

Becky: Welcome everyone! This call is now being recorded. I would like to thank you for being on the call this evening. **Our Speaker today is Dr. M. Ron Feldman, Director of the Autoimmune Blistering Disease Clinic and Assistant Professor at Emory University.** Thank you for joining us today! The call today will focus on **Prednisone and its side effects and Dr. Feldman will be answering any questions you have.**

Dr. Ron Feldman earned an MD, PhD from the Medical University of South Carolina and completed his dermatology residency at the Cleveland Clinic. He then completed an autoimmune blistering disease fellowship at the Center for Blistering Diseases. Dr. Feldman is currently a Assistant Professor in the Department of Dermatology at Emory University. He now directs the Emory Autoimmune Blistering Disease Clinic where they strive to better understand and develop novel therapeutics for these devastating diseases.

Now, it is my pleasure to introduce **Dr. Feldman** to discuss a bit about **Prednisone and the side effects it has** and to answer your questions.

Dr. Feldman: Thank you so much and for inviting me to this call. As a disclaimer, I will provide broad explanation of Prednisone. Anything specific to your case, you should always fall back on the dermatologist who is treating your condition. Just in general systemic steroids such as prednisone, they were developed back in the 1950's believe it or not. They are a synthetic compound that mimic naturally produced steroid hormone called cortisol. All of us have cortisol that's being produced by our adrenal glands and the different types of synthetic steroids include dexamethasone, prednisone, and hydrocortisone. Each one of these steroids has different levels of hormone suppression in our bodies and they are used in various scenarios with these diseases. Prior to steroids, there really were no effective therapies for people with pemphigus and pemphigoid. Many patients ran into many problems and the rates of mortality were really high before the 1950's. The good news is that once the steroids came on board we were able to use high doses to induce clinical remission. The problem is that this came at a high price because steroids had a significant side effects including some of those that many of you are probably experiencing- weight gain, high blood pressure, diabetes, severe cramping, glaucoma, cataracts, stomach ulcers, and so on and so forth. In addition, as you wean down on the steroid it's not uncommon that you can suffer from severe fatigue, low blood pressure and a lot of joint pain issues. I'm hoping to answer some of these questions obviously related to many of these aspects of steroids, especially prednisone is probably the most common ones used to treat pemphigus and pemphigoid. We'll start with some of the questions.

Becky: The first question is from Martin, he says he was diagnosed with PV 3 months ago and he's been taking some prednisone. He said that in the last month he's been getting some hand cramps and muscle spasms about 2 to 6 times or more a day, it's more of a frustration and inconvenience. In the information provided in the medication it makes no mention of this side

effect but he find when he googles in that many people have the same issue. She he be concerned about this or just accept it?

Dr. Feldman: That's a very good question and a common complaint. Yes, cramps and muscle spasms are a common side effect of prednisone especially at higher doses. I would encourage you to talk to either your dermatologist or your primary care doctor to get options to help treat it especially if it's becoming more bothersome. If it's just a as you mentioned, sort of a nuisance, and it should get better as you wean down. It's a very common side-effect of prednisone.

Becky: Diana says she was on 40mg of prednisone for a month and then dropped to 30mg and then began to taper by 2mg and then getting to 8 mg and started to drop to 1mg. After dropping to 4 mg of prednisone she says that she was wrecked with insomnia and anxiety, mood swings and fatigue for a week. So she went back up to 5mg a day and planned to drop to a lower amount about a half. Is there anything that you can do to help your system begin producing the cortisol again as the taper doses get lower and lower to combat the side effects?

Dr. Feldman: Good question, and really there's not much that you can do than allow your body more time to start producing it. So, your body naturally produced about 5 mg to 7.5 mg or cortisol daily. Roughly the same dose of prednisone we use. As you mentioned, it's not uncommon as you mentioned when you dropped down to a lower dose. Below that physiological level you feel really tired and fatigue until your adrenal glands start kicking in and producing its own cortisol. There's really nothing else you can do unlike you said you went back up a little, you should start feeling better. You do need to go a little slower on your taper. It does seem that patients, the younger you are the better you are able to kick start the adrenals. In my experience the elderly patients tend to take a bit longer and we tend to have to go longer and slower tapers to get them back to their normal level and feeling better.

Becky: Along the same lines, Lisa is asking and saying that she's having some long term side effects of fatigue. Is there anything that can be done to help with that?

Dr. Feldman: Nothing really, unfortunately. Other than if the fatigue is coming from the change in prednisone, I think you have to sort of reevaluate how your taper is and again potentially go a little slower until you start feeling better. If you can exercise, exercise does tend to help with some of these issues. I would also speak to your dermatologist and primary care doctor. Other things- a good night's rest, assuming you're not having insomnia from prednisone will help, reducing stress in your life in general. Ways to reduce stress however you can do that and like I said, exercise tends to help too. A lot of it is just time. It takes a little bit of time till your adrenal glands come back on board as you wean down on the prednisone.

Becky: The next two questions are kind of related, Kevin and John sound like they are having similar symptoms. What are some cognitive side effects of prednisone and how long can they potentially last? John says that he was on 80 mg of prednisone and recently lowered the dose to about 10 mg and he's having a hard time remembering things like words that he should know,

he forgets appointments and if he's interrupted in any way he forgets what he's doing. He also finds it hard to focus his attention, organize information and plan things like he use to do and never had this problem before prednisone. Is this a common thing that happens with prednisone and are there any treatments and should it be mentioned to the primary care doctor as well?

Dr. Feldman: Very very common. Especially higher doses of steroids especially prednisone. Although it really is individual dependant. Some people at higher doses tend to function actually better. They can somehow be more focused and can concentrate. I have a lot of patients who give me a hard time who don't want to go down on their steroid because they seem to get a lot more work done, require less sleep and so on and so forth. Other patients and like this patient it sounds like it's unfortunately the opposite. They have a harder time focusing, they're feeling confused, sometimes difficulty organizing information. I think that probably the more common scenario is that people tend to not feel well. They just don't feel normal they're not functioning, their thinking is kind of clouded. You should always talk to your primary care doctor if there is something else going on that should be explored as well. But it's not uncommon at higher doses of some of these steroids to have some of these side effects that he's mentioning.

Becky: Great, after tapering to a lower dose of prednisone or getting off of prednisone completely, how long should it take to get your "normal" energy back or back to your own self?

Dr. Feldman: There really is not exact time frame, it varies again by individuals. I would say like I mentioned before that the younger patients tend to get it back a little faster than my older patients. In general when you wean down to lower doses and eventually off, you should start feeling better over time. It varies by individual but you should get back to normal energy levels.

Becky: Great, thank you. Evelyn wants to know, "Are nosebleeds common with prednisone?" She is also experiencing some hair loss. Is there anything that you can recommend, like any supplements or anything that can help with either of those conditions?

Dr. Feldman: Nosebleeds, not so common in my experience with prednisone necessarily. Hair loss can be an issue. Again either as you start prednisone at the higher doses or as you transition rapidly to the lower doses. Fluctuations in the steroid doses can definitely have implications in hair growth and hair loss. I would again speak to your physician about that. Options, there are vitamins such as biotin. Topic options such as Rogaine to restore or enhance growth but I would speak to your dermatologist about that in terms of other specific options they may prefer. But it is not uncommon to see hair loss. Nosebleeds I am not so sure, perhaps it is related to your underlying blistering condition more so than the prednisone.

Becky: Great. For the next question, this patient has had bullous pemphigoid for a few years and they took 4 milligrams of prednisone with Methotrexate. Recently her body has had more pain and sometimes they can't use their arms. Could prednisone be contributing to this?

Dr. Feldman: Well I don't know. Sometimes when you wean down on the prednisone or methylprednisolone in this case, you can have some issues with joint pain that is not uncommon particularly in our elderly patients. So prednisone is also anti-inflammatory so if you had joint pains as you get older the prednisone will sort of mask those joint pains. And then of course as you wean down as you tell patients, you went from the joints of a 30 year old to the joints now of your current age. It is not uncommon to have severe joint ache especially in feet. I find anecdotally a lot of patients complain that their feet are very sore when they are walking. That tends to get better with time and exercise but how long that takes it varies on the individual patient. In terms of not being able to use arms or walking, I am not sure if that is the case here. There may be something else going on. Sometimes for my elderly patients I may have to go back on a baby dose of prednisone if the joint pains are very severe but I would talk to your dermatologist and primary care doctor to confirm. I am not sure I can explain everything the way it is described here with just prednisone.

Becky: Sure. And I think you kind of answered our next question which comes from Pat. His brother has been on prednisone and has developed a progressive peripheral neuropathy and has even developed a foot drop and they are concerned that he will lose the ability to walk. The question was if this was prednisone related and you said just previously that there can be pain but this doesn't sound like this would necessarily be prednisone related correct?

Dr. Feldman: Not a common symptom necessarily with prednisone usage, neuropathy. But with long term usage of steroids you can develop steroid induced diabetes and of course diabetes can be associated with peripheral neuropathy. I am not sure how that can explain this case. But not a common symptom with prednisone.

Becky: Okay. Dalia asks, "How long can somebody use prednisone and is there a dose that is considered "safe" to be used long term?"

Dr. Feldman: Good question. How long, there really is no time frame. I have some patients that have been on prednisone for over 20 years. For whatever reason they are not able to completely taper off so we tend to keep some of these patients on low dose steroids. What does low dose mean? It tends to mean the dose of the physiological levels which I mentioned earlier, so somewhere between 5 or 7.5 or lower. I wouldn't say that it is considered "safe" but it is considered an acceptable dose in terms of the risk-benefit ratio that we would use. In other words the benefits of the low dose steroids outweighs the potential risk of even a low dose steroid. So I wouldn't necessarily use the word safe but acceptable doses that we use for long terms. And like I said I have had patients on it for many years.

Becky: Great, that it comforting for a lot of us so thank you. Kathryn asks, "How effective has treatment with prednisone proven in patients who have had a recurrence of bullous pemphigoid? And does the dosage seem to need increasing, or is a lower dosage as when it is not the first time it has been used?"

Dr. Feldman: In terms of efficacy I can't give you an exact percentage but it is completely reasonable that yes prednisone can be used in patients in which their pemphigoid has relapsed or recurred and really the doses are going to depend on the severity of the relapse and the comfort level of the treating dermatologist. If you are asking in terms of evidence based therapies for bullous pemphigoid long term or for maintenance therapy and for relapse we really don't have that data. So we rely a lot of individual experience, anecdotal experience but it is completely reasonable yes, to go back on the prednisone if the relapse is severe enough to require it, in my opinion.

Becky: Okay, is there any thoughts even after a patient has gone for a period of time when they haven't had any lesions from pemphigus or pemphigoid, is there any thought of staying on that low dose even when everything has been cleared?

Dr. Feldman: Sort of using prednisone as a maintenance therapy?

Becky: Yes.

Dr. Feldman: I think some dermatologists do that. We always have to decide when is the appropriate time to completely wean people off steroids. Sometimes it is not an easy decision to make but if the patient as you mentioned is totally clear and if we are able to use some of the blood tests to look for the levels of pemphigus or pemphigoid, and if those seem very low then we usually have an in-depth discussion with the patients to suggest that they could wean off completely. Some patients are okay with that and some patients are really nervous that the disease may come back so we may leave them on a lower dose for an extended period of time. There really is no evidence necessarily, good evidence to guide us in that scenario. So that is a conversation that needs to be held between the treating dermatologist and the patient to make sure that both of them are comfortable either keeping on a low dose, that it is doing something, or completely weaning off and it is not necessary anymore. Hope that answers your question.

Becky: Yeah it does. Rosa says that her brother is 40 years old and was diagnosed with pemphigus about 5 months ago. He is currently taking prednisone on an alternating schedule so on day one he will take 5 milligrams, then day two 10 milligrams, then back and forth like that. He has also had Rituxan in the spring and his current side effects that he is experiencing is excessive sweating and he has never had this problem before. Is this probably related to the prednisone or could it be related to something else?

Dr. Feldman: I am not sure actually. Not a common side effect mentioned with prednisone. It may very well be but I am not aware of it necessarily in at least my patients that I have treated. No one has really mentioned any excessive sweating. I could be related to the changing in doses of the prednisone but I would discuss with the treating dermatologist if there is something else going on because I am not sure.

Becky: Okay, and I think you kind of eluded to this question before but you kind of explained how some people get more acute and astute and other people become extremely fatigued and sluggish feeling and you mentioned age in relation to that. Are there any other indications or any other thing that might be able to predict how a patient could react to prednisone?

Dr. Feldman: No, I wish there was. There really is not. Sometimes a patient have other comorbidities which means they have other psychological issues or underlying propensities to have issues related to thinking or otherwise mental reasoning, they could definitely have problems with that. But assuming the patient is otherwise thinking clearly and are focused, we have no way to predict. Everybody is a little bit different. I wish we had a way to predict what was going to happen.

Becky: Great. That would be easier on us patients too so we knew too. So Vynette is asking why is it that when she goes on prednisone her stools become green? She has mentioned it to her general doctor and they told her that other patients have told him the same thing but he has no explanation for it.

Dr. Feldman: I don't either. I don't know how to explain that one. It is not in my experience that I have heard that before. Great question but I do not have an answer for.

Becky: Great, thank you for being honest with us. Laurette says, "How does you dose of prednisone affect any dental surgery procedures? Is this something that should be considered when having dental surgery?"

Dr. Feldman: I think that is a good question in relation to any surgeries, what do you do about the steroid? It is really up to the discretion of the treating dermatologist. I will say that sometimes when it is a major surgery the dermatologist should consult the surgeon and they can decide if some patients will need "stress doses" of steroids. Sometimes particularly in elderly patients, they may need higher doses of steroids in order to handle the major surgery more than a younger patient may need. But those are discussion that have to be held between the dermatologist and the surgeon. For minor surgical procedures, my experience I usually do not necessarily adjust the steroid dosage per say especially if they are on lower doses. If the patients are on higher doses sometimes I will find, as you had mentioned earlier the dentist, the dentist might not be comfortable with the higher doses of prednisone and may want to wait for the procedure until the patient is on a lower dose but that really is up to the comfort level of and to the discretion of the treating physician's to make that choice.

Becky: Great thank you. Our next question comes from Carol and she wants to know, "How long should prednisone take to work and how long should she wait to contact her doctor before requesting that her dose be adjusted?"

Dr. Feldman: So that is a good question and that sort of gets to the point of why do we still use prednisone in this day and age? The thing about prednisone which is why we go to it relatively

quickly is because it works very fast. So, prednisone is one of the few medications we use for these diseases and other autoimmune diseases in general because we know it works, it's efficacious, and we know that it works fast. It is anti-inflammatory, works very quickly and it slows down the production of the antibodies that are attacking your skin in pemphigus and pemphigoid. There really is no other medicine that works that fast, unfortunately not yet anyways. So we still utilize prednisone to gain rapid control of the disease and to try and start induce clinical remission and then sort of taper it with the addition of steroid-sparing medicines. That's sort of the strategy that is still the case today, until we find better drugs prednisone still works the fastest. So, in other words it should work very quickly. Within a few days thing should start to improving in most patients, not everybody but in most patients. And then assuming you get control of the disease you can start tapering and or adding other medicine called a steroid-sparing medicine. There are many different options now a day for steroid-sparing including with the recent FDA approval of Rituximab for pemphigus. So that is the most common scenario and the main reason that we still utilize prednisone.

Becky: Great, thank you. Our next question comes from Linda who asks, "What vitamins or supplements are recommended when using prednisone?"

Dr. Feldman: That really depends on the discretion of the treating physician. Most common one I would say usually most of us would use so one of the common side effects of prednisone, at least long term, prednisone at higher doses can bone thinning or osteopenia or osteoporosis. So I tend to recommend vitamins as far as calcium and vitamin D to help counteract that issue. As far as other vitamins, it is really up to the patient and the treating dermatologist to decide based on the individual needs but in general to sort of head off some of the potential steroid side effects, for vitamins I would recommend calcium and vitamin D supplements.

Becky: Great, thank you. Because you sort of mentioned this, Natalie is asking what is the long-term use of prednisone have on bone density and is a bone density scan recommended after long-term use and how often?

Dr. Feldman: We tend to recommend that patients that are going to be on steroid usage of over three months, typically above 5 milligrams it is not unreasonable to recommend getting a bone density scan or a yearly bone density scan if the patient is maintained on a higher dose for a longer period of time. The way that we think that prednisone effects bones is that you typically have a balance of bone growth and bone resorption. It seems that prednisone pushes the bone resorption higher and it lowers the bone producing ability so in other words you get a turn over of bone too quickly which is why we think that patients develop osteoporosis. So in general the recommendations would be to start supplementation of calcium and vitamin D and or at the discretion of the treating physician patients who are going to be on long-term steroids and if the bone density scan suggests that there is osteopenia or osteoporosis that additional medications may be necessary to prevent bone loss.

Becky: Great, What side effects would a patient experience that would warrant a call to the dermatologist?

Dr. Feldman: Side effects could be many. Anything that is obviously life threatening I think should be a call to the EMS and the emergency room. In terms of specific side effects it's hard to say, it is really individual dependant. I think you mentioned earlier that cramping is one of the common side effects that patients can experience. Sometimes headaches patients can experience. If there is change in blood pressure the patient should really take that up with the dermatologist and primary care doctor. It is important to also follow blood sugar because on higher doses of prednisone blood sugars can go up and if patients already have underlying diseases such as diabetes it is important to monitor blood sugars. Hopefully most dermatologists are checking blood work along the way as well and any kind of abnormalities in the blood work, that should be followed up. Otherwise those are the common ones I would say to call about. If the patients are feeling weak or dizzy they should contact either their dermatologist or their primary care doctor. Typically those things would be related to blood pressure issues which can be affected by prednisone usage. Those are the most common ones that come to mind anyways that I think it is important to be aware of to contact your dermatologist.

Becky: Great, thank you. Anna is asking if it is okay to have the new shingles vaccine, the Shingrix vaccine, while taking 40 milligrams of prednisone?

Dr. Feldman: That's a great question. As of today, the guidelines may be changing soon, we tend to not recommend getting live vaccines when patients are on immunosuppressive therapies. Typically the prednisone doses would be 20 milligrams and above so in her case I would say wait until she drops down below 20 milligrams and after having discussions with her dermatologist and primary care doctors. But we tend to not recommend live vaccines and that would be the shingles vaccine in particular. Some patients are getting the booster of the pertussis in some cases, we would wait. Or the MMR booster, the would be the measles, mumps, and rubella patients are having boosters for those and we don't recommend those as well. The attenuated vaccines or "killed" vaccines such as the flu vaccine we think is acceptable to get while you are on steroid usage as well as the pneumonia vaccine especially in patients that are typically 65 and older. So those would be okay but the live vaccines if you are on higher doses of steroids we tend not to recommend but again I would have the discussion with your dermatologist and primary care doctor, it really depends on the individual situation. But in general, the general guideline those are the rules we adhere to until the further guidelines are released in the next few years for the way we typically handle these scenarios.

Becky: Great, thank you. Is there are standard dose of prednisone to decrease the amount that I am currently taking? Is there a number of milligrams that is too much or too little to drop my dose by?

Dr. Feldman: That is really individual dependent. How the dermatologist decides how to drop the dose, taper as we say, many dermatologists will taper by a certain number based usually weekly if you will, say by 5 or 10 milligrams per week. Some dermatologists prefer to taper by every other day dosing, in other words you would take for example 10 milligrams one day and the next day you would take either 5 or zero, then 10 milligrams the following day. There are really many different ways to taper prednisone it really is individual dependent and a discussion between the dermatologist and the patient. So there is no magic numbers in other words.

Becky: Okay, Is prednisone safe to use in pregnant woman?

Dr. Feldman: Yes it is safe to use. Obviously we prefer the lower dose the better to use in pregnancy because it does not cross the placenta easily so that is a medication that is commonly used in pregnancy in patients that have pemphigus or pemphigoid. Again this needs to be a discussion between the OB as well as the dermatologist but it is technically safe to use.

Becky: Great, thank you. As a side note to that, one thing that I did when I was coming down on my prednisone and was really interested in starting my family was to find a high-risk OB or a fetal medicine doctor who was familiar with autoimmune disease and they are very familiar with a lot of the medications used in many autoimmune diseases can be used in pemphigus and pemphigoid and those doctors are familiar with that and they can provide a wealth of information. So that is just a side note from me, from my personal story too.

Dr. Feldman: Yes, I agree. It is always helpful to speak to your OB and if they have a colleague that handles more high-risk cases it is completely reasonable to try and go that route for sure, if it is available in your community.

Becky: Absolutely. Dale from Dallas is asking, "How can diet be adjusted to help ease the side effects of prednisone?"

Dr. Feldman: Good question, for those of you taking high dose steroids it is very common that you are going to raid your refrigerator. For some reason prednisone makes you crave sweets especially, so I always have to try and counsel patients on the higher doses you really want to try and throw away all those sweets from your house. So ice cream and cookies. You want to try and at least maintain a lower carbohydrate intake if possible, more lean meats, high protein sources, fruits and vegetables especially on the high doses of steroids because they will make you crave sweets. And you also tend to gain weight because you hold water. It makes you retain fluids. So retaining fluids and eating a lot more than you would normally eat, patients tend to gain a lot of weight on higher doses of prednisone. So that is an important component of treating patients with prednisone. If we are going to use higher doses we have to counsel patients that diet is really important so you really have to be careful with your intake of carbohydrates, you know breads pastas and sweets. You want to try and limit them because it tends to make you gain more weight. And then of course urging regular exercise tends to help keep that weight off, if you can if you are not too fatigued. So those two things would help a lot.

As far as other dietary issues related to prednisone it is really individual dependent, I would have the discussion with the dermatologist or primary care doctor with questions about specific foods should you avoid or not with prednisone. Those are sort of general guidelines though about definitely about the carbohydrates at higher doses of steroids.

Becky: Well great, thank you.

Dr. Feldman: I hope that answered your questions about diet.

Becky: Yeah, I think you did well there. Topical steroids are said to thin the skin, but what does taking it systemically do? Does it have any effect of my skin or my internal organs?

Dr. Feldman: That is a very broad question, yes it can have effects on the skin. Again higher doses and longer treatment periods, oral steroids can result in the same side effects. Skin thinning, easy bruising, increased blood vessels if you will we call it telangiectasias is very common. Patients can develop steroid acne or rosacea, the flushing of the face and or acne-like bumps on the face not uncommon with high doses of steroids for longer periods of time. Internal organs really can be sort of a difficult question not necessarily direct issues with internal organs but obviously indirect effects can be related to side effects of prednisone. So we talked about the adrenal suppression that can cause issues with not producing enough cortisol. Obviously if patients develop high blood pressure and or diabetes those can have direct effects on various internal organs especially the kidneys. Blood pressure can also affect the heart, obviously the function of the heart. But those tend to be indirect effects potentially of prednisone, as far as direct effects on the internal organs it really varies by the scenario. I would say that I would be more concerned about the indirect effects from the side effects of prednisone. And as far as the skin those are the most common ones we experience.

Becky: Great, thank you. I have heard that I should tell my surgeon after I stopped taking prednisone that I was on it. How long is that window of when I should tell my providers before I have a procedure?

Dr. Feldman: There is no set time frame. I would say that if you are off prednisone then I think you are probably going to be in most cases okay. If the time frame is very short, the surgeon may be worried about wound healing. So it is true that prednisone can potentially, higher doses, can potentially affect wound healing. But if you have been off for a period of weeks to months I think it is okay. I am not sure the surgeon would have any issues unless they were worried about your specific surgery in general. But typically if you have been completely off prednisone for periods of weeks to months I think mostly likely it will not be an issue.

Becky: Okay, great. What is the best time of day to take my prednisone? And can splitting it into two different doses help me with some of the shakiness and the inability to concentrate?

Dr. Feldman: Typically we recommend taking prednisone in the morning because it will help with the issue of insomnia so your normal doses of cortisol tend to increase early in the morning so we try to sort of mimic that with giving oral prednisone. So most scenarios you will take prednisone in the morning with breakfast. You can split the prednisone dosing up it really depends on the individual scenario. When you split it up it tends to be more immune suppressing in general. Typically we don't do twice daily dosing unless we need a good or very strong immune suppressing effect especially at higher doses. So you can potentially split it but you may run into issues with having trouble sleeping if you take a nightly dose. So I am not sure that is going to have an effect on reducing the shakiness or concentration other than lower the total dose of the prednisone in general. By splitting it you may run into other side effects which may be an issue. So most of us use prednisone in the morning, a daily dose in the morning.

Becky: Great, thank you. The next question has to do with Rituximab and prednisone. The question is, "What is the dose of prednisone generally given with Rituxan and can Rituxan be given without the prednisone?"

Dr. Felman: Good question, in terms of evidence-based medicine the clinical trial, the phase three trial that was published for which the FDA approved Rituximab the patients were on prednisone along with the Rituximab. But the dose varies by individual patients there is no set number we look for as far as the prednisone. It really depends on the severity for in that case pemphigus or patients who have pemphigoid who get Rituximab. It really depends on the severity of their disease and at the discretion of the treating dermatologist in terms of what dose they would consider appropriate. There is no specific dose we look for with Rituximab. And yes you can have Rituximab treatment without prednisone. That is also done in patients who cannot tolerate steroids. So for example patients who may have severe diabetes or patients who have severe glaucoma or patients who have severe osteoporosis. Many of these patients can't tolerate steroids especially higher doses of steroids. So sometimes we do treat these patients with Rituximab therapy alone. Anecdotally there is some evidence that perhaps they work together, prednisone along with Rituximab, what we call a synergy seem to help patients get better faster. But we don't have more evidence than that phase three trial that's been published in terms of large numbers of patients. So really it is up to the discretion of the treating physician what dose of steroids they want to use and whether they want to use steroids with Rituxan.

Becky: Great, thank you. Our next question asks, "My skin seems to have reacted more quickly with prednisone than the mouth ulcers. Is this normal or why does this happen?"

Dr. Feldman: It is not abnormal it really varies by patient. Some patients the skin disease will get better before the mouth disease does some patients vice versa. It really depends on the patient.

Becky: Okay, great. A patient says that they had a brain MRI that shows white matter and hypersensitivity suggesting microvascular changes. Could prednisone cause these microvascular changes?

Dr. Feldman: That I don't know. I would ask the question to a neurologist and or a radiologist. I don't know I would say just off the cuff I don't think that it is necessarily directly related to prednisone. It could be related to changes of aging or other issues but I would clarify that with your physician and your neurologist or neuroradiologist.

Becky: Great, thank you. This patient says that they have read that there is a risk of having prednisone induced psychosis in the literature that has accompanied her paperwork. How common is a prednisone induced psychosis? And what kind of treatment is necessary for this?

Dr. Feldman: Thank goodness not very common it tends to happen in patients who are elderly and patients on very high doses of steroids that rapid administration of high dose steroid that induce some changes in the patient's thinking and result in psychosis, that is patient's mental status changing dramatically sometimes requiring hospitalization. Not very common and I don't have an exact number in our patient populations but very rare thank goodness.

Becky: Great, thank you. Michael asks, "Once prednisone has been significantly lowered, is there a real concern for PNP to come back?"

Dr. Feldman: PNP, so I would assume that is paraneoplastic pemphigus?

Becky: I believe so.

Dr. Feldman: I don't know about a concern for it, it really depends on the scenario obviously. As you wean down on prednisone and I am not sure if Michael is on other therapies at the same time. If he is just on prednisone therapy, what we call monotherapy, yes assuming that as you lower down if you start developing new lesions or some of your biomarkers suggest that there is more activity, than yes we worry about the disease coming back but like I said it really is up to the treating dermatologist. They should be following these things very carefully in close concert with the patient's clinical symptoms, blood tests and will need to make a decision whether or not the patient is ready to wean off prednisone completely. But PNP, yes can be very difficult and a recalcitrant disease to treat and yes it can tend to either not respond to or as quickly or come back potentially as you wean down. It may require other therapies besides just prednisone. I assume that is what the patient is asking.

Becky: I believe so, yes, thank you. Nancy says that she was diagnosed with PV several months ago and was started on 40 milligrams of prednisone for about 3 ½ weeks, tapered down to 20 milligrams for several days then switched to extended release doxycycline and it seems to be keeping things under control but if at some point another short-term treatment of prednisone is needed, are there any cumulative effects of short-term treatments of prednisone?

Dr. Feldman: It really depends on how short-term and what the doses are but in general, the doses that you mentioned were 20 and below for short periods of time are not an issue assuming the patient is healthy otherwise or doesn't have other comorbidities, that is other

disease that influence the way they tolerate the steroids. Whether they have issue with their GI tract, whether they have as I mentioned earlier diabetes, osteoporosis, eye issues, blood pressure issues, cardiac issues. So assuming those aren't the case with her, it is not unreasonable that she can tolerate doses of steroids. It really depends on what the final outcome that her dermatologist wants to achieve and whether or not other medicines may be just as effective to try and avoid the prednisone. So that is a conversation I would have between you and your dermatologist.

Becky: Great, thank you. A patient asks, "have you ever seen a recurrence of cataracts after corrective surgery to replace a lens with the use of prednisone?"

Dr. Feldman: No, not typically. It shouldn't, once the lens is replaced, it typically is replaced with a synthetic lens there should not be an issue as far as prednisone unless there was something else that we are not aware of. But once you have had cataract surgery those issues with prednisone tend to not be an issue anymore unless something else is going on.

Becky: Great, thank you. Erin says that she was on high doses of prednisone that caused her to have osteoporosis in her back. She is wondering as she weans down will her bones become stronger again?

Dr. Feldman: They can, you can get bone formation. I am not sure what she is on as far as treatment for her osteoporosis but I would encourage her to have repeat bone density scans each year to see if in fact she does get an increase in her bone density over time with the treatment that she is on. Yes, as you lower prednisone those side effects should improve you should have less bone resorption and in theory she should get some bone growth back. But that really depends on the medication she is on and if she has included exercise, weight-bearing exercises also tend to help prevent bone loss and or supplementation with calcium and vitamin D as I mentioned earlier. So assuming she is being treated for osteoporosis I would expect hopefully that as she does the yearly bone density scans it should at least stabilize, hopefully and or not get worse.

Becky: Is treatment for osteoporosis, is that compatible with taking prednisone at the same time?

Dr. Feldman: Yes, it is.

Becky: Perfect, thank you. There is another question, you have referred to younger patients from time to time, how do you define a younger patient?

Dr. Feldman: Good question, don't want to get in trouble here.

Becky: It kind of feels like I am setting you up.

Dr. Feldman: Exactly, on average the pemphigus patients their average age tends to be forties to fifties so me that would be younger. Here at Emory we see patients even as low as teenagers with pemphigus. So my younger would be I would say fifties age range and below and my older patients would be sixties and above. So you know the average age for bullous pemphigoid for example tends to be in the seventies. So don't have an exact cutoff but what I'm eluding to younger would sort of be my pemphigus group of patients or my younger pemphigoids fifties and below and then sixties and above tend to be older patients. Is sort of the way I would "soft" divide if you will. Hopefully I am not offending anybody.

Becky: No, that kind of helps. It helps in understanding the discussions. Lori is asking do you recommend potassium to counteract the impact of prednisone and its side effects?

Dr. Feldman: That's a great question. It kind of depends on the scenario if patients are already on patients called diuretics in which they may lose some of the potassium in general from the medications they are on. It may be appropriate to add in a daily dose of potassium, because yes she is right prednisone can result in a loss of potassium through issues with the kidney filtration. So yes, some patients you can start but really it is a discussion between the dermatologist if they are comfortable supplementing potassium and or the primary care doctor. Or the other option is as you start therapy as you repeat lab work you can follow the potassium level and if it drops you can always supplement. And of course I always recommend food supplementation and diet supplementation of potassium is important. So everyone can do this on prednisone you can eat foods rich in potassium assuming you don't have any other GI issues you could have problems as far as absorption. But foods that are rich in potassium tend to be yogurt believe it or not, sweet potatoes especially here down in the southeast and bananas are typically recommended by most physicians but don't necessarily have the highest levels of potassium. So I would encourage you to look at the nutrition serving on your foods and you can always start taking foods that are rich in potassium if you are on higher doses of prednisone. If the labs suggest that the potassium levels are dropping I would definitely have a discussion with your primary care doctor and dermatologist whether or not you need daily supplementation. I think in general most dermatologists don't start potassium right off the bat usually, but it really just depends on the individual patient and their other comorbidities they may have. So hopefully that answers her question.

Becky: Great, this next question goes back to insomnia and the patient is asking is there any way to cope with insomnia caused by prednisone other than taking sleeping pills?

Dr. Feldman: That is a good question, there really is not one magic pill that we give to help with insomnia. Like I said I would try and take the prednisone with breakfast, the earlier you take it the better tends to help. Try to be careful with taking caffeine sources later in the day this will hopefully help as well with the insomnia. Daily exercise and activity obviously helps with allowing you to relax at night or other stress relief mechanisms. But short of taking other therapies as you mentioned, pills to help with insomnia I don't really have any recommendations but I would talk to your treating physician to see if they have any magic tricks. But in general we

don't really have anything in other words in patients we start on prednisone I don't recommend anything unless they have brought to my attention that they are having issues with insomnia.

Becky: Great thank you. This next question is asked by a patient and she is wondering if there is any work being done studying the interaction of prednisone and perimenopause?

Dr. Feldman: Prednisone and perimenopause, I don't know about research from the dermatology side of things but I imagine there is from the endocrinology side of things. But yes, prednisone can have potential side effects in patients who are perimenopausal or menopausal and that can vary by patient. So in terms of, I have had patients complain of their cycles changing on higher doses of prednisone so the menstrual cycle may lengthen or shorten, patients may have heavier cycles or lighter cycles, or sometimes lose a cycle completely on higher doses of steroids. In perimenopausal in terms of other side effects such as hot flashes can be enhanced with prednisone. So higher doses of prednisone can result in worsening hot flashes, I have seen that a lot. So it makes that very difficult but we do the best we can in terms of minimizing that. Other changes in hormones, we don't tend to check them necessarily unless the primary care doctor is asking for them or if the endocrinologist is asking for specific hormone levels to monitor while on prednisone. We typically don't do that as a dermatologist. So those are the things that come to mind around perimenopausal that many women can suffer when they are on high dose steroids. So obviously the goal for us is to wean the prednisone down assuming the disease is getting better to try and minimize all of these side effects that you may experience.

Becky: Great, that was a quick hour and we are getting close to the end here but I think we have time for one more question. This patient says they were on prednisone and then had their immunofluorescence biopsy done and the immunofluorescence biopsy came back negative but the doctor still believes that they could have pemphigus. Is it common to be on prednisone and to have prednisone cause the biopsy to be negative?

Dr. Feldman: Yeah we call that a false negative it is very very common. I just had one actually, so yes this is something that is tricky especially at higher doses of prednisone. It can influence the lab testing, the biopsy testing as well as the blood tests testing for antibodies, they can be falsely negative. You may find sometimes as you wean down prednisone and you repeat the study they actually become positive. So yes I agree it does not rule out the disease if it is a negative on a high dose of steroids. It really is up to the dermatologist to sort that out in terms of whether or not to repeat testing as the prednisone is tapered or based on the clinical findings you may have to make what we call, a clinical diagnosis, in the absence of a positive biopsy or blood test. So yes, it is very common.

Becky: Okay, one last question. Are there any sort of calcium or vitamin D supplements you suggest considering there are a lot of controversy over calcium supplements causing colon polyps? And between bone density and the colon polyps is there one that we should consider more serious than the other as patients?

Dr. Feldman: There is not one calcium or vitamin D product that I would recommend in particular I would really discuss that with your dermatologist in terms of which ones they recommend. I agree, there are some studies coming out that suggest that sometimes with supplementation of the calcium in particular, you can have too much calcium possibly. But I think you have to weigh the risks and benefits of the calcium supplementation in the presence of prednisone which can influence bone loss. So I would have the discussion with your dermatologist. I don't have a particular product in mind in terms of recommending but we do in general guidelines say that we do recommend calcium and vitamin D supplementation due to the risk of bone loss with prednisone. As far as the colon polyps I don't really have an answer to that.

Becky: Well great, thank you so much Dr. Feldman. I feel like we just sort of pepper sprayed you with so many questions during this past hour. So thank you for being on the call with us today.

Dr. Feldman: Well thank you so much for having me.

Becky: I would like to give everyone on the call with us a big thank you for joining us. Before we go I just want to let everyone know that the IPPF has kick-off our third quarter fundraising. Funds raised this quarter are used to support Patient Services such as this call today. Other patient services include our Peer Health Coach Program and Local and Regional Support groups. Please consider visiting our website today to make a tax-free donation to support these valuable free programs and assistance the IPPF provides to pemphigus and pemphigoid patients.

As a reminder, the IPPF Annual Patient Meeting is right around the corner! The 2018 conference will take place in Raleigh-Durham, North Carolina from October 12-14th. Registration is now open! Visit our website at www.pemphigus.org to register for the conference. This is a great opportunity to meet others within the pemphigus and pemphigoid community and learn more from the world's leading experts about these diseases. We hope to see you there! This year we will also be having an extra field trip. With your conference registration we will be including a visit to the University of North Carolina Dental School for a day filled with learning and hands-on workshops for the patients.

Don't forget to register for the IPPF Natural History Study, a new patient registry sponsored by the National Organization for Rare Disorders (NORD) and the US Food and Drug Administration (FDA). Register today on the IPPF Website under the research tab. And a reminder the IPPF is still looking for Awareness Ambassadors to visit local dental offices. Please click on the Awareness Ambassador link for more information.

Lastly, If you have a question that didn't get answered on the call, or have additional questions please e-mail our Outreach Manager, Becky, at becky@pemphigus.org, or call me at (916) 922-1298 x:105, and I would be more than happy to help.

This call recording will be sent out with the survey following this call. Thank you all for being on the call today.

END CALL (1:02:54)