

April 9, 2020 COVID-19 Patient Education Series

Becky: Welcome everyone. This call is now being recorded. I would like to thank you for being on the call with us this evening and a big thank you to our sponsors Genentech and Principia Biopharma for making today's call possible. Our speakers today are three members of the IPPF's medical advisory Council. Dr. Emanuel Maverick is an Immunology researcher and associate professor at the University of California Davis Department of Dermatology. There he runs a clinic that specializes in the treatment of patients with severe immune-mediated diseases involving the skin. Next at the University of Pennsylvania, Dr. Aimee Payne serves as the Albert M Klingman Associate Professor of Dermatology, Director of the NIH funded Penn Clinical Autoimmunity Center of Excellence, Core Director for the Skin Biology and Disease Resource-based Center, and Associate Director of the Medical Scientist (MD-PhD) Training Program. Dr. Payne's clinical practice specializes in the diagnosis and treatment of patients with autoimmune blistering diseases. Our third panelist is Dr. Mary Tomayko. She is a physician scientist who specializes in the diagnosis and treatments of autoimmune blistering diseases and other immune-mediated skin diseases. Dr. Tomayko is the Director of Dermatology Education at Yale University School of Medicine. Thank you all for joining us on the call today.

Dr. Payne: Thank you.

Dr. Tomayko: Thank you.

Becky: On the call today we will be discussing COVID-19 or the coronavirus and pemphigus and pemphigoid. So now it is my pleasure to introduce to you Dr. Mary Tomayko, Dr. Aimee Payne and Dr. Emanuel Maverakis to answer your questions and to give us some more information about COVID-19 and pemphigus and pemphigoid.

Dr. Tomayko: Hello and welcome to everyone. This is an important topic that is on the front of all of our minds. We are happy to be here to help answer questions and hopefully alleviate some concerns and give you some tools to help protect yourselves today. So I'm Mary Tomayko and I'm going to begin. We're going to, first the three of us are going to give an

overview to you, which actually Becky if you can go advance to the next slide. So this is how the overview is going to go. First, I'm going to give you some background on the virus and on symptoms and then Dr. Payne will talk about risk factors for more severe COVID-19 disease and give current data on outcomes and then Dr. Maverakis will give some advice about how to protect yourself during this COVID-19 outbreak. At that point we will proceed to a panel discussion with questions and answers.

Dr. Tomayko: So we can go to the next slide, please. Okay, so here let's go over a basic primer on the terminology to make sure we're all on the same page. So coronavirus, what is a coronavirus? So coronavirus is a name for a very large family of viruses that cause respiratory illness in humans as well as other mammals. Some famous coronaviruses that we've heard about in the news over the past two decades have been the SARS virus, the MERS virus and now this new virus which is the SARS-Co-V2 virus. In addition to these very famous viruses, coronavirus causes many other upper respiratory infections both in adults and in children. So SARS-Co-V2 that is the official name for the virus that's causing this current Global pandemic. It stands for severe acute respiratory syndrome coronavirus 2, also called the novel coronavirus to distinguish it from the SARS that was the outbreak in 2003 and much of Asia and then COVID-19 stands for Coronavirus disease 2019, and that's the name of the disease caused by infection with the virus SARS- Co-V2. So what do we mean by novel? This was a question that was asked by some of you before this meeting. So novel means new. It's a new virus. It's not a virus that we in medicine and science have encountered before it has many similarities to other family members, coronavirus family members, particularly to the SARS virus but it is new to us. And so it is causing new disease in humans that has not been recognized before and probably didn't really exist before. Here is a link to some general information on the CDC website. It's an outstanding website for any of you who have not gone there yet.

Dr. Tomayko: So how does the respiratory virus, how does this virus spread? So the major route of spread is person-to-person. It happens from respiratory droplets that come out when a person sneezes, coughs or even talks. These are heavy because they're water, they're based in water so they don't typically go more than a six foot range. This transmission is similar to that of the influenza virus. How it's transmitted is very similar. Transmission is very easy, so

transmission between household contacts happens very readily. It's difficult if one person in a family has the virus, it's very difficult not to have that virus spread to other people in the household. Virus can be spread by people who have no symptoms, people who are asymptomatic. This is very important. We estimate that somewhere between 20 and 25 percent of people who are infected with this virus have no symptoms at all. So that means that when you're in public there can be people who have the virus who are exuding virus in their respiratory droplets, but who don't have symptoms and so who are not aware that they're contagious. In addition to the respiratory droplets traces of the virus can be found on solid surfaces like doorknobs, elevator buttons, bathroom fixtures, office fixtures. They're particularly hardy on solid surfaces so something like a doorknob. They don't last as long as on something like paper or a fabric. We did get some questions that we thought we would address here because they were common questions. So one question was if a grandparent and their adult children had been in separate isolation for weeks. Is it okay to move in together? And we thought that generally this should be okay, but with some important caveats. When you're moving in together, that should be with travel that's isolated, meaning inside in your own car or by I suppose walking. The movement shouldn't be by something like mass transit or travel on a train or an airplane because during that transit time there would be opportunities to become newly infected. Another important thing if you're thinking about combining households is that it's very important that no members of the household then would be going in and out and possibly contracting the virus in the outside world and bringing it back if there are people in that household who are particularly vulnerable to having serious disease if they're infected. And Dr. Payne is going to talk about who is particularly at risk for having severe disease. People asked about whether the second wave of the disease would be worse. Why would it be worse? That's an excellent, excellent question that we are not ready to answer at this time. We're going to need to see how this proceeds and gather more data and we do hope to have more guidance for you as time goes down. And another question is, if this virus can be found not just in the air but also on surfaces? People wonder, is it important to wipe down groceries or grocery bags when you bring them home? Is it okay to get takeout food? The risk of transmission is primarily by these respiratory droplets coming from surfaces. The issue is if you touch something with your hands that has the virus on it and then you touch your eyes, your nose, or your mouth. You can then give yourself the virus for your eyes or nose or your mouth. It's probably quite reasonable to wipe down packages when they come in. The virus won't last that long on paper, but wiping it down is very reasonable. Okay, and then we'll go on

to the last of this set of slides before a Dr. Payne goes on. So Becky if you don't mind advancing. So disease symptoms. So what if you become infected, what are the disease symptoms? So usually people are going to start to have symptoms of infection 2 to 14 days after exposure. The most typical symptoms are fever, cough, shortness of breath, and fatigue. Less commonly people have a loss of smell or taste, red eyes, or diarrhea. If you have symptoms, what you want to do is to call your primary doctor, explain your symptoms, have a discussion and see if testing would make sense for you. So 80% of people have mild or moderate disease. So what is mild to moderate disease? That is fever that lasts for many days and fatigue. Something that's different about this illness compared to many other respiratory infections that we're accustomed to, is that this is a prolonged illness. So for mild or moderate disease, the recovery typically takes two weeks. For severe disease, the recovery is even longer, 3 to 6 weeks. So that's what mild or moderate disease is. So, when do you decide that you actually need to do more than just call your doctor? So the emergency symptoms would be if you're having severe trouble breathing. You suddenly can't walk up the stairs anymore, you're having trouble completing or you can't complete a sentence when you're speaking. Chest pain, chest tightness, feeling confused or severe dizziness or weakness or signs of having congestive heart failure, like a sudden weight gain by fluid swelling in your legs. And those are the times that you need to call 9-1-1 or the ER. So it was asked, some people did ask so why is this new disease COVID-19 a serious health concern? So the answer is that this new virus, this COVID-19, causes severe disease at a higher rate than most other respiratory infections that we're accustomed to and Dr. Payne will talk about this too. But really about overall about 16% of people who are diagnosed are going to require hospitalization. This is a new disease that no one in the world has had until now which means that everybody can become infected, everyone's susceptible. There is no what we call herd immunity to protect us. Everyone can get the disease. So this is different from influenza or other viral infections where lots of people are immune, so they by extension protect people who are not immune. This is a pandemic which means it's on all continents except for Antarctica, it spread all over the world. And caring for individuals with severe disease has the potential to overwhelm the Healthcare System making it infeasible to treat everyone who has a serious disease and also importantly interfering with treatment of people who have other medical needs other non COVID medical needs like pemphigus and pemphigoid. So those are some of the main reasons this is a health concern. Also on an individual level another important thing to keep in mind is that compared with other respiratory virus infections, even

influenza, the severity of this COVID-19 disease is worse. The overall mortality rate of the COVID-19 disease compared with influenza is probably 10 times higher. So it is a significant disease. People wonder are the symptoms for a COVID-19 disease different for pemphigus and pemphigoid patients compared with other people in the population? We don't think so. Generally the symptoms appear to be the same for people who have blistering diseases compared with people who don't. Also many people wrote in asking, will Rituximab or other therapies how are they going to affect COVID-19 disease and Dr. Maverakis will touch on this in detail. But specifically one question that we wanted to address here is will it blunt your symptoms? Will it make you not have these symptoms? And for the most part we think no, that being on medications for pemphigus and pemphigoid are not going to make it less likely that you have symptoms with the one exception being prednisone. Prednisone can blunt fever and blunt symptoms of not feeling well. In the final question here before I hand this over to Dr. Payne, people asked, we hear that the next few weeks are going to be the most dangerous. How are these predictions being made? And the answer to that is that it's based on data looking at the curve of infections in populations. And so it's based on what we are anticipating being the numbers of people who are being affected and the numbers of people with serious disease needing to go into the hospital and require medical care. So that's a basic introduction about COVID-19 disease. And then Dr. Payne.

Dr. Payne: Great. Thanks so much. Dr. Tomayko gave a great overview and I think that it really lays the ground work pretty well. So in this next part I guess this is sort of the scary part but we don't want to scare you too much. We just want to give you some facts that you might be hearing on the news and put it in context for you. So these are the risk factors for people to get more serious disease from COVID-19. So why is it that some people are asymptomatic and some people may end up in the hospital. So the people who tend to get or are at higher risk for serious illness are people over age 65, people living in nursing homes or long-term care facilities, chronic lung disease or asthma, serious heart conditions, people who are immunocompromised, severe obesity, diabetes, chronic kidney disease, and chronic liver disease. So we had received some questions asking if pemphigus and pemphigoid in and of itself, you know in the absence of any of these other risk factors would make you more susceptible to serious disease? And to our knowledge that is not the case. However, we do know that a lot of patients with pemphigus or pemphigoid may be over 65 and

immunocompromised. So that would be what would drive your risk not having pemphigus and pemphigoid in and of itself. So another question that we received was, does being immunocompromised only apply to those on certain medications or does it apply to all people with autoimmune disease and if your immune system is overactive because of autoimmunity does that put me at higher risk? So Dr. Maverakis will go over specific medications in a few slides and I know we posted some of that information on the website. But again, as of right now, we don't have any data to suggest that people with autoimmune disease or pemphigus and pemphigoid in and of itself are at greater risk. Okay. Another question we got was, can we make antibodies against the virus? So we think that in general most people in the United States don't have pre-existing antibodies to the virus. Dr. Tomayko had mentioned this is a novel or new virus so most of us don't have pre-existing antibodies, but our immune system is able to make new antibodies if people are not on immunosuppressive treatments. And so again, Dr. Maverakis will go through which medicines suppress your immune system and which don't in just a few slides. A final question was, would having severely dry eyes or dry throat be an additional problem. And we think that that should not increase your risk if you follow the general precautions that Dr. Maverakis will get into. Okay so we can go on to the next slide.

Dr. Payne: Okay, so for COVID-19 outcomes, this is a study that was published by the CDC. It's on their website if you're interested in seeing it and we simplified it a little bit here. And I want to also put in the big caveat there in red at the bottom that right now we are not widely testing people. So basically we're probably missing cases with mild or no symptoms and we're only capturing the more serious cases because you have to have symptoms or be in a hospital to be tested generally speaking as of right now for this reporting period. So what these data have shown, that if we just look at the overall population, there are 7,000 cases that have been reported by the CDC up until this time point of February 12th to March 28th. We know that 20% of patients are hospitalized and 6% will ultimately require ICU admission. That means that 72% of the patients don't require hospitalization and can recover at home. And if we go to the next slide, these are data that actually look at the specific risk factors. So they list out all of the risk factors. And that was what I showed you on that first slide, which is heart, lung, kidney disease, asthma, diabetes, obesity. And then also they list out people who are immunocompromised. And what you can see is that the risks are about the same across those

groups. So 40% of immunocompromised cases are hospitalized and 16% of those patients will require ICU admission. And it's about the same risk as somebody with heart, lung, kidney disease or diabetes. That line also includes people who have one or more conditions. So, you know, I think sometimes people have asked what if I'm immunocompromised and I have heart disease or I'm immunocompromised and I have diabetes from my steroids, you know again, when we group all of these conditions together, they're about the same. So we think that this is about what the data is reporting right now. And if we go to the next slide. So they've also broken apart people who have no apparent risk factors. And so if you look at those data and just the middle columns here like the 7% versus 24% what this means is that if you are immunocompromised it increases your risk of hospitalization by about threefold and if you compare the 2% to the 16% it increases your risk of ICU admission by about eight fold compared to people without risk factors. I know that that sounds scar but at the same time it's sort of a circular argument that these are risk factors for a reason because they increase risk. So these are basically the things that have been identified that are more common in people who are hospitalized and in the Intensive Care Unit. So, Dr. Tomayko touched a bit on the mortality rate of COVID-19, which again is very, very difficult to get the exact numbers right now because we're not broadly testing. There have been some statistics published. It ranges from as low as 0.1% in New Zealand to as high as 13% in Italy and right now it's a little over 3% in the United States again realizing that we're not broadly testing so we're probably missing a lot of cases with mild or no symptoms and we don't think that it's necessarily any different in pemphigus and pemphigoid patients unless they have one of the other risk factors namely being immunocompromised heart, lung, kidney disease, asthma, diabetes, obesity, etcetera. We got a really advanced question, which was what is cytokine storm? Some people have mentioned that on the news and are people with low immune responses less likely to have cytokine storm? So some people may have heard that there's two phases to the infection. So the first is when the virus is dividing and making more of itself so you're sort of getting sicker during that time and the second phase which is something that leads to most of the complications with COVID-19 is the inflammatory phase and that's when your body is trying to fight off this infection. So your body's natural response to a virus is kill it, let's try to kill it. Sometimes your body can make an over exuberant response to the virus so over exuberant that it's actually part of the problem that lead to an ICU admission. So it's basically trying to throw every weapon it has to kill this virus and in the process it can clog up your lungs making you need oxygen or a ventilator and that's part of some of the cytokine storm or the

complications that people have been reporting. It is relatively rare overall and so far there's no evidence that the medicines that are used to treat pemphigus and pemphigoid will reduce cytokine storm. Okay, and so that is the bad news if you will, then negative data. So let's go to something a little bit more positive with Dr. Maverakis which is how to protect yourself from infections.

Dr. Maverakis: Thank you. Thank you Aimee. I want to thank everybody who has lasted this long on the call. Hopefully not too many people have dropped off. We're going to go into basically the CDC guidelines, which I think most people have heard before and then we'll dive into a little bit more the nuances when we answer these questions because I think some of the questions hit on some of the important aspects that are not quite covered by the CDC guidelines. So how to protect yourself from infection? Currently we say, stay at home to the extent possible, wear a cloth face cover when you go outside for food or other necessities. If you go out, stay 6 feet away from other people and avoid non-essential travel in mass transit. Wash your hands with soap and water, the CDC says to scrub them for 20 seconds. If soap and water are not available then you can use a hand sanitizer and then avoid touching your eyes, nose, and mouth with unwashed hands. So the first question is, is it safe to go outside? It's definitely safe to breathe the air outside, this virus isn't going to be traveling around in the wind and get you when there's nobody around. It doesn't have any type of heat seeking missile to find you like a mosquito might so it is safe to go outside. But you know depends on what your area looks like if there's other people around that could absolutely transmit the virus to you. If you're going outside and touching surfaces like to the grocery store and you touch the shopping card or you touch the credit card or you give your credit card to somebody else, these are all things that are going to increase your risk. That's why we recommend that you stay inside as much as possible but for your own sanity, if you want to go for an early morning walk when there's not a lot of people out, you know, feel free to do that. But you should follow the guidelines as much as possible when you're outside. So we got another question here, are protection guidelines different if you're immunocompromised? And the answer to that is no, they used to be a little bit different because we used to say wear a mask if you are immunocompromised and now everybody should be wearing a mask. Currently I don't see any recommendation that's different but obviously if you're immunocompromised you're going to be in a higher risk category. So you should be more stringent with the guideline. The next

question is something that's very dear to me because I have some differing opinions from CDC. It says why is hand-washing better than using hand sanitizer? I have open blisters on my hands, how should I protect myself since hand sanitizer is not an option? The CDC doesn't say hand sanitizer is not an option they just said if you can't get to soap and water then you could use a hand sanitizer. But what I don't think the CDC really takes into account is that scrubbing your hands for 20 seconds is a little bit harsh on your hands and you know we're not genetically engineered to wash our hands 30 times a day. Whereas we could easily apply hand sanitizer for 30 applications a day. Do I think hand sanitizer is going to be as effective as hand-washing? If you really scrub for 20 seconds but I would imagine that hand washing is going to be better than hand sanitizer, it's just that can we do that every time we come into contact with the doorknob or any type of surface? And the answer is probably not so hand sanitizer should be an important component of your daily hand hygiene. But there is one problem and that's there's not a lot of hand sanitizer out there. So if you go to the stores you might not see hand sanitizer, so what do you do? If you don't have alcohol and glycerol or if you don't have like a little mini chemistry set it might be a little bit hard to make your own hand sanitizer. So in this case, you know definitely washing your hands is still going to be important. And then the second part of this question is, are gloves a good idea? So gloves will not protect you from coronavirus because it's just like having another surface that the virus could attach to. So if you touch your glove to a shopping cart that has coronavirus on the surface, you transfer that coronavirus to the glove and you're still at the same risk of touching your face. So if you have like a million pairs of gloves, which I don't think we do, and you could change the gloves every few minutes, then gloves would be okay, but you could get you know contact derma or other problems from wearing gloves all day. But in itself, if you just put on a pair of gloves in the morning go outside spend your day and think that you're protected because you have gloves on and this virus isn't going to come in contact with your skin, that's a very bad strategy because the problem is not when the virus comes in contact with your skin it's when the virus comes in contact with your skin and then you touch your face. You might think that it's easy not to touch your face, but you know studies show that we touch we touch our faces all the time, we just do it subconsciously. We're not thinking about it all the time that our hands come up for our face, but they're constantly coming up to our face. So it's also not touching your face is something that's very hard to do and then wearing gloves won't help much with that. Okay, we have another question. I have to use eye drops and medications in my mouth so I touch my face all day. Should I wear glasses, gloves or masks when I go outside? And I

think possibly the question is more, should I wear gloves when I have to put in these eye drops and stuff? If you're going to be touching your face to put in medication then then you should sanitize your hands before they touch your face. Yes, you can use gloves in that setting, like put the gloves on then put in your medication and then you would take the gloves off right after. So it is possible to use gloves in that setting but the most important thing is that you have some type of hand sanitization before you do any of those activities. One thing I'm going to touch on when we get to masks as well, but it holds true for hand sanitization some things that have to be considered when you're developing these policies are compliance and feasibility. So you can imagine that washing your hands might be a little bit of a problem. Let's say you go to a restaurant, I mean we can't go to restaurants now, but when this shelter-in-place lifts, we're still going to have the risk of this virus. So let's say you go to a public place and want to wash your hands, you have to get into the bathroom and there's probably a lot of contaminated surfaces or a lot of doorknobs to get into the bathroom. Then you have to touch the sink which probably has a potential to be colonized with this coronavirus. And then you have to wash your hands and you have to exit and the amount of time that it takes to get into that bathroom and to get out of that bathroom that's a feasibility issue. And the number of times you could do that, there's not sinks all over the place. So if you could use hand sanitizer frequently and if you had it, then it's something that we definitely recommend. Don't feel that you should go outside without your hand sanitizer because CDC says preferably to wash your hands. You should have hand sanitizer on you as much as possible. You should use it as frequently as possible. And that's how I differ a little bit from the CDC. Okay, we have another good question here. Are dietary supplements recommended to protect against the infection like garlic, onion, or vitamin C. I don't think vitamin C would be dangerous, I think it's probably fine if you take Vitamin C. Since the infection is so complicated, I don't think any type of supplement is going to have much of an effect. So for example, you might feel that this particular supplement is going to boost your immune system. Well, maybe you don't want your immune system boosted because you're going too strong of an immune response to the virus. And that's going to damage your lungs or maybe you need a boost, we don't know. Everybody is going to be different. We don't know where you fall on the spectrum and most supplements and I'm part of the Foods for Health Institute, and I actually study certain supplements in immune response. So it's something that I'm pretty interested in. There's not good data on how this is going to work with everybody and it's just way too complicated of an infection to make any type of recommendation around food supplements. I don't think that some supplements will harm me

like vitamin C but at the same time this is not something to try to protect yourself through dietary means. Instead, stay six feet away, wash your hands or use hand sanitizer, wear a cloth mask, these types of things are what's going to be able to protect us.

Dr. Maverakis: Okay. Can we go to the next slide which is guidance on masks. So again following the CDC guidance on masks. And as I'm talking, I find myself touching my face a couple of times even though I'm not supposed to but it's very hard not to touch your face which brings up, you know, why are masks so important? So currently the CDC does not recommend medical grade masks for the general public due to shortages. On 4/3/2020 the CDC recommended a cloth mask or cloth face covering for the general public to reduce the ability to spread and also inhale respiratory droplets. Face covering should not be used for those under 2 or for those who can't remove the mask without assistance. Don't forget hand washing and physical distancing in addition. Perfect is the enemy of good, so this strategy conserves precious medical resources and also reduces risk of spread among the general public. Okay, so let's go into these in a little more detail. The first question is a very good question. It says, are fabric masks made of bandanas as good as surgical masks to keep me safe? And this is where I go into feasibility and also into compliance. So if you start with the medical mask that is very good at protecting us, those are called the n95 masks and those are the ones that people who are intubating patients in the hospital really need and there's a shortage of those. It's been shown that certain procedures that the doctors do really increase the risk of COVID-19 and one is intubation where they're actually inserting something into the airway of a patient, but it's imperative that those types of masks are reserved for people doing these types of activities. But just to point out that even if you access an n95 mask the very best mask out there doesn't mean that you're going to be more protected because the n95 mask is something that basically sucks onto your face. It has two straps and it forms a seal around your whole face and it's very stuffy inside of that, it's hard to wear that all day long and it's something that your hands would probably come up to to manipulate the mask a lot because it would be like too tight or you might want to take a quick breath or something. Your hands will come up for adjustments a lot. What they found is that people who wear n95 masks versus people who wear surgical masks, which is a lot looser fitting, their chances of infection from the influenza are relatively the same and that's not to say that the n95 mask is not as effective or just as effective as the surgical mask. The n95 mask is much more effective at protecting yourself, but it gets into the feasibility

issues and other parts. So the mask is just one component of the safety protocol. You still have to keep your hands clean with hand sanitizer or washing, you still have to distance yourself. These types of things are just as important as masks. The mask is not going to protect you in itself. You need the mask plus everything else. So then that brings us back down to the question of surgical mask versus a bandana to cover your face? Now a surgical mask again just like the surgical mask versus the n95, the surgical mask is probably a little bit better than a bandana. It has a filtration unit that the bandana won't have and these types of things. The main point is to filter out the droplets, we don't get the droplets on ourselves. And if we're sick, we're not spreading the droplets to other people. These masks, even the n95 masks that stops 0.3 microns and the virus is like .12 micron so these masks are not filtering out the virus they're filtering out the particles that carry the virus. That makes sense. So in terms of surgical masks versus bandana, so the surgical masks are going to be a little bit less comfortable to wear than a bandana and the bandana is not necessarily going to be inferior to the surgical masks in everyday practice. Is it better at filtering out the droplets and those types of things? The surgical mask, of course, is going to be a little bit better in those regards but any type of protection is going to be better than no protection and if you're comfortable wearing the bandana and if you're not monkeying with it all time then that is probably the most important thing. Are you going to use it, is this something feasible for you? And those are things that you got to consider as well. Let's go to the last slide and then we could go back and answer some other questions.

Dr. Maverakis: So the last slide is on therapy, balancing pemphigus and pemphigoid therapy with risk of COVID-19. And before I go into this, I want to emphasize that you don't want to necessarily tough it out. If you know, you have pemphigus or pemphigoid and you know that when you don't therapy you feel horribly. Well that's going to be a lot worse, flaring horribly is going to be a lot worse because you might end up in the hospital and the hospital is where all these infections are so you definitely want to keep your disease controlled. If this is no excuse to not have your disease under control. Let me go through the slide and then we'll go through the questions. So the goal is to maintain disease control on the least amount of immunosuppression and avoid as disease flare that they require hospitalization. Topical steroids, Doxycycline, Dapsone likely don't affect the risk of serious infection unless you're using more than 20 grams of high potency steroid, like Clobetasol daily. Immunosuppressives

such as oral steroid, particularly greater than 20 milligrams daily, Mycophenolate, Azathioprine, Methotrexate Cyclophosphamide, Cyclosporine and Rituxan may increase your risk of infection and more severe disease. An advantage of IVIG is that it is not really immunosuppressant and may be able to be given at home so you don't even have to go to the infusion center to get an infusion. I'm going into the questions now. Somebody asked what about low-dose immunosuppression? Well, this is absolutely something you talk with your doctor. The idea is that you want to be on the lowest dose of immunosuppression that's going to keep your disease from flaring badly. You don't want to skip out on immunosuppression and let the disease come back and then fight as much as you can and then end up in the hospital. So you definitely want to be on the lowest dose that you need to be to stay in remission. So let's say you're usually on like 2,000 milligrams of Mycophenolate, your doctor might say well you haven't had a flare in many years maybe we come down a little bit on that and see what happens. So those types of discussions with your doctor are reasonable but stopping Mycophenolate or stopping whatever medication you're on is probably not a reasonable discussion to have with your doctor because we don't want you to flare badly and sometimes when you stop a medication it might take a long time before you rebound flare. So let's say you skip a couple of doses of your meds and you're like, oh I could do pretty well without them. Don't do that. Everything should be done through your doctor, and this is not the time to experiment with stopping your medication. Although you might want to talk to your doctor about titrating them down a little bit, that's up to you and your doctor. This patient says in starting to flare, what should I do? What should the patient do? Well definitely a lot of the Dermatology practices are closed now, but hopefully your practice will have a telederm visit. You need to communicate with your doctor if you're starting to flare, preferably through a telederm visit, but even if you could just message them and they message you back, some type of communication with your doctor is really important at this point. If you're actually flaring then you're probably going to need some immunosuppression and depending on how bad your flaring is, will determine what type of medications you're going to need. Like we said one advantage of the IVIG is that it's not really immunosuppression and you can get it at home. But medications like IVIG don't work overnight so it's not a solution if you're flaring and that's why we want you to try to not be in the situation where you're really actively flaring and then you're in big trouble. We want you to make little baby steps not big steps. If you want to go on IVIG, that's some kind of discussion you should have with your doctor early. IVIG is incredibly expensive and it's sometimes hard to get insurance approval and it's kind of a pain because

you do it for 5 days well I don't know how Aimee and Mary do their regiments but we do it for 5 days in a row. So for some patients it's not very tolerable and you don't have good veins. So it's not a perfect medication for everybody is what I'm trying to say. But it has some advantages in the setting of this COVID-19 infection. The other question that I feel is very important is should I delay my infusion? So this is a question I've been getting my patients all the time. Now most of us like to use this medication called Rituxan these days to treat pemphigus and a lot of our pemphigoid patients get this medication too and sometimes the patients are doing just fine and we give them their second dose of Rituxan because it's the 6 month mark and patients often not always but get a second of that six months. Well here it might be reasonable to postpone the second dose if you absolutely have no symptoms of your pemphigus or pemphigoid returning. Again, this is something that you would want to talk to your doctor about. Rituxan doesn't kick in overnight so if you wait until you're flaring really badly and then you get your dose of Rituxan it's going to take some time for that to kick in and you're going to have this period where you have horrible blisters and the last thing we want again, which I'm repeating myself but the last thing we want is for you to end up in the hospital. So typically pemphigus doesn't rebound overnight when you had a medication like Rituxan so it is possible for you to extend the day of your infusion, not take it at the 6 month mark or the year mark, or wherever your doctor usually gives it to you. You can extend that out a little bit and then if you see even a little tickle of your pemphigus coming back and that would be a good time to call your doctor and schedule a new infusion or to do one of these other therapies instead of getting your infusion. Maybe you'd be a candidate for IVIG? Not everybody is going to be a candidate for IVIG. And after this I don't want people just calling their doctors and saying, Dr. Maverakis told me I need IVIG. It's an individualized decision whether or not you should be on that medication but it is one option that some of us are talking about in the setting and what I've been doing with my patients which may or may not be a good decision for you is that if they're due for an infusion and they absolutely have no signs or symptoms of their immunobullous disease I usually am extending it out until they start getting a some symptoms and that's mainly because the disease doesn't come on as quickly after a round of Rituxan and I could get the patients in pretty quick for Rituxan. I think that's the end for me. I'm happy to turn it back over to one of the other experts now or to the moderator.

Becky: Well, thank you. That was an amazing amount of information in a very short amount of time and I sincerely appreciate all the information that you've shared with your community. We do have some other questions that were submitted and not answered. The first question is from Margaret and she says, is there concern that Cellcept will be unavailable during this pandemic and I guess we should probably add is there a concern about any medications used to treat pemphigus and pemphigoid being in shortage?

Dr. Tomayko: You know, that's an excellent question. Medication that you've probably heard about in the news that is in short supply right now is a medicine that's called Plaquenil or hydroxychloroquine. This is the medication we do use for a lot of autoimmune disease including autoimmune skin disease but is very uncommonly used for people with pemphigus or pemphigoid. That is in shortage because there are questions about whether or not it could treat COVID-19 disease. I don't know and I would love to hear what if Dr. Payne or Dr. Maverakis have different insights. I have had no indication so far that Cellcept or Azathioprine or Rituximab or Dapsone or Doxycycline or Methotrexate are going to be in low supply. One General concern is that many of our medications are produced in China and we are dependent on China having its manufacturing running optimally to provide those medications to us, but I have not had any trouble so far renewing or getting these medications out and I have not heard any warnings.

Dr. Payne: Yes, I would second that as well. I think the only thing that the American Red Cross and other people have mentioned is that because IVIG depends on blood donors and blood donation has gone down a little bit with the stay-at-home guidance, although they make it very clear that if you're going in to donate blood that's an acceptable reason to go outside. But they did say that it's possible, nothing has happened yet, but it's possible that if the blood donation drives decrease that theoretically in the future IVIG could run low, but as of right now it seems to be okay.

Becky: Great. Thank you so much. So Nancy asks, are there any precautions that she needs to take? Do gum grafting procedures work with mucous membrane pemphigoid?

Dr. Payne: Do you want to take that Emanuel? Maybe we'll go Marry, Aimee, then Emanuel and that way will divide them up.

Dr. Maverakis: So I don't think grafting is a treatment for mucous membrane pemphigoid. It's definitely not something that would prevent the disease. If you're in remission and your oral surgeon feels that they could improve your gum health with a graft that would be a separate discussion. But anybody who is experiencing mucous membrane pemphigoid, we would not recommend them to be treated in any fashion by grafting and often the question is is it safe for them to have dental work or things like that? If I'm answering correctly, I don't feel that it's a treatment for mucous membrane pemphigoid. If you're in remission and don't have any disease then it would be a reasonable option if that's something that the oral surgeon felt that would help your gums. But otherwise I wouldn't recommend it.

Dr. Payne: That sounds great. And I think that every doctor's different. So I would recommend discussing with your oral surgeon at the end of the day, but the Academy of Oral Medicine has released guidance that right now oral procedures are thought to be high risk for COVID-19 transmission so they are recommending not to have procedures done unless they're considered emergency. And so we were discussing this with Marc and Becky because obviously we have the Biopsy Saves Lives Campaign at the IPPF and that still does hold true. But in this particular circumstance, we are asking questions, is there a way that we can defer that procedure and try to get people through symptomatically just to basically get them to the point where it's a little bit safer to interact with the Healthcare System. Again, we're definitely in this perfect is the enemy of good situation we back to the art of medicine rather than the science of medicine. And really I think the best discussion is just to talk with your provider about what the best plan of care is.

Becky: Great. Thank you for that information. Jory asks, if one's immune system is fighting off a disease or a virus will the immune system cease fighting one's own self so it can fight the problem?

Dr. Tomayko: And that's such an excellent question.

Dr. Maverakis: If your immune system is fighting off a virus it doesn't mean that your autoimmunity will get better because the component of the immune system is fighting off the virus. There's different components of the immune system one component is called the innate immune system and that's kind of a nonspecific attack and then there's what we call the adaptive immune system. The adaptive immune system in part is what's causing your pemphigus or pemphigoid and the Adaptive immune system eventually, maybe not right away, but eventually it's going to be what's fighting off the virus as well. It's like the second person on the field. The adaptive immune system takes some time to get up and running but the adaptive immune system is very specific. So the part of the adaptive immune system that's going to be fighting off the virus is going to be a little bit different than the part that's actually attacking your skin and both could occur at the same time. It's not, like oh now that we have this virus to attack let's let's stop attacking the skin and let's all go join forces and fight the virus. The immune system isn't that strategic. With that said there could be cross reactivity between the virus and the autoimmune response, but that again probably wouldn't lessen the auto immunity, if anything you would be at risk of getting more of an autoimmune problem depending on the types of cytokines and the other soluble factors that your body is using to mount the fight against the virus. That might be able to stimulate a little bit of the autoimmune response, but that's going to be highly dependent on the person and how they're interacting with the virus. Aimee's an expert and Mary's an expert so maybe they have some different opinions.

Dr. Payne: No, I think you covered it well, we can go on unless Mary you want to add something.

Dr. Tomayko: No. No, I agree.

Becky: Okay, so there's another question that came in during the webinar and it says I know that there are not many clinical trials for pemphigus going on but our trials that use oral medications still ongoing?

Dr. Tomayko: So for the most part, trials that are ongoing are continuing to proceed however most have halted new enrollment temporarily. So patients who are in a trial can continue to get the treatment that's available to them in the trial. But most trials are not taking new patients right now.

Becky: Great. Thank you. Bonnie asks, how do I know I won't get COVID-19 from getting a blood product like IVIG?

Dr. Payne: Yeah, so right now there's currently no evidence that there is virus in the blood. So we can find the virus in the saliva and in respiratory secretions like when you sneeze or cough, but we don't really see a lot of virus in the blood at all really. So the IVIG product should be safe in and of itself. Now, of course, you know the act of getting the infusion is the part that where you're interacting with the healthcare system. And so that's just standard precautions for interacting with other people but the IVIG in and of itself we think should be okay.

Dr. Tomayko: And to add on to that, blood collection centers and the blood banks are screening donors for symptoms. Currently, they're not screening for COVID-19 infection directly, but as Dr. Payne says currently we don't have any evidence that the virus is in the blood anyway.

Dr. Maverakis: I also want to add that the IVIG is a highly, highly purified product. So let's say there was some COVID that somehow got into the batch it hopefully would be purified out because the once you get down through all the purification steps you almost have pure IVIG, you don't have other blood components. And IVIG is made from thousands of donors so if it was something that was easily transmitted infection that it would have been it would have been a problem. But after they finish the batch then they highly screen each batch to make

sure it's safe before it goes in people. So I wouldn't worry about catching an infection from IVIG.

Becky: Great. Thank you. So much. Ellen is asking can a viral infection like COVID-19 cause a pemphigus or pemphigoid flare?

Dr. Tomayko: We don't have any data so far suggesting that that's the case.

Becky: Great, does any of the other doctors want to comment?

Dr. Payne: Yes, I would second that.

Dr. Maverakis: I think that if you look in the literature, lots of studies that say autoimmune disease could follow a viral infection but that doesn't mean that every viral infection is going to do it and it's very rare to get autoimmunity and that's related to a viral infection so I wouldn't worry about any of that happening from COVID-19.

Becky: Great. So Michael asks, many of us need ongoing medical care, will help systems make provisions for these needs so that we don't develop flare-ups?

Dr. Payne: Yes, I think that the healthcare system has done a lot to address people who need ongoing medical care. So, number one the stay-at-home order doesn't apply to people who need to see their doctors. So you are able to go see them. I do know that a lot of doctors offices are closing, but they have already approved telemedicine. They're also doing a number of things such as approving emergency out-of-state licenses for doctors so they can treat their patients remotely. Here in Philadelphia, we're right in the corner of the state so I have patients that might come from New Jersey, Delaware, Maryland New York, and we're actually able to treat all those patients through telemedicine right now and they are still recommending that in-person visits be reserved for only the most essential evaluations and procedures. But if you

need ongoing medical care by all means, you should be able to reach out to your doctor and ask them how best to proceed.

Dr. Tomayko: Just to add to that, the important thing is to have an ongoing conversation with your doctor. So the telemedicine has been a critical component of this. Other components are having a way to go in and to see your doctor when it's absolutely pressing because we want to keep you out of the emergency room. We want to keep you out of the hospital. That is the primary goal right now of healthcare workers and doctors across the country, so it's important to have a good relationship with your doctor.

Becky: That's a great Point. Thank you. Kevin is asking, can I have my infusions at home now and are insurance is covering home infusions?

Dr. Maverakis: I don't think Rituxan is given many places by home infusions. I would have to have a confusion company that agreed to that but IV isIG often given at home.

Dr. Tomayko: Insurance coverage for home IVIG will of course differ from company to company and area to area. But insurance companies are being more generous with that benefit now then typically.

Becky: Great. Thank you. This is also a question about infusions are hospital systems closing and infusion centers, to care for patients with COVID-19?

Dr. Tomayko: I can say what I observe in our health system. So we're here. I'm here at Yale University in New Haven, Connecticut with a draw from also New York and Massachusetts and Rhode Island. Centers are not closing, we're shifting. So we have emptied out large portions of out-patient facilities that are in our hospital. We've moved them to other locations, so that the hospital can be reserved for in-patients with COVID-19. And those services like the infusion are being offered outside partly to sequester those patients who are getting infusions from people who are COVID-19 positive and partly to give more room to care for the patients

who are COVID-19 positive. And hearing colleagues around the country, and I'm sure Dr. Payne and Dr. Maverakis can comment. I suspect it's very similar.

Dr. Payne: Yes, that's right our infusion centers are not closed but they are recommending only essential infusions and we are trying to switch to home and fusion as much as the insurances will allow us.

Dr. Maverakis: Yes, we are open. We haven't had any problems at UC Davis either.

Becky: Great. There's a question about IVIG that came in during the call as well. And it says that there is some talk about COVID-19 possibly being a hypercoagulable state, could IVIG further increase that risk?

Dr. Payne: One of the risks of IVIG the risk, the hypercoagulability, is usually the greatest in the few days immediately following the infusions. So it would probably just be in the couple of weeks immediately following the infusions, but not an ongoing issue afterwards. You would probably fall back to about the same level as a normal individual after that point in time, or around the same.

Becky: Great, thank you. Deborah asks should people with a serious form of pemphigus fallacious or any form of pemphigus or pemphigoid stay away from the COVID vaccine when it's finally created?

Dr. Tomayko: I'd say it's much too soon to say. That will be something that will be super important for us to discuss and to do an update on when we have vaccines, when we have vaccines and trials to discuss but it's a really excellent question and an important question, but it's too premature for us to have a meaningful answer.

Becky: Great, and I have a feeling it will be a similar answer for the next question. That with talk of a vaccine how will medications used to treat pemphigus or pemphigoid affect how well the vaccine will work?

Dr. Tomayko: So another great question, right. So many of the medications that we use that are immunosuppressive medications will most likely interfere with the ability to mount an effective immune response and to make effective antibodies. So medications like Mycophenolate Mofetil (Cellcept) or Azathioprine or high doses of Prednisone and certainly Rituximab will probably inhibit individuals ability to make effective antibody responses. So that being said Rituximab is one of the main medications that we use certainly for pemphigus and we often use it in bullous pemphigoid. From what we know from basic biology and from data looking at influenza vaccines, probably when we have a vaccine if you're on Rituximab, we will target the time of vaccination carefully. So we'll want it to be at least 4 months after you've had Rituximab. But also at least 1 month before you have the next dose. So when the vaccine comes out, it will be important to discuss with your dermatologist or your doctor who's giving you who's treating your autoimmune blistering disease will be very important to coordinate when you get that vaccine compared with when you have your infusions.

Becky: Great. Thank you. Lauren asks our next question. Where can we get the antibody test so we know if we don't need the vaccine when it comes out?

Dr. Payne: So right now antibody tests are not generally available they're being developed, but they're not out yet. So I think that's another situation where we just sort of have to say stay tuned for more guidance as those tests become approved.

Becky: Great, Carolyn sent in a question during the call and it says will those individuals who test negative for antibodies, will they need to stay in quarantine or at home until either a vaccine is developed or they become ill and develop antibodies. She asks will she need to stay at home until a vaccine is found?

Dr. Payne: That's a really tough question because it's more of a public health guidance. So I would basically say that that's something that it's probably best to just stay tuned and see what people say. There is right now a stay-at-home order which is mainly a public health guidance about "flattening the curve" which I think you've heard about. So the general idea is that the same number of people will ultimately get infected. But if all of those people become infected in 1 month versus if all of those people become infected and are spread out across 5 months, then it will make a significant difference on the strain on the healthcare system. So I think the most notable examples of that are New York City and Italy where there were not enough ventilators to take care of all of the sick individuals leading people to have to make some really tough choices, in some circumstances about who would get the ventilator. So that's basically what the guidance of stay-at-home order right now is basically trying to avoid. So again, I think a lot of these questions are a little bit too hard to answer right now because we're sort of in that exponential phase of the curve if you will and we're all just kind of staying tuned, listening to the guidance, looking at the data and then seeing what they recommend from a public health perspective.

Becky: Great, Bobby asks, I hear there are studies being conducted using malaria medications and antibiotics. How can I participate in this trial if I get COVID-19?

Dr. Tomayko: What's happening right now, is there will be regional variation. The way we're doing it in our hospital system is we have one algorithm for treatment of people who are having mild to moderate disease who are at home not in the hospital and we have a separate algorithm for people who are having severe disease and who are hospitalized or who are in the Intensive Care Unit. So you're going to hope that you're not going to end up in that situation where you are one of those people with severe disease, but if you are you're going to rely on the expertise of the doctors who are taking care of you who will offer you the ability to participate in in studies or trials of those medications.

Becky: Great, and then are those medications safe for patients to use in conjunction with the pemphigus and pemphigoid medications?

Dr. Payne: Those questions are a little bit hard to answer. So we do know things like Azithromycin are probably fine and hydroxychloroquine, but ultimately the treating doctors will determine if you're eligible to participate. It's a little bit too hard to just get a blanket answer because everybody has different medical conditions, other medicines that they're on and also specifically for the trial, they have very specific criteria for inclusion and exclusion so it would be too hard for us to say.

Becky: Thank you all! Dr. Maverakis, Dr. Payne, and Dr. Tomayko you have provided us phenomenal information in not a lot of time. Thank you for staying over with us for about 15 minutes. I know that it was extremely educational for me and our whole community having you on our call and I'd like to give a big thank you to everyone joining us as well as Genentech and Principia Biopharma for making today's call possible. I know that there are a lot of questions that didn't get answered today. And so I encourage you to know that we are planning another webinar to get some more questions answered in the future and we will keep you posted on that as well. Before we go, I do have a few announcements. Our next patient education webinar will be next Wednesday, April 15th with Dr. Ron Feldman from Emory University to answer your questions about pemphigus and pemphigoid symptoms and side effects. So if you can and you are interested, please register today.

We need your help to continue to spread awareness about pemphigus and pemphigoid. The IPPF's awareness program aims to accelerate the time it takes pemphigus and pemphigoid patients to get diagnosed by stressing the importance of a biopsy. Your tax-deductible donation today will support our Biopsy Saves Lives Campaign that will educate and encourage dental professionals to consider a biopsy sooner in order to diagnose patients faster. We're counting on you to make a difference in the lives of pemphigus and pemphigoid patients and their families by helping us accelerate diagnosis time. Donate today and help us reach our goal of \$15,000. Also if you haven't registered for the IPPF's Natural History study we encourage you to do so. 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). You can register today at www.pemphigus.iamrare.org. This online data system collects stores and retrieves patient data for analysis and research studies. The more data we can collect the better information we can give to researchers, the sooner they can find better

treatments, earlier diagnosis and one day even a cure. Lastly again, if you didn't your question answered the call today or you have additional questions, please email me Becky Strong at becky@pemphigus.org or call me at 916-922-1298 extension 105, and we'd be more than happy to help. This recording will be sent out with a survey following tonight's call. Thank you everyone for joining us. Goodnight.

Dr. Tamayko: Thank you.

Dr. Payne: Thank you. Take care of everyone.