Oral Care Patient Education Webinar Transcription-May 21, 2024

Becky Strong: Welcome everyone. The webinar is now being recorded. I'm Becky Strong, IPPF Outreach Director, and I'll be your host for today's webinar. I'd like to thank you all for being on the call with us. Before we begin, I want to remind everybody that information is a key factor when treating and living with any condition. However, everybody's situation is unique. So the IPPF reminds you that any information found online or during presentations like today's webinar should be discussed with your doctor or healthcare team to determine if it applies to your specific situation. Today we're excited to have Dr. Victoria Wu with us to discuss oral disease, treatment and care. Before I hand it over to her, let me introduce you to her. Dr. Victoria Woo received her D.D.S. with distinction from the University of Western Ontario in 2001. Following dental school, she completed a General Practice Residency at Brigham and Women's Hospital/Harvard-wide Hospitals and specialty training in Oral and Maxillofacial Pathology at Long Island Jewish Medical Center. She received her Certificate in Oral and Maxillofacial Pathology in 2005. She served as an Assistant Professor at the Columbia University College of Dental Medicine from 2005 to 2008, Associate Professor in-residence at the University of Las Vegas UNLV School of Dental Medicine from 2008 to 2014, and Professor in-residence at UNLV School of Dental Medicine from 2014 to 2020 and now she is at Texas A&M University. Dr. Woo is a diplomate of the American Board of Oral and Maxillofacial Pathology, and fellow of the American Academy of Oral & Maxillofacial Pathology.In addition to maintaining an active clinical oral pathology consultation practice, she was the founding director of the UNLV Oral and Maxillofacial Pathology Biopsy Service. Dr. Woo is licensed to practice dentistry in Texas, Nevada, and New York. Before we begin I would like to go over a few housekeeping items… (Reviews Housekeeping Slides). Now, it is my pleasure to hand it over to Dr. Wu.

Dr. Woo: Thank you so much Becky. I'm going to go ahead and share my screen. I'm hoping everybody can see the screen.

Becky Strong: Yes.

Dr. Woo: Alright, hi everybody. Good afternoon. My name is Vicky Woo. I'm one of the oral pathologists at Texas A&M School of Dentistry. I want to thank Becky so much for the kind introduction. In addition to being one of the faculty members here, I'm also the Program Director for the Oral and Maxillofacial Pathology Residency program. So one of the most wonderful things that we do here is we educate dental students as well as dentists who are training to be oral pathologists. So I wanted to extend my heartfelt appreciation to Becky and Amethyst for putting together this webinar and giving me the opportunity to speak today. So I'm going to go ahead and stop my video and progress with the presentation. So welcome again to the IPPF Patient Education Series and before I begin, if I can advance my slide.

Dr. Woo: Okay, there we go. I did want to share that I have no conflicts of interest and no financial relationships with commercial interests.

Dr. Woo: So back in February when Becky asked me to give this seminar, I jumped at the opportunity. I was so honored and so flattered. Many know Becky to be one of the kindest, one of the most generous people on this earth, and I've had the pleasure of knowing Becky and working with her for about 10 years. We were involved in the curriculum committee for IPPF in the early years and then for the past three years she has been giving our third year dental students a lecture talking about her personal journey with pemphigus vulgaris. So it was a wonderful thing. After two years of Zoom meetings and presenting this presentation, which I will say it's probably the most appreciated and loved seminars of the entire course, I finally had a chance to meet Becky last November, and this is a picture of us in one of our classrooms. Don't be concerned about the empty seats in the back. Our classrooms are usually full, and particularly with that presentation, it was very, very full. So I did want to share this picture and again say thank you to Becky for inviting me to speak today.

Dr. Woo: So I was asked to speak on oral disease and treatment for pemphigus and pemphigoid. I thought it would be appropriate to show this little guy here. This is my son's tooth pillow wearing the very famous sunglasses, the heal our skin sunglasses, which Becky was so kind to give me in November.

Dr. Woo: This is just a general overview of some of the information that we're going to talk about today. I know that you've received excellent patient education seminars from various clinicians on pemphigoid/pemphigoid treatment, skincare, mental health, so many different things. I thought it still would be helpful to just give a general overview of mucous membrane pemphigoid and pemphigus, talk a little bit about etiology, demographics, clinical presentation, diagnosis and differential diagnosis. We'll spend a few minutes talking about treatment options. Once again, I do know that you've received excellent seminars on treatment options for both of these conditions. Some potential complicating factors, and then devote most of our time to talking about oral hygiene and care. And Amethyst was kind enough to send me some questions that you had posed beforehand. So I have a few slides trying to consolidate the questions, but I'll also be available for a live Q&A after the seminar.

Dr. Woo: So I did want to start off by just talking about the autoimmune blistering diseases, also known as the immune-mediated vesiculobullous disorders and immunobullous diseases. Really the root of this group of lesions is the autoimmune mediated pathogenesis. Autoimmune is related to any disease that's caused by the production of autoantibodies. In particular with pemphigus and mucous membrane pemphigoid, the autoantibodies are directed at components of the epithelium and the epithelial connective tissue complex. Blistering, it's a clinical term referring to a fluid-filled lesion and they can be small or they can be large. Smaller blisters are known as vesicles and larger blisters are known as bola. So that's really the root of this group of disorders.

Dr. Woo: Obviously under this category we have a number of different conditions, mucous membrane pemphigoid and pemphigus vulgaris, which is going to be the focus of today and also the focus of the IPPF. We've got the pemphigoid family, which includes a number of different disorders including bullous pemphigoid. The pemphigus family, which includes pemphigus foliaceus, paraneoplastic pemphigus and many others. And also some very, very

rare conditions, one known as epidermolysis bullosa acquisita, linear IgA disease. All of these will also fall within the category of AIBDs.

Dr. Woo: I just wanted to start off with a quick overview of pemphigus, and I do know that Dr. Amber had given an intro pemphigus maybe several months ago. So this is just meant to really jog our memory about some of the things that he may have talked about. Pemphigus vulgaris is an autoimmune disease and it really involves an interplay of genetic susceptibility and perhaps some environmental triggers. Some of the postulated or proposed environmental triggers include exposure to a chemical or drug. This is really the basis for most autoimmune diseases. If a patient is genetically susceptible to developing the disorder, there may be some sort of environmental trigger, sometimes a virus that will trigger that susceptibility and lead to the full manifestation of the autoimmune disease. So with pemphigus vulgaris, what's happening is the body is producing auto-antibodies towards a specific antigen. The antigen is found within structures known as desmosomes, which are adhesion proteins that bind the epithelial cells together. This is going to be very important in terms of being able to appreciate the clinical findings that we see with pemphigus as well as the histologic findings. We kind of think of desmosomes as the glue that holds the epithelial cells together. So when there's some sort of antibody that's disrupting that bond, it causes the epithelial cells to fall apart. Most often than not, we do see pemphigus in the adult population, but we can also see it in young adults and children as well. It's not very common in the younger population, but it has been described in the younger individuals. There is an approximately equal sex predilection, and that's a little bit different from mucus membrane pemphigoid, which really does have a female predilection. This is what's known as a mucocutaneous disease, meaning it can affect the mucosa as well as the skin. The oral findings of pemphigus vulgaris are very important because they often are the first sign of disease, the first presentation of disease. Later on, patients may develop skin lesions. It's not definite in every case, but there is the potential for cutaneous involvement. And also we can sometimes see involvement of other mucosal sites, the pharynx, the larynx, as well as the nasal mucosa and the eye.

Dr. Woo: So this is just a very basic schematic showing the structures that are really involved in the epithelial connective tissue complex. These are going to be the structures that are basically targeted by some of the autoimmune blistering diseases. So as you can see with pemphigus, the structure that really is targeted here is going to be the desmosomes. We talked about the fact that these are kind of the structures of the glue that hold the epithelial cells together. So with pemphigus, the autoantibodies are directed at a component of the desmosomes known as desmoglein 3. There's different types of desmoglein, but desmoglein 3 is the main target for pemphigus. So on the skin, pemphigus vulgaris will usually present as these fluid-filled blisters. They could be small like vesicles or a little bit larger like bullae that rupture to form erosions. And the erosions will usually have kind of these irregular or rugged borders.

Dr. Woo: One of the classic clinical findings that we see both on the skin as well as the oral mucosa with pemphigus, is a positive Nikolsky sign. You may have heard about this maybe when you've talked to your care team, but this is a clinical test that we sometimes use where there is the ability to induce the formation of a blister with gentle lateral pressure.

Dr. Woo: So this is an example of a positive Nikolsky sign. And basically what's happening here is that the tissue adjacent to an area of active disease, gentle lateral pressure is placed on that area and there is an induction of this fluid filled blister or a bullae. We can see this or we can observe this both on the oral mucosa as well as the skin.

Dr. Woo: So the oral findings of pemphigus vulgaris, again, are very important to recognize because they usually represent the first presentation of disease. The saying, “the first to show and the last to go” is really quite appropriate for pemphigus because the oral lesions are usually the first presentation of disease, but they're often the most recalcitrant and difficult to treat, so that's where the last to go comes. Clinically, we're going to see lesions that resemble the skin lesions. So redness, these erosions which represent superficial loss of the skin, the epithelial portion and ulcerations, which are deeper where you get loss of the epithelium and superficial connective tissue. They typically have these ragged borders and oftentimes at the periphery of the erosions we can see the epithelium kind of piling up. I didn't want to put too many clinical photos here, but this is kind of the classic clinical description for pemphigus vulgaris. Rarely do we see intact vesicles or bullae with oral pemphigus. And the reason is because the split that occurs is fairly superficial. And so oftentimes because it is superficially located and because the mouth is constantly exposed to low grade trauma with speaking and eating, the vesicles will often rupture and just instead form these ulcerations or erosions. With pemphigus vulgaris, a very common side of involvement is the gingiva. And it can sometimes produce this clinical presentation known as desquamative gingivitis. That's a term that we use to describe sloughing of the gingiva, and it really elicits a very specific differential diagnosis. So when we see desquamative gingivitis clinically, we're usually thinking about one of three diseases, and of course intra-orally we can also elicit that positive Nikolsky.

Dr. Woo: So the diagnosis of pemphigus is really made by correlating clinical presentation and histopathologic findings, and that's where the tissue biopsy procedure comes into play. It is really important for us as clinicians to be able to understand that when we do a biopsy in a patient that we suspect may have pemphigus or pemphigoid, that we do need to biopsy the tissue that's adjacent to the ulceration or erosion. The reason is, or the reason behind that is because the pathologist will need to see the relationship of the epithelium to the connective tissue in order to establish a definitive diagnosis. If the clinician's going to biopsy the eroded area or the ulcerated area, the epithelium is going to be missing. So the pathologist doesn't have the information that he or she needs to be able to make a diagnosis. In addition, when this biopsy is performed, ideally half of the biopsy should be submitted for traditional histology and formline. So that's what we see the majority of the time under the microscope with hematin and eosin staining. But half should also be submitted in a very special solution known as Michelle solution for direct immunofluorescent studies. And the direct immunofluorescent studies is important because it's really the study that helps to distinguish between mucous membrane pemphigoid, pemphigus vulgaris and and the third differential, which is lichen planus. In addition to that, your doctor may collect some serum or some blood, and with that serum they can perform indirect immunofluorescence studies or ELISA studies. Indirect immunofluorescence is quite successful with pemphigus. About 86% of patients with pemphigus will show a positive finding on indirect immunofluorescence. With ELISA, these are kind of newer techniques used to be able to detect the auto autoantibodies and this can also be a very, very good study as well.

Dr. Woo: So without going too heavily into histology and microscopic, I did want to show you what happens when a biopsy is submitted for immunofluorescence studies. Again, once a biopsy is taken, half of it really should be submitted for light microscopy and half of it should be for direct immunofluorescence. And what happens with direct immunofluorescence is that the biopsy itself represents the substrate and there is a solution that contains anti-human antibodies that's tagged with fluorescein that's applied to the biopsy and it will specifically localize to the areas of the biopsy that have autoantibodies. So depending on where this fluorescein conjugated solution localizes, it will tell the pathologist if this is the pattern that's consistent with pemphigus or the pattern that's consistent with pemphigoid. Very similarly is indirect immunofluorescence. There are a few extra steps here because instead of using the patient's tissue, we'll be using the patient's serum. So the serum will contain the autoantibodies if it is serum from a patient with pemphigus or pemphigoid. Then it's applied to a commercially available substrate. And then after that, once the autoantibodies have bound to the correct structures, then that solution containing the anti humanic antibodies with the fluorescein will be applied. So basically from this point on, it becomes like indirect immunofluorescence. And once again, the pattern of fluorescence will tell us if this is an example of pemphigus or pemphigoid.

Dr. Woo: So this is what the histology looks like. And because I'm a pathologist, it's really hard for me to give a presentation without at least showing a couple of microscopic slides. So please forgive me if this is very boring, but I think it's very interesting because this speaks to what the underlying etiology is with pemphigus. So with pemphigus we have the production of autoantibodies that are specifically targeting the structures that hold the epithelial cells together. So when these structures are disrupted, it results in basically a cleft which clinically translates to the vesicle or the bullae. And what we're going to see microscopically is the formation of this cleft right above the basal layer of the epithelium. It's known as a superbasal or cleft or intra-intraepithelial separation. And this will become important because if you undergo a biopsy, you'll receive a biopsy report back that indicates this particular finding and this finding is very, very characteristic for pemphigus vulgaris. Down below we can see what we see with either direct immunofluorescence or indirect immunofluorescence. And with this particular study we're going to see deposition of antibodies in the intracellular spaces. This is basically where those desmosomes are located and it results in a very classic pattern known as a chicken wire pattern, which again is diagnostic for pemphigus vulgaris.

Dr. Woo: Okay, so when we have or we see patients with a potential diagnosis of pemphigus, it's not always straightforward clinically. The diagnosis doesn't always declare itself. Sometimes there are other conditions that we consider in the differential, and a differential basically represents a list of conditions that can have very similar clinical features as what the condition represents. So I kind of mentioned before that very commonly pemphigus will occur on the gingiva and produce this clinical presentation of desquamative gingivitis. Desquamative gingivitis really has a list of three main differentials, lichen planus, mucous membrane pemphigoid and pemphigus vulgaris. So to be able to distinguish between the three involves clinical correlation as well as the findings on microscopic examination. Other potential differentials include chemical thermal injury, allergic mucosal reactions either to systemic medications or contact with certain agents such as dental restorative materials, cinnamon flavored agents. Lichen planus has a very long list of differentials, about 10 different entities that

we consider in the differential for lichen planus and those need to be ruled out by clinical correlation. For other conditions, there was a question that was posed about ulcerations or canker sores and how they differ from pemphigus vulgaris and there are things clinically that can help us make the distinction. For instance, with canker sores, those are going to be transient, meaning that they'll self resolve in about 7 to 14 days, whereas pemphigus vulgaris is a chronic condition that tends to persist unless it's treated.

Dr. Woo: Again, I didn't want to show too many pictures, but I did illustrate how there are other conditions that can have very similar clinical features as the desquamative gingivitis. So I'm hoping you can see this. There's probably a panel maybe that's covering up the top. But to the upper left we've got erosive lichen planus, in the middle we've got mucous membrane pemphigoid and to the right we have pemphigus vulgaris. You can see that each one of these is presenting as erosions or redness of the gingiva. There are some subtle clinical differences with erosive lichen planus, oftentimes at the periphery we can see these white lace-like striations and that's very, very classic for lichen planus. With pemphigoid, it tends to be more kind of generalized erosions. With pemphigus vulgaris we talked about the fact that the periphery of the lesions tends to have a little bit more of a ragged type of look, and oftentimes the epithelium piles up at the edges and that's a little bit different from what we see with pemphigoid. To the lower left we've got an example of an aspirin burn. This can mimic some of the vesicular bullous diseases, but it can be easily ruled out by clinical history. So being able to ask the individual if they have applied any type of caustic chemical to the area, and once again, once the offending agent is removed, this should completely resolve. And then to the right, we have one of my former patients or one of my former students' patients, this was a patient who had kind of redness almost like a lichenoid type of pattern on the right buccal mucosa and this ended up being an allergic reaction to denture materials. So again, the collage of images is really just to show you that there is some clinical overlap with a number of different conditions. So the key is really to be able to correlate the clinical history and histology in order to establish a definitive diagnosis.

Dr. Woo: For treatment very quickly, once again, I know I think it was Dr. Wu and Dr. Czernik, if I'm pronouncing her name, they talked about the treatment of pemphigus vulgaris. Immunosuppressive therapy is really the treatment that's given at least first-line treatment for pemphigus vulgaris. Most of the time that will be systemic steroids that can be complemented with immunosuppressive medications, also called steroids sparing drugs. Dapsone and tetracycline can also be used. If it's a condition or if the patient has more refractory disease or recurrent disease, a very good option is of course the anti-CD20 agents, rituximab as well as intravenous and immunoglobulin therapy or IVIg. There was a question that Amethyst had brought up. It was actually the very last question in the two and a half pages that she provided about low level laser therapy. And I just want to speak a few minutes about that. So with low level laser therapy, the main kind of biologic effect of that is to reduce inflammation and to accelerate healing. And there are a few small case reports and case series as well as pilot studies on using this mostly as an adjunct in addition to systemic steroids in pemphigus vulgaris. The conclusion of one of the largest studies is that there's just not enough evidence to be able to make a universal recommendation for using this therapeutic modality. And so the recommendation from that study was just basically to consider performing randomized

controlled clinical trials in order to determine whether this could be effective in terms of an adjuvant while on systemic steroids. So the jury's still out with low level laser therapy, but hopefully there'll be some information in the future and more robust scientific evidence to support its use for pemphigus vulgaris.

Dr. Woo: Okay, so next we're going to move on to mucous membrane pemphigoid. So very similar slides as pemphigus vulgaris. This represents an autoimmune disease, again involving interplay of genetic susceptibility and an environmental trigger. And with mucous membrane pemphigoid, the target's going to be a component of the basement membrane and hemidesmosomes. Hemidesmosomes are like desmosomes, adhesion proteins, but instead of binding the epithelial cells together, they're going to bind the basal epithelial cells to the basement membrane. And again, this is very important in terms of what we see clinically as well as microscopically because the disruption of the hemidesmosomes will lead to a very specific pattern that we see both clinically as well as microscopically. So mucous membrane pemphigoid, unlike pemphigus vulgaris, is really a disease of adulthood. We do tend to see this in the adult population rather than younger patients, and there is a definite female predilection. So more often we're going to see it in females than males. Oral mucosal involvement is very common. About 85% of patients will have involvement of the gingiva, but also ocular mucosal involvement, genital mucosal, nasal mucosa can be affected as well, but very rarely do we see cutaneous or skin involvement with mucus membrane pemphigoid.

Dr. Woo: So here we've got that schematic again showing you the structures that are involved with mucus membrane pemphigoid. So they're going to specifically, or the autoantibodies are going to specifically disrupt the hemidesmosomes, which are the structures that hold the basal epithelial cells to the basal lamina. So when these structures are disrupted, we're going to have a split that occurs specifically between the epithelium and the connective tissue.

Dr. Woo: So oral involvement is very common with mucous membrane pemphigoid. It is often the presenting sign of disease and the lesions can present as intact vesicles or bullae that rupture to form erosions and ulcerations. And unlike pemphigus, sometimes we're able to appreciate intact vesicles with mucous membrane pemphigoid because the location of the split or the separation is a little bit deeper. So the epithelium is a little bit more robust and can actually withstand some of the low grade trauma that we see intraorally. Again, this is one of those conditions that can present clinically as desquamative gingivitis and also will be associated with a positive Nikolsky sign. Ocular involvement occurs in about ¼ or 25% of patients with mucous membrane pemphigoid, and it can unfortunately result in adhesions or scarring of the ocular mucosa.

Dr. Woo: So this is again a very familiar slide because it's the same as what I use for pemphigus vulgaris. The diagnostic approaches are going to be the same. It involves correlation between the clinical presentation as well as microscopic findings. There are ELISA studies that will aim to detect antibodies against BP 180 and BP 230, which are components of the hemidesmosomes, which are targeted by the autoantibodies of mucous membrane pemphigoid. However, indirect immunofluorescence does not tend to have a higher rate of positivity as

pemphigus vulgaris. So when we do indirect immunofluorescence for mucous membrane pemphigoid, only 5% to 25% of patients will have a positive result.

Dr. Woo: So this is what mucous membrane pemphigoid looks like on microscopic examination. So once again, because the structures that are going to be targeted are those that hold the epithelium to the connective tissue, the split that we see is going to be between the epithelium connective tissue. It's known as a subepithelial split. So if you've ever received a biopsy report that says something like chronic inflammation, chronic mucosal inflammation with a subepithelial separation, that's basically depicting what we see on microscopic examination. And with direct immunofluorescence, we're going to see deposition of the antibodies as well as C3 complement along the basement membrane in a linear type of pattern. So this is going to be different from what we see with pemphigus vulgaris with the chicken wire pattern.

Dr. Woo: Other than that, the differential diagnosis is quite similar as pemphigus vulgaris. I just wanted to show you a few pictures. So on the very top, these were two of my patients who had pemphigoid. You can see that in each one there is buccal mucosal involvement. Down below we have a very similar appearing lesion, which happened to be an oral manifestation of systemic lupus erythematosus. And then to the right, we have a contact allergy to cinnamon flavoring agents. So there really are, I think, a number of conditions that we have to include in our diagnostic consideration list for mucous membrane pemphigoid.

Dr. Woo: So treatment is going to be immunosuppressive therapy. In my experience, with mucous membrane pemphigoid, I don't often see patients with severe pemphigoid more in the mild to moderate category. I've had very, very good luck with topical steroids. And so topical steroids applied correctly at the correct frequency, I think can be very, very helpful for gingival or oral mucosal involvement with pemphigoid. This can be supplemented with immunosuppressant medications. In more severe disease, we may need to consider the possibility of systemic steroids. Dapsone and tetracycline, I know I received a question of a patient who mentioned that they were on Dapsone. Those can also be therapeutic considerations as well. And the anti-CD20 agents are used in a small number of cases, but I think it tends to be, or at least the literature I read, it tends to be a little bit less effective in pemphigoid versus pemphigus.

Dr. Woo: So these were the patients that I showed you earlier and my patient at the top had kind of these ulcerations and erosions of the posterior buccal mucosa, and this was two months after topical steroid therapy. So we can see a very nice result on the lower left, this patient of mine had more severe involvement. It was a little bit more recalcitrant, so I did try topical steroids, but he didn't respond as favorably as I had hoped. So eventually I did end up providing steroid injections and you can see to the lower right that he had a very nice result. So there are a number of different delivery systems that we can use for steroids. Most of us do favor topical steroids, but in some occasions we'll need to provide it in an injectable type of format or even systemic.

Dr. Woo: Okay, so this was a study in preparing for the seminar that I read. It is a very interesting study, it was out of the UK. But basically looked at a five-year history of their clinic. And their clinic was very unique because it was a combined clinic of oral medicine specialists

and dermatologists. So it was a really good example of interdisciplinary or multidisciplinary care. What this chart is showing you is the different therapeutic regimens that their patients were on. The vast majority of patients did receive prednisone, but you can see some other therapeutic regimens that were used here as well. So I really enjoyed reading the study just because it was a unique situation where there was a group of individuals that came together to form this clinic. So every patient that's seen in this clinic is seen by an oral medicine specialist as well as a dermatologist.

Dr. Woo: What they really emphasized in this study was really the consideration or having a strong consideration to seek care, enter a multidisciplinary or interdisciplinary team. And what this really offers is the ability to see multiple experts in multiple disciplines. Experts that really have a good range of knowledge with these particular disorders and having them work together in a concerted way so that communication is facilitated, communication is effective, and all of this will serve to enhance patient care, improve outcomes, and improve patient experience.

Dr. Woo: So who are some of the members that you might consider to have as part of your care team? In the dental arm, you can consider maybe having the participation of an oral pathologist, an oral medicine specialist, an oral surgeon, and a periodontist. So all of these clinicians will be able to perform the biopsy. They'll be able to provide treatment as well as follow up, but only oral pathology will be able to provide histopathologic or microscopic diagnosis. So there was a question that Amethyst had asked, what's the difference between an oral pathologist and oral medicine specialist? And it really has to do with training. Oral pathology and oral medicine are very, very closely aligned in the sense that we both provide patient care, but oral pathologists will also be able to provide the microscopic diagnosis or microscopic aspect of diagnosis.

Dr. Woo: In the medical arm. A dermatologist, an otolaryngologist, many of you are probably under the care of one of the other or both. And these clinicians can provide or perform the biopsy and they can provide treatment and follow-up. And a dermatopathologist, so this would be a medical expert who's trained in clinical dermatology as well as reading slides can also provide histopathologic diagnosis. As needed, we may need to involve an ophthalmologist if there's ocular involvement, a rheumatologist, even an oncologist who may help to facilitate the rituximab infusions. And then last but definitely not least, is to have a group of individuals that's known as allied health professionals or resources. And these are critical individuals that really help with some of the other aspects of management. In this group of very special individuals, we have dental hygienists, nurses, registered dieticians, psychologists and counselors, and of course our wonderful support resources such as the IPPF. So I know that Dr. Daveley, I apologize if I'm mispronouncing the name, but he did a seminar of mental health. And I think that this is something that's really important to recognize the importance of maintaining the mental component and being able to appreciate that this is a very, very difficult group of disorders and diseases to have. And so we do need to rely heavily on our allied health professionals to be able to maintain a level of mental health as well as social health.

Dr. Woo: Okay, so the next few minutes, I just wanted to talk a little bit about complications. And again, I believe that a lot of this was probably discussed previously with patient seminars. Medical complications usually fall into the arm of medical complications related to the condition

itself and related to treatment. Many of the treatments are unfortunately associated with adverse events. One that pertains to me as a dental practitioner is candidiasis. So topical steroids as well as systemic steroids can predispose to oral candidiasis because it's suppressing the immune system, but that's very easily treated. Oral candidiasis isn't anything to be too concerned about because we have excellent medications to manage that. Skin infections, I believe Dr. Wu had talked about skincare in the setting of pemphigus and pemphigoid, so that remains a potential medical complication. And scarring really is mainly a complication associated with pemphigoid, not as much with pemphigus. Oral complications really surround the impact of disease on maintaining proper oral hygiene as well as eating. So unfortunately, especially when the disease activity is quite high, it can be very difficult to maintain oral hygiene. So home care, and this can unfortunately predispose to development of cavities or caries as well as periodontal disease. This is really where being able to receive care, professional care with your dentist and hygienist is going to be very important at those time points. In addition, because the ulcerations and erosions can cause difficulty with eating, there could be the secondary effect of nutritional deficiencies. It is really important to maintain proper nutrition in the setting of pemphigus and pemphigoid because it's really the building blocks that allow for healing of the oral mucosa. The psychosocial implications, again, I think Dr. Daveluy did talk about this, but of course recognizing that stress, physical functioning, relationships and lifestyle can be affected in patients that have pemphigus and pemphigoid.

Dr. Woo: Okay, so oral care recommendations, I think these are fairly straightforward. There was a question as to whether diet can make pemphigus or pemphigoid worse. To the best of my knowledge, there isn't anything specifically that we can eat that will make the disease worse, but there are certainly things that we can eat that can exacerbate disease. So spicy food, sharp crunchy food should be avoided if at all possible. Also, to avoid excessively sugary or cariogenic diets. If there are difficulties in maintaining oral hygiene, we don't want too many sugary foods which can predispose to cavities or caries. So trying to stick to foods that don't have as much sugar would be ideal. In terms of professional dental care, very important I think to maintain a very regular schedule of dental visits and professional cleanings. You may want to interface with your dental professional team and try to request multiple appointments so that there's not too much being done at each appointment to be able to maintain comfort. And also you want to ask your hygienist and dentist to be very, very gentle. Basically, any type of manipulation of the oral mucosa can lead to formation of lesions in the area. It's basically a Nikolsky sign. So whenever we manage patients with pemphigus and pemphigoid, we tend to do hand scaling rather than cavitron. We avoid anything with harsh abrasives or ale polishers. We try to avoid high volume suction. Again, the tissues are very, very fragile, so any type of suction or trauma to the area can be very, very uncomfortable.

Dr. Woo: Okay, so the second component in addition to professional dental care is home care. Home care really represents the second major component of trying to maintain oral health. So things that we like to recommend for home care is the use of soft toothbrushes and mildly flavored toothpaste. There was a question about water flossers. I think water flossers are very difficult to say. Some of those water flossers are very, very powerful. So I think if you want to consider using a water flosser instead of traditional floss, you want to use that at very, very low power. So don't use it at very, very high volumes. Avoid products with abrasives such as baking

soda, strong flavoring agent. So this would be a toothpaste with baking soda, which can be a little bit abrasive to the oral mucosa. Consider chlorhexidine rinses. Chlorhexidine is an antimicrobial rinse and in addition to having antibacterial effects, it also has very minor or mild antifungal, antiviral effects as well. So it can be very, very effective, particularly during times when it's very difficult to maintain oral care or home care. And then for pain, we can sometimes prescribe a suspension that contains viscous lidocaine and this will kind of numb the tissues a little bit to make it more comfortable and we'll often mix it with Benadryl as well as Maylox, certain ingredients basically to soothe the oral mucosa. And of course professional cleanings, I think I was reading and also I've recommended for patients when it's very difficult to maintain home care, this is the time I think when you want to go to your dentist and try to get your teeth cleaned professionally because they can apply topical analgesics or even provide anesthesia that will make the cleaning a little bit more comfortable. And that way we're sure that we're maintaining the health of the dental apparatus as well as the oral mucosa.

Dr. Woo: Okay, so just for the next couple of minutes, I wanted to bring some of the questions that Amethyst had sent to me. I have just a few slides here. I'm hoping you're seeing the questions at the top. There were about two and a half pages of questions. So I did try to go through them as well as I could. And one was really pertaining to why these diseases start in the mouth. And if I have oral lesions, will I eventually develop skin lesions? This really has to do with the localization and concentration of the auto antigen. In particular with pemphigus vulgaris, the autoantibody is going to be targeting the desmoglein 3, which has a higher concentration in the oral mucosa versus the skin. And this is the reason why with pemphigus vulgaris, oral mucosal involvement tends to be very early, it tends to be more severe than the skin. There is, however, some desmoglein 3 in the skin, so in some cases patients may develop skin involvement, but the oral mucosa is going to be the primary target for. So hopefully that kind of answers why these diseases have a predilection for the oral mucosa. MMP rarely involves the skin. There are other forms of pemphigoid that are primarily cutaneous diseases, but with mucous membrane pemphigoid pemphigoid, as the name implies, it really tends to be mucous membrane predominant. So involvement of the oral mucosa, the nasal mucosa, ocular mucosa tends to be more common with that particular disorder.

Dr. Woo: Okay, so the second group of questions really surrounded dental work. There were a lot of questions about will the dental work make mucus membrane pemphigoid or pemphigus worse? Does it cause it? Is it okay to have dental surgery or dental work with this disease? Can I have dental surgery or implants when I have active disease in my mouth? And there were several questions pertaining to situations where you had been advised to get maybe a crown or a filling and when should I get this done? And so first off, the dental work will not cause the disease itself. This is an autoimmune disease that's really caused by certain factors within the body, but trauma from dental procedures can definitely exacerbate or worsen the disease. And so it's really important I think to have that open dialogue with your dentist and your dental hygienist to try to be as gentle as possible. We want to have as little manipulation of the tissues as possible. We don't want to be too rough with the tissues because it is very delicate. Besides professional cleanings and emergent dental care, there should be a consideration maybe for elective dental work, to delay it until the disease activity is under control. You may not want to undergo this elective dental work when you're at the height of disease activity. You might want to

get it under control before having the elective work done. However, more emergent work will be necessary. Oftentimes with dental types of situations, it's bacteria driven and so absisis and pulpal necrosis, those are all bacterial mediated conditions. And what we do understand is that when we have a lot of bacteria in the mouth, it can exacerbate disease. So trying to reduce that bacterial load is very important. So I think in those situations where maybe there is a bacterial component and that needs to be taken care of, then there should be consideration to perform that dental work. But anything that's elective can maybe be delayed until disease activity is controlled. And once again, just the importance of open communication with your dental team, making sure to find a group of individuals that you feel really comfortable talking with maybe trying to produce a schedule or create a schedule that will help to maintain your comfort during these dental appointments.

Dr. Woo: So third set of questions was really related to how frequently should I see my dentist for cleanings when I have active disease in the mouth? And this is a nuanced question, I think everybody has a different schedule for their cleanings as well as their dental appointments. The typical one is every six months, but some of us have periodontal disease, we need to see our dentist every three months or every two months. So it really depends on the condition of your teeth as well as the periodontium. The ideal maintenance regimen will be recommended by your dentist and you may want to go more frequently if you're having some problems or if you have to space out your appointments to make it more comfortable. Consistency is really the key. So being able to stick to a constant kind of time interval for your cleanings as well as your dental appointments. You would want to consider increasing the frequency of cleanings when it's difficult to maintain home care that way, at least we know that the teeth are being cleaned professionally because home care can be very difficult when you have a lot of ulcers. And then again, I think really this is very nice to say, but sometimes it's very difficult to find a dentist and hygienist who feels really comfortable managing patients with pemphigus and pemphigoid. So I think that's where we really need to rely heavily on our support networks, the IPPF in terms of finding a group of individuals, even medical dental individuals that can refer you to clinicians that feel comfortable managing pemphigus and pemphigoid. So trying to find a group I think that speaks to each other that have a good relationship with each other and that can work together to really provide you the best care possible.

Dr. Woo: Okay, fourth question was, is it possible to have scarring in my throat? If so, what doctor should I see? And the scarring is primarily a complication of mucous membrane pemphigoid, and it's really the result of involvement of pharyngeal and laryngeal mucosa. So I think when we have activity farther back in the mouth, this is really when we need to start seeing clinicians that have the ability to visualize those areas. So an otolaryngologist or ear, nose and throat physician may be necessary at the time to involve them in order to be managed properly.

Dr. Woo: And I think the last set of questions, are there any diets or foods that can help to make this better? What type of foods are best to keep blisters from getting worse? So not necessarily any foods I think that can make the condition better, but there's certain foods that we can avoid to prevent exacerbation of disease. I always like to tell patients best, your symptoms are really going to dictate what foods to avoid and what foods are a little bit better during disease activity. I mentioned before, avoiding spicy or sharp foods, avoiding excessively sugary foods. I think

those are very good for all of us, but certainly when we have pemphigus and pemphigoid, I think those are very good things to adhere to as well and try to maintain a balanced diet to prevent nutritional deficiencies. Nutrition is really important again to ensure that we have the proper healing mechanisms to be able to manage some of these ulcerations and eruptions.

Dr. Woo: So this is my last slide, which is the take home messages. What I really found as I was kind of researching the seminar was how important and how valuable it can be to have a multidisciplinary team. And I think that makes a lot of sense. We might not think about it a whole lot, but the ability to have a group of individuals that can really speak to each other and understand, I think can really provide the best patient outcomes and best patient experience. And that's as a clinician, all we really care about is our number one goal is to make this as positive as an experience to help you as much as possible. So again, finding a multidisciplinary team I think can be very, very valuable. At least from an oral standpoint, maintaining a regular schedule of professional dental cleanings in conjunction with daily home care. And realizing that you're not alone. There's wonderful groups, the IPPF, other support groups, allied resources that you can rely on to be able to provide that kind of mental health and the ability to discuss this with other individuals that are going through the same experiences. And of course, your medical and dental specialists are always there to help as well. So that's all I have, and I wanted to thank you so much for your attention and this is my email address, so if you have any questions for me, feel free to reach out to me by email and I'd be happy to answer those at any point going forward. And just want to know if you have any questions. I do have a couple of references here, so if you'd like me to send that, I'd be happy to. But now I'm happy to answer any questions that you have.

Becky Strong: Well, thank you Dr. Woo. You put a lot of information and a lot of work into that, so I sincerely appreciate that.

Dr. Woo: My students are always telling me that if it's not a hundred slide PowerPoint, it's not a Dr. Woo presentation. So I'm so sorry if I went through too much or if I went through too quick.

Becky Strong: No, that was great. Jackie is asking, can a person have antibodies to desmoglein 1 or 3 only and then develop antibodies to both or later in life?

Dr. Woo: Yeah, so that's a really good question. Desmoglein 3 primarily is pemphigus and desmoglein 1 is usually pemphigus foliaceus, which as would expect we have a higher concentration of desmoglein 3 on the skin. So with pemphigus foliaceus we're going to have primarily skin ulcerations. There's something known as a desmoglein compensation theory where actually antibodies towards one will kind of help, I think to protect against the other. I don't know if it's possible then to convert to developing autoimmunity against the other desmoglein, but it could possibly represent one of the explanations for why patients might develop skin lesions later in disease with pemphigus vulgaris. So not a hundred percent sure. There's a lot of great research on the desmogleins. One of the seminal groups out of University of Toronto and Japan really studied desmoglein. They were the pioneers. So if I can find the answer to that, I'll definitely let you know. But I'm not sure, just knowing that the clinical

manifestations are primarily related to the concentration of desmoglein in the skin versus oral mucosa.

Becky Strong: Great. Frank is asking a similar question. Over time with MMP, is it likely for antibodies to shift the area in which they attack, such as from the mouth to the eyes?

Dr. Woo: I don't know about the shifting. I think the autoantigens are fairly well defined with MMP. If we go back to the slide, there's about six of them, I believe. And so oral or ocular involvement, it does fall within the spectrum of MMP. So I'm not sure it's a shift per se as much as just increasing involvement in that area. I think it's very well known with pemphigoid that there can be ocular involvement, but not everybody with pemphigoid develops ocular involvement. It's really only about 25% of patients. I'm really not sure why an individual with pemphigoid will develop ocular involvement versus not. Some of it might have to do with delays in treatment. So I think if treatment is instituted early, then we might be able to keep the disease localized to one area versus involving other parts of the body.

Becky Strong: Great, thank you. We've had a couple of requests to go back to your slide with the references.

Dr. Woo: Oh, okay. Sure. This is by no means all inclusive. These are just the ones that I put together yesterday. I included a few on the low level laser therapy. I thought that was very interesting and I really appreciated that question that Amethyst sent to me because I wasn't aware that this was something that was being used. The only thing I wanted to emphasize with that, again, the studies really use it more as an adjuvant rather than a standalone therapy by itself. So the immunosuppressive still really plays a major role in the management of pemphigus.

Becky Strong: Great, thank you. So there was a question, you were talking about topical steroids, and I think you covered it in the webinar, but can you just reiterate what kinds of topical steroids are generally used?

Dr. Woo: There's a variety. Topical steroids are split into different groups depending on their potency. And so mostly with oral, we'll use dexamethasone elixir, which I think is the mildest. Fluocinonide, which is moderate to high potency, and then clobetasol, which is high potency. They are in different formulations. Clobetasol can be in a gel, fluocinonide is usually a gel and dexamethasone is a rinse. and They're given at different frequencies. The key I think with topical steroids is really compliance and also making sure that the topical steroid contacts the oral mucosa. It only works as well as when it touches the oral mucosa and there's absorption in that area, which then initiates the anti-inflammatory immunosuppression in that area. One of the things I find is that it's very difficult to make gel stick inside the mouth. The mouth is very moist, it's got saliva. So oftentimes I'll recommend patients just gently dry the area without being too rough because again, the mucosa is quite thick, but drying it really helps the gel to stick a little bit more.The rinse is a little bit easier, but then with the rinse, we have to make sure to just lavage the area for long enough to be able to allow that absorption of the medications. And that actually, if you don't mind, it brings me to another point. There was a question about a lot of

these medications being for external use only. That's something that we talk about a lot with patients. When I prescribe fluocinonide for various oral mucosal disorders, I'll always let the patient know that the container or the box will save for external use only, and in my prescription I'll actually say approved for internal use so that the pharmacist isn't concerned about it. So the reason it says that is because these medications, they're not necessarily approved by the FDA for intraoral use, but we have been using the medications with safe results for decades and decades and decades. So that would be the reason why there is a warning. But just rest assured that this is pretty much our mainstay treatment for oral mucosal disease, and as long as it's used as directed that it shouldn't have any deleterious or adverse effects except for candidiasis. That's the only thing. But again, we can manage that with antifungal therapy.

Becky Strong: Great. Michael is saying that triamcinolone, a dental paste will cost $83 for a small 5 gram tube. Is there quality evidence to show that it actually helps the oral lesions to heal faster, and is there a cost effective alternative?

Dr. Woo: Yeah, that's a fantastic question. So thank you so much. So triamcinolone orabase is that dental paste. Triamcinolone itself is not a very expensive medication, it's generically available. I think what makes it kind of expensive is the orabase. My experience with orabase hasn't been great. It tends to have a very gritty texture. It's really meant to be a vehicle that sticks to the oral mucosa and therefore allows the topical steroid to contact the mucosa. But in patients with pemphigus and pemphigoid, that grittiness can be very, very uncomfortable, I think to spread on the oral mucosa. So I tend to not favor orabase. So an alternative I think would be fluocinonide gel, which is generically available, that might be a little bit less expensive. Or if your clinician feels comfortable, just using a slightly higher potency steroid clobetasol cell gel is also an option as well. So sometimes it's just really a matter of trying the different medications. If it's really a cost prohibitive type of medication, there are other topical steroids available that can have similar effects. In terms of the potency of triamcinolone, it's quite low, so it's under fluocinonide and it's under clobetasol in terms of steroid potency. So as long as your clinician feels comfortable just prescribing something a little bit stronger, then fluocinonide I think is a really good alternative.

Becky Strong: Great, thank you. We also got a question from somebody who was using a steroid dental paste on the gums for a flare and they ask, can topical steroids accelerate receding gums?

Dr. Woo: So that is a question that we receive quite frequently. So what we know about topical steroids on the skin, and the reason why we tend to be very careful is that it can thin the skin, but that doesn't happen as frequently intraorally because we have saliva and we have saliva that washes a lot of it away. And so we don't worry too much about mucosal thinning with topical steroids. Any type of recession really has to do with the dental apparatus. So that would be the bone support system, the gingiva, which shouldn't be affected with topical steroids. Any recession that's appreciated might be because there's a reduction in swelling or inflammation in the area. So the recession may have been there already, but it’s kind of declaring itself because there's less inflammation and swelling in the area. So to the best of my knowledge, it doesn't cause recession specifically. And a lot of that is because applying topical steroids intraorally is

quite a bit different than applied topical steroids on the skin. On the skin, it stays there and it can't go anywhere until you wash it off with the oral mucosa, it's just naturally washed off with saliva.

Becky Strong: Great. John is asking a question that we get here at the foundation a lot and then reach out to our medical advisors. Is it possible to get whitening treatments now that my treatments for pemphigoid have stabilized my symptoms?

Dr. Woo: Yeah, so that's a good question. I don't think that there's any contraindication for that. I think it would depend on how the whitening is administered. So if you do more of an in-office situation where it's one and done, as long as they maintain the solution on the teeth there really shouldn't be any problems. But some of the whitening systems are delivered in trays, and so I would just say that the trays are fine as long as fabricated in a way that they only stay on the teeth and they don't have sharp edges because the last thing we want are trays with sharp edges irritating our oral mucosa. So I think the trays are okay as long as they're well fabricated and they're very smooth on the edges. The other thing with trays, it's done at home, so you're squirting the whitening solution in the tray. So you don't want to over fill the trays because we don't want that solution necessarily touching the oral mucosa. So that might be a situation I think we're having more of a professional in-office procedure might be a teeny bit better because they can be very careful about making sure that the solution doesn't touch the oral mucosa and also you don't have that tray issue with that constant irritation from basically a mouth guard in your mouth every single night.

Becky Strong: Great. I know we're over time already, but can I ask one more question?

Dr. Woo: Sure.

Becky Strong: Okay. Marqueta asks, do you have any opinion on how to polish teeth in the dental hygienist practice if the pumice paste can hurt the gingiva?

Dr. Woo: Yeah, this is a great question. Something that we discuss all the time with our residents, not even in the context of mucous membrane pemphigoid and pemphigus. The polishing is not a hundred percent necessary. Please, if there's any dental hygienist in the audience, please correct me if I'm wrong, but it's really more of a satisfaction type of thing. It kind of soothes the teeth. The issue with pumice is it really contains these granules that can become embedded within the tissue, particularly if the mucosal interface is compromised by ulcerations and erosions. And what we're finding, and this is really kind of something that we're discovering, it's evolving over time, is that many of those pumice pastes contain components or ingredients that can elicit an inflammatory response. It's what's known as foreign body gingivitis. So we've now gotten to the point where we don't even recommend using any type of polisher after a dental cleaning, to wait a couple of days for the oral mucosa to heal before polishing or just not polishing at all. Because we know that when we go through the dental cleaning, there is some abrasion of the gingiva and the sulcus, which is the lining between the gingival pocket and the tooth. And when that's compromised, we can get this material stuck in it and can have some long-term effects. So I think if possible, to avoid the polishing, and again, I'm very open to

anybody who has objections or maybe if there's real value to the polishing besides the feeling of nice smooth teeth, to try to avoid that. I think in the setting of any type of mucosal trauma, whether it's just a professional cleaning or mucous membrane pemphigoid, there really isn't anything out there. There are some pumices that don't contain silica. Silica is really the main ingredient that we're concerned about. So if there's a possibility, I think of finding a practice where they have some sort of paste that doesn't contain silica as an ingredient but most of them do. I think that's what we're seeing can create some problems, whether it's pemphigus or pemphigoid or just a patient that has abrasion related to a professional cleaning.

Becky Strong: Great. Thank you so much. This has been a very educational time. I know we went over time, and so I appreciate everybody hanging with us, and I really appreciate all the hard work and the questions that you've answered today. Dr. Woo.

Dr. Woo: You're most welcome. Thank you so much for everybody's attention, and again, feel free to email me if you have any additional questions. If I can't answer it, I'll look it up or I will ask my very nice family of oral pathologists here at the university and we'll get you an answer.

Becky Strong: Well thank you. Before we go, I do have a few announcements. I hope you'll join us on our next webinar on June 3rd where Dr. Animesh Sinha will be discussing social determinants of health and pemphigus. Then on June 10th, Dr. Rachel Lipman, we'll be discussing immunosuppressant treatments for pemphigus and pemphigoid. You can scan the QR code on the screen or go to the website to register for these webinars. Please be sure to register for each webinar individually that you would like to attend.

Becky Strong: Next, if you want to stay updated about upcoming webinars, events, and important news in our community, you can opt into our emailing list. You can join our emailing list by visiting our website, www.pemphigus.org. Scroll to the bottom of the page and enter your email into the join email list box.

Becky Strong: Next, we are excited to announce this year's patient education conference will be held in person in Newport Beach, California. We hope to see you there so we can finally meet in person. The conference will be held October 26th and 27th, so please mark your calendar. Registration will be opening soon and space is limited, so see you in October.

Becky Strong: Next, have you checked out the IPPFs newest resource, the IPPF Guide to Pemphigus and Pemphigoid. This guide is intended to provide medically reviewed information relevant to the most common questions people have when first diagnosed with pemphigus or pemphigoid, as well as educational information about ongoing disease management and treatment options. Through this guide and other IPPF resources, we hope to empower the community with essential knowledge that can make living with pemphigus and pemphigoid much more bearable.

Becky Strong: Also, you can check out the IPPF Find a Doctor directory. We now have a directory style of listings of providers that allows you to search by many criteria to find doctors in

your area who are familiar with pemphigus and pemphigoid. You can scan the QR code to access the directory or you can visit our website.

Becky Strong: Next, do you want doctors and researchers to understand our disease better? 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 and the US Food and Drug Administration, the FDA. Your information is private and the IPPF Natural history Studies follow strict government guidelines to ensure patient information is protected. The IPPF will use your participation and the data 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 affect the future of all people affected by pemphigus and pemphigoid. So get involved today. Visit www.pemphigus.iamrare.org and join the Natural History study today.

Becky Strong: We would also like to thank everyone in our community for their continued generous support of the IPPF. Your donations help connect patients with support, resources and disease experts, as well as raise awareness with your support. We also shared the patient experience with medical and dental students and professionals, advocate at the government level and promote research. Scan the QR code on your screen or visit www.pemphigus.org/donate in order to donate today. You can ensure that our programs are available to all that need them today, tomorrow, and for years to come. Also know the IPPF has virtual support groups across the country. If you're interested in attending a meeting, please check out the IPPF's event page to register. We're also looking to expand our network, so if you'd like to start a support group in your region, please contact me, Becky Strong at becky@pemphigus.org. It's a lot easier than it sounds to start a group and you can help connect others in your area affected by pemphigus and pemphigoid. Please know a recording of today's presentation will be sent out following this webinar. Thank you everybody for joining us. Goodbye.