Patient Education Webinar-December 9, 2020 COVID-19 Update

**Becky:** Hi everyone, welcome. This call is now being recorded. I'd like to thank you for being on the call with us this evening and a big thank you to our sponsors, Genentech, Principia Biopharma, a Company, argenx and Cabaletta Bio for making today's call possible. Today's topic is a COVID-19 update with a question and answer session. But before we begin, I'd like to take a quick poll to see how many people on this call have had COVID-19? This information is important to share with our researchers and doctors in our community so we can learn about how COVID-19 and affects people with pemphigus and pemphigoid. You'll see the poll pop up on your screen and if you can take a quick second to answer that. While you're answering the poll, let me introduce you to our three IPPF Medical Advisory Council members, who will be speaking today.

**Becky:** Dr. Emmanual Maverakis is an immunology researcher and an 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. Payne is a 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 treatment of autoimmune blistering disease and other immune-mediated skin disease. Dr. Tomayko is a director of dermatology education at Yale University School of Medicine.

**Becky:** So, now we're going to show our poll results. Before I hand it over to our speaker, it looks like 1% of us have had COVID-19 on our call. And 99% have not. So we're staying healthy and that's a good sign. Now, before I hand it over to our speakers, I'd like to go over a few housekeeping items. (Announces Housekeeping Rules...). We have received many, many questions before the call, and we will do our best to answer as many questions as we possibly can. So now it is my pleasure to introduce Dr. Maverakis, Dr. Tomayko and Dr. Payne to discuss COVID-19 updates. Thank you for being on the call with us today.

**Dr. Payne:** Thanks for the invitation.

**Dr. Tomayko:** Thank you.

**Becky:** That's my fault, I am sharing my wrong screen. I'm sorry. There you go.

**Dr. Tomayko:** Perfect, So you can advance. I'm gonna do the first portion, so go ahead and advance. So this is our fourth COVID-19 update that we're doing together. The last one was in June, so there's been a lot of things that have happened since then. We're going to break this into three parts. I'm going to start with an update, what have we learned since the last webinar? After that, Dr. Maverakis will talk about risk factors for more severe COVID, and particular concerns that we may have about medications that are common for pemphigus and pemphigoid. And then finally in a very meaty part of the webinar, Dr. Payne will talk about COVID treatments and COVID vaccines. Afterward, we can also have a question and answer. Okay, can you advance the slide, please?

**Dr. Tomayko:** So let's just start, what have we learned since our last webinar in June? Two key things that we have learned are, number one, that children can become infected, and that may seem very simple now, but in June we really weren't sure. It turns out that children can become infected, they can transmit the virus, probably just as easily as anybody else. However, thankfully most children have mild disease compared with adults. Another really important thing that we have learned is, we're gathering more information about how durable, how long lasting is immunity to COVID and can people become reinfected? So the duration of protection after COVID-19 infection is not established, and it's an active area of research. But we do know now that in most individuals, immunity lasts, at least for three months. Reinfection can happen, but it's unusual, at least, at this point. It may be that with a longer period of time, a year after infection, two years, three years after infection, the story may be different. But for right now, for the duration of our experience with COVID-19, reinfection is not common. Another key thing to think about is our expert evaluation right now is that we anticipate that vaccination is going to induce more reliable immunity than infection, Okay. So, we have many questions. For example, what are the major long lasting side effects that we're seeing after this virus has been around, for more than nine months? What is meant by long COVID? So, long COVID is a term that we're now using to describe the observation of lingering debilitating health issues that can persist for months after infection. The common effects that are seen months after infection are fatigue, shortness of breath, cough, chest pain, joint pain. There are other effects as well. Difficulty thinking, concentrating. People refer to a brain fog. Also depression, headache, muscle pain, fevers, palpitations which is your heart beating, quickly or pounding. And then more serious, we can see strokes that can happen way after the initial infection. You can get inflammation of the heart muscle, lung function abnormalities, kidney injury. You can see profound hair loss, long lasting smell and taste problems, erectile dysfunction. People have sleep issues, difficulty concentrating, memory problems, depression, anxiety, and changes in mood. So, how common are these? This is an active area of research. The NIH just had a two day meeting about a week or two ago. Nature Medicine just put out an editorial about this. I put some links here at the bottom for anyone who is interested. The estimates vary widely. Several studies are suggesting that maybe 25% of people will have these lingering symptoms. Some studies have shown much higher rates. What are the risks for long COVID? This is not clear. Individuals with very mild illness can experience persist or late symptoms. So, are people with pemphigus or pemphigoid or people who are on medications that we treat pemphigus and pemphigoid for more at risk?It’s just not clear. Somebody asked, why do tests for long COVID

patients come back negative? And the reason for this is that when long COVID occurs, the viral infection itself is cleared. The tests that we're typically doing are these RNA tests that are testing for active infection however now the infection is gone, and that's why the test is negative at that point.

**Dr. Tomayko:** So the second wave, lots of questions about the second wave. It's being said that the second wave will be more deadly than the first, why? How long should it last? Why is this timing happening now? What should I be paying attention to? So what is the second wave? This is a graph that commonly appears in the newspapers of numbers of infections, COVID infections, SARS-CoV2 infections in the United States, and where each day is plotted. And you can see going from April to really September, that was what we call the first wave. Really, there are two humps. Those two humps are showing the virus really spreading across the country but together we call them the first wave. Then there's a bit of a lull and now we're having another very rapid increase in the number of infections. So that's what the second wave is. And why are we having a second wave, well, we are having a second wave because the infection is now widespread, geographically. There are large case numbers. There's community spread. And the main reason behind this is human behavior. It's just a simple virus, it just sees humans and other mammals and it infects whatever's close by. Things that make this worse are that it's winter months and much of the country where it's colder and people are more likely to be indoors. With the holiday season, people would like to be gathering socially, they would like to be traveling. So how long this second wave will last is something we can't really answer, it depends completely on human behavior. Will we stop the behaviors that are causing transmission or not? So this is something we'll only really be able to say in retrospect. Next slide.

**Dr. Tomayko:** So, one question is, How do I know, I'm feeling sick, could this just be the common cold? So, how do we know if it's a COVID or a common cold? You really can't tell. there's a wide range of COVID symptoms. So, I've depicted that here in the blue. Up to 40% of people can be asymptomatic, have absolutely no signs. Then, there's this wide spectrum between lows with small symptoms or less severe symptoms and then more severe disease. So common symptoms are many. It can be fever, even just up to 99.9, not necessarily high. Chills, cough, shortness of breath, difficulty, breathing fatigue, muscle aches, muscle and body pains. Headache, loss of taste, or smell, sore throat, congestion, or runny nose, nausea, vomiting, diarrhea. People who are in the workplace are probably used to answering these questions now every day when you're going in. So you can see that when you look at this list, and really any one of those symptoms could be a symptom of COVID you really can't say you have that symptom, is a COVID or is it a common cold? We really don't know. So what do you need to do? You need to test. You need to isolate yourself until you have the results of the test, and especially our patients, our people, our community with pemphigus and pemphigoid, you must notify your doctor. Okay, we can go ahead.

**Dr. Tomayko:** So you have some symptoms, what do you do? It's COVID testing. And just as a reminder, there are different types of tests that you can do. There are the tests that will ask, are you infected right now and tests that can ask were you infected in the past? The primary type of testing that is happening right now are the, are you infected right now tests which are RNA test QPCR test, PCR tests. These are tests that are testing for the genetic material of the virus, the RNA. These are the most commonly done tests right now, really the most sensitive and specific. There is a question that was asked to us, tell us about this, the FDA just gave emergency use authorization for an at home kit. So this at home kit is actually an at home PCR kit. How do you get it? How sensitive is it? I can tell you that right now, it's not something we can go out and purchase ourselves. It's something that you get when a doctor has written a prescription for you, and it seems to be fairly inexpensive. The cost is supposed to be somewhere around $50. How sensitive is it compared to a PCR test done in a laboratory? Probably not quite as sensitive, based on what I have read about the test, but it's probably pretty good. Another type of test that can say are you infected right now is not commonly done, these are called antigen tests and they're looking for viral proteins. These tend to be less sensitive. I don't think this is really something we have to think about too much, right now. But one thing to keep in mind is, there are these tests, that say, were you infected in the past? These are called serological tests or antibody tests. They're looking for the presence of protective antibodies in your blood. There are many, many different versions of these. How sensitive they are or how specific they are varies tremendously. We are not using them clinically. They are not a primary clinical tool for us right now. Again, I put a couple of links here. One is, for people who are interested, there's a nice page on the FDA website about testing basics, it even has a video. And I also put in a link for the page talking about this home use COVID test. Okay, we can go ahead.

**Dr. Tomayko:** Contact tracing. There's some really good questions here. Somebody asked, what have we learned from contact tracing and has tracing changed what we thought we knew in the spring? Really great question. So we've learned a lot from contact tracing. We've learned that masking and personal protective equipment and social distancing are effective at stemming or slowing the spread of the virus. We have learned that there are activities that are higher risk and they include indoor dining, bars, indoor sports, contact sports. There are also risks that are lower. Kids who go to school with masks on where and where social distancing is really put into effect are at low risk for transmitting the virus while they're at school. They can easily pick it up when they're in their afterschool activities or visiting their families. But that schooling with masks and with social distancing can be a lower risk activity. However, right now, contact tracing is increasingly becoming more difficult and less effective. Why is that? It's because we have community spread. So what I mean by that is that it's no longer isolated to some specific cruise ships and some specific long-term care facilities, or maybe a few specific hotspots in cities. It's now so widespread that it's becoming more common for people to come down with COVID-19 and really not know where they got it. Not to have somebody else who they know that you had it, who they were in contact with. There are so many numbers, it's also difficult to do contract tracing because of the large numbers of new diagnoses. Contact tracing is extremely time consuming, and when you have large numbers of infections, the system just

becomes overwhelmed, it can't do it anymore. And the fact that restaurants and bars and workplaces and social events have been open also means that there are many more opportunities for people to have become infected. And the more opportunities the harder the contact tracing is. Okay, we can go ahead.

**Dr. Tomayko:** So protection against infection, what should we do? This really has not changed since June. We know how the virus is transmitted. It's transmitted through airborne droplets and aerosols. So aerosols being tiny, tiny droplets that come into contact with your eyes, your nose, or your mouth. So the protection is simple. It's wearing masks, wearing eye protection, washing your hands, doing social distancing. What's a good social distance we talk a lot and you hear it's the six foot rule. Six foot outdoors with a mask is probably good. Now, UCSF, University of California, San Francisco, did some interesting work for the San Francisco Opera Company. The people who speak more loudly or singing, your respiratory droplets travel further. And so the opera wanted to know, well, if we're going to do any singing as a group, how far do we have to space our people? And the number they came up with was 12.5 feet. So 12.5 feet, no mask, outdoors is probably a safe distance. What else do we need to do? When you're going to gather, gather outdoors whenever possible. Gather in small groups when possible because fewer people around means lower risk of one person having COVID-19 and therefore, a lower risk of having it spread. Then isolate if you have a possible exposure or symptoms. So people do ask, is there a safe number of people to gather with? I think the thing to just keep in mind is there's no one magic number, right. It's all about probabilities. It's about decreasing your risk. It depends on how prevalent the virus is in your community. How likely is it that another person you're gathering with could have been exposed? So, it will vary community to community but the smaller, the better. And then, lastly, lots of questions about travel. Is it safe to travel? What are the best modes of transportation? I've heard that being on an airplane is safer than going to the grocery store. Is this true? So travel, recommended routes of travel would be to drive by yourself or with your household members only. To bike or to walk. You want to be very cautious if you take a bus, train or an airplane. So, the kinds of things to ask yourself before travel is, first of all, is the travel essential? If it isn't essential, we all need to be seriously reconsidering the travel at all. So if travel is essential, then be thinking about what are the rates of COVID-19 in your community of origin. What about the destination to which you're going? What about the transit points? It's all about, what's the probability that you're going to be coming into contact with somebody who has the virus and is infectious? If you're going to be traveling on some sort of communal transportation, you want to be also thinking about, what's the community adherence to your CDC recommendations? Meaning, are people wearing masks? Are people social distancing, are people who are sick socially isolating themselves? How available is testing in your area? That can differ tremendously and if more people are adhering to these guidelines, the risks are going to be a little bit lower, and if people aren't, the risks are going to be higher. Also, ask, what is your ability to protect yourself? What's your personal protective equipment like? Do you have a higher filtration mask that fits well, that you can put on and leave on? Do you have glasses that's protective or goggles or a face shield? Those are important questions to ask. For airlines in particular, there are movements by some airlines to do COVID testing of passengers. And this certainly is a positive sign if all passengers

are COVID tested, then the chances of somebody being COVID positive are less. They're not negative, because these tests are not perfect. People can have COVID-19 brewing, but not be positive yet. So these aren't perfect tests, but they together will cut down on the rates of transmission. So that's it, and we can move on to Dr. Maverakis.

**Dr. Maverakis:** So congratulations on the group for being so good with your protective measures. Only 1% having COVID is amazing. Even in my department, we're getting lots of people coming down with COVID. Let's fast-forward through the first slide, because we'll come back to questions. So today we're talking about factors associated with severe disease. The initial slides were very nicely provided by Dr. Payne. So in terms of hospitalizations, because usually you consider severe disease as people who require hospitalization. I think most people kind of know now that the older people, the older you are, the more likely you're gonna be hospitalized. It really starts to tick up after the age of 70, although, after the age of 50, it's going up. People with comorbidities, heart disease, lung disease, diabetes, and kidney disease, those all will increase your chances of being hospitalized. And, of course, if your kidney disease is worse, your chances are going to be worse. In terms of immunosuppression, people who are on immunosuppression, we'll go into it a little bit more later, are going to definitely have an increased risk of having worse disease. It appears that it's related to the dose and the type of medication. So if you're on prednisone, but if your dose is lower than 10 milligrams, you're going to be a lot safer than if your dose is above 10 milligrams. And I know that some people, depending on how active your pemphigus is, sometimes people are on 100 milligrams. So, of course, if you're on a high dose of prednisone, you're going to be extremely sensitive to COVID. Next slide.

**Dr. Maverakis:** So, this is going into a little bit about the drugs, the different immunosuppressants that we could give for immunobullous diseases and the risk of COVID. And more data is continuously being accumulated. So, there's gonna be some additional data on Rituxan published soon. But from what we have now, it looks like patients who have received Rituxan are going to be at increased risk of COVID-19. Cyclophosphamide, Azathioprine, Mycophenolate, are all going to increase your risk of COVID-19. Rituxan probably will increase your chances more if you recently received it. The more months you are out, the more protection, not protection but the more your immune system will be getting back to normal and you will have more normal immunity against COVID. But, even after a year, you can be susceptible to having a higher risk of getting severe COVID. If we go by data from Influenza vaccinations and things like that, I would say the first six months are really critical that you don't get exposed during the six months. After six months, of course, your risk is probably still a little bit higher but definitely not during the first six months where you're really, really susceptible to COVID and other viral diseases. Let's go to the next slide.

**Dr. Maverakis:** This gets into the age a little bit. So I told you that if you're above 70 or 80, it's gonna get up high. But as you can see here, people from 50 to 59 they're going to have a

greater chance of getting severe COVID-19 compared to people 40 to 49. But once you get up to around 80, is when your chances of getting severe COVID really, really escalates. Males might have a slightly higher chance of getting severe COVID than females. People who are severely obese. You know, we're all a little bit fat around the mid-section because of the holidays but as you get up into a really high body mass index, is this when your chances of severe COVID really goes up. Again, we talked about this a little bit, if you have diabetes, your chances of getting severe COVID are going to be higher but if you have your diabetes really well controlled through diet and exercise and insulin and any type of medication, your chances of getting severe COVID are going to be less than if he had uncontrolled diabetes. And the same with kidney function. So if you have a little bit of kidney, renal insufficiency, your chances are not going to be as high as if you have severe renal insufficiency. So most of this stuff appears pretty intuitive. If you have comorbidities, your chances are going to be increased. If you have really severe comorbidities, your chances are going to be much higher. Next slide.

**Dr. Maverakis:** So now I just wanted to talk briefly about some animal data, because this is not as intuitive as the slides that we just talked about. So, one of the things and most of this animal data was done with these other coronavirus diseases that are very severe like MERS and SARS which are very similar to our COVID-19 infection. They're kind of like those viruses that came before them. So, if we look at animals and what we need to do to get an animal with severe disease, one of the most important things is how much you inoculate the animal with. So if you inoculate the animal, if you give them just a few viral particles, they might get sick, but they often don't have severe disease. The chances of them dying is much less than if they got higher loads of the virus. And also, the people who do die, or the animals who do die from the virus, if you give them a large viral load, they'll die sooner. So that means that the animals not only died in higher percentages, but they also got more severe disease and died sooner. So it's very important that if you do get an infection that you do everything that you are supposed to be doing in terms of distancing and wearing your mask because even if you do get an infection, it might be less severe because you're wearing your mask or because you're doing your hand washing or using your hand sanitizers. I hear in the news a lot, depending on the radio station, people complaining about, “My aunt, she wore the mask all the time. She was very careful, and she still got COVID. No, so what was the use?” But actually, if she was very careful wearing her mask and everything, she probably got a less severe disease than if she was just reckless and going to parties and getting in front of people while they cough on you and things like that. So even if we can't prevent ourselves from getting COVID because it's all over the place, if we take good precautions, hopefully, if we do get the disease will be less severe. And I'm gonna go to the next slide  and we'll go into this a little bit more. Next slide.

**Dr. Maverakis:** So this is a very similar idea. So animals who got a little bit of COVID, they actually are still protected from rechallenge. So if the animal gets a little bit of COVID, I’m sorry this is MERS. So if the animal got a little bit of coronavirus or a lot of coronavirus, there's still protection from rechallenge which shows you that any type of infection will most likely give you

a little bit of protection afterwards, although you shouldn't be relying on that if you do get infected, you should still be cautious afterwords. Next slide.

**Dr. Maverakis:** So this is interesting, this one is on, not the dosa virus that you get, but the amount of volume you got it in. So if you get exposed to a small droplet with a certain amount of virus in it, it's going to be less severe disease than if you got the same amount of virus in a larger droplet. This is evidence in favor of you wearing your mask because if you're not wearing your mask you can get a big droplet inside of you, versus a small droplet that the mask can protect you from that came in from the side or something like that. So the volume, regardless of the amount of virus, the volume of fluid that you get exposed to will likely be one of the things that will dictate if you get severe or mild disease. So basically, you don't want to get exposed. If you do get exposed, you want to get exposed to the least amount of virus and the least amount of volume of those droplets Okay, next slide.

**Dr. Maverakis:** So this is all animal data. And then this is the same idea with the volume. This is looking at old and young animals. So this volume effect is very present in old and young animals, especially in the older animals, they're more susceptible to the same amount of virus in large volumes. Okay next slide.

**Dr. Maverakis:** So, does this translate to any human data? And we don't know. But this is the human data that we have. One is that if they look at people when they first test positive, and you look at their viral load by these PCR reactions, people who have more virus tend to have more severe disease, they tend to die more frequently. If you have a larger viral load at the time of your diagnosis, and this was done for SARS which is very similar to COVID-19. Next slide.

**Dr. Mavericks:** This is the same, basically, the same thing. This is looking at people who have severe disease versus non severe disease. People with severe disease tend to have more virus when they're diagnosed. People who die tend to have more virus when they're diagnosed. People in the ICU tend to have more virus when they're diagnosed. And the amount of symptoms you have tend be worse if you have more virus. Okay, I think that might be it for me. Go to the next slide. I don't know what that is, but that was probably one of my slides that didn’t translate.

**Dr. Payne:** Oh, it was a cute cartoon of the two people with a mask on.36:09

**Dr. Maverakis:** Oh yes, that was just a reminder to wear your mask. I did draw a cartoon.

**Dr. Payne:** Great, that was a great introduction to all the key concepts. And so in this section, we'll tackle all, well try to tackle all of your questions on treatments and vaccines. So we can go forward one slide. So, one of the questions that came up is, What is Emergency Use Authorization? So this is the official definition, which is, during Public Health Emergencies, Emergency Use Authorization allows the FDA to allow unapproved drugs to be used to either diagnose, treat, or prevent serious or life-threatening diseases when there are no adequate, approved and available alternatives. So, in order to get an emergency use authorization, what you have to show is number one, reasonable efficacy, where there's reasonable evidence to believe it will be effective. Number two, that the benefits likely outweigh the risks both known as well as potential based on just the biology of the disease and the therapy. And number three, there's no adequate, approved and available alternative. So, one question was, “I heard there are as many as 10 or 11 vaccines in the running. What would this mean if Pfizer or Maderna got an or an emergency use authorization?” So, the answer is as long as there are not enough available alternatives, and the vaccine is reasonably effective and the benefits likely outweigh the risks, the chances are that those vaccines will continue to get approved, as long as there are not enough available vaccines. So going forward.

**Dr. Payne:** So COVID-19 treatments. So, the general thought now, in terms of how we approach therapy, is that in the early phase, number one, we want to just prevent infection to begin with. But if you are infected, it's all about controlling that viral load in the beginning. As Dr. Maverakis was referring to. We want to reduce the viral load. So a lot of those treatments go towards that. So Remdesivir was one of the first drug that was initially approved for emergency use for COVID-19 and it's now FDA approved. It actually inhibits viral replication and its clinical uses in hospitalized patients. The study results have been somewhat mixed. So there were three major studies that contributed to its approval and are described in the FDA label for the drug. So, in study number one, what they showed was that Remdesivir reduced the recovery time from 18 days to 11 days for patients with severe disease. There was no effect for mild or moderate disease, and death at 29 days was reduced from 15% to 11%. But obviously, any reduction in death is a good thing. In study number two, there was actually no effect on recovery or death. And in study number three, there was a 1.65 higher chance that you would improve with a five day course of the drug. And then there was a 1.3 chance that you would improve with a 10 day course of the drug, which was a little all over the place. But at the end of the day, the idea is that reasonable evidence of benefit, benefits likely outweigh the risks. It was one of the first ones approved. So this is a drug that's now on the market. Subsequently, there was an additional study where they paired it with a drug that's used for rheumatoid arthritis, Baricitinib, that's known as a JAK inhibitor. It is thought to blunt inflammatory responses and so the data suggests that Remdesivir plus Baricitinib could improve outcomes compared to Remdesivir alone. Then go forward one.

**Dr. Payne:** To get the Baricitinib. And then finally, if we go forward one more time, Dexamethasone you've probably heard of the President received Dexamethasone when he was in the hospital. This is a steroid that blunts the inflammatory response after an acute phase

of infection. So Dr. Tomayko covered long COVID and the general idea is that an acute phase of the disease, it's all about viral replication and getting sick. Once that sort of acute phase passes and the viral load is going down, and your body can have its delayed reaction, where it's like, Woah, what just happened? It's trying to throw the kitchen sink at it. It's overreacting in the response to the virus, and that can be deadly. So you want to actually blunt that second inflammatory response, and that's a steroid known as Dexamethasone. And that's indicated for use in hospitalized patients. The data showed that it reduced death from 41.4% to 29.3% for patients who are on a ventilator, and it reduced death modestly for patients who just needed a supplemental oxygen mask. And there was no effect, and possible, tiny increase in death in patients, not on respiratory supports. It sort of underscores how these drugs have very, very specific applications. And so, we'll get into this a little bit later, but there were a lot of questions about, "How do my immunosuppressant medications help or hurt me? It's actually good to be on immunosuppressive drugs, because I've heard that steroids are actually good for COVID?" It is really about the timing of the disease, so I think Dr. Maverakis showed you that one graph where early on, a low-dose of prednisone may not hurt that much, but a high-dose of prednisone will probably hurt as it will make you  more likely to have severe disease because it will suppress your immune system as the virus is replicating. But later on, past that point, the steroid probably helps. Swe can go to the next slide on antibodies.

**Dr. Payne:** So, this has had a lot of news coverage. So, you've likely heard of antibiotic treatments or cocktails for COVID-19. So, for example, Chris Christie received a release, monoclonal antibody therapy, Bamianivimab. I'm going to try to pronounce it. Usually, as doctors, we're trained not to  use the pharmaceutical name with it so I'm just going to call it the Lily Antibody, because it's got a really long name. And the President received Regeneron's Antibody cocktail, which is the two antibody regimen. So both of these, basically, if your body's not making the antibody response, we're giving you the antibody response, that your body needs to make clear that virus. So, with the Lily monoclonal antibody, it's meant for patients who are age 12 or over, they're actually not hospitalized. They have mild to moderate disease, but they're at high risk for severe disease. So, maybe they have lung disease, kidney, liver, diabetes, obesity. You ideally need to give us within 10 days of symptom onset and what they showed in the trials that it reduced hospitalization rates from 10% to 3%. Regeneron, same application reduced hospitalization from 9% to 3%. Convalescent plasma was something that was also in the news. That's basically where you take the blood donation from somebody who had COVID and recovered. Isolate the plasma, and then give it to somebody who has active disease. Same sort of idea but the problem is you just don't know how much antibody the person has in their blood. It's very variable and you could only figure it out sort of in retrospect. So, there were some trials on this where they showed that it reduced death in non intubated patients. So, again, milder patients, from 49.4 to 41.5%, and in people who are younger than 80 years, it had a much more significant effect. More like 46% to 33%. So basically, the data suggests that the monoclonal antibodies, you want to use that, again, in the early phase of the disease when somebody has mild to moderate symptoms to prevent severe disease. So, one way to think about these two slides is in someone that has early signs of a high risk for severe disease. So, for example, multiple comorbidities, worsening symptoms, then a physician could

consider a monoclonal antibody therapy plus or minus Remdesivir right in the very beginning, reduce that viral load, clear out the virus and then followed later by Dexamethasone to help avert any late complications from the inflammatory phase and the disease. So, that's sort of how we think about therapy right now. But if we go to the next slide to think about prevention.

**Dr. Payne:** So these are the COVID-19 vaccines and there were a lot of questions on vaccines. How safe and effective are they? How do they work? How will they be distributed? So, I am going to hit safety and efficacy sort of quickly on the next two slides. So, as probably many people in the audience know just from watching the news, there's sort of three major vaccines that are being covered right now, the Pfizer/BioNTech vaccine which is an mRNA type vaccine, Moderna which is also an MRNA vaccine. The AstraZeneca/Oxford, which is an adenovirus type of vaccine. And, what the data has shown, I feel like if you're watching the news you can probably state this data back, as well as I can because it's been constantly run on banners across the newsfeed. But basically, the Pfizer as well as the Moderna vaccine are roughly 95% effective at preventing infection. The Pfizer trial looked at any infection at four weeks. There were no serious safety concerns reported to date. The Moderna Trial looked at symptomatic infection at six weeks with no serious safety concerns reported to date. And the AstraZeneca vaccine reported I think, as you heard, 70% effective efficacy rate at preventing infection, but it ranged from 62 to 90%. And the data collection analysis is still ongoing for the AstraZeneca/Oxford trial. In addition to those, there are multiple other vaccines and phase three trials around the world by Janssen, Novavax, International Pharmaceuticals in China. They're based on a variety of different vaccine types and these are all ongoing with no data, or at least so far. So, one person asked,are these live vaccines? None of these are live vaccines. So, that's good, in that people who are immunosuppressed can’t receive live vaccines. Now, one interesting thing is that immunosuppressed patients were actually excluded from all three of these trials. So, if you are immunosuppressed or were at risk of getting future immunosuppression, you weren't allowed to enroll in the Pfizer, Moderna, or AstraZeneca trials. So, if we go forward.

**Dr. Payne:** COVID-19 vaccine, so a lot of questions on possible side effects. So these are the side effects that were reported. Fever, greater than 39 degrees Celsius, which is a little over 102 degrees Fahrenheit for 2% of patients. Fatigue is very common, 4% to 10%. Muscle aches are very common, just about 10%. Joint pain, headache, pain and redness at the injection site. So, actually, the photo that I have here is of a patient who actually received a shingles vaccine. But these types of reactions are being reported in patients who also received the mRNA based vaccines. And some people feel that it's a good thing because it means that you know that your immune system is responding, but obviously if it lands you with 103 degree fever, you're gonna feel pretty rotten for about 24 to 48 hours. So, we can go to the next slide.

**Dr. Payne:** So, hopefully, this is not too complicated, but I'll see if I can walk you through it and translate into a lay person. So, if there are any scientists in the audience, hopefully, you'll love it. And if there are non scientists in the audience, I'll walk you through. So on the upper upper left, where it talks about how it works. What a typical vaccine, not the mRNA vaccine, so this is like if you go and you get your flu shot or something like that. You are injected with a dead vaccine, so basically inactivated germs and inactivated virus into you and basically those germs then go into your muscle and they release things called antigens which are the proteins. And then large cells called antigen presenting cells come over and their job is to eat anything that's injected or germs, viruses and then their job is to show those antigens to the immune system and say “hey, what do you think? Is this good or bad?”. And so then the T cells, which are actually shown in blue there, coming up to the big pink cell of the left, basically say, “I don't know. I don't care about that one, it looks fine to me”. But then sometimes it will say, “Whoa, that's really bad! We don't want that around”. And then they're going to proliferate and basically start to like warn the troops that there's something bad in our body and we need to get rid of it. And so if you go to the upper right, then, what it does is it trains the army. So T cells and B cells get ready. T cells are basically directly stab infected cells and kill them. B cells make antibodies, which basically neutralize and clear out the virus, and that's how your body responds to a vaccine. So then, if you go to the next slide.

**Dr. Payne:** After you get the vaccine, then the idea is that the vaccine was like a boot camp for your immune system. It kind of gave you the test infection with something that can’t make you sick, trained the army against it. So now if you actually get a real infection where the germ actually comes in, now they're already. The antigen presenting cells are there, they still pick up the germ and basically say, “What do you think guys, this is something that looks bad to you?” And the T cells and B cells are like, “I have definitely seen that before. We do not like this thing, we're ready to go, we're totally trained, and we're gonna get rid of it really quickly.” So basically, the T cells and B cells kick in and they make antibodies a lot faster. The T cells are a lot better at killing because they actually know what to look for. And that's how your body then clears a subsequent infection. So that's sort of how vaccines work in a nutshell. And then on the next slide is the mRNA vaccine versus just these classical inactivated vaccines.

**Dr. Payne:** So really the only differences are the ones in red. So instead of injecting this dead virus, where we take a virus and kill it with formaldehyde or other chemicals, what they ended up doing was putting messages called mRNA.. So these are basically temporary instructions to the cells on how to make the coronavirus spike protein because that is really the key protein that you need to neutralize to get rid of the infection. So basically, we inject these temporary instructions, that then goes into the antigen presenting cell directly. So basically, immune cells are recruited to the injection site that's why a redness at the injection site is actually a good sign, because it means your immune system is responding to the vaccine. They swoop in then they basically pick up all of that mRNA particle, they themselves make the spike protein and show it to the immune system and be like, “Hey guys, what do you think? Do you like this or not?” And then the T cells and B cells ultimately will respond. So if you go forward one.

**Dr. Payne:** The advantages of the mRNA vaccines, and the reason why scientists are sort of excited about them as a general class of drug, is that they're much faster to produce than inactivated vaccines. So theoretically, you could adapt them mid-season if the virus mutates. So, for example, when people say, “Oh, the flu shot didn't match this year.” Part of the problem is it takes months and months and months to make the flu vaccine. So if it's a mismatch we missed it for the year. But with the coronavirus vaccine, everybody was commenting how quickly it was developed and that's one of the advantages for the mRNA platform. Theoretically speaking, if the virus should mutate, there is a possibility that they could change in 2021 and have that released by the end of 2021. So potentially broader and more effective antigen presentation is also thought to be the case because basically since you can inject a decent number of mRNA nanoparticles, you can really dose those antigen presenting cells so that they're just showing a lot more of the viral particles to the immune system. Okay, if we go forward.

**Dr. Payne:** So then a lot of questions were then directed to, are there any treatments that are better for me to be on, so I'm eligible for a vaccine? If I am on Rituximab can I get the vaccine? If I'm on these other therapies, can I get the vaccine? So this is data that really hasn't been studied, obviously because immunosuppressed patients were excluded from the trials. But we're just basically going on how we know these drugs affect other immune responses. And I have an important disclaimer at the bottom, which is that formal recommendations really await the FDA recommendation after review of these emergency use authorization requests. Like, are there any contraindications to receiving the vaccine, the label will tell us. So that's basically what we'll use to generate formal guidance, after the FDA has rendered an opinion. But in general, prednisone, Methotrexate, Azathioprine, Mycophenolate are thought to reduce vaccine efficacy, relative to dose. So if you're on prednisone 1 milligram, probably not going to have that much effect. If you're on prednisone 10 milligrams, mild, moderate effect. Prednisone 100 milligrams is going to blunt the effect. But the general idea is that you immunize while on these medications. With Dapsone, it's uncertain whether it will be beneficial or harmful. The thought is that probably shouldn’t have a major effect. So, the thought is that you would immunized while on the medication. Doxycycline is thought to have a minimal effect, so you would just immunize while on that. IVIG actually impairs the ability of antigen presenting cells to show that antigen to the immune system. So, that it's actually thought to reduce vaccine responses, but it's time dependent because when you get the IVIG infusion the IVIG level is very high, then it declines over time. Then you get the repeat infusion and it goes high and declines over time. So, the general recommendations for IVIG and vaccination is to get the IVIG more than two weeks before the vaccination, and then wait at least two months after the vaccination. I'm sorry, wait at least two months after the IVIG to get the vaccination. And with Rituximab it's expected to reduce because you'll have no B cells to make antibodies depending on the dose that you received and how long ago that was. So, for example, if you get a four dose infusion of Rituximab and then you go to get that vaccine the day after the fourth dose, there's probably very little chance you'll respond to the vaccine. But let's say you've got a 500 milligrams booster of Rituximab and it's seven months later, there's probably a decent chance you're going to respond to the vaccine. So, the formal recommendations are that you don't want to get a

vaccine within 2 to 4 weeks after Rituximab because it's just unlikely that you're going to respond. I'm sorry 2 to 4 weeks before. So if you're going to get a vaccination, get it at least 2 to 4 weeks, complete the second dose of the vaccine, at least 2 to 4 weeks before the Rtiuximab. And if you're going to get it afterwards, wait at least 4 to 6 months. But, again, speak to your doctor about it. And once you get to 12 months after Rituximab, you're considered to be within normal range. Okay, and then if we go forward one.

**Dr. Payne:** So one person had a question, how does the efficacy of these new vaccines compared to other vaccines? So, again, Moderna was looking at prevention of symptomatic infections starting two weeks after the second dose of the vaccine. And they gave the 2 doses 4 weeks apart. Pfizer just looked at prevention of infection at 28 days and they gave two shots that were three weeks apart. AstraZeneca also gave two doses that were four weeks apart. So these efficacy rates at 94, 95% are really as good as measles, polio. You're not gonna get much better than 94 to 95%. Compared to the flu, a flu ranges from 44 to 60% at preventing infection. But one of the key things about vaccines that's not just about preventing infection, but preventing death from infection. So, for example, even in years when the flu shot only prevents 44% of infections, in most years, it decreases the death rate by a half to two thirds. So it's very effective at reducing death from the disease, which is really the key. Okay, we go forward.

**Dr. Payne:** Then there were a lot of questions on distribution. So, how likely are they to be distributed widely? How quickly will it happen? Who will get the vaccine first? Will having an autoimmune disease push me to the front of the line? So, this is going to be officially voted on tomorrow, I believe, but the Advisory Committee on Immunization Practices at the CDC made recommendations on what they think the appropriate priority list should be. So, in Phase 1a would be healthcare personnel and long term care facility residents. And the rationale for doing this was, one of the questions was, is our goal to prevent the maximum number of infections, or is it our goal to prevent the maximum number of deaths? I think the idea was that in Phase 1 they wanted to prevent the maximum number of deaths. So basically the highest death rate is basically in elderly, individuals living in congregate settings and long-term care facilities. So that's basically where that will go. Phase 1b will be essential workers, education, food and agriculture, utilities, police and firefighters, basically if you were working in March and April of this year, you're probably considered an essential worker is easily one way of thinking about it. And then Phase 1c is then adults with high risk medical conditions and adults who are 65 and older. If you are an adult who has an autoimmune disease and you are not on therapy, it's not clear you're going to be in Phase 1c if you are under age 65 because having an autoimmune disease alone does not actually put you in a high risk category, it's only if you're on immunosuppressive medication for that autoimmune disease, that would put you in Phase 1c.

**Dr. Payne:** Sandra, actually asked a question about this article. So I looked it up. And I thought this is kind of fun, I'm going to share it. So basically, she found this article in The New York Times, it was an opinion piece where they can find your place in the vaccine line. Basically,

what it is, is it's just a survey that gives you an idea of how many people in your community meet every single one of those tick boxes that was on the prior slide. So it asks, how old are. If you're greater than 65, you'll be bumped into a higher category. Less than 65, you'll be in the lower one. What county do you live in? And actually they use that to determine how many people in your county like are above or below, you know any certain rate. Then it basically says, do you work in any of these professions? Are you a healthcare worker? They know exactly how many health care workers live in that region. Are you an essential worker? Are you a first responder? Are you a teacher? None of the above? Do you have COVID related health risks? For example, that would be chronic kidney, liver, lung, or heart disease, diabetes, severe obesity. So you check that off, and it will basically say, according to our calculations, you're going to be one of the first in line. That's if you check off over age 65, health care worker, COVID related health risks, you're gonna be first in line potentially to get the vaccine. If you're 39 years old, you don't work in any of those professions and you have no health risks, you're actually going to be one of the later stages in the vaccine. And so, the general idea is that Phase 1a will be rolled out across December and January. Phase 1b we will sort of look at like February range, and then basically Phase 1c is looking at like March, April. Then for everybody else, April to June. And they feel like it should become widely available to everyone by June. And those timelines are obviously subject to adjustment. They're expecting about up to 70 million vaccines by the end of the year. And by the middle of summer of 2021, well over a billion to a billion and a half vaccine doses being available just from Moderna and Pfizer, that's not accounting for any of the others that are in the works. So that covers my section. We can go to a final slide. This is probably only for science nerds who can appreciate it. My lab member texted this to me and I broke out laughing and I thought, that's the sign you are a complete science nerd. This is a little ribosome. Ribosomes are like little factories in your body that read the RNA and make protein off of that, so they basically go along and basically make protein for all of your cells. So, this is basically one going along doing its job, encountering an mRNA and coding for coronavirus spike protein and keeps going. So that's also the cartoon version of how the vaccine works. So we will close there.

**Becky:** Great, thank you all, that was wonderful. We've been getting a lot of questions too. You've answered a lot of the questions. Going back to some of the earlier questions that were submitted. One question that came in is, "What extra precautions, we all know about washing our hands, social distancing as much as we can, and wearing masks but what extra protections should the older crowd,we will say like the 60 and over crowd, also do to protect themselves from getting COVID-19?"

**Dr. Tomayko:** One simple thing is wearing glasses. This is data that initially came out looking at a city in China. Looking at the data and realizing that people who are myopic and therefore were wearing glasses, had lower rates of getting COVID-19. That was one of the initial ideas that inspired it. But your eyes are a mucus membrane, and it makes sense that you could become infected via your eyes. So one other simple measure would be to have eye protection.

**Becky:** Great. And so that really is something that is helping and can help our community then. We've gotten a few other questions about that as well. So thank you so much. Another question came in, and this is about the vaccine, is that patients with food allergies or medication allergies, it's been out in the news about possibly, not doing as well with the vaccine. Between having multiple food allergies, or medication allergies, and having pemphigus or pemphigoid, should somebody like that in our community, take the vaccine?

**Dr. Maverakis:** I think you should still take the vaccine regardless, especially if you're in a high risk group. It is true that there are different antibodies, not all antibodies are going to be able to block this virus the same. So, if you have a tendency to make a different type of antibody, which we would call IgE or something like that, it is possible that that won't be as protective. But absolutely, everybody should take the vaccine because even if you're somebody with that type of immune response, it's not like you're not going to make any protective antibodies in fact the vast majority should still be protected.

**Dr. Tomayko:** I believe there was something in the press about a couple of people in the UK, who had a history of food allergies, who had severe reactions. It didn't sound like they died, but they had severe reactions. So I read that there was a question against people who have a history of food allergies. I think I agree with Dr. Maverakis, that this isn't something that should automatically preclude a person from taking a vaccine, but just like if you have an egg allergy, you let your doctor know before you get your flu vaccine. It doesn't necessarily mean you won't get your flu vaccine, but let the doctor know and then make a decision with your doctor, but it can likely just be that you're gonna have extra monitoring. Maybe it's going to be in the office and there's going to be an epi pen on hand, for example.

**Dr. Maverakis:** I haven't read the package inserts of the vaccines, but the vaccines will come with the warning if you have an egg allergy or something that you might get increased risk. Since these are mRNA vaccines, I'm not sure about formulation. Because when you give a split vaccine, which is a killed vaccine you get a live virus, and then you want to infect the people with this virus. But before you do you want to kill it. So that's called a split vaccine.You need to include lots of things to induce the immune response. I'm not sure about formulations of the mRNA vaccines, if you need these types of alum or whatever things they add to the vaccine to make it more immunogenic with the mRNA.

**Becky:** Great, thank you. Janet says she's had some minor allergic reactions to the shingle and pneumonia vaccines in the past, and it was just reported that two people in the UK just had allergic reactions. Would you recommend any of the other vaccines to treat COVID-19?

**Dr. Tomayko:** Dr. Payne, do want to take that? I'm thinking about your picture of the arm.

**Dr. Payne:** Yeah. So I guess one question is what the allergy was? So, for example, there was that one picture where somebody had a big sort of goose-egg response. That's almost thought to be an intended response and it's not actually considered an allergy. I don't know if that's what Janet was referring to but those similar types of injection site reactions are not uncommon. I'm trying to remember the exact data, I think they occur in 2% to 4% of patients so you know people will definitely notice that.

**Becky:** Thank you. George asks, will the COVID-19 vaccine or other government approved remedies reboot my immune system and possibly cause a recurrence of my disease, which has been in remission? And we've got  a few questions that ask, how does the vaccine trigger our B cells, what will that do to our disease and our remissions? Or will it increase if we already have active disease?

**Dr. Maverakis:** So, vaccines have been associated with autoimmune diseases. Like Guillain-Barre for example, people who get Guillain-Barre a certain percentage of them will have had a vaccine previously within the last month before their onset of symptoms. So vaccines are absolutely known to do these types of things. Again, we're dealing with a different type of a vaccine, so we don't have data on how many people are going to develop autoimmunity from the vaccine or who are gonna get worsening of their autoimmunity after they get the vaccine. But usually, the vaccine risk of autoimmunity is very small. And when they do population based studies. One of the problems is that 70 million people are getting the flu vaccine. So, if 70 million people get the flu vaccine most likely if somebody did develop autoimmunity, it might be around that setting. When they do population based studies not all of the autoimmune or inflammatory diseases pan out. So, many of these diseases where you have case reports, saying that a patient developed Lichen Planus after a vaccine or something like that, not all of those diseases really pan out when they do population based studies. But we do know that there are a variety of immune mediated diseases that do pop up after vaccines. However, those risks, in general, are very tiny and the risks of getting COVID is very high. And the risk of death from COVID is very high. So, these are all things that you have to weigh and for me, I would still want to get the vaccine. But as more data will come out, we'll know. One of the good things about the trials of the vaccine is that they did put a lot of people on the vaccine Usually any clinical trial is power for efficacy, not safety. But the FDA before they awarded this emergency approval for these vaccines, they waited 60 days for any type of late reaction to pop up. And usually the vaccine associated autoimmune diseases or immune mediated problems, they usually pop up in 30 days. So the FDA weighted 60 whole days, in my opinion, was longer than need be. So there is some data already with the people who did receive the vaccine, and I imagine that this is going to be rapidly coming in, as more and more people are vaccinated. I mean, we're going to have massive amounts of people being vaccinated soon. So we'll know more about what type of autoimmunity, what type of immune reactions they have. Lastly, this is something that the government is very interested in because vaccine companies are protected from lawsuits. So, every time someone gets the vaccine, a certain amount of that dollars that was paid for the vaccine goes to these vaccine adverse event funds. So they're monitoring that

very quickly. There's databases of all the different adverse reactions for the different vaccines. So, we'll know very, very soon but right now, we don't have a lot of information.

**Dr. Payne:** It's always a little bit difficult to have this conversation and make formal recommendations before the FDA has reviewed. So my final answer will always be, let's wait until we see what the FDA formerly recommends if there's any contraindications of the vaccines and any kind of follow up surveillance. Because as hundreds of millions of people start to be immunized, we'll start to get a much broader data set. And it is possible that the recommendations will change. But just from a poll of some of the autoimmunity health care centers around the country, the standard recommendation right now is that patients with autoimmune disease should get the vaccine.

**Dr. Maverakis:** The package insert will definitely have the data as it evolves, so you can always take a peek at the package insert. They might veer towards the caution side in package inserts but it will definitely say if you have egg allergy, use with caution, or something like that. I did look really quickly on the Internet. So, it was a few people who got the Pfizer vaccine, not too many people who got an allergic reaction to it.

**Dr. Tomayko:** They were both people with severe allergies who carried epi pens with them routinely.

**Dr. Maverakis:** In terms of allergies, everybody knows somebody with a history of food allergy, but there's a wide spectrum of how severe those allergies are. And there's people who literally have like tens of thousands of units of these allergen specific antibodies in their blood. Let’s say the normal value is like 100, and you get up to like 20,000 or 30,000. So, I don't know what those people were, but the vast majority of people who have food allergies are just going to be having IgE levels of 100 or 200. Sometimes it's even normal levels, so these people with sky-high values are not incredibly common.

**Becky:** Great. I know the FDA approval still is forthcoming but we're getting a lot of questions on preliminarily looking at things, is the mRNA vaccine or the adenovirus vaccine probably going to be better for patients with pemphigus or pemphigoid? Good question?

**Dr. Payne:** Yes, I guess based on the preliminary data that's been released, basically there were no significant records of safety concerns for any of the three vaccines so far. But again, AstraZeneca/Oxford have not released final data yet. I know that they did publish a paper, I believe it came out yesterday or today. But right now, the data is 95% effective roughly for Pfizer and Moderna and 70% effective for AstraZeneca. So, one way of thinking about it is if we're faced with what we think is equal risk, you should probably go with the one that's more effective.

**Becky:** Then another question, I know, that it wasn't trialed with any patients with an autoimmune disease but is there any potential interaction between the vaccine, and any immunosuppressive medications?

**Dr. Tomayko:** I think the real interactions that we need to be concerned about are the fact that immunosuppressive medications can decrease the efficacy of the vaccine. When you get a vaccine, your immune system is responding to it, similarly to how your body responds to the infection. Immunosuppressive medications will dampen your immune response. So vaccines are going to be less effective when you're on immunosuppressive medications. And as Dr. Payne tried to outline with different classes of immunosuppressive medications, some will suppress your effective immune response more strongly than others. So that's what the main type of interaction would be.

**Dr. Payne:** It's not a dangerous interaction that would cause ill effects but more that it would dampen the efficacy of the vaccine.

**Becky:** Okay, great. Debra asks, if you've had COVID, would that put you at the end of the line for the vaccine?

**Dr. Payne:** That's a good question. I don't know the answer to that.

**Dr. Maverakis:** I don't think they will know if you have had COVID because you're going to be going to CVS to get the vaccine and they're not going to have access. Excuse me, I don't know if it's CVS, but you're gonna go to someplace to get the vaccine and they're not necessarily going to have access to your medical record. For the early people, I imagine that you might need something from your doctor that you have some type of health issue to get it but they're not going to be able to look it up and say, oh you've already gotten COVID, you're not going to get it, this vaccine is not for you.

**Dr. Tomayko:** The preliminary recommendations that I have read so far say that if you had COVID, you should still get vaccinated.

**Dr. Maverakis:** Yeah, just like if you've had zoster they still want you to get the zoster vaccine.

**Dr. Tomayko:** And the immune response that people make to a real infection with COVID-19 is quite variable. So how durable or how effective the long term immunity is by natural infection is

still in question. Probably has a lot to do with what was the viral load that you got like Dr. Maverakis was talking about? What is your age? What are your other health statuses? How robust is your immune system? Are you on different medications? So, even though we don't really have a full dataset, based on what we know, we really do believe that the vaccine is going to induce more reliable, more effective, more durable immunity on average than in true infection and natural infection would have.

**Becky:** And, I know you said that, after having COVID you have a natural immunity for three months or so. Is there an estimated length of how long you would have immunity to COVID-19 with the vaccine? Is it a permanent thing, or is it an annual trip to the doctor, like the flu vaccine? Is there any data out there on that yet?

**Dr. Tomayko:** There's a little bit of pretty intriguing, unpublished, basic science data out of UCSD, the University of California, San Diego, Shane Crotty's group, who has done some fabulous work, really showing how durable immune responses are to measles and smallpox. He's the person who showed that 80 years after getting smallpox, people still have memory B cells and long-lived plasma cells against smallpox. His group has work that hasn't been published, but actually was even discussed in the New York Times and being quoted by all the right leaders in the field. He's suggesting that from what he can see, he thinks that natural infection will give long lasting immunity. So that's encouraging, but this is nothing we can hang our hats on clinically, at this point. But it was very encouraging in comparison to the data that we had back in February, March, where we were looking at studies from other coronaviruses. There were a limited number of studies done where people were intentionally exposed to a coronavirus, some of the common cold viruses and then reinfected a year or two later and for many of these other coronaviruses, it was pretty clear that natural immunity waned. That after a year and a half, you could get reinfected. Or if you got reinfected, in some cases, people didn't get as sick but they continue to spread the virus to other people. So really, just 8 to 10 months ago, we had some serious concerns that immunity wasn't going to be that durable. But I think that's newer data set is encouraging to let us think that we have to keep an open mind.

**Dr. Maverakis:** One of the things to remember is that we get a new flu vaccine every year, not necessarily because we lost immunity, but there's a new strain of virus the following year. So, we need to be vaccinated against the new strain of virus. So, whether or not there's going to be new strains popping up after everybody gets vaccinated, will remain to be seen. But, hopefully, we could just make a new vaccine if that happens.

**Becky:** Great. This is a question about testing. And I imagine it might depend on the type of tests that you're getting, but Victoria asks, if you get sick and can't get the test right away, how long will you test positive?

**Dr. Maverakis:** I could answer that. So there have been reports for people to test positive for many, many months. So it's not clear if you're one of these people who have lingering positivity in terms of the PCR test, how infectious you are. Usually, the recommendation is for 14 days that you be extra careful, that you're not affecting anybody, but I wouldn't base it upon a negative test. In the past, the CDC was recommending two negative tests before you exposed yourself to anybody that you bunker down for that time. I would say, definitely, regardless of what the test is, you shouldn't be going out and exposing people for two weeks. So, even if tests are negative, stay bunkerd down for two weeks. Let's say you got sick and you just want to see if you are positive, and you couldn't go in, and it's been two weeks, I think the utility of the test at that point, is probably a little bit questionable and there might be people who need to be tested more than you. So, depending on what your doctor says.

**Dr. Payne:** I would agree with that. And it also depends on whether you're getting tested because you actually have symptoms, or whether you're getting tested because you had an exposure. So, if you, for example, went out to an event where there were a lot of people who weren't wearing masks and you were worried about that situation, they actually recommend that you don't go out and get tested right away. Because if you went out the next day and got tested, it can very well be negative, even though you actually exposed the virus. So they recommend that if you are exposed, that you wait 5 to 7 days and then get the test. So the idea is it's an asymptomatic exposure, you wait 5 to 7 days after the suspected exposure to get the test. If you're symptomatic it should be positive, then you'd want to get it probably within 10 to 14 days of the onset of symptoms.

**Dr. Maverakis:** Yeah, I totally agree. At my work, if we get exposed because of somebody at work has it or some patients come it and then I have to do my little question thing on my phone, and answer my questions whether I'm sick or not and at the end it asks me if I want to test,? And I am like, what for? I just got exposed yesterday. I'm not going to convert overnight, I have to wait a little bit. So, I usually don't run off and get tests right away when I get exposed.

**Becky:** That kind of leads into our next question. Dr. Maverakis, you said that some people do come into the office and are positive. Is there any data out there on any patients with pemphigus and pemphigoid? Even if it's just in your own experience with patients that get COVID and what you're seeing in our patient population?

**Dr. Maverakis:** Okay, I'm sorry, I haven't seen any of my patients get COVID. It's amazing. I see patients who get COVID but they're not like my autoimmune patients. They're the people who don't care and they're complaining about wearing the mask, things like that. But I know there's many people who take all precautions and they still get COVID. I would rather be one of those people because hopefully I would get milder disease. None of my autoimmune patients that I can think of have gotten COVID, maybe one at the most.

**Dr. Payne:** I want to say that maybe seven or so of my pemphigus and pemphigoid patients have had COVID and they were on mix, some were not on therapy anymore or for example, were greater than a year after Rituximab. Some were on the maximum doses of Cellcept and a lot of people were on various different things in between. Just my sort of back of the envelope kind of estimation of how they did is probably more driven by their age and other comorbidities then by the pemphigus or pemphigoid per se. So, I think that the people who did worse for people who are over the age of 80 and in a nursing home. And the people who did better were in their 40's and 50's and did not have that many other comorbidities other than their pemphigus and it's treatment.

**Dr. Tomayko:** I'd have to say my experience, again, is small, probably about six patients total. And people have done different sorts of courses. When you're dealing with small numbers like this it's hard to say what the real correlations are but certainly people who are older with many comorbidities, people in long-term care facilities, some of those people did worse but not all. And people who were just generally healthier tended to do better.

**Dr. Maverakis:** Dr. Payne and Dr. Tomayko are on the other side of the U.S. where they got the cases first. Now, it's just getting really bad in California but they were hit before me. So they have more experience with patients getting COVID I'm sure.

**Dr. Tomayko:** Right, that's what it has to do with, right? I mean, my state for a lot of the spring was like number 4 or 5, highest cases. So Dr. Maverakis is correct.

**Dr. Maverakis:** Yeah, we're catching up to you and I'm sure, probably past that now.

**Dr. Payne:** And so hopefully everybody is aware, the IPPF in general has also nucleated an international pemphigus and pemphigoid physicians group, and the group in the Netherlands and Germany are organizing an international registry. They're encouraging all the pemphigus and pemphigoid physicians to actually log in cases. It's actually hard in the United States, though, to actually officially login the case because they want written confirmation about the COVID test. In the very beginning no one could get a COVID test so a lot of people would just go into Rite Aid and they get a report on their phone. But it's hard for us to actually get the official tests in our records. But the type of data they're collecting is basically, what's their age, comorbidities, what was the outcome? Did their pemphigus or pemphigoid get worse? All of these sorts of data that are trying to collect to answer this question.

**Becky:**Great.

**Dr. Maverakis:** Are they doing that with the vaccine as well Dr. Payne?

**Dr. Payne:** Go point. No, they're not. It's only related to infection.

**Becky:** Great information. Thank you. We're getting some questions about just a clarification about the better and worse treatments for pemphigus and pemphigoid to be on during a pandemic? Just how dangerous it is to be on, specifically, a lot of the questions are in relation to Mycophenolate Mofetil and Rituximab.

**Dr. Maverakis:** The one thing with Rituximab is that it's going to increase your risk of getting severe COVID after you receive it. But it's therapeutic effect sometimes lasts longer than its immunosuppressive effect. So, you might get Rituxan then maybe you might be in remission for two years afterwards, or at least a year afterwards. And your immune system might recover it before then so it's really hard to answer that question. If you're on Mycophenolate I would guess and this is not based upon data, I would guess that Mycophenolate which is Cellcept, which would predispose you to COVID infection but that predisposition would be all the time while you're on it. And it's not like you could stop it right away, you can stop it right away when you have COVID but that immunosuppression will also linger for a couple of weeks after which is like the natural course of the COVID. So it's not clear which medication would be safer. But I would guess that if it was right after you received Rituxan that would be worse than being on Cellcept because at least he could stop the Cellcept. But if it was six months after, it might be safer for the Rituxan group than if you're in the Cellcept group.

**Dr. Payne:** Becky, can you go to slide 14? So basically, this was data for the Global Rheumatology Alliance that's basically tracking over 3,7000 patients who are on various different therapies. Basically, an odds ratio is basically like how much more likely you are to end in death. Methotrexate was their baseline comparison. Antimalarials are things like Plaquenil and Hydroxychloroquine. And then Azathioprine, Mycophenolate and Cyclophosphamide were seen with a two fold increase in death. And Rituximab was associated with a 3.68 fold increase in death in the study.

**Dr. Maverakis:** So this is unpublished. Is this the same data as, I forget the name of the investigator. Anyways, I've heard of an investigator that their data showed that people on Rituxan did actually very poorly but it wasn't published yet. I just noticed that this is also unpublished. So it might be the same group that was telling me about their data?

**Dr. Payne:** This is not a dermatology group. This is actually from an Arthritis Seminar that was about a month ago run by Betty Diamonds from Zachary Walls. It’s under review right now but basically a prospective registry of patients with Rheumatologic diseases. So, incidentally the

Rituximab data, we have to take with a grain of salt because a lot of this would be patients with rheumatoid arthritis, autoimmune vasculitis, they may have kidney disease in addition. So, we have to take it with a little bit of a grain of salt because these are not pemphigus or pemphigoid patients but it gives you a general idea of what they found in that autoimmune patient population.

**Dr. Maverakis:** Unpublished data I heard for immunobullous diseases was also a little bit concerning for Rituximab. Again, though, I would think that it's going to be related to the timing of when you got the Rituximab. So, if you got it a year ago, your disease might still be controlled but most likely, you're not going to be as suppressed as if you were on something like Cyclophosphamide or something like that.

**Dr. Tomayko:** So anecdotally, here for some of our neural neurology patients, multiple sclerosis patients who get a different version of Rituximab, Ocrelizumab, which is very similar. Anecdotally, it looks like they've done worse, with COVID too. But like Dr. Maverakis is saying, it's the same for things like rheumatoid arthritis and for vasculitis and multiple sclerosis those patients are almost always getting fusions every six months and sometimes even every four months. And some of our pemphigus patients go longer than that.

**Dr. Maverakis:** At least here, we are probably pushing it longer but I don't know how they're doing it in Europe, but I'm sure many of you don't necessarily redose at six months if the patient looks really great.

**Dr. Tomayko:** I think you have to think about what are your other risk factors in your life? If you're able to stay home, work from home, if your household is sort of controlled, who's coming and going. If people are maintaining social distance and masking, et cetera, then you're at lower risk for contracting the disease, Rituximab can often be the most effective treatment. And you don't want to withhold treatment for that reason. However, if you have to go to work and your family member is working in a grocery store and another is a young person who's coaching kids or if you're a family member and household members are in and out of the house that puts you at a much higher risk. And maybe you do need to to re-evaluate. But it's really complex medical decision making.

**Dr. Payne:** I think we're going to update the IPPF website, because that's a common question. So even though we think Rituximab increases the risk of poor outcomes, including death with COVID-19, at the same time, there was a clinical trial that was run where they compared Rituximab and prednisone to high dose prednisone alone. If your pemphigus is so severe that you're on 100 milligrams of prednisone they've actually shown that the rate of any infection with prednisone is actually the same as or higher than the rate of infection with Rituximab. So at that rate, go with the one that's more effective.

**Dr. Maverakis:** Yeah, I agree with both Dr. Tomayko and Dr. Payne.

**Dr. Payne:** Essentially risk of disease versus risk of infection from the treatment.

**Becky:** And you had mentioned in a previous call, too, that if you're on 40 milligrams of prednisone, it's not necessarily good to stop it now, because if you do and then have this rebounding flare, then it's possible you're going to need 70 milligrams of prednisone or a stronger medicine, and then be in a worse situation and more immunosuppressed then you are currently with your current treatment. That still stands from the earlier ones as well, correct?

**Dr. Payne:** Yes. Never stop prednisone suddenly! It's interesting, your body gets addicted to prednisone very easily, and you literally need steroids to live. It makes your heart beat, it literally makes your body function. So if you go cold turkey and suddenly stop prednisone there will be very, very bad outcomes. We've had people that have literally passed out and needed a pacemaker if they just suddenly stopped high dose prednisone. Definitely don't do that.

**Becky:** Well, great. Thank you so much. This is then a very educational hour and a half for us, and we appreciate all the time that you guys have dedicated to preparing for this. You can tell a lot of work went into this, and this is a very difficult subject and you broke it down pretty well. So I think both are science nerds and our average joes will be able to understand. So, I really thank you for all of the work and the effort and a big thank you to our sponsors who made this called possible, Genentech, Principia Biopharma, a Sanofi Company, argenix and Cabaletta Bio. So before we go, I do have a few announcements. Our goal at the IPPF is to create a brighter future for all those affected by pemphigus and pemphigoid. As a community, we've made great strides in recent years, but there's still much work to be done. Your support is critical to fund the future for pemphigus and pemphigoid patients. Help the IPPF reach their goal of raising $40,000 by the end of the year by making a donation online today.Thanks to a generous gift from the Unger Family Foundation, all new or increased Healing Hero donations will be matched through the end of the year. Your donations will ensure that our patient support programs are available to all those who need them today, tomorrow and for years to come.

**Becky:** Also, if you are interested in continuing to help support the IPPF you can become a healing hero. Healing Heroes fund the future of the IPPF community by making sustaining, monthly gifts to support our mission of improving the quality of life for all those affected by pemphigus and pemphigoid. No amount is too small, even a $5 or $10 monthly donation goes a long way and continues to allow us to provide for the greater good of our community. If you have not registered for the IPPF's natural history study we encourage you to do so. The IPPF 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 in research studies. The more data we can collect, the better the information we can

give to researchers, the sooner they can find better treatments, earlier diagnosis, and one day a cure! Our next Patient Education Webinar will be next week on Wednesday, December 16th with Lynne Mitchell, a registered social worker and PV patient to discuss Mental Health and Stress going into the holidays. Lastly, if you have a question that didn't get answered on the call, or have additional questions please e-mail Becky Strong, at becky@pemphigus.org, or call (916) 922-1298 x:105, and we would be more than happy to help.This call recording will be sent out with a survey following this call. Thank you everyone, and goodnight tonight.