

Siegel Rare Neuroimmune Association 'Ask the Expert' Podcast Series
Vaccinations and rare neuroimmune disorders

The audio of this podcast is available at <https://youtu.be/20y9cwrSbF4>.

00:00 Hello everyone and welcome to the SRNA Ask the Expert podcast series. Today's podcast is entitled Vaccinations and rare neuroimmune disorders. My name is Erin Coriell and I will be co-moderating this podcast along with my colleague GG deFiebre. SRNA is a nonprofit focused on support education and research of rare neuroimmune disorders. You can learn more about us on our Web site at wearesrna.org. This podcast is made possible in part by the generous support of Alexion Pharmaceuticals Inc. Alexion Pharmaceuticals is a global biopharmaceutical company focused on serving patients with severe and rare neuro disorders through the innovation and development and commercialization of life transforming therapeutic products. Their goal to deliver medical breakthroughs were none currently exist. It is driven by the knowledge that people's lives depend on their work. This podcast is being recorded and will be made available on the SRNA website for download via iTunes. During the call if you have any additional questions you can send a message and chat option available within GoToWebinar

01:14 Thank you Erin. I'm GG deFiebre. For today's podcast we are pleased to be joined by Dr. Augusto Miravalle and Dr. Teri Schreiner. Dr. Miravalle is an associate professor of neurology, Associate Chair for education, and chief of the Multiple Sclerosis division at the University of Florida College of Medicine. He's sub specializes in multiple sclerosis and related neuro-immunological disorders of the brain and spinal cord. Dr. Miravalle has been involved in both clinical and basic science research. Before moving to the University of Florida, he served as the residency program director and vice chair of education, chair for the clinical competency Committee, for the residency program, and chair for the adult residency Education Committee for the Department of Neurology at the University of Colorado. Dr. Miravalle received his medical degree at the University of La Plata, Buenos Aires, Argentina. he completed his neurology residency training at Loyola University where he served as chief resident of education.

02:16 He subsequently completed a clinical neuro immunology fellowship at Harvard University. Dr. Miravalle was the recipient of the 2012 American Neurological Association Medical Education Fellowship Award.

02:32 Dr. Schreiner is a neuroimmunology specialist and pediatric neurologist at the University of Colorado and Children's Hospital Colorado. She sub-specializes in pediatric onset demyelinating disorders of the central nervous system and has begun a multi-disciplinary clinic for children with these disorders. Dr. Schreiner sees patients at both the Rocky Mountain MS Center at the Anschutz Pavilion of the University of Colorado and at Children's Hospital Colorado. Her areas of interest include immune mediated neurologic disease spinal cord syndromes including acute flaccid myelitis quality of life in pediatric patients with demyelinating disease biomarkers of multiple sclerosis and clinical trials she earned a master's degree in health policy and administration. Dr. Schreiner also worked in healthcare consulting for several years prior to her career in medicine. So, thank you both for joining us today and welcome to the podcast. We very much appreciate you joining us today.

03:27 Thank you. Great to be here.

03:31 Thank you. So to begin we did receive a lot of questions from the community and so we did kind of try to you know group them together and themes to be able to get to as many of them as possible and people can still submit questions via GoToWebinar as well. But to start Dr. Schreiner would you mind just giving us an overview of vaccinations and rare immune disorders. You know and if there's any theories that could explain in association you know if there is one yes absolutely. **04:01** Well first of all let me again thank you for including us in this discussion. I think this is an important discussion to have and something that comes up for me in clinic and talking with my patients and their family is quite frequently. So I'll start by talking a little bit about what vaccinations are and then extrapolate into how they work and why they are questioned to be a factor in the development of transverse myelitis and other neuro inflammatory disorders. So in any discussion of vaccinations I feel like we need to start with the benefits and the benefits are that vaccines have in some cases eradicated or near eradicated diseases that formerly caused mass death and illness and death. And so there has been a tremendous role for vaccines in in our history and really have contributed to much of the healthy living that we have today.

05:09 They work in various different mechanisms. And we have different groups that we put the vaccines in to. And the groups are constructed according to how they work. So for example we have live vaccines and we know like varicella, yellow fever, rotavirus are all in this category. We have another whole category of vaccines that are called live attenuated. They are they are vaccines in which the virus causing the disease that we're trying to prevent has been changed in a way that makes it no longer able to cause the disease that able to trick the immune system into thinking that it has seen that disease and therefore knows how to fight it. And then we have some other varieties that include conjugate vaccines which are combinations of proteins and different elements of either bacteria or viruses that we're trying to prevent them from causing infection.

06:16 So what each of these categories of vaccines do what vaccines do is prime our immune system make our immune system think that they have seen this invader before and they know how to fight it and our immune system is smart it has a long memory. It's it knows and can respond to an invasion of something that it has seen before very quickly. And the vaccines work by maximizing this introducing something into our body that triggers or immune system in a way that it believes it's fighting an invasion when in fact we're really just teaching it how to fight this particular virus. So, if we are exposed to that virus or bacteria in the future our immune system is like OK I've seen this before I know exactly how to fight this and therefore prevent illness.

07:23 So that is what vaccines do. The reason there has been such I guess inquiry and interest into exploring whether or not vaccines may be the cause of an immune mediated problem is that there is this thing called Molecular mimicry. What that means is our immune system responds to particular sequences of proteins. It's sort of like the signature or how it recognizes what it is fighting against. If the signature on one virus matches the signature on a protein in

our own body, then the immune system can get confused and say Oh well I know that if I see this signature on that particular if I see that signature then I need to rev up production of the antibodies of cytokines that need to fight. But if that signature is similar to something on our own bodies are our spinal cord or neurons and then the immune system actually can cause damage to itself and that is molecular mimicry.

08:37 So this is the way in which are there reason that there is what we call biologic plausibility there is a possibility that vaccines could have this effect and we'll talk much more about what the evidence has shown us and how this plays out in in our scientific querying into whether or not this is in fact what happens. But there's the theory behind it and there's another theory of something we call a super antigen and that just means. Well there are some things that can rev up the immune system to a normal degree and there are other things that can trigger an all-out assault and those are super antigens and might there be something like a super antigen that could trigger our immune system in a maladaptive way as well.

09:40 And so maybe I'll pause right there and see Augusto if you have anything to add absolutely and Teri and you know it was a very eloquent description of the mechanism behind the potential trigger of neuroimmunological disorders as a consequence of vaccinations. In this case. But the truth is that that could happen from any time the immune system is exposed to and an antigen and just to expand on what Dr. Schreiner explained before. So, she mentioned vaccines are a way to in a sense manipulate the immune system to think they are being exposed to the real disease and the purpose for that is to obtain the benefit of neurological tolerance meaning that then of training they need the system to be ready to respond to certain antigens in a way that might protect against disorders. What happened is that in certain circumstances through the mechanism Dr. Schreiner explained you are creating also a pool of immune cells or lymphocytes that will have the ability to respond to cell antigens as well.

11:01 And that's the basis to explain many of the autoimmune disorders including Transverse Myelitis, Multiple Sclerosis, Neuromyelitis Optica.

11:14 So the question here is whether the use of vaccinations is linked to these disorders in a way that is different or increased from the natural infection that the vaccinations are trying to prevent.

11:30 And that's where the evidence argues against evidence that vaccines are actually more harmful than the disease or trying to prevent. So virtually all of these reports that you see that for the most part are case reports of neuroimmunological disorders that come after vaccinations. They're also present as a consequence of the infection that the vaccination is trying to prevent. And so, the question here becomes is that a factor that is directly linked to the vaccine itself or this is a factor a response that the immune system is doing perhaps in maladapted response that the host of that infection whether it is the individual who has the disease is not able the immune system is not able to discern between the subtleties of the antigen presenting the vaccine or the infection and the self-antigens. So, that's the basis behind

the that perhaps some individuals have an immune system that has been developed to the point of discerning between the subtle things some individuals may not.

12:40 And that's why even though these reports are real for the most part are rare disorders. You get thousands and thousands of individuals receiving vaccines and only a handful will have these neuroimmunological disorders associated with them.

13:00 Thank you very much Augusto.

13:02 So several of our members reported that they were diagnosed with a rare neuroimmune disorder within a few weeks of getting a vaccination. So, what would be the time frame for which the association could be likely?

13:20 OK well I will I'll jump in and talk to that one a little bit. And then Augusto,

13:26 I'll have you as before sort of comment as well. And so there I think there are there's some issues in this question that I want to address sort of separately.

13:40 So one is we all know of case reports in which and maybe we ourselves know our loved one a friend a colleague someone who has had a vaccine and then within a period of time has developed a rare neuro immunologic disease like transverse myelitis, like optic neuritis, multiple sclerosis. And the question is really is that causal. So, I think in many ways tempting to say you know one thing happened and then a subsequent event happened. Therefore, the first thing caused. The second thing and that's really what we have tried to investigate in the research that has been done in this area is the temporal association. Actually causal. So many people will joke and say Oh well I know what I know it's going to rain tomorrow because I took my car to the car wash today and so that would be something that may be temporally associated maybe sometimes we go to the car wash and it does bring in the next day but we haven't actually caused the rain by going to the car wash as much as it might feel that way.

15:02 And I offer this example not to minimize any of this but just to sort of illustrate that sometimes something comes before an event that is not actually causing that event. Now with that being said in the context of plausibility is it plausible that a vaccine could trigger a rare neuro immunologic disorder. There is a time frame that we think about we know basically how the immune system. We think we know how the immune system works or responds to a vaccine and that is you know generally within a couple of days we are producing antibodies. We know that the number of antibodies that are produced for example after a vaccine peaks around two weeks.

15:54 And we know that when the immune system is being triggered to attack the cells divide very quickly on the order of once every six hours or so. So, if we take these things into account and we say OK so is it the immune system were triggered by a vaccine. What is the time frame in which we would expect to see a sequelae. We think generally about you know a few days later maybe up to five days to a month. In the studies that have been done and there was one

just recently published by an author named Baxter that his group looked at a five to twenty eight day window following vaccination in a large group a group organized through something called the vaccine safety data link and they looked at something like 63 million vaccinations within a period of time and they said OK well let's look at the people in this large population that developed something like transverse myelitis and look at the five to twenty eight day period before their presentation and see whether or not there was a vaccination and that in that time period they also broadened their scope and said OK well maybe that's too narrow why don't we also look at a time period of two days following vaccination to 42 days.

17:31 So they made the window a little bit broader. And in this particular cohort where they were looking at people who developed TM in a period of five years and then trying to compare whether or not they had received a vaccine to everybody else in the cohort who had been receiving vaccines but did not develop TM.

17:55 They found that there was no association. So, I know I'm jumping ahead a little bit to talk about one of the specific studies that has been done on this topic but to answer the question of the timeline that we would think about.

18:10 I generally think about that window of maybe five days to 28 days after

18:20 I agree with Dr. Schreiner and just to just to expand on that the way we look at some if not most neuro immunological disorders is looking at a multi modal a situation in which multiple factors play a role in triggering and initiating the disease for the most part. Whether you look at transverse myelitis, multiple sclerosis neuro myelitis optic it's not that we have a single factor that is responsible for causing the disease. So, there are genetic factors. There are environmental factors and there are factors that actually relate to the host itself. And in this case I want to emphasize the fact that there are certain individuals that are more susceptible for the development of auto immunity and you see that through even though disorders outside neurology whether it's asthma or lupus.

19:21 And even some of these disorders actually run in families so the thought behind that is that independent of the trigger. These individuals have an immune system that is more prompt to respond in a way that may not only protect against the antigen that they are trying to fight but also cross react with selfantigens.

19:46 That is because these immune cells as I mentioned before and they're not sophisticated enough to discern between molecular differences between cells and foreign antigens whether it's because their regulatory cells that are intended to prevent autoimmunity from happening are not working well whether the process of initialing intolerance that happens when we are kids has been somehow interrupted.

20:13 So there are many factors. But the truth is that the current thought behind these disorders is that the immune system already starts by being more prompt and predisposed to react in a way that is maladaptive and conducive for autoimmunity. So, the question becomes

you still something has to trigger that something that has to be an event that is going to activate the cells that we know these individuals have and we call them auto reactive cells. So why all of a sudden transverse myelitis so in some way when they're in their 50s you're thinking that these cells have been present there for their entire life. What triggers those cells to all of a sudden get activated and cause disease. And that's way that's where the roll of vaccines may play a role but is not unique to vaccines. Right. So, we know that infections can do that.

21:10 And that's why we have an entity that we call post infectious transverse myelitis, post infectious encephalomyelitis. So, they are these entities that were labeled based on what we know of not only on the disease itself but sometimes when possible based on what triggered that.

21:31 So there is a role as Dr. Schreiner mentioned before of biological possibility between vaccines and disease is perhaps as a trigger but not as the cause right thank you and this is a think related to what you just mentioned dr. Miravalle some one of our listeners wrote and you know had I not been stricken by this vaccine and in this case the flu shot something in the future have gone ahead and had a similar effect I guess with their diagnosis. If you could just adjust that.

22:01 Yes. And actually, the flu vaccine is one of the exceptions because for the most part we tell individuals and patients who suffer from these side effects. Well if you had a bad reaction to any vaccine or any treatment before it becomes Don't do it again because you know when you look at these large studies you know for the most part know it exist. But if you look at individual cases if somebody has an adverse reaction to a vaccine for the most part I recommend to avoid revaccination with the same type of vaccine. Interestingly the flu vaccine is one of the exceptions and the reason for that is because the way the vaccine is being manufactured is trying to mimic the strain of this seasonal virus. And as we all know the virus itself mutates every year and this strain differs.

22:55 So when we when you manufacture the vaccine and you're trying to mimic the strain of the virus that you're expecting to have in that season. So, that's why you see that even if you have reactions to the flu vaccine in prior years that doesn't necessarily mean that you may have similar reactions in the future. And this came very clear with a now famous pandemic of a flu in the 70s in 1976 that there was a large number of patients who develop Guillain-Barre right after that. And there were numerous studies looking at that serious disease after vaccination with flu. And the latest one came from the Sweden national database that they looked at over two million individuals and they could not identify any increase risk of Guillain-Barre with the current strain of H1N1 flu vaccine.

23:56 So that may be one of the few exceptions but for the most part we tend to recommend do not revaccinated if you had an adverse reaction before.

24:07 Right. And I'll just add to that. I agree. Absolutely.

24:12 And to go back a bit to the discussion about how there can be many triggers of disease multi-modal factors involved in triggering something like TM and how that it may not be one thing that causes a disease but a trigger that tips the scales that we're you know predisposed towards that so to speak can we think about genetic predisposition towards autoimmunity we think about environmental exposures. And so, if the question was that that was posed was if it hadn't been this one immunisation that triggered my TM would it have been another. I think there is a possibility I think there is an argument to be made to say yes in a predisposed individual and someone who already had certain features that were making an inflammatory response more likely the trigger could be one thing or it may have been the infection that happened the next month or the immunization that happens you know years from now.

25:32 It's really difficult if not impossible to say that. But I think there is a rationale a mechanism behind saying yes in a predisposed individual it could be one of any number of triggers that actually tips the scales and causes the disease.

25:55 Thank you very much. And Dr. Schreiner you mentioned earlier about live vaccines.

26:01 So is there a difference between live vaccines and other vaccines I think you might have spoken to that earlier. You know there are recommendations for people with neuroimmune disorders.

26:13 OK. Yes, I can I can address that. So, we did speak a little bit in the very beginning about how there are different types of vaccines different ways in which the vaccine is made to subsequently trigger an immune system into thinking that it's fighting a disease when in fact we're just teaching it how to fight a disease or a virus an infection. And so, the live viruses are one type of vaccine. And it is not. And the more proper term would actually be live attenuated meaning that we take the virus and we change it in a way that it is not able to cause disease in an individual when vaccinated with that virus. But it is able to teach that host that person's immune system how to fight the actual live virus. And so, a live attenuated vaccine is a vaccine that is it comes from an actual virus but it's been weakened it's been changed so that it should not cause actual disease in in somebody with a normally functioning immune system.

27:38 Now there are exceptions unfortunately to that in history where we go back to look at the oral polio vaccine and have and that did cause paralysis in a subset of people who received it unfortunately. But the that is the exception to the standard with live attenuated viruses is that they do not cause infection. They just teach the immune system how to fight it. And often times have a greater duration of protection than some of the other viruses, excuse me, vaccines. So. So, we have we have killed viruses and this is these are killed vaccines. There are vaccines that come from viruses that yes have been killed have been changed in a way so that they promote an antibody response and the host to give temporary immunity against something like Influenza. Pertussis is another one in this category Rabies is in this category in something that hopefully many of us will not will not need.

28:57 And then the third category is combine something called conjugate vaccines as well as recombinant vaccines. And these are vaccines that are created by taking certain aspects of the antigen of the invader and attaching it to a protein that helps the immune system respond more effectively more vigorously against to be the would-be invader. And so, in this category we have pneumococcal conjugate. We have meningococcal vaccines. Hepatitis B is a recombinant vaccine.

29:42 And so each of these different mechanisms is to achieve basically the same thing which again is to teach the immune system how to fight an invader that they have not actually seen before. Augusto, do you have anything to add there.

30:03 Yes absolutely. And the question that I often get asked is but if the live virus vaccine or the attenuated vaccine carries a slightly more risks of developing the disease or many countries trying to prevent. Why do people still use that. And I always like to use these comparisons so look at your immune system as you or the police in your city. Right so you're trying to train the police which is your defense mechanism to learn how to recognize a criminal. So, if you only show the police a fingernail of that criminal they might not know who to chase because it's only a little piece of the body of evidence.

30:52 But if instead of that we show them a picture of the person with a face they might be more specific in order to mount a defense mechanism against that. So, in vaccine manufacturing processes there it's nice balance that you have to play between how much of the antigen you show are you exposing your system to in order to mount a stronger immune response sort of more accurate in my response versus how much risk you introduce to the host of potentially creating the disease you're trying to prevent. And that's why you have different models of vaccines will call for different protection against the disease you're trying to fight as well as different ways.

31:43 OK great. Thank you. And so, I know we've talked about this a little bit but you know so if someone was diagnosed with something like TM but they you know wasn't after a vaccination you know is having just a rare neuro immune disorder contra indication to getting vaccinated. And then you know what if their doctor recommends that they don't get vaccinations.

32:11 Teri, you want me to address that or yeah.

32:12 Why don't you go first on that one.

32:15 Sure. Yes. So basically, as we mentioned before so there is a clear temporal relationship with a side effect or adverse event from the vaccine. That cause competition in a patient I usually recommend a patient not to do that same vaccination again the exceptions that we mentioned before with the flu vaccine for individuals who already have an autoimmune disorder and they are two things that we have to take into account. One as we explained before because of the nature of their disease and their immune system they might be more prompt to develop an auto immune response after being exposed to certain vaccines. And that's why for

example in multiple sclerosis patients we tried to avoid the use of live virus vaccines when possible example being for example there's intranasal flu vaccine. It's live attenuated vaccine where they were the intramuscular flu vaccine is a killed vaccine so we always recommend to use intramuscular when possible and avoid the use of live virus vaccines.

33:34 The other consideration that we have to take into account in these patients is the fact that for the most part they are also receiving immune suppressive therapies to control their disease. So, then you're talking about a different level of complexity which you see in an individual who has an underlying autoimmune disease and is now on treatment with anti-immune suppressants. And two things can happen in that scenario. One is that the immunity that you're expecting to generate by exposing the vaccine to this individual may be weakened by the fact that the system is not competent. So even if you vaccinate individuals for immune suppressive medications they might not mount the level of immune response to convey protection.

34:31 The second consequence will be that because the immune system is weakened they may develop the symptoms from the disease that you're trying to prevent. So for the most part individuals who are receiving these medications. We tried to avoid live virus vaccines as we mentioned before. And when possible we try to coordinate the use of certain vaccinations prior to starting immune suppressive medications.

35:00 Yes. Well said and I agree. And I will sort of point out again to cycle back to the discussion about influenza and particularly in the disease multiple sclerosis which is the disease characterized by ongoing inflammatory effects and attacks. There is more risk to be if there's more risk associated with getting the infection of influenza than there is with the vaccine of influenza. So, So, I want to just you know point that out. Not only that multiple sclerosis is a much different than an idiopathic transverse myelitis in which we think it is a one-time event not to occur again and a disease like MS where there can be ongoing relapses over time and concerns specifically in that disease about whether or not to vaccinate against something like the flu. And again, I agree Augusto with you and the evidence supports that the infection can be much more significant and detrimental to the patient than the vaccine itself.

36:23 And so if I may I'll talk a little bit more about transverse myelitis and idiopathic transverse myelitis and myelitis itself is a broad term that refers to inflammation in the spinal cord that can come from many different etiologies. But to look specifically at idiopathic transverse myelitis which we believe to be a one-time event should those patients go on to receive vaccinations after that. And I believe and the evidence would support that the answer is yes you should continue to be vaccinated. And there was a time I think in which we thought, well if your immune system is prone to overreacting as evidenced by this onetime event of transverse myelitis, perhaps we shouldn't give live virus vaccinations. Perhaps we shouldn't give vaccinations, but truthfully the evidence is that there is not an associated risk with having additional myelitis events or other demyelinating events after transverse myelitis when vaccinations are given.

37:57 And just to second that particularly true when you're looking at older individuals with the concern around pneumococcal vaccine and just to expand on that the risks of acquiring a pneumococcal infection are larger and more detrimental than the potential and small risk of developing complications. Let alone the fact that this is a killed inactivated bacterial vaccine so the risk itself are minimal.

38:24 And when you're looking at the immune suppressed individuals or individuals over 65 years of age the risk of complications and sometimes fatal complications from the infection itself outweigh the risks of the possibility of complications.

38:44 Thank you both so much for that. So, we had a question coming in. And it reads I'm a 68-year-old female with NMO on Rituxan

38:56 What vaccine should I take and when as it relates to infusions. And what about what about with steroids or other acute treatments.

39:07 Augusto maybe I'll let you address that one.

39:12 Sure as we mentioned before so we try to vaccinate patients particularly with the intramuscular flu vaccine when indicated individuals over the age of 65 they should receive the pneumococcal vaccine.

39:28 There are two types of vaccine the conjugate vaccine that is usually used for anywhere from infants to elderly individuals that confers immunity to 13 strains of the bacteria. That's Prevnar. And then you have the polysaccharide vaccine which confers immunity to 23 strains of bacteria. So for the most part and that's Pneumovax. for the most part individuals that are 65 and older should be vaccinated with Pneumovax vaccine and just as I mentioned before in order to even minimize their already small risk of complications when possible I try to coordinate all these vaccinations prior to the initiation of immunosuppressive therapies if a patient's already on a medication and needs to be vaccinated. Really depends on the medication they're receiving with Prevnar the biological half-life of the medication. It takes up to three to six months for the B-cells to restore to their baseline they also will be safe eventually to wait until a week or two prior to the next infusion and to administer these vaccines.

40:51 For example in the case of MS patients receiving Glatiramer which is another immunosuppressant medication we usually have to interrupt treatment for at least four weeks. Vaccinate if needed and then wait an additional weeks a couple of weeks to restart the medication. So, treating patients with the medication in a patient is receiving. But for the most part when possible we try to coordinate timing and try to prevent as much as we can and both situations the immune suppressive lack of response to the protection of the vaccine as well as potential complications.

41:32 Great. Thank you very much. And we got another question that their TM was one of our members asked stated that their TM was apparently had an attack on indolent herpes zoster

chicken pox and that was in their cervical spine. And is there any sort of risk for taking a shingles vaccine since it was you know the initial event could have been related to chicken pox. Dr. Schreiner Yeah.

41:57 Er Doctor Yeah, I think I'm a suspect. This question was actually about varicella zoster which is the chicken pox virus. And that can reside in a very specific part of the nervous system called the dorsal root ganglia. But I think I might ask could Dr. Miravalle to answer this question as an adult neurologist.

42:29 Sure. And so, the zoster vaccine. Again, it's a live attenuated vaccine for individuals who had prior exposure to the virus. Often individuals remember. And they have symptomatic infection in the past with chickenpox for the most part. The revaccination with the Zoster vaccine is safe. Whether you have or you don't have an underlying autoimmune disorder then the question becomes in individuals who never been exposed to the chicken pox in the past. And that's usually when we try not to expose patients to this Zoster vaccine just to give an example of the medication I mentioned before Glatiramer a type of immunosuppression that the medication will result will increase the risk of reactivation of or if a large immune response to their exposure to these types of viruses. So, for that the FDA requires that patients have to be vaccinated prior to initiating therapy.

43:43 And in that case what we do is we vaccinate individuals who've never been exposed to the virus by using a vaccine. But in terms of the Zoster vaccine each individual has been exposed through natural infection in the past for the most part is safe. The question comes into when somebody had shingles clinical shingles. And I always give this example. Your immune system is already being exposed to the virus. So, by having the clinical shingles you're already inducing a refresher in the immune system to remember how to protect against the recording of these viruses. So, the question becomes is that actually necessary. That's a different question but in terms of safety when somebody has been already exposed in the past the risks are minimal.

44:42 Thank you so much.

44:43 So this next question is for Dr. Schreiner says Should my child be vaccinated and given that I had reaction. And then she notes that she is that her daughter is vaccinated but that she's always nervous on how she will react.

45:00 OK. So, if I interpret that correctly the person posing the question has been affected by a neuro immunologic disorder like TM And the question is Should her daughter continue to be vaccinated. So, I would say yes, I know it is it is anxiety provoking to think about a loved one a child having a reaction that to a trigger that has caused you know a sequelae a negative event and that person herself. But I think it's important to think again about how complex our immune systems are and how many factors go into causing a particular disorder like TM. So, to sort of revisit what we talked about before. There are probably genetic triggers we can't change our genes. They are you know the blueprints of our body including our immune system and

they may have a predisposition towards inflammation are environmental factors however are going to vary significantly from one person to the next even within a family.

46:30 So a mother to a daughter may still have very different environmental exposures throughout their lives customizing and training their immune system. And so because just because one person in a family has had a reaction to a particular vaccine that does not imply that other people within the family will have the same effect. And the benefits of vaccination are great. And I think we've seen in recent years unfortunately a resurgence of some diseases that had previously been controlled by vaccine like you know an outbreak of measles at Disneyland. There's been an outbreak of mumps in Iowa I believe. So, these are vaccine preventable diseases that have you know unfortunately had a resurgence because a portion of our population is not vaccinating anymore. And this is this is risky.

47:44 Then it introduces the possibility of so. So if the daughter in this situation were not to be vaccinated and she were to come into exposure to one of those viruses that was previously well controlled but now because of lack of vaccination it's got a foothold in our population again she could become very very ill from that disease. And I think it is worthwhile remembering that some of these diseases are much more than just a rash and they have caused death and significant sequelae in the past. And so my summary is that yes I think I think the child should be vaccinated.

48:36 Thank you very much.

48:39 So you gave us some really wonderful information on vaccines and we have another question asking if there is any reason to space out some vaccinations so Dr Miravalle if you could answer that question I'm sorry a reason to do what? Any reason to space out vaccinations Oh no the only reason being as we mentioned before somebody is receiving an immunosuppressive therapy and we can eventually wait for the immune system to be restored to baseline levels before vaccinating. But

49:17 other than that as Dr Schreiner mentioned for the most part of the reason why these vaccines are given in these pre-determined intervals is because that's been shown to be the most effective way to prevent disease. So for the most part we try to adhere to their calendar and just to sync on what Dr Schreiner mention you know when you go through medical training one of the first things you learn is that the first and foremost an important role of physicians and health care providers is to cause no harm. And that's the last thing we want to do in our patient population. So, do not harm. It's always in our minds where we recommend any type of interventions including vaccines. So, it is difficult sometimes to wait. The well-known and well established benefit in communities of vaccination as ways to prevent disease versus these isolated cases that perhaps the vaccine had a role not of causality but her role in perpetrating or activating an already auto reactive immune system.

50:33 The question is do we need to generalize that into now recommending no vaccinations. Well it's difficult. I don't I don't for the most part I don't recommend to stop vaccinations.

50:47 And what I try to do is say on an individual basis looking to avoid the potential risks that we can determine and then try to work around that individual patient

51:02 Yes and I can speak to this question as well so as a pediatric neurologist I'm oftentimes asked this question you know a mom a pregnant mom will say you know I'm about to have a child and I know there are you know six different vaccinations that are required at two months at four months. And again, at six months you know is there any reason not to spread them out so that instead of giving you know six immunizations on one day every two months maybe we give three every month for six months. And I don't think there is a reason not to do that. I think the most important thing is getting the vaccines.

51:51 But I think the one of the downsides of spacing out you know at least those early vaccinations is that the you know your infant is getting poked twice as often or however many times greater number of pokes in order to get the immunizations. So, I don't know if that was maybe the question that this person had. But I think I'll say there are some rules about how vaccines need to be spaced out. You know the hepatitis B vaccine is given at birth and then you have to have a second dose this many months later and a third dose between this many months later. So, there are some rules that that are known created by the CDC to try and maximize the efficacy of the series. But is there a downside to spreading out vaccines in an immunocompetent patient. No I don't I don't think there's a downside.

52:55 OK.

52:55 And then you know just. Are there any particular side effects or benefits of vaccinations for people with rare neuro disorders for example you know the potential for something like autonomic dysreflexia or worsening of symptoms after the vaccine or you know for example also helping make sure that people don't get sick who have you know whose ability to cough is impaired for example. If you could just speak a little bit about specifically in this population you know what the potential side effects or benefits could be.

53:30 Sure. Teri If you want I can take that basically look at vaccines as a way to challenge the immune system and any individual already has in an autoimmune disorder the immune system is going to be susceptible to anything that will trigger activation of their cells where the infection whether it's a UTI whether it's the flu or whether it's a vaccine. But I want to emphasize what has been said before that when we look at the overall risk benefit of vaccination it is still the most powerful way that we have to prevent infections and even the rare but possible case of the vaccine causing similar symptoms to the infection you're trying to prevent for the most part those symptomatic side effects of the vaccines tend to be a milder form of what could have been their symptoms from the infection you're trying to prevent. So for the most part and you mentioned actually a perfect example of that somebody has a significant disability that has what we call bulbar symptoms in which swallowing coughing is impaired imagine that individuals develop pneumonia or infections on their respiratory airway system.

54:54 The consequences of that and the complications are greater. So for the most part you know again we are sensitive to the potential risks but we are still for the most part recommending vaccinations for individuals at risk yes.

55:11 And I agree. I will add that for people who have suffered any insult to the nervous system following a vaccination they may develop a fever. They may have what we call recrudescence or reappearance of symptoms that they have had before so they might have a temporary worsening in the immediate period after the vaccine. That is similar to you know patients with multiple sclerosis being very susceptible to heat and having a temporary worsening in those situations. So, there may be in the short period after vaccination for someone who has had a rare neuro immunologic disorder there may be return of prior symptoms but that is temporary. And I again will reiterate that I think the benefits of a vaccination to prevent illness in this population outweighs the risk.

56:19 Thank you both so much for your time today. We're unfortunately you know at the end of our time but we hope to continue this conversation and you know various forms in the future. But thank you both very much for your time. We really appreciate it.

56:34 You're welcome.

56:35 Before the meeting you for the invitation and just to announce to our listeners we will have another podcast next month. It's

56:42 managing your health after a rare neuro immune diagnosis and we should be sending information about that shortly and then there's also all of these podcasts are available on our website in our resource library at myelitis dot org So if you missed it part of this time you can always check back in and listen to the recordings. So, thank you.