflammatory cells on the eye. They lubricate the surface so that every time the eyelid blinks we're not causing further damage and they can be available in this different viscosity, right? There's the artificial tears that are just tears and there's the gel kind and there's the ointment kind. Patients always ask me which one is the best? Honestly, there is no best. Every patient prefers one or the other the keys to just make sure they are preservative free. We do not want to be adding any further to damage the surface of the eye. Punctal plugs are also often used in patients to help keep the tears around a little longer. They can be dissolvable, or they can be semi permanent, and we put them in the drainage system. So these little punctal that drain the tears off the surface of the eye. And they take about two minutes in the office. You know, again, something we use pretty cautiously because sometimes doing those two early can actually retain those inflammatory cells and make the inflammation worse but generally very benign, very well tolerated. And

highly, highly recommend doing these earlier rather than later. The third aspect is getting that lipid layer we talked about. So, we use hot compresses, and I always emphasize to my patients, these need to be hot. And the goal is to really open up those oil glands. The higher the heat, without burning your skin, the better. So, we often ask our patients to use high heat for about five minutes, followed by a gentle massage of the eyelids and cleaning the eyelid margin. Another mainstay for most of us treating OCP patients is anti-inflammatory antibiotics. These kind of work two different ways. First is they decrease the eyelid flora. So they decrease any bacteria that live on the eyelid that can lead to further inflammation, and they also change the composition of the oils, and the oil glands with those oils are better functioning. They also have some direct anti-inflammatory effects. And oftentimes, these are pretty low dose doxycycline, or minocycline that are commercially available. We can also use topicals as in azithromycin bursts or oral azithromycin. They tend to be a little bit more expensive, but they can work as well. Another very popular and often used modality is something called serum tears. So these are tears that we take from a patient's blood, spin them down, and use as tears. And they are thought to have a lot of healing properties and healing proteins, and vitamins and lipids that are generally present in normal tears that our patients don't have. They are compounded, and they can also be compounded as platelet rich plasma tears. There's not many compounding pharmacies, at least where I live, that make these. So they are pretty specialized. That are thought to have higher concentration of growth factors. Again, cost is an issue. These are compounded. So they are all out of pocket, accessibility because you know, it is not everywhere that there is a compounding pharmacy available and these two have to be kept in the fridge. So they're not very portable and that's a huge barrier to using these as well. Amniotic membrane can also be into some of our patients. These are available as cryopreserved, and freeze dried. They are what sound like the amniotic membrane harvested from new moms and their amniotic membrane. And they are thought to have a lot of growth factors and restorative properties that can really help improve the surface. They are thought to have anti-inflammatory mediators within the membrane itself, and that can trap inflammatory cells. And they also just act as a nice quote, unquote, kickstart to healing inflammation. We often use these in patients who have epithelial defects or abrasions that are really hard to treat and it can really make a big difference in patients. They are thick so they have blurred vision. Cost is also an issue, because while insurance covers them, they are expensive, and they're not also available in every doctor's office. Not as common these days, but not necessarily every doctor has these available.

Now, once we've treated the local inflammation with all these different medications, I mentioned, we want to prevent any further damage. And what I mean by that is we don't want these eyelashes turning in and constantly rub against the cornea. So in the Appalachian works we have patients get those lashes plucked. A bandage contact lens, or a large contact lens that acts as a barrier between the eyeball and the eyelid can also work really well. And they are also specialized lenses called sclera lenses. That can be a godsend. So, bandage contact lenses, essentially, just act as a barrier between the eyelid and the eyeball. So there isn't this constant persistent inflammation that continues to occur because of those eyelids rubbing against the cornea. It also gives our patients significant relief, because those lashes sticking in the eye can feel like a giant grain of sand in your eyes all the time and these can make the eyes feel so much better. Unfortunately, these cannot be kept in the eye long term because of risk of

inflammation and infection. So we do switch them out every 2 to 6 weeks, depending on the patient. And we do use an antibiotic drop just as a prophylaxis. But these can be very, very critical in the early stages when we're getting that inflammation under control. The biggest treatment that has revolutionized really the care of Ocular Cicatricial Pemphigoid is probably scleral lenses. I do not fit these, it's a contact lens specialist who specializes in these lenses, who do them. And these are big contact lenses that have a chamber that can be filled with tears. In the eyeball is essentially bathed in tears. These can be incredibly helpful not only to prevent further damage but to really restore the surface of the eye. As you can tell, these are large lenses. So, it is very important that we don't have a significant scar tissue to be able to put these lenses. And now, if a patient comes to me that so much simpler for, on our scar tissue, that I cannot get a lens, and it's really difficult to make these work. But if there's a patient who has a fornix that, that space between the island and the eyeball, and we can get a clear lens. And these can be game changers in terms of vision, in terms of healing, and in terms of any further damage. Of course, cost, right, these are not always covered by insurance. In these can be anywhere from 600 to \$1200 per eye as far as cost is concerned. And, you know, once we get to that point, where we feel like the systemic inflammation is as good as we can get it to be for at least 3 to 6 months, that the surface of the eye has been as calmed down as possible then restoring that normal anatomy can be critical. Oftentimes, our ocular, plastic surgeons, fixed the eyelids and the eyelid turns out again and either us or an oculoplastic surgeons depending on the degree of damage to surface reconstruction to remove or recess a lot of that scar tissue on the surface of the eye and restore some sort of normal anatomy. Of course, if we do either of these surgeries too early, if we do these while the inflammation is still very active, I can make things much, much, much worse. So while they seem like we should be getting to day one, that a patient shows up to our clinic, because sometimes we are doing more harm than good by doing these two. The toughest part of taking care of Ocular Cicatricial Pemphigoid patients is that despite everything we do, sometimes, just because of late diagnosis, they still continue to have severe scarring, loss of the stem cells that lead to a healthy surface and what we call almost end stage disease, where it is so difficult to really do much of anything when when patients show up at this stage. We can try reconstructing the surface. We can try turning that eyelid out. But oftentimes when there are no stem cells left, even with surgery, they're not likely to regain normal anatomy of the patient. At that stage, there's a few things we can do. Again, these are pretty intensive interventions. We can do a stem cell transplant. So, oftentimes, from a cadaver or from a family member and these stem cell transplants can help us get some stem cells so that any further surgery is actually successful. The tough thing about the stem cell transplant is that they require heavy immunosuppression, which, sometimes, if the disease doesn't cause problems, the immunosuppression can really cause problems. So, it's not everybody who can tolerate them. We can do a cornea transplant. Again, cornea transplant is only likely to succeed if there are stem cells left. So, this again isn't an option for every patient. We do plastic corneas, sometimes called a keratoplasty either Type one or Type two, that can restore vision despite less than ideal stem cells, but these are high risk surgeries, they are prone to infection. They're prone to melt and oftentimes, these surgeries can lead to other complications like severe glaucoma or retinal detachment or infection. So it's sometimes trading one bad thing for, for another high risk thing. I know as you've kind of gleaned from our conversation, taking care of Ocular Cicatricial Pemphigoid patients is very much a

multi-disciplinary approach. Often requires Cornea specialist, an eyelid specialist, so an ocular plastic surgeon, a contact lens specialist. And of course, our immunologists, so either rheumatology or dermatology. And all four of us and in glaucoma, oftentimes because the steroids can lead to glaucoma. Every specialty we really do have to work together as a team to time any interventions or really help restore vision in these really high risk patients. But as we all know, early diagnosis is key, but recovery requires a very high index of suspicion and can often be easier said than done. And it is very important that we treat inflammation early and aggressively and require that multidisciplinary team approach to help take care of our patients. Any questions or concerns? I'm happy to answer them now.

Amethyst: Great. Thank you so much. That was a great presentation and I definitely learned a lot. We've had a lot of questions come in so I'm going to just jump right in here. Sue was wondering how soon after diagnosis with Pemphigus or Pemphigoid should an ophthalmologist be consulted for their care?

Dr. Thulasi: Great question. As you know, not all Pemphigoid patients are made the same flavor. So, oftentimes patients have eye issues. I would say about 75% of CP or mucous membrane pemphigoid patients have eye issues. So ophthalmologists are consulted very early on. But there is a small percentage where they have no manifestations. And in that case, an ophthalmologist isn't necessarily as critical. It is still nice to see an ophthalmologist to make sure there aren't any subtle changes that could be identified early. I guess, to answer your question, early is always helpful especially if you have symptoms.

Amethyst: Great, thank you. And are there any special, like, phrases or even like accreditations that a person should be looking for in a doctor's bio to make sure that they are familiar with these conditions?

Dr. Thulasi: Yeah, so if you see a Cornea specialist or an oculoplastic specialist, these are something that we are extremely familiar with. These are you know, unfortunately or fortunately we know patients that do need a high level of skilled care and are a very common part of our practice. A comprehensive ophthalmologist is something that every is taught about in school and should know to look elsewhere. So it's not necessary that you go to one particular person especially if that means you have a pemphigoid. We would rather you see an eye doctor early and get filtered to the right person than wait for the right person for months and months.

Amethyst: Great, Thank you. Are there any resources to find these specialists or doctors for patients with these conditions?

Dr. Thulasi: I know organizations like the IPPF can often be helpful, But, again, I would encourage you to start with your local eye doctor, because they are probably your best resource in terms of knowledge on who in their community takes care of these patients.

Amethyst: Great, thank you. So, once a patient does find a specialist or the right ophthalmologist, how often should they be going to be seen?

Dr. Thulasi: Again, it really depends. It really depends on severity. Really depends on how aggressive those CPs are and how much is there to be done. That's a very, very, very much personalized question. I have patients with OCP that I see once a year. I have patients with OCP that I see every six weeks. So it all depends on what stage I'm seeing, and what I'm having to do if it's the end stage, or if it's well controlled.

Amethyst: Great. Thank you. Melinda asks, does having PV make her eyes more susceptible to other eye diseases such as glaucoma, cataracts, maybe if they're not on prednisone?

Dr. Thulasi: If you are not on any systemic or topical steroids, my assumption would be that you are probably just as likely as anybody else to get a cataract or glaucoma. I wouldn't imagine this. I don't know if there's ever been a big study that's been done looking at it, but just understanding the pathophysiology. If steroids weren't involved, I don't see the risk of glaucoma, or cataracts would be any higher in our ocular cicatricial pemphigoid.

Amethyst: I know you talked about the risk of being on prednisone and the effects of that, but do you know if there's any other side effects for the eye, for things, such as Mycophenolate or Rituximab?

Dr. Thulasi: No eye side effects. But, you know, they certainly have their share of systemic side effects. Absolutely. And you know anything that is immunosuppressive makes you more likely to get an infection in your eyes or elsewhere. So, of course, that should be kept in mind that there's no particular eye-related side effects from cellcept or Mycophenolate or Rituximab.

Amethyst: Does being on Prednisone cause vision loss or like, distortion of the vision?

Dr. Thulasi: Because of glaucoma, yes, because of cataracts, yes.

Amethyst: Great, thank you. Daniel wants to know what is the best method to diagnose linear IGA disease of the eyes?

Dr. Thulasi: Biopsy. So, when we send the biopsy for immunohistochemistry, or immunofluorescence they do test most of the common antibodies, including IG, IGG IGM and, you know, very, very common assuming it's ocular cicatricial pemphigoid and that they're going to have the classic IGG better and they come back as IGA. So very, very common.

Amethyst: Great. Thank you. If a person has Pemphigoid is there anything that they can do to avoid or prevent ocular disease?

Dr. Thulasi: Systemic inflammation control. Control that inflammation.

Amethyst: Brian's asking or saying that they have had difficulty getting their compounded Tacrolimus and Cyclosporine filled. Do you know of any compounding pharmacies that ship across throughout the US?

Dr. Thulasi: I personally do not have a list of compounding pharmacies that ship across the US. There's a few, and again, this is such a regional question. They can't answer them in broad terms, but you're right, there's compounding pharmacies that have closed recently, or have stopped making Tacrolimus and Cyclosporine. I don't know of any that ship across the US. That may be, again, a great question for you to list.

Amethyst: Ed wrote in and asked or said that six years ago he experienced a laceration on the lower left eyelid. He currently sees an eye specialist, and has an ocular plastic surgeon and they were not able to resolve the laceration and still has constant oozing. Do you have any suggestions to help it?

Dr. Thulasi: Again, without seeing the patient or understanding the whole case, it's very difficult to answer that question unfortunately.

Amethyst: Do you see patients, often, with any eye trauma prior?

Dr. Thulasi: Not as often. You are allowed to have normal other things, besides OCP or PV, right? You're allowed to have just good old birthdate related cataracts and just general glaucoma, normal trauma and, of course, all of those things and they don't all have to be from OCP. But, you know, is it a common thing in OCP patients that they have prior trauma, or that it's more common in OCP than others. Probably not.

Amethyst: Thank you. Elizabeth asks- do you ever use Intense pulsed light treatments or lipiflow for treatment of the gland treatment for dry eyes for Pemphigoid patients?

Dr. Thulasi: I don't have access to IPL intense pulse light treatment. I do have access to lipiflow which is institutionalized and we do use it in patients. I have not specifically used it with Pemphigoid patients, And, again, oftentimes it is a referral bias. By the time they're making it domain, they're pretty severe and you do need a pretty normal anatomy to be able to get lipiflow. But I don't see why that wouldn't have, if that's your question.

Amethyst: Dick wrote in and asked If their Pemphigoid was just in their mouth, is it common for it to move to the eyes as they get older and age?

Dr. Thulasi: So, when we look at data out there, I think about 70% or so of Pemphigoid patients do have some eye manifestations. We don't have a great idea for the order in which they come on board. Whether its mouth first then eyes, or vice versa, but it is common for eye involvement to be a very prominent part of Pemphigoid. So, to answer your question, I think it would be great to make sure you are being seen by an ophthalmologist. You know, at least initially after 50 years. So we do need to have an exam at least once every few years or just a general recommendation, and a good idea to be seen regularly.

Amethyst: Good recommendation, thank you .Dave said that their doctor mentioned that they have a central serous retinal myopathy related to taking prednisone. What does that mean and how do I manage this going forward?

Dr. Thulasi: That's a good question that is a retina colleague question. I know another specialist that often comes into play here. Steroids can have lots of side effects and one of the rare but very possible side effects is they get swelling. For lack of a better word in the retina is something called CSR or Central Serous Retinopathy, and it is the treatment unfinished stopping this. So that is where your rheumatologist or dermatologist comes into. Put you on a non steroidal anti-inflammatory. But, again, this is one of those things where you've gotta balance vision and inflammation, certainly.

Amethyst: Wonderful. Michael wrote in and asked, have you ever seen adhesions go into remission? Their optometrist believes that the adhesions got smaller and less severe. Although, they don't say if they've been on treatment.

Dr. Thulasi: The adhesions don't go away. They can become less inflamed and so the anatomy can look more normal. Once you have us and you have a symbol of, they don't direct track, go back. Now, adhesions I'm not sure which ones the eye doctor was referring to. But, you know, that's the caveat there. The serous retinopathy doesn't go away. But they can look less inflamed and that can look more normal.

Amethyst: Great. Thank you. I think you may have covered this during your presentation, but just curious, again, if a patient's been on like cyclosporine or an eye drops for six months, is there a next step for treatment to help keep the eye disease from advancing?

Dr. Thulasi: Again, case by case, single thing here. If topical anti-inflammatories aren't enough, then, that's where systemic anti-inflammatories would have to help us out.

Amethyst: Great. Susan says, What would I expect if I needed surgery for glaucoma or cataracts if I never had disease activity in their eyes prior. She had laser treatment in the office once years ago for her glaucoma with no issues.

Dr. Thulasi: If the eye has been quiet, then your surgery should be similar to anybody else's. Certainly would be watched. And you certainly, I presume, would watch a little closer than most people to make sure there's no inflammation on the eye surface. Sounds like, you know, if you don't have any ocular involvement, that's wonderful.

Amethyst: Someone who's curious, are there any supplements that they should be taking to help them keep their eyes healthy?

Dr. Thulasi: What's good for your body is good for your eyes. Eat healthy, exercise, eat lots of leafy greens, protect your eyes from UV light. So all that good stuff that helps your body helps your eyes.

Amethyst: Great. That's good advice. What about, like any holistic treatments? We get people asking about holistic treatments often.

Dr. Thulasi: Anecdotally, patients whereby one or the other. Unfortunately, I cannot be driven by anecdotes, right? I do have to do my job based on some clinical data. There aren't any serum tiers used to be holistic at some point, until it really became more mainstream. I guess I don't have any particular suggestions. There's tons of anecdotal things patients swear by that we just don't have data on, or have any evidence for that I could share with you. But, you know, again, it's something, a question that is, you know, a better answer with particulars.

Amethyst: Great, thank you. Miriam was curious which is more beneficial for OCP. Systemically, is there any data doxycycline infusion versus Rixiximab infusion?

Dr. Thulasi: Very, very different strength of anti-inflammatories. So doxycycline is a pretty mild anti-inflammatory, and Rituximab is a pretty big gun. So it depends on how bad the OCP is and I wonder if you mean Dapsone versus doxycycline. Again, certainly different potencies. Dapsone is not as strong as Rituximab. In some, that's all patients need to calm the inflammation down.

Amethyst: Great, thank you. Jane was wondering, or is said that you mentioned, like environmental triggers that can cause disease. Are there any special environmental triggers that are associated with the disease?

Dr. Thulasi: Not necessarily just the honest truth is, and I hope I got this across in my presentation. There is a lot about OCP we just don't know. And I have patients that come into my clinic and I'm gonna go: when did that start? They tell me a story that's immediate or two years ago my doctor noticed my eyelashes turning in. But then when you dig deeper. The dry eyes had been an issue for 5 to 7 years prior. Right, so it's very difficult to really understand, or know when the symptoms of OCP started, and therefore it's very difficult to know what could have triggered them, if that makes sense. There is just very little data, like longitudinal follow-up of OCP patients from onset all the way to even 5, 10 years out. So, we don't know. We think something triggers it. Just like any autoimmune disease, right? There's oftentimes a trigger either of, you know, a viral illness or some sort of stressor. Something happens that makes these immune system's to kinda become funky. There's not one thing I can point to. The big picture is that it's just that we just don't have great data.

Amethyst: Pat asked, is it common to feel like I constantly have stuff in my eyes? They're always hurting.

Dr. Thulasi: Yes, Unfortunately, yes.

Amethyst: Great. Someone was curious. Why does my doctor want to treat them with Cytoxan for their eye disease rather than Mikafanalate or Rituximab? Does Cytoxan work better to halt eye disease?

Dr. Thulasi: There is no good data that certain kinds of immunosuppression works better for eye disease versus others, because this question gets asked all the time, should I get on Dapsone or you know, there's just no good data. There are certain different strands of immunosuppressants. So, Cytoxan is incredibly potent, Rituxan is pretty darn cool. You know, so they're all differently effective, you know in terms of how strong they are. There are certain patients who cannot get Rituxan for whatever reason, and they may be better candidates for Cytoxan. If you know certain liver disease or kidney disease, I wonder if that's what's happening. But again, it's a very personally driven treatment regiment. It's hard to draw big, bold strokes about treatments there.

Amethyst: Gotcha. What about the eyelashes being removed? How frequently do you remove the eyelashes from a patient that has inward growth?

Dr. Thulasi: I'm so sorry, y'all. These are all, unfortunately, very personally driven. You know, some people's lashes grow every two weeks and some don't have any till six weeks out. If they had alopecia, sometimes even longer. So, it really is personal. Personally driven question. Oftentimes patients tell me, up in two weeks, I'm going to need those lashes out. It very much varies.

Amethyst: That makes sense, Thank you. I know sometimes it's hard to answer everybody's questions, they are certainly individual and personalized. Ann was wondering is there a percentage of how often OCP does end in blindness?

Dr. Thulasi: Again, comes down to whether or not we are truly capturing the entire breadth of OCP. Most of the papers out there come from very few institutions, very few academic bases like ours. You know, I'm not, unfortunately, seeing the early OCP that by the time the patient makes it to me, they are already at stage 3 stage 4 of OCP. Therefore, my likelihood of seeing somebody who has gone blind is much higher than somebody in the community whose screening early OCP. The problem is everybody around papers or publishing tends to be from academics where we see the severe stuff. If that makes sense, right? So the data out there, it's for severe patients. Going blind OCP is, unfortunately common, but I don't think that's all OCP patients. I don't think that's all Pemphigoid patients. I think there are so many good eye doctors and good immunologists that catch early, treat early and prevent blindness. It's just the data doesn't reflect it, because those aren't the folks who are getting published.

Amethyst: Debbie was wondering, is onset of conjunctivitis prior to Pemphigus a coincidence?

Dr. Thulasi: Difficult to say, so was this conjunctivitis, or was this a really bad layer of Pemphigus or was there a positive culture? What kind of conjunctivitis, right? Was it very viral or bacterial? Conjunctivitis is a big basket term for many, many things, viruses are often triggers for autoimmune things. We know that for many, many autoimmune diseases. So it is very possible that whatever this particular person had could have triggered her particular autoimmune disease, or maybe that conjunctivitis was always part of OCP and was just misdiagnosed. Most folks would treat it as just a garden variety conjunctivitis.

Amethyst: Great, thank you. Janet was curious If there is a risk of having cataract surgery while having active BP. And if there is a risk, what's the risk of delaying treatment?

Dr. Thulasi: So we avoid any surgery when somebody has active inflammation. The caveat being if a patient is blind and can't get around. You sometimes have to make an exception. Right? So if there is, if a patient has help, if they are ambulatory, if the cataracts are not that bad, waiting is never the wrong answer. But I certainly have patients where they can't drive, and because they live alone, they can't cook. They can't see their meds to take their meds, they can't pick up the phone and answer phone calls. I certainly have patients who have terrible cataracts where there certainly is an inability to get something done. I guess treat the patient, not the condition right, is sort of what it comes down to. Cataracts are not life-threatening. They're not sight threatening. We can always take them out anytime. It's not like we have to take them out now or else they become so big that they cause permanent loss of vision. Cataracts are always elective. But if the cataracts are so big that she can't see, is running into things and getting into car accidents, or can't do her job or can take care of her kids, maybe we still need to do the surgery.

Amethyst: Thank you. Well, that was a very quick hour. I'm going to ask one more question before we go. Isabel was wandering or saying that she was told by her optometrist that she's not a candidate for LASIK surgery because of her Pemphigus Vulgaris. Is this common or true and can you speak on Lasix for people with OCP?

Dr. Thulasi: Pemphigus Vulgaris doesn't affect eyes as much for the most part. I am going to say though, it is in general, LASIK patients. You only choose somebody to have LASIK if they are very much healthy, otherwise. It is an elective refractive almost cosmetic procedure. And we would never offer that to a patient if there's even a slight chance that we can make one of their other conditions worse. The other thing is that a very common side effect of LASIK is dry eyes, and of course, our cicatricial patients have a lot of dry eyes. And so, it does not make sense to add another variable to make their dry eyes worse. So, I agree in the sense that LASIK. It's very much an elective procedure that we may choose to do when we are very sure we're not going to do anymore harm. And there is a good chance they can be caused by eyes and can make the Pemphigoid worse. And that's a very smart decision. Not to choose too have LASIK.

Amethyst: Great. Thank you. Wonderful. Well, thank you again for being on the webinar with us, and thank you, everybody, for being on the call with us today as well. Before we go, I'd like to make a few announcements and give a huge thank you to our sponsors Sanofi Regeneron Genentech, and argenx, for helping to make today's call possible. I am excited to announce that we will be hosting this year's Patient Education conference which will be held virtually from October 21st to October 23rd! We invite leading bullous disease experts to present on research and trends, educate on disease management, and answer your tough questions. The 2022 Virtual Patient Education Conference will be an exciting and educational event for any patient, caregiver, physician, researcher, or stakeholder in the field of bullous disease. Keep an eye out for emails about registration.

Do you wish there was a better understanding of our diseases by doctors and researchers? Do you wish there were more FDA-approved treatments and better treatments available? Well here's your chance to get involved and make these goals a reality - Join the IPPF Natural History Study today! 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! You can find the Natural History Study by visiting www.pemphigus.iamrare.org

There are many opportunities coming for our community to get involved with research. From clinical trials for potential new medications and online surveys to patient opinion panels, telephone and video interviews, there may be an activity that would be right for you. This is a great opportunity for us - as patients - to really have our voices heard and to be part of scientific research to help others with our disease. Please keep an ear out by signing up for our mailing list to learn more about these opportunities.

Do you want to become a hero in our community and continue to support the free services and support the IPPF provides to you, such as today's webinar, the IPPF's Peer Coaches and our find a doctor map? If so, become a Healing Hero today! 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 \$10 or \$15 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. Thank you all for joining us today. And thank you again Dr. Thulasi for educating our community today. Well, have a great day, everybody. Thank you, again.