

**Becky:** Hi, welcome everybody. Thank you for joining us on this webinar today. Today's webinar is now being recorded. I'm Becky Strong, IPPF Outreach Director, and I'll be your host for today's webinar. I would like to say a big thank you for everybody joining us and also a thank you to Sanofi and Regeneron for the support that they offer to make today's webinar possible. We're excited to have Dr. Victoria Werth with us to discuss supplements in autoimmune disease and vaccination. So let me move on and introduce our speaker.

**Becky:** Dr. Werth received her Medical Doctorate from Johns Hopkins School of Medicine, followed by residency and a postdoctoral research fellowship in Immunodermatology at New York University. Dr. Werth moved to Penn in 1989 as Chief of Dermatology at the Philadelphia VA Hospital. At Penn she directs the Autoimmune Skin Disease study unit, and performs clinical and translational research studies in autoimmune skin disease funded by the National Institute of Health, autoimmune foundations, and industry. She has performed a number of industry trials for pemphigus and bullous pemphigoid. She has a basic research lab at the VA devoted to autoimmune skin disease and photobiology, funded by NIH and the VA. Dr. Werth's clinical practice specializes in the diagnosis and treatment of patients with autoimmune skin diseases, including autoimmune blistering disease, lupus erythematosus, and dermatomyositis. She led an international effort to develop disease severity tools for several autoimmune blistering diseases, including pemphigus and bullous pemphigoid. These tools are now used in international trials that are developing new drugs for autoimmune blistering diseases, including the trial leading to the recent FDA approval of Rituximab for pemphigus vulgaris. Dr. Werth has also performed studies to determine the impact of bullous diseases on Quality-of-life. She has been on the IPPF Medical Advisory Board since the beginning of the foundation. Dr. Werth has received numerous honors for her work. Before I begin. I'd like to go over a few housekeeping items... (Reviews Housekeeping slides).

**Becky:** It is now my pleasure to hand things over to Dr. Victoria Werth.

**Dr. Werth:** All right. Well, thank you for that lovely introduction, and let me get my slides up here. So this is a very challenging but important topic because I think that when people have an autoimmune disease, and in particular blistering disease, we really need to pay attention to the fact that many of the medicines do dampen down the

immune system. But on the other hand, the problem is that the immune system is overactive so you want to be really careful not to further stimulate the immune system. And so I think it does bring up a lot of questions. I hope to present some data today that will make you think about what you're doing when it comes to taking supplements, and we'll talk a little bit about vaccinations as well.

**Dr. Werth:** These are the 2 topics, and I'm going to start talking about supplements. I have no conflict of interest. I don't receive any funding from supplement companies or people who do vaccinations. It's just that, in the process of taking care of my autoimmune patients I've made some observations that has led to me wanting to do additional studies.

**Dr. Werth:** The use of complementary and alternative medicine is prevalent among people with dermatologic and chronic disease. There are certain of these complementary and alternative medicines (CAM) that are immunostimulatory or associated with adverse autoimmune dermatologic effects. The first article there that was published in the Journal of American Academy of Dermatology really reviewed the literature. I'm just listing some of the substances that have been studied enough that I'm pretty confident in saying that they can stimulate the immune system in a way that when you have an autoimmune disease may not be helpful. We'll go over some of the data for this. But there's spirulina, echinacea, alfalfa, chlorella, blue-green algae, and elderberry.

**Dr. Werth:** I can tell you that I now have a number of years of experience of reading the backs of all these different things that come out. Whether it be, for instance, Naked Juice here, but a lot of the green juices, and really looking for these types of herbs and trying to guide whether or not it's something that's safe or not safe. Sometimes if you look in these herbs they will show some kind of substances and they don't even define what they are on. And so that's a problem because you don't really even have anything you can look up, it's proprietary. When you see a proprietary blend, that's probably not helpful. But I will point out that herbal supplement use is increasing in the United States. We had initially, at least in some of our autoimmune patients noted that, IsaLean which is a weight loss powder, have been associated with one autoimmune disease, dermatomyositis, onset of the disease or flaring of the disease. I will mention that Herbalife has some of the many of the same ingredients as IsaLean and these are used by many, many people. The herbal substances that can simulate the immune system

we kind of already talked about. So I want to go forward and talk a little bit more about why I'm concerned about these.

**Dr. Werth:** So with the weight loss powder, it's called IsaLean, we dissolved it, and we use it to stimulate peripheral blood cells from patients with autoimmune disease. And we were able to show that when you had increasing concentrations, as you can see here, going along the X-axis from 0 to 0.5 to 5, that the amount of a cytokine that can be part of the immune simulation, went up and up and up. We also saw the same thing with the interferons which we know are drivers of autoimmunity in a number of patients, interferon Alpha and interferon Beta. Again, with increasing concentrations of IsaLean you get more and more stimulation of these interferons, which stimulate the immune system.

**Dr. Werth:** Then we were really interested in understanding how this was working so we started doing some studies where we would try to block receptors like a toll receptor for, and could show that when you put IsaLean on the peripheral blood mononuclear cells, you could actually block the effect of increasing TNF with an antibody against that one specific receptor. So that really helps us figure out, how is this working? So we found that to be the case with IsaLean.

**Dr. Werth:** More recently we started looking at spirulina. Spirulina is a blue- green algae which is thought of as a superfood. There are many things that have been attributed to it, including effects on lipids, antioxidants, anti-inflammatory properties. So it's been very confusing, because it sounds like a good thing to do. What is even more amazing is how widely it's used in tablet form, or as a powder and in many energy bars, smoothies, and green juices. It's hard to escape actually. If you start reading the labels of many of the foods that you buy or the drinks that you buy, you'll start finding this in it. And I'm going to show you some data about that.

**Dr. Werth:** What's really interesting and I learn a lot from my patients because they teach me what's going on in the market, now we've got spirulina creams. I can't say anything about these. I have no idea what they do, but it's fascinating to me how things evolve. I'll show you later in the talk, another evolution that happened.

**Dr. Werth:** So we decided to look at spirulina and we extracted it from the original powder, and we're doing very similar experiments to what I showed you with the weight

loss powder, the IsaLean. Here we took different amounts of spirulina. Here is 0.3, here is 1 and you can see again when we took our peripheral blood mononuclear cells that we were stimulating TNF with this concentration of spirulina. And at higher concentrations we would simulate the interferon gamma, which is again pro inflammatory. We looked at a number of cytokines and we found this to be pretty interesting. What we had done was, we recruited patients from one of my databases of autoimmune patients and we used this spirulina that we'd isolated and then we stimulated these peripheral blood mononuclear cells and we looked at various pathways that could be activated that we were particularly interested in.

**Dr. Werth:** There are lots of ways to look at cells. We can look at something called flow cytometry, which tells you what's going on with individual, different types of immune cells and what they're making and how what they're making contributes to problems with simulating the immune system. You can look at tissues with something called imaging mass cytometry. That's another study that we've done.

**Dr. Werth:** Obviously, we have to analyze the data very carefully. So what we did was we did flow cytometry and here what you can see is we were looking at how many cells had one particular type of inflammatory cytokine, namely TNF in a specific cell type, mainly here it was a conventional monocyte. What's also really interesting is that the patients who had autoimmune disease here, with DM meaning dermatomyositis, that there was stimulation of TNF producing inflammatory cells, something we did not see in the healthy controls. We saw that in both the low dose here of spirulina and then the higher dose of spirulina. And it is obviously very different from the untreated, control peripheral blood.

**Dr. Werth:** So what this is telling us is again, we're stimulating the immune system and the cells and they're making these inflammatory cytokines and we're not seeing it in healthy controls. So what I think that's telling us is that people are predisposed to having autoimmune problems, I will talk more about how to interpret that, or maybe more susceptible. And certainly for most people, it's not a problem. But for people who are more pro autoimmune, it probably could be a problem.

**Dr. Werth:** Then this is looking at another cell type. It's another type of dendritic cell. Here again, you can see stimulation with spirulina but not with healthy control and this is

a high dose, same thing. This is looking at individual cells and doing flow cytometry and we can look at drill down on what cells are being affected. Then we could do similar studies where we can block different pathways and see which ones are causing issues and problems and what would get rid of the stimulatory effect. So we've done these kinds of studies. But I'm going to show you this, here on the right hand side, which is what a flow cytometer result looks like. This is like normal and here on the x-axis is TNF. This is just looking at the fact that there are no cells there, there's nothing in this quadrant here, so there's really no TNF producing cells or very few. Then when you add the spirulina, all of a sudden look at all the cells that are making TNF. These are all the individual cells that you can look at. Really indicating how stimulated the immune system can get.

**Dr. Werth:** One of the things that we've been sort of interested in looking at is what are the pathways that are affected by some of these immunostimulatory herbs. This is really beyond what we're going to talk about today but I think it's important to understand that these really have biological effects.

**Dr. Werth:** So spirulina induces production of these inflammatory cytokines in a number of different cell lines that we showed from people who have autoimmune disease compared to healthy control. We were able to block in when, for instance, blocking the one particular receptor, we could block the stimulation by this, so we kind of have some ideas of how this is working. Our concern is that spirulina may promote autoimmunity via production of these inflammatory cytokines in the cells and the peripheral blood and in the skin and, then that be a concern for patients who have autoimmune disease.

**Dr. Werth:** There have been previous individual cases documented of acute onset or a flare of a number of autoimmune diseases, including, I will point out, autoimmune blistering diseases with some of these herbs. So we decided to do a study analyzing the exposure among patients with autoimmune skin disease, including dermatomyositis, lupus, and also autoimmune blistering disease, to see what people were doing.

**Dr. Werth:** So what this is showing is that some autoimmune diseases may be more susceptible than others. Here's the dermatomyositis, and you can see that of the patients who had dermatomyositis, almost 20% were using a herbal supplement that

was immunostimulatory. You can see there was some increase with autoimmune blistering disease but nothing like this. And here is the control, 5% and with lupus it was not that different. So if there is a little bit of a drift here, it's nothing like here with dermatomyositis but it's still concerning that autoimmune diseases can be associated with the use of an immunostimulatory herb. Then we looked at spirulina and here you can see that there were many people taking it with dermatomyositis but not much difference between, in fact, no difference between lupus and control, and in the 31 people that we carefully discuss this with with autoimmune blistering disease, none of them were taking spirulina but they were taking other immunostimulatory herbs.

**Dr. Werth:** So that brings me to another one, elderberry. This is one that's only recently come to my attention. As we've seen now, a number of people who seem to have had an onset of their problem with their autoimmune disease shortly after starting, taking elderberry and leading to really significant autoimmune issues. There's been some really good studies, I'm referencing one here, a fairly recent one, talking about the effect on maturing the dendritic cell which is one of the ways that activates T cells that are part of what mediates a lot of autoimmune problems. Then there are also T cells that are simulated, and there's an induction of inflammatory cytokines. This is actually a quote from the article, "There is interesting potential to stimulate antiviral immune responses". I think in this era we've had so much trouble with Covid and people are so worried about infections, it really speaks to why people are using these preparations more and more because we think it's a good thing. In the right setting it probably is. In fact, there's some data to say that it may help. But, on the other hand, if you have an autoimmune disease, it can also be a huge problem.

**Dr. Werth:** So this was from that article. Again looking at dendritic cells and when you add in different fractions of elderberry, you can see the TNF alpha and Interferon gamma, these are pro-inflammatory cytokines, are stimulated as you can see here. This is a control. And when you add in these different fractions of elderberry, you stimulate these pro-inflammatory cytokines. Again, maybe that's great for infections, it's not great, probably for autoimmunity.

**Dr. Werth:** Very recently, somebody came in and was coughing, and said, well, because I was coughing I went and got Robitussin. And I was typing away on the computer and then they said, with elderberry. And I'm like, huh what is that? Well, it turns out, now

we've got this thing, it's new Robitussin with elderberry. So again, if you have an autoimmune thing, maybe that's not the best thing to take, maybe we better go back to just an old Robitussin. But these new things are creeping in everywhere, and it's just good to be aware of it. In fact, elderberry supplement sales increased 415% in the single week period ending March 8th 2020, as you remember, is when Covid started to take off. Then this was a link talking about how dietary supplement sales were skyrocketing during the Covid pandemic. However, the link is no longer active but again speaks to why people are taking many of these things.

**Dr. Werth:** That's pretty much what I wanted to discuss. I think there's really lots of room to do more work. Maybe it's not the same for every single autoimmune disease. But I think it's good to be aware that there can be problems.

**Dr. Werth:** Now the other thing I wanted to talk about today then was about vaccines and autoimmune blistering disease. I can tell you that whenever controlled prospective vaccine safety studies have been done in patients with autoimmune diseases, there's not really been evidence of an exacerbation of existing autoimmune diseases or induction of new rheumatic diseases or autoimmune processes found. That's pretty standard, and I think that in fact, many of the vaccines have been around for many, many years and are incredibly safe. It's not good to get the flu. It's not good to get pneumonia. It's not good to get herpes zoster. There probably are a very small number of patients in these studies, and so we may not detect rare events. If you look in the literature there may be a few case reports of patients flaring with their autoimmune disease with regular vaccines, but it's very, very rare. And I think in general it's really easy to say one should continue to get vaccines. Many of these illnesses can be life threatening or life altering in terms of quality of life so the risk benefit ratio here is pretty clear in favor of getting vaccines.

**Dr. Werth:** That brings me to the Covid vaccine, which as we all know, came out very quickly. It didn't have the chance to be tested as much. I think many people got it, not everybody. They've been some reports of immunobullous disorders that have been induced or exacerbated after Covid-19 vaccine. Some of these are here, and you can see which vaccine it was. Here they're talking about, this one here is Pfizer, the BNT is Pfizer. The Moderna is the mRNA-1273. What this is showing is that there have been some scattered, not so many reports of new onset of pemphigus in this case. Here's a

case of a flare of pemphigoid and some flares of pemphigus. This was in the literature about a year ago. Not a huge number of cases but I think that it is something that is worth being aware of. What I would say is, most of these outcomes that have happened with flares, with the vaccine have been relatively mild. Some have required increased medication treatment, and most flares have settled down over time. But they did happen but not to everybody.

**Dr. Werth:** So I wanted to review a little bit of our data and I was just going to start with dermatomyositis where we had a number of patients who either had Covid infection or Covid vaccine. There were patients by the way, and you should know that the infection itself can trigger autoimmune flares. So it's another argument for, although few people have had trouble with the vaccine or even serious trouble, it's not great to have Covid. It's always a risk-benefit and it's just a little harder here to know but I think most people, even with autoimmune disease, who have gotten the vaccine have done fine. But this is just showing you that in 2022 we saw 8 people, half of them in the setting of infection, and the other half in the setting of the vaccine, with new onset dermatomyositis. It definitely happened, but again not so common. Then this is looking at new onset versus flare and you can see that there was some new onset of disease associated with the patients who got Covid. We also saw this with the vaccine as well as the infection. So it is really hard to say since some were new onset and some were flare. So people with autoimmune diseases can have issues.

**Dr. Werth:** So we decided early on since I was seeing some people flaring after getting the vaccine, and we decided to very systematically study the patients we were seeing. Everyone was asked the same questions rather systematically. We had a template about the vaccination status, who the manufacturers were, the vaccine dates, autoimmune symptoms after the vaccine and the timing of symptom onset. We wanted to see over a number of different autoimmune diseases what we were seeing.

**Dr. Werth:** This shows you a lot of what we were seeing in terms of the baseline autoimmune disease. You can see we had people with pemphigus, pemphigoid, mucous membrane pemphigoid. We had some people that were not vaccinated, about 13% and 85% were fully vaccinated of the people that we were seeing.



**Dr. Werth:** When we were looking at what happened to people who are fully vaccinated, with one disease, mainly dermatomyositis, about 22% of people had some kind of a flare. Most of the time mild enough, but some people had worse flares and or even new onset versus about 8.6% with lupus. It's not zero but you would expect to see some flares in populations but it's clearly more here. So we went on and looked at all the different people that we just talked about. We have to almost ignore the blue line here because it was only 2 patients but they both happen to exacerbate with the vaccine. What this is showing you is that with pemphigus, about the same as with dermatomyositis, there were some flares that we saw after getting the vaccine. With MMP we had 1 out of 10 people had a flare. With BP we didn't see anything but I'm sure that it can happen and there are reports in the literature. But this gives you some idea of the relatively low level of flaring that was seen in some people after getting the vaccine.

**Dr. Werth:** So we wanted to know which vaccine did people get and it was about 12% Pfizer, 19% Moderna, and then J&J, 10.5%. This is in terms of people who reported exacerbations of their autoimmune disease. So a little bit more with Moderna, which was thought to be, overall more immunogenic when it was rolled out and this kind of fits with that approach.

**Dr. Werth:** So what about the timing? Of the people who had autoimmune exacerbations after vaccination, 20% had symptoms after their first dose but most people, if they had an exacerbation, it was about 82% after the second dose. So not the first dose but the second dose and then a few after the third dose. Subsequent immunization seemed to be much less problematic. It was really right at the beginning. Then the timing after the second injection was usually around 14 days and it was pretty consistent. I was really within 1 to 2 weeks, typically 2 weeks, with the 14 to 21 being the median. It was after 7 days with the first one, for the few people that had that, the 20%.

**Dr. Werth:** So that's what we saw. Our conclusion from this was that in general, from these studies that I'm showing you, immunosimulatory herbs probably should be avoided if there's a family history or personal history of autoimmune disease. When I tell people about this, I think it is one of the most helpful things to also share this with your family members because they likely share some genetics and are more predisposed to having problems. So that is one take home message. If you think that you have a

problem with your immune system, it's likely to be overactive, not underactive. And you don't want to be taking these herbs if it's going to cause problems. Then, both the Covid vaccine and the Covid infection can be associated with exacerbations and new onset autoimmune diseases. So it becomes very difficult. I think the vaccine for most people did not cause any problems and it was protective from bad infection. It's very hard to make that determination. I think, especially with subsequent immunizations, although fewer people are getting them, we're not seeing the same amount of problems. But it's harder to interpret, because fewer people are getting subsequent vaccines. But I think it's pretty well tolerated and the flares are usually mild.

**Dr. Werth:** The take home, think before you drink. This is something we hand out to lots of our patients and something to really keep in mind as you move forward and think about the many products now that are on the market that I think that we really need to be really cognizant about. With that, I think I'm going to stop so we'll have time to talk about some questions.

**Becky:** Great. Thank you, Dr. Werth. Before we jump into a lot of questions, there have been a couple of questions about what is TNF? You were discussing that by discussing that when discussing the supplements.

**Dr. Werth:** So that's a protein that is part of the immune system response. Just like the interferons which are part of an antiviral response, it's part of a response to sometimes bacteria or different things, but it turns out that when tumor necrosis factor (TNF) goes up, that's the sign that the immune system is revved up. It's one of the ways to show that the cells are more active. Very good question.

**Becky:** That's great. Thank you. Our first question is about turmeric. It has been said that it's an anti-inflammatory. So does this help if somebody takes this with an autoimmune disease? Does it help to calm the immune system as well?

**Dr. Werth:** Yeah, that's a very good question. Turmeric has actually been studied in trials. It is not pro-inflammatory. It is probably a weak anti-inflammatory, it probably isn't that effective but it's probably not going to hurt people. I think it's really important to not lump everything together, but to really be careful about the things that we know simulate the immune system. If you have a product that you can't even tell what's in it, that's a problem. But turmeric is not one of the ones that I particularly worry about. I think it's probably relatively safe.

**Becky:** Okay, our next question says, for those who take corticosteroids, is it recommended to take berberine or chromium that are often used to control blood sugar? Is there any research being done to show if there's any impact on pemphigus vulgaris?

**Dr. Werth:** I have not seen anything about those being immunosuppressive. I don't think those are problems and if your doctor is telling you you should take it for that indication, I don't have a problem with that. I'm not aware of so much literature in regards to the immune system.

**Becky:** Great, Joanne says that she was diagnosed with the bullous pemphigoid 2 weeks after having the flu and Covid vaccines at the same time. Is there any research saying that getting both vaccines at the same time could have had an increased cause in developing her disease?

**Dr. Werth:** Yeah, that's a tough one to answer. As I mentioned, some of the other vaccines very rarely can cause problems. We know that the Covid vaccine alone can cause problems, so it is very hard to tease that out. I think it's probably better not to get multiple immunizations at the same time. But there's not a lot of data to speak to about that

**Becky:** What about using zinc? A lot of times people will take zinc when they're sick or told to take zinc when they're sick and it helps to shorten the length of their cold. We've gotten quite a few questions about zinc.

**Dr. Werth:** That's great. Anytime it's thought to help with the cold I get a little bit worried. I'm not aware of literature that says that zinc is a problem, but you would actually want to look specifically at that but I'm not aware of literature that talks about them. But if something really shortens the cold you have to ask how and why, and actually look into it more. I don't know if I've seen anything much about zinc in terms of that. I mean, I know it's used to try to deal with infections.

**Becky:** So moving on to vaccines, we've gotten quite a number of questions about the shingles vaccine. And is it okay to get it with pemphigus or pemphigoid and about timing as far as having treatments. What is your advice on the shingles vaccine?

**Dr. Werth:** I think shingles is so common. As people's immune systems as you're being treated with medicine that lowers the immune system, it's really frequent to get shingles.

You can get chronic pain from it. It's really not fun to go through that. I think the chance of flares is relatively rare, again can probably be managed pretty readily with most people. The timing I think should be for instance like if you are getting Rituximab you might want to wait until your B cells have recovered a bit before getting it, because if you get it shortly after getting the Rituximab you may not mount a very good immune response. But I don't think that means you should not get it.

**Becky:** We've gotten a couple of questions. Let me go back because I'm trying to put a couple together here. Bonnie said, "It seems like the number of patients in the Covid vaccine study, you had listed 8, is incredibly low to be considered a good control group. Is it normal to have such a low number in a study?"

**Dr. Werth:** Yeah, that wasn't the control group. We were looking at people with new onset of disease that would come in to be enrolled in our database. It wasn't a control. It was more like, who did we see and was it people who had either flare of their disease or new onset disease. But you know, it's a very limited sample so it's not a control. It's more to say, these people really associated with the timing of either the vaccine or the virus. It's not it. It's not a big population study or 100% right. But that would be really difficult to do. I will mention that there were some studies that were done with the vaccine where they combined a lot of different diseases and there were a few people that had autoimmune problems, but many fewer than what we saw of the almost 400-500 people that we actually systematically followed and that we saw over that year. And when you started mixing a lot of diseases together, they did not see much. And it's really when you focus on autoimmune disease and have a large number, that you can begin to see some patterns. Again, not overly concerning, but it helps us to understand a little bit more about what to expect.

**Becky:** Great. We're getting questions about patients who are taking corticosteroids and doctors are saying to take calcium and or vitamin D, and I was hoping that maybe you could address the need for that and why those suggestions are being made.

**Dr. Werth:** One of the concerns about steroids is the effect on the bone. We try to do everything we can to try to make sure that people don't lose bone, and one of the ways is to replace calcium. Calcium goes out more in the urine and it doesn't get absorbed as well when you're on steroids. So calcium replacement is a fairly standard approach.

Vitamin D as well can help. Those are just really standard, but have nothing really to do with the immune system so much, but more about the bone.

**Becky:** Great, is there a form of calcium that's better for patients who are on corticosteroids to take?

**Dr. Werth:** There are issues with absorption. I think calcium citrate can be particularly good for absorption. Calcium carbonate does not always get absorbed. I think that there's some preparations that are combined with vitamin D. I'm not aware that there's so much, but I think it's more a matter of taking it or not taking it, but I guess if you have a choice, calcium citrate might be better.

**Becky:** We got a couple of questions about, are vitamins and supplements governed by the FDA like my prescriptions? Or how do I know how to measure a quality supplement to be take?

**Dr. Werth:** I love that question. There was a decision by Congress, I think in the 1990's, that more or less removed over the counter preparations from regulation by the FDA. So there is really no oversight. I think if there was a problem there are ways of reporting it. As you probably know, the over-the-counter, if they start to say that they have effects of their drugs that are pharmacologic then that gets them into trouble. And then they get into trouble with the FDA because they're not supposed to really do anything. But I think from the data I'm showing you is that there these some of these herbal things do, in fact, have pharmacologic effects, and one could argue that it would be a really good idea to have some of this regulated.

**Becky:** Great, thank you. That's helpful for everybody to hear. We've had quite a few people ask about taking fish oil supplements to help protect against autoimmune disorders, specifically for rheumatoid arthritis. Is there anything in the evidence that says that fish oil can help with autoimmune blistering diseases as well?

**Dr. Werth:** So it's not gonna hurt. I think there's some thought about its impact on lipid levels, which I think is maybe one of the reasons why it's offered. I'm not aware that it has effects in terms of inflammation. Fish oil is often used more for cholesterol and things like that.

**Becky:** Thank you. We've also got a couple of questions about probiotics. Is there a need for probiotics? And does it help with controlling the disease or reducing a flare?

**Dr. Werth:** Great question. I don't think we know all the answers. Probiotics are not all the same. There can be, "good bacteria" I guess they are good for the gut but there is a lot of gut skin connection, and I don't think we know since there's so much variation in the probiotics. I don't think it's been really studied enough to understand what happens in terms of the immune system. I think it's really a hard question to answer. I wish there was a simple answer but I don't think there is a simple one, and I know lots and lots of people take probiotics.

**Becky:** Great. Thank you. We've also got quite a few people interested in participating in research for Covid or other vaccinations. And they were asking if they could enroll in your trials or do you need to be a VA patient in order to enroll in your study? And if they can participate, how can they do that?

**Dr. Werth:** So I really feel like the work we did, it was really a unique time, because everybody was getting immunized so we were able to very systematically collect the data. I think now, there's so much recall bias, in terms of being able to determine something like, when did you get the vaccine and when did something happen, it's really difficult to tie things together. I have patients that I was seeing during that year who would for instance, flare the disease 2 weeks after the second vaccine, and only a few of them got quite so sick and could not recollect like 6 months later, that it's somehow tied to the vaccine. So I'm not, right now doing any ongoing studies but I definitely think if we introduce new vaccines, it really speaks to the need to do very, very careful studies, particularly in autoimmune patients.

**Becky:** Great. Thank you so much for that. We also got some questions about how many Covid vaccines should a patient have and what should the spacing be? Especially if you're on treatment?

**Dr. Werth:** Again, I don't think there's a right answer. I think we heard about the bivalent vaccine that came out like a year ago. That was going to be good for people who were immunosuppressed but I think it was a little more immunogenic. I saw a few things with that. I think it really depends a little bit on what happens with Covid. It's really mutated a lot. We have better treatments for Covid and the vaccines don't seem to be as protective at this point as maybe they were originally when it was much more severe.

It's like a moving target, and the CDC doesn't even really know what to recommend. So there's not a right answer here. Some people are very worried, and they're up to number 5 or number 6 immunizations. There are other people that don't want to get any immunizations. And I think that's also problematic, because those people really are not protected. Some of them have become recluses and don't go out of the house and I think that's really unhealthy. I think there's got to be a balance and there's not a right answer.

**Becky:** Okay, we've gotten some questions, about live vaccines versus attenuated, and which is better for patients with pemphigus and pemphigoid. And if you could just give them a brief primer over the different types of vaccines and what patients should be getting when they go to the doctor for vaccines.

**Dr. Werth:** I think the live vaccines, and even the attenuated, if you're on steroids and other medications that might not be that safe because you're not going to be able to mount a response and you can get sick from the live vaccine. There's certain vaccines, for instance, yellow fever that you wouldn't want to get if you were on steroids and high doses of immunosuppressants. I think it's just a good discussion to have about which vaccine one is getting at what time and what medications you're on in order to decide, what's safe or what's not safe?

**Becky:** Great, thank you. Are there any medications or treatments for pemphigus and pemphigoid that affect the effectiveness of a vaccine more than others? Does Rituximab make a vaccine less effective, or one of the immunosuppressants like Mycophenolate, or Azathioprine, or corticosteroids?

**Dr. Werth:** That's very true. We have learned from many of the vaccine studies that when people are on Rituximab, they did not mount an immune response to the Covid vaccine. And people who were on Rituximab could potentially get sicker if they got Covid. Now that we have treatment for Covid, that is less of an issue but it was a huge issue at the time. But the same thing can be said about higher doses of steroids and also higher doses of immunosuppressives, they all suppress the immune system in a way that could potentially make the vaccines not work as well.

**Becky:** Okay. We've also got a couple of questions that we're pre-submitted about getting the flu vaccine and there's a different dose for seniors. Should patients with pemphigus and pemphigoid, whether they meet the age criteria or not, request the vaccine for the older adults or is the regular vaccine dose safe for patients?

**Dr. Werth:** Yeah, it's a great question. Part of the reason the higher dose is that older people don't mount as good of a response to the vaccine and if somebody's on a lot of immunosuppression they're not going to mount a response, so one could easily make an argument for getting the higher dose. I don't know that there are official guidelines on that, but it would make sense to have that discussion with your physician to see whether you should in fact get that, it would make sense.

**Becky:** Great. There have been a couple of questions about taking vitamin D or niacinamide as part of their treatment regime, and people are wondering why their doctors are recommending that. Do the treatments make them deficient in that?

**Dr. Werth:** With vitamin D, there is some thought that the immune system may not work quite optimally if you have a low vitamin D. That is certainly one of the things. Also, if one is on steroids, potentially it might be a little bit lower and we worry about bone. The niacinamide is really quite different and there was one study that was an open label study that suggested that when you combine niacinamide with doxycycline or tetracycline that it might be one way to control blistering diseases. But that doesn't really have much to do with infections or anything like that. It's really much more about trying to dampen the immune system without using a steroid or an immunosuppressant.

**Becky:** Great, thank you. Frank is asking, are there any supplements or vitamins that are advisable to take when you're taking Dapsone?

**Dr. Werth:** Dapsone, as you probably know, even if you have the enzyme that metabolizes it, everybody hemolyzes and gets a little bit anemic and that is a known side effect. For most people, it's not a big issue as long as your bloods are being followed, and you're on a dose that doesn't cause that to happen. There's really nothing that will prevent hemolysis. There was some thought that there might be one medication that may cut down, it's not a supplement, it's an actual medication on hemolysis but there's no supplements. It's not like you're iron deficient. The problem is that the cells that you have are breaking and then your bone marrow is good enough that it's making new red cells so that it kind of replaces most of the ones that are not doing as well. So there's not really a supplement that could be recommended for that.

**Becky:** Okay, thank you. There was also a question about the HPV vaccine from somebody in their 20's. Their doctor is recommending that they get the vaccine, but they're afraid that it can cause a flare, because that also is a disease with blisters. Is



there a reason for any cross-concern between our autoimmune blistering diseases and the HPV vaccine?

**Dr. Werth:** They're really different. Typically the warts are more verrucas and not so much blisters. It's a really different process. So I think it's a good idea to get that.

**Becky:** Okay. Thank you. How does IVIg affect vaccines? Are there any special considerations and timing in relation to getting IVIg treatments?

**Dr. Werth:** With IVIg, the way we think it works is that it helps clear existing autoantibodies. It really actually has nothing to do with antibody formation and that's a good thing because it's really not immunosuppressing. So people that have problems, maybe an underlying malignancy, and we don't want to give them medicine that suppresses their immune system, IVIg is actually relatively safe to give. So it doesn't interfere with the vaccine taking at all. You are getting immunoglobulin so it's actually not a problem, you're actually getting lots and lots of immunoglobulin so if anything it probably helps with infections and it is not a problem with vaccines.

**Becky:** Great, so this is an interesting question to me. Do collagen supplements help to repair damage done by lesions to our skin?

**Dr. Werth:** Yeah, I don't think there's much evidence for that. Sometimes people are taking it for their bones as well, or for arthritis. I don't think there's much evidence in the skin that that can be helpful.

**Becky:** Okay, thank you. How quickly would somebody know if their vitamins or supplements are causing a flare, or that they are aggravating their immune system?

**Dr. Werth:** That's always a tough one. The only way I can even talk about this at all is because I have people that started it and then a short while later, they had a problem. But you know we don't know the other end of it, which is somebody could take it for a year and suddenly have more trouble. That's much harder to predict. I think it is just better to avoid them if you have a personal or family history. You don't need these supplements. They're not helping, and they really can only hurt.

**Becky:** How long do they take to leave your body? I know medicines have different times that it takes to get out of your system. Is there any research on supplements and vitamins? I think by and large, they're water soluble and they kind of don't last forever. But the problem is that the effects on the immune system can last longer. It's almost like

it's a trigger and then the disease takes on a life of its own after that and it's not because the medicine is still there, it's just a trigger. We see that in other autoimmune diseases, where there might be a medication exposure, and you start the process and then you've got to take other medications to get it back under control.

**Becky:** Thank you. There have been questions, you had talked about taking pills and drinking the supplements and taking them systemically. Is there any problem with using a topical use of a Spironolactone?

**Dr. Werth:** Yeah, I showed the creams that I didn't even know existed until people told me about it. The only analogy I can make is that there are some topical antivirals that, in people who have autoimmune problems when they put them on their skin they can actually trigger the autoimmune disease in the skin. I don't think that we know much about these others, for instance spirulina cream. Would that do something? I have no idea. I do know that when you have other receptors that have been stimulated by antivirals that are cream, we've seen problems. But I have only recently become aware of this cream. I don't know how long it's been out there. I think it is going to take a while to know about the safety.

**Becky:** Nancy is asking if any of your other patients had lichen planus? And what is your opinion with fresh, whole vegetables, or anything to add with fresh foods?

**Dr. Werth:** Yeah, the lichen planus question is a really good one. I think there's a feeling that it's happening more. I don't know if there's any systematic studies looking at that in the same way that we've done it with the autoimmune problems but it's possible that some of these immunostimulatory herbs are causing problems we just haven't identified that yet. I mentioned that alfalfa can be a problem. I think with smoothies, when people make their own or eat regular vegetables that's not the problem. The problem is when you throw in the powders and the extra things that could stimulate the immune system then that's a problem.

**Becky:** Is there any test that can be done to see if a vaccine has caused their blistering disease? Is it more a cause and effect or is there any definitive way to figure out if a vaccine has caused your immune system to go haywire?

**Dr. Werth:** That's a great question. I don't think it really is. I think it's again, the only reason why I can talk about this at all is because I just saw, like 400 people get vaccinated at once so I could see what happened. And most people were fine and a few

people were not fine. I don't think you can prove it. Before this vaccine, people were getting autoimmune diseases. And in fact, when I started talking about this early on, people told me, well people are going to just get these diseases anyway and this is just what is normal. I think it is really hard to know the cause and effect for a particular person.

**Becky:** Great, thank you. This is an interesting one to me as a high-stress person. Is there any research showing that taking supplements for stress hormones can be effective in helping to control pemphigus or pemphigoid?

**Dr. Werth:** Well, I'd have to know more details about what those supplements might be. What I would say is that controlling stress is really important. I think that's part of the exacerbations for people and stress makes things worse. But I don't know that I can point to an herb that would not be immunostimulatory and would work in that way. But it's really important to address stress.

**Becky:** Great, thank you. Judy is asking if there's anything that can help with the itching as far as supplements or vitamins?

**Dr. Werth:** I think it depends on the cause of itch to some extent. It's not all the same but often treating the underlying disease will get rid of the itch. If somebody has bullous pemphigoid and they are itchy, getting medicine that will help that will make the itch better. You can also take antihistamine that can help with at least sleeping, if not the itch itself. They're topical antipruritics such as Sarna lotion which has menthol that can be used and also topical steroids can help with itch. That's where your doctor can help you with that, I think.

**Becky:** And are there any vaccines that are contraindicated for anybody with pemphigus or pemphigoid? We've gotten some questions about DTap, RSV shots, the herpes zoster vaccine, as well as chicken pox. People are worried that they would cause a flare. So is there anything that we shouldn't take, or that we should be a little leery, or think twice or or truly take a deep dive in before getting?

**Dr. Werth:** I think, by and large, with these vaccines if there are problems, they're very rare. And I think that it is not enough of an issue to avoid getting the vaccines to keep you healthy.

**Becky:** Okay. Well this has been very educational Dr. Werth. And we really appreciate your time and for answering so many questions for us. I know a lot of our questions are

hard because we're just searching for answers and a lot of answers just aren't there. The research isn't showing out there. So we really appreciate you taking the time and sharing what you do now with us.

**Dr. Werth:** Thanks for all the great questions and the opportunity to speak about these things.

**Becky:** Great. So before I go I do have a few announcements. We have a very exciting announcement, this year's Virtual Patient Education Conference will be held virtually from October 27th- 29th! We have invited leading bullous disease experts to present on research and trends, educate on disease management, and answer your tough questions. We hope you will join us for this exciting event! Registration will be opening soon.

**Becky:** Do you wish there was a better understanding of our diseases by doctors and researchers? Do you wish there were more FDA-approved treatments and better treatments available? Well here's your chance to get involved and make these goals a reality - Join the IPPF Natural History Study today! The Natural History Study is a patient registry sponsored by the National Organization for Rare Disorders (NORD) and the US Food and Drug Administration (FDA). Your information is private, the IPPF Natural History Study follows strict government guidelines to assure patient information is protected. Your participation and the data will be used by the IPPF to help advance research, better understand the patient journey, find better treatments, and hopefully one day a cure. By sharing your journey and answering some questions, you directly have an effect on the future of all people affected by pemphigus and pemphigoid. So get involved today! Visit [www.pemphigus.iamrare.org](http://www.pemphigus.iamrare.org) and join today.

**Becky:** It's your turn to pay it forward to other patients just like you in our community by becoming a Healing Hero. Our Healing Heroes make much-needed monthly donations to allow us to provide free programs and services like today's webinar and our Peer Coaches. With your monthly donation of only \$15, you help the IPPF screen and add new doctors to our Find a Doctor map which increases patients' access to care. Or a \$30 contribution allows our Peer Coaches to support you and other members of our community by providing resources and tips on how to live and thrive with their disease. Scan the QR code or visit [www.pemphigus.org/hero](http://www.pemphigus.org/hero) to become a Healing Hero. The IPPF has a number of upcoming virtual support groups across the country. If you are interested in attending a meeting, please check the IPPF's Event Page to register for a meeting. Also, we are always looking to expand our support network. If you are interested in starting a support group in your region please contact Becky Strong at [becky@pemphigus.org](mailto:becky@pemphigus.org). It's easier than it sounds to start a support group and you can help connect others in your area with other patients. This call recording will be sent out with the survey following this call. Thank you all for joining us.

