Hello everyone and welcome to the TMA Ask the Expert Podcast Series. In today's session, it is entitled Understanding Vaccination and Autoimmune Diseases. My name is Roberta Pesce and I'm the research and project manager at the Transverse Myelitis Association. We are a nonprofit focused on support education and research and are immune diseases. You can learn more about us on our website at myelitis dot org. Chitra Krishnan, executive director of the TMA will be moderating our podcast for today. a few housekeeping pieces before we get started. This podcast is being recorded and will be made available on the TMA website at myelitis dot org. You can also be downloaded by iTunes. During the call if you have any additional questions please send them to us our Facebook page at Facebook dot com slash myelitis.

Great thank you Roberta. Very excited to be joined by Dr. Benjamin Greenberg and Dr. Teri Schreiner on today's podcast. Dr. Greenberg is an associate professor at University of Texas Southwestern Medical Center. He is recognized internationally as an expert in rare autoimmune disorders of the CNS. Dr. Teri Schreiner is a neuroimmunology specialist at the University of Colorado and a pediatric neurologist at Children's Hospital Colorado. She is sub-specialized in pediatric onset demyelinating disorders of the central nervous system and has begun a multi-disciplinary clinic for children with these disorders. We are so grateful to both of you for joining us. We've received many questions from our community and this topic of great concern and interest. We really appreciate you both taking the time to address what is clearly a very complicated and difficult issue. And to start us off perhaps I can get with you Dr. Greenberg.

There's so much conversation in the community as I said about vaccinations and a lot of concern that vaccinations actually caused TM or NMO or ADEM. you know from a public health perspective and we talk about causation. We talk about many factors like the timing of biological possibility and so much more when you think about the context of vaccinations and these rare neuroimmune diseases. Is it possible that even biologically plausible that vaccine can cause TM, NMO, ADEM or Acute Flaccid Myelitis?

Well first Chitra let me just thank you and Roberta and the TMA for sponsoring this podcast and the podcast theory series and Dr. Schreiner for taking part in what you’re correct. A controversial area in an area that needs a lot of work and research done for many years in fact decades’ people have talked about the potential complications of vaccinations leading to a difference neurologic conditions. And it's been well-documented in the lay press as well as the literature concerns about links between vaccinations and autism concerns about link between vaccinations and multiple sclerosis. Concerns between you know about vaccinations and the link to transverse myelitis or Guillain–Barré and in all
of these areas there has yet to be a study that proves a link between now the lack of evidence does not disprove that theory. But it’s important from the outset of the conversation to have a framework for this conversation and what I’d like to do is just take 60 seconds and talk about these two different theories that would biologically link a vaccination to one of these conditions like transverse myelitis.

03:48 And the two theories are first the theory of molecular mimicry and what that theory says is that parts of the vaccine part of the proteins of the organism that we are exposing a human to in order to build protection. So, for example a flu vaccine or measles vaccine has the whole or part of the measles virus or the flu virus. And we inject it or ingest it so that the human being develops resistance to that organism. The molecular mimicry theory states that there are proteins within the spinal cord or within the nervous system that look very similar to the proteins of the virus.

04:30 And as for the immune system gets activated against flu or against the measles or hepatitis or any of these viruses in the aftermath by mistake goes in and causes inflammation in the brain or spinal cord leading to one of these autoimmune conditions. So, the molecular mimicry theory states that a specific protein in a specific vaccine triggers an immune response against the host. The second theory that links vaccinations to these autoimmune conditions does not specifically need a certain protein from the virus. This theory states that there are people who are predisposed or are in fact incubating these autoimmune conditions meaning they are walking around with everything necessary in their biology to have a transverse myelitis event or ADEM event or multiple sclerosis attack or NMO attack and that the vaccination leads to generalized inflammation that triggers a preexisting condition.

05:36 Those two theories are very different and have a huge impact on the way we do research relative to vaccination because in the first theory we would need to prove that a very specific act. So just flu vaccine that was a trigger for people transverse myelitis and in the second theory what we need to show is frankly any vaccination when exposed to a trapped individual would lead to these conditions. So, there are two biologically plausible theories that could link vaccination to these events. Unfortunately, as we talk about on today’s call we’re going to go through the data and talk about where we’re missing data and where the data has either substantiated or not substantiated framed.

06:21 OK. This is Teri Schreiner. I think I'll just jump in there and say I think that is a wonderful overview of the scenario that we are looking at which is very complex and comes up so often in clinic and so it's a pleasure to be able to have a discussion today and to address some particular questions regarding this very pertinent topic. I will add just a couple things to it. Dr. Greenberg as always all
already very eloquently described which is that we referred to vaccines as if they are all the same and we know that there are different types. That's important to consider as we look at all the evidence and think about you know which types if there were any link would be more prone to cause an immune response. And also, we think and in some circumstances, have had research evaluate the interaction between the different types of vaccines and the different types of the demyelination.

07:39 But we know that not all the demyelination is the same. So, multiple sclerosis is a much different disease than acute disseminated encephalomyelitis and that myelitis itself has many different causes. And so, there's a complexity within the system. When we look at all these different factors that we need to take into account as we weigh the evidence that's great.

08:06 Thank you Dr. Schreiner. I know that's a fantastic overview from both of you. So, if I just sort of pick you know a particular vaccine that we've gotten many many questions about. And most of them have been that you know I've received the flu shot and two days later I was diagnosed with transverse myelitis or six weeks later I was diagnosed with transverse myelitis. So are there any known risks associated with receiving flu shots for those with TM and conversely are there accompanying risks to contracting flu that might have been prevented with the vaccination. Dr. Schreiner Do you want to start this one.

08:46 Yeah, I will I will start this one. So, this is I've mentioned that vaccines in general are a topic that comes up quite often in clinic but I think of them this is the question that I receive most often is you know should I get a flu shot. I've never had the flu. I'm not going to get that because you know I just never get sick. And I think that this is something worth clarifying that the evidence that we have shown that the potential impact on disease and I'll just say demyelinating disease in general is much more significant from the influenza infection itself than it is from the vaccine. So, one particular study looking at this look just at multiple sclerosis patients and what they found was among patients who were already diagnosed with Multiple Sclerosis the risk of having an exacerbation and a new neurologic problem related to demyelination was significantly higher in the three months after having had the flu the actual infection than it was after getting a flu shot.

10:06 And so I recommend for all of my patients that they be immunized against influenza to prevent the infection. Now you know all of us have we have to accept the certain uncertainty and how efficacious the flu vaccine is going to be and unfortunately this year we're seeing that the flu vaccine is not very efficacious but it is still something that is recommended to prevent the infection in at least 23 percent of the people who receive it.
Dr. Greenberg do you have anything to add with regards to the flu so I guess there's a couple of things when it comes to flu that I would add. So, one thing and this is specific to the flu virus vaccination is no two vaccines are the same. Year to year. So, there is no such thing as a singular flu vaccine. So, when people have concerns that in the past they had a reaction or end of the flu vaccine and I get that question can I ever have it again. The answer is you're never going to have that flu vaccine you're going to have a very different flu vaccine. And so, one of the concerns that comes up with repeated exposure is not one we have when it comes to flu vaccine. The second issue that comes up and Chitra you alluded to that is people will report that I had a flu vaccine and in the days, weeks or months after I had my event.

So that is what is used as evidence to show causation. And unfortunately, it is can be a misnomer in what we see is that it is human nature. We're all i do it myself that if A proceeds B, A must have cause B. And in this respect, it's even more so along those lines because there's a theory that would link the two. Unfortunately, when you do the statistics of how many transverse myelitis cases there are a year and you break them down into seasons and you look at well if there's let's say there's a hundred cases of transverse myelitis. There's more than that but to make numbers simple there is 100 cases and it's evenly distributed throughout the year.

That means 25 cases are going to happen in November December and January the peak for flu vaccinations are September October November. That means even if there was no association no cause between the flu vaccine and transverse myelitis a quarter of transverse myelitis cases will happen within three months of the vaccination. So even in a world where there is no association we could be fooled individually into thinking there is one just by random chance. So, from an epidemiologic perspective what we would want to show is gee there is a spike in transverse myelitis cases in the time period after vaccinations. And every study that's looked at the myelinating diseases has failed to find this temporal association that we can find individuals. And in fact, you would expect to find individuals who have the event after the vaccination but at a population pattern that pattern hasn't been there in the last comments I make which is to echo what Dr. Schreiner said about the dangers of flu this season.

I have personally cared for more children with post flu neurologic events than for children with post vaccination events. I have not had thankfully a child in a house with transverse myelitis in the 90 days after flu vaccine yet this season but we have had two to three kids in hospital with post flu neurologic events and so while we all weigh the risks and benefits of putting things in our body we do have to recognize there are distinct advantages when rolling the dice with taking the vaccination.
Great thank you. And you know so this also of you know you mentioned 90 days and we've got a question on Facebook about this as well you know. So, what would ordinarily be a timeframe that you would consider a biological possibility three months the cutoff?

Yeah, I don't think anybody knows. So, it depends on which theory you're talking about.

So if you're talking about molecular mimicry in theory there isn't a specific time cutoff. In theory, you could get a vaccination this year that primes your immune system against the protein and then far later in your life it gets triggered to actually give you the event whereas in the other theory where the vaccination is the trigger for the preexisting autoimmune condition you would expect for it to trigger it. You know I would argue scientifically within 60 days really within 30 days. And likewise, you can make the argument that some reactions would be too soon to be biologically plausible. So, for example somebody having symptoms within 24 hours after the vaccination that's probably not long enough for it to trigger a spinal cord event. And so, there's probably a window anywhere from three days to 30 days. We're biologically I would consider it plausible that there was a potential link.

Again though if you do the math on a population level if people get transverse myelitis by eating a bad turkey sandwich and they happen to have that turkey sandwich around the time they get the vaccination there is no way to separate out which was the culprit. In fact, I should mention at this point because I do want to recognize one thing I see sometimes I think comments like this in conversations like this since it is such a charge area can come across as being dogmatic about this and I and I don't want to come across that way. I do believe and in fact there is proof that certain vaccines have induced neurologic events in the past specifically ADEM or TM in the best example of this is the simple rabies vaccine. This was when we used to grow the rabies virus in neurons in brain tissue basically and then injected into humans to vaccinate against rabies.

Well if I inject brain and spinal cord tissue into humans that it's quite probable then I'm going to get an immune response against brain or spinal cord. And so, I know that in the past there have definitely been vaccines that clearly had an association with neurologic events. Fortunately, today the manufacturing processes don't involve those human tissues or neuronal tissues.

So I think we've gotten to a place where the odds of that happening are just significantly lower and I'll make that decision if I may that in looking at the literature the number of cases that have linked a vaccination with development or presentation of demyelinating episode the spectrum of time between the vaccination and the presentation of neurologic symptoms that would be the
disease is quite variable. Anything from days, as Dr. Greenberg mentioned, to up to five or six months or even years and that is worrisome. We've talked about examples like the turkey sandwich of trying to identify causation when there are different things happening to us every day of our lives and how to draw a link between one thing such as a vaccination and a disease that will develop months if not years later is really fraught with so many difficulties and presumptions.

18:29

So I think we need to be conscious of thinking about things like that. But I do share the thought that we probably can't assume that anything happening within a couple days of a vaccine in any demyelinating episode happening within a couple of days is causal. Likewise, I carry a heavy dose of skepticism that anything happening you know months later up two years later with a I seriously doubt that that would be related.

19:06

Great thank you. So you know given the timeframe and given the fact that you know there are like you said rabies vaccination has been shown etc. Are there any circumstances where you would tell a person not to get vaccinated? Or is it a specific vaccination or do you give them sort of any guidance that if it's a live virus you need to be or live attenuated virus you need to be careful or if you're sick don't get it. I mean are there any guidelines one should think about if you've been diagnosed with any one of these diseases?

19:37

You know when you should get vaccinated and when not? Yes, I’ll join in on this one the issue of live versus killed vaccines and it's important just to know the difference for listeners who may not be aware of this. So, there is there are two ways to two three ways. In theory to vaccinate people against infections or complications of infections. So, one is to take a weakened version of the live virus. So, you take a flu virus you grow it over many generations to a point where it's really not going to make you that sick. And then we ingested or injected into a human. So, for flu this is the nasal mist of the flu mist that gets unescorted into a nose and it will give you a mild infection that really doesn't make you sick but gives your body a chance to mount a response.

20:27

So that's a live attenuated virus vaccine. The second type is a killed virus where you take the whole virus. It's killed and the carcasses are injected into the person and you mount an immune response because the proteins are there and the means as you can see the proteins and learn to attack and in the future and it won't replicate and can't cause the actual illness. It can make you feel sick. So, most people who get a flu shot will get a low-grade fever. It's not because they get the flu it's because their immune system is getting activated as if they had the flu and is mounting that response. And then what's left of the vaccine is a conjugated protein vaccine where instead of giving you the whole that carcass of a virus or a live virus we just take one piece or two pieces of proteins and inject it in.
21:14 So the tetanus vaccination is to a protein. So, one of the big discussions that comes up is there a difference in danger between these different vaccines and the most attention that gets cast towards live viral vaccinations versus the dead or protein base. And in general, the safety record for each of them has been exactly the same relative to triggering auto immune events. We do not see any difference in history between the live attenuated viruses and the killed or the protein base viruses. There is one exception to this that our patients need to be aware of and that specifically is most appropriate for our NMO patients and that is for anybody who is on an immunosuppressive whether it be a steroid or Mycophenolate which is sold as CellCept, or Azathioprine which is sold as in Imuran or Rituximab which is sold as Rituxan any of these drugs any immunosuppressant is a contra indication to taking a live attenuated virus because now you're what was a weakened the virus to a normal host may become a full blown virus to you.

22:22 So for patients who are immunosuppressant or have recently been treated with immunosuppressant So maybe you're just getting over your transverse myelitis and you're on a steroid taper. Just finished the steroid taper then it is worth discussing the timing and whether or not you should take a live vaccine. For individuals who are not on immunosuppression or have not had a recent exposure to immunosuppression.

22:44 In general I consider the safety risk profile of the live and the dead viruses to basically be the same. So, for an idiopathic transverse myelitis patient I would not personally in my clinic distinguish between those two.

23:03 Yeah, I agree and I think it's worth noting as well that many live virus vaccines are used only in very special circumstances so yellow fever vaccine, oral typhoid or BCG for tuberculosis. These are vaccinations that are used only upon traveling to specific destinations or going into endemic areas.

23:28 So they are not in the vaccine vaccination schedule of the CDC or nor are they anything you are likely to encounter unless you're traveling to an endemic area.

23:40 Likewise the oral polio vaccine which has in the past been implicated with vaccine associated paralytic polio that is no longer used in the U.S... So, among the live virus vaccines that one is likely to come into contact with that would be the FluMist the intranasal influenza and measles and rotavirus which is only used in very very young children. So, so we're talking about a small subset of vaccines that are used commonly.

24:16 And thank you both. And can you sort of bring up you know childhood vaccinations. We've received quite a few questions and concerns around you know if someone's been diagnosed with idiopathic TM How long would you wait
following the acute episode before resuming childhood vaccination and part
two of this is it safe to give you know all the childhood vaccinations the
recommended schedule. Would you spread them out? Would you give them
one at a time? Would you give them the way given? You know there you a lot of
concern around receiving vaccination. Dr. Schreiner, Can I ask you this question
to start us off?

24:58 Yes. Yes absolutely. So, I'll start with the first question that you posed which was
if a child is just getting over what is presumed to be an idiopathic transverse
myelitis when might it be appropriate to resume a vaccination schedule. And I
will second what Dr. Greenberg had said a moment earlier which is if you were
within I would say a month or perhaps two of receiving high dose steroids which
is commonly used to treat transverse myelitis I would probably wait to give
vaccinations until after that time period. And the reason is the high dose
steroids that we use on purpose to calm down the immune systems or to quell
the inflammatory response in an idiopathic transverse myelitis. It doesn't
discern calming down in one area of the body but not in another. And so,
administering a vaccine to someone who has a lowered immune system is not
only unlikely to benefit the patient because they won't be able to generate an
immune response that we're hoping for it with a vaccine.

26:16 But if they are getting for example a live virus vaccine it's risky. And that would
be an exception that I would take but I do believe that everybody should be
getting their vaccines.

26:30 Now the CDC has a very prescribed time period for giving each of the
recommended vaccines and they also have a complimentary schedule which is
OK if you get if you fall behind if you miss a vaccine or six. You know here's how
you go about making up for the delay in vaccination. And so there is a very
formal way of catching up if you have missed a couple.

27:04 Is there any advantage to breaking them up. So, for example you know at four
months two four and six months and I know we're talking about very young
patients here. There are you know five six vaccines that are recommended at
each of those time points. And so, one question I often get is you know I really
don't want to give all of these vaccines on the same day even in a healthy child.

27:32 You know can I can I break them up? Can I do it instead of you know six doses
on at two months and six at four and six at six months can I give half of them at
two months or half of the two months' shots at two months and the other three
months and so forth can I spread them out? Can I give you the vaccinations over
a longer period of time? And I don't think there is a contra indication to do and
that I don't think there's any disadvantage other than perhaps you know most
certainly having more injections spread over a longer period of time. But I don't
actually feel that it's necessary per se even in the case of getting over a demyelinating event assuming you are not immunocompromised. I don't know that there's an advantage to taking a let's say a combination vaccine like diphtheria, tetanus and a cellular pertussis.

28:40 And breaking that down into three injections instead of just one. So, I'm not opposed to it when families come to me wanting to do that but I don't think that there's a strong advantage to doing so.

28:40 Dr. Greenburg any thoughts to add?

29:00 No I mean I agree I think Dr. Schreiner kind of laid everything out quite nicely I will just mention one thing that we haven't brought up yet but falls into this category of delaying or even avoiding childhood vaccinations and that is we do need to remember that the reason we're vaccinating is to prevent some very serious sometimes life threatening conditions like measles like pertussis. We've had outbreaks of pertussis here in Texas that killed multiple infants. We've had a measles outbreak in California going on right now and the people who are most susceptible are our youngest in several cases in fact to my knowledge all of the cases so far have been in people who either delayed or did not get vaccinated. And so, we just need to remember that we are taking risks when we delay. And it's during those delayed times that the kids are most susceptible to the really scary versions of these diseases.

30:04 Now that said I will mention that there are times after an acute transverse myelitis that I do hold off on a vaccination partly because of getting off the steroids but also partly because with vaccinations it's very common for all of us to get low grade fevers because your immune response is being activated against the vaccine and we want that. That's the whole point. But for a lot of our kids who are working through rehab and trying to get into management under control sometimes they'll say you know what let's just wait a couple months. If it if we have the luxury of waiting so that we don't derail or take away from any of the rehab during flu season however for all of our patients, we want them vaccinated. It's a killer virus that can be done. And the worst thing that would happen is during recovery after an event to get actual flu would actually just set people back tremendously.

30:58 So we advocate for flu. Thank you both.

31:03 There was you know very very clear response to the questions that we get asked a lot. So, you know talking about a combination vaccine even within kids in adults some people are traveling or people are getting safe flu and hep B you would sort of say the same thing that it's you know is it safe to have you know
multiple vaccinations when you're traveling abroad if you've been diagnosed with TM? Yeah, I'd tell you in general the answer is yes.

31:34 I would just say that people need to be prepared for this phenomenon. During that low-grade fever, you know could their symptoms transiently worsen. So, I definitely have patients who've had transverse myelitis who get a vaccine home or abroad or anywhere for a few days after old symptoms become more intense and everybody worries about a relapse occurring or brewing. You know we look at these folks we don't find any evidence of new information but it's pretty common with those low-grade fevers just to have cold symptoms come back. So, if you're doing it for traveling you just need to be aware in the days after vaccination you may not feel so great but it should wear off.

32:11 And that's a great point you bring up because people have asked you know are you aware or in your practice you know having a recurrent attack after receiving a vaccination. And in many cases as you say it's just the worsening of symptoms. At what point do you sort of differentiate between worsening of symptoms and a recurrent attack.

32:33 Well I can tell you our approach and I welcome. Dr. Schreiner’s comments on this as well because everybody I think has a slightly different approach. So, in general when we have a patient who's had prior inflammatory neurological disease, transverse myelitis, ADEM, Neuromyelitis Optica, contacts for clinic or presents with symptoms. They fall into two categories from the outset there are either symptoms that have been experienced before or they are symptoms that are completely new. So, for example if somebody's transverse myelitis gave them leg weakness and numbness five years ago, and they come in with a recurrence of weakness and numbness in those legs then that would fit into a category of it's the old stuff returning. Whereas if they come in and say my right arm isn't working and I never had the right arm issues then it's in the latter.

33:27 For the latter, we always presume it's new information until proven otherwise. So, it's an area of the body that's never been affected is affected that we work that out as a relapse. If somebody comes in and it's a reemergence of old sometimes in our experience statistically it's almost always something else going on. Not new inflammation. This is something called Raynaud's phenomenon. So, either there's a urinary tract infection or there's a sinus infection in there they haven't been eating well they're dehydrated. They haven't slept well maybe they got a vaccine and their immune system is activated but something to throw their compensation off such that old symptoms become more pronounced. In my experience, we definitely have had that occur after vaccination. I have had several of my patients who in the couple of days after a flu vaccine have had an intensification prior symptoms. I personally have yet to document for any of my idiopathic transverse myelitis patients a single...
recurrence after vaccination. I am not aware one but I would definitely welcome Terri’s perspective on this.

34:33 No I agree I have not seen a recurrence of transverse myelitis following vaccination or even illness. After just an idiopathic TM So meaning I have not seen new symptoms develop in a patient who has had just an idiopathic transverse myelitis. I do agree that anything that really disturbs the homeostasis of a patient who has had a priority demyelinating event is going to cause a unveiling of return of symptoms that they have had in the past. And so when I receive a phone call from a patient or a family of a patient who says you know these the patient is experiencing these symptoms. Yep it's the same stuff they had a year ago, two years ago, five years ago, then we had to launch into an investigation of what’s disturbing the homeostasis is the patient. Well do they have any sick symptoms.

35:32 Is there any sign of a urinary tract infection? How have things been going? Sleeping well? Eating well? and so forth. And most often that is where we find the explanation. There's something that has caused the unveiling of those symptoms from before and once you attend to whatever that cause might be the symptoms abate and then the patient will return to their previous prior baseline duration of symptoms can also be a clue. So if there is some disturbance of homeostasis there's something going on and we attend to it and the symptoms still don't improve and we need to think a little bit harder about that. And if there is any new inflammation going on it's going to last more than 24 hours and so it's not going to be something transients that resolves within five minutes or 45 minutes or two hours or whatever.

36:35 Great thank you. You know I have about four questions that are about specific vaccines and the first one is about shingles. Most people are being told. I mean the question is the primary doctor won't give it to me until a doctor who knows TM clears me since it's a live virus. Should I get the shingles shot? We've had a few questions about shingles. Do you have any thoughts about shingles specifically Dr. Greenburg?

37:04 I think shingles hurts. That's my thought about single specific thing. I don’t want to get it.

37:10 But in seriousness it's a live vaccine so it fits into that category that I discussed before relative to it’s probably got the same safety profile as the Killed vaccine. Relative to risks for transverse myelitis or triggering an event. It's got its own safety profile in terms of can people get mild cases of shingles with it that’s extraordinarily rare. But in terms of triggering neurological events it's got a very good safety profile. Now when talking about vaccinations you know we lump them we send a lot of time lumping them all together. And I think it's a good
idea to talk about some of the nuances for each. We mentioned that for example flu vaccine is different every year. The shingles vaccine is the same all the time.

37:54 But the other thing that is different about these conditions is about what we're trying to protect against. So, there are certain conditions we're trying to protect against. I think measles and flu are great examples where they are highly contagious.

38:11 They can spread from person to person before an individual is symptomatic and they are both linked with various serious complications neurologic complications. And we have to remember that between 30 and 50,000 people die every year from flu or flu related complications. So these are serious life threatening quality of life threatening illness shingles which for most if we're talking about adult populations the shingles vaccine is being given to people who had chicken pox as a child and it is being recommended to reduce the risk of having a shingles outbreak later in life. Shingles a painful blistering rash. It can be associated with neurologic complications although they are relatively rare. It's just really painful to get in so in the adult populations if I have adult to for any reason they you know I'm just not interested in this. And shingles vaccine it doesn't represent the same level of outright concern to their health and well-being frankly as flu or measles in terms of risk to life or limb now in children.

39:21 It's different. The reason we are vaccinating children is to prevent them from getting chickenpox varicella which the primary infection is associated with neurologic complications. So even kids who have never had a chicken pox exposure I put the shingles vaccine into the category. We should get it as long as you're not on immunosuppression in the adult. And I'm open to the conversation of saying it you know. You know the risks and benefits them and make a decision. All indications are vaccines are not made equally and so I think we have to take each one and I think Shingles is a good example.

40:04 And Dr. Schreiner What about MMR? I mean there have been a few questions about MMR vaccine. People are terrified to give it you know give boosters after one for example you know have there been any studies that have link MMR with any one of these demyelinating diseases?

40:23 There have been studies looking at MMR which is measles mumps and rubella. So vaccination one vaccination against three different diseases and study studies looking at not only MMR with separate immunization of varicella but also the vaccination that is MMRV which is all four of them together in one shot. And I don't know of any evidence that has linked that with an episode of demyelination. What is associated with the MMR vaccine is an increased risk of febrile seizures particularly in young patients but even so it's a risk that less than
1 percent of all vaccinations. I think that's point three percent. But there is that risk that seven to 10 days after the vaccination with an MMR particularly because of the measles component that their child would be at risk for a febrile seizure. And there are other side effects not neurologic side effects that have an associated rarely with MMR as well. But I think again to sort of reiterate what has been said the benefit of being vaccinated against MMR and all through varicella in there as well outweighs any of these risks.

41:53 And so I am a proponent of using either MMR with the separate varicella or doing all four together in the MMRV.

42:02 The one aspect of vaccinations that I think has led to some degree of comfort in the population presently is this thing called herd immunity. And so, if you vaccinate enough people in a community then the ability of that virus if it breaks into the community to spread and infect people is significantly inhibited because you have a preponderance of people within that community who are vaccinated who will not be able to get that disease. So, there are unvaccinated people in the community who may benefit by the fact that everybody else in the community is vaccinated and they don't have to be until something until an outbreak occurs and which is not the same degree of herd immunity like you know Disneyland in California or whatever where the patients who have not been vaccinated will now be susceptible and very much at risk for getting the disease. That is not just an inconvenience and a rash but it can cause serious side effects.

43:21 Thank you. So, you know we're talking about herd immunity and other important questions that we get asked a lot about pregnancy and receiving the pertussis vaccine which you know most pregnant women are asked to get if someone's been diagnosed with transverse myelitis prior to becoming pregnant. You know should I mean should there. Should they get the whooping cough vaccine in general.

43:47 I would say yes. I think it's going to a tremendous safety record. We don’t know of a specific association with these neurologic conditions. And based on the fact that we are still seeing infants at each year dying from pertussis we have to remember the reason for vaccinating mom is to ultimately protect the baby.

44:08 And so it's obviously a personal choice but I think the safety and the benefit of far outweighs the risk and I would agree I know of no evidence of you know risking a bringing a risk to either a pregnant mother or her fetus by vaccinating with either an inactivated virus or a tetanus toxin late for example.
And on this point, I think it's worth to reiterate one other aspect of this and that is from my perspective there is nothing we do that is risk free. So, I'm not here on the podcast to say vaccines are 100 percent safe.

They're never ever going to cause a harm take it because it's only good enough that we fully accept that there are unknowns out there in there are unknown.

That means there is a potential risk but we also have to put it into the total view of why are we doing it and what the potential benefit if we look elsewhere in medicine for hints of what we're willing to do. without really give it a lot of thought. It's pretty interesting.

So for example anybody who's had a heart attack he's going to go on aspirin or another medication and people will go and buy aspirin and take it every day and really not give it much thought. But the percentage of people who have major bleeding events is been statistically defined. We've seen it in every study. They can be life threatening life changing events and that rate is statistically going to be a long fold higher than the complication rate of vaccinations because we're having a hard time even measuring the impact of vaccinations and yet with the aspirin we can do it.

And yet there's not a as much thought given to aspirin or major bleeding risks in patients who've had heart attacks or diabetics trying to prevent the vaccination world has come under scrutiny for a lot of different reasons. All of them legitimate but we have to keep the relative risks in perspective. Unfortunately, this area I think has been mired by some bad science in the past and even some science with political motives on both sides of the coin. And when trying to weed through what's out on the Internet about any of these issues it's a very scary and concerning area with people being adamant about certain things. And it's also hard from a human perspective if you've had a health event after anything after a vaccination or I hear the same thing after procedures. I had surgery and then two weeks later I had transverse myelitis and the surgery caused it.

It's very hard for us to ever shake the feeling that there was an association. But when we take a step back in the science it's been hard to prove that if there is one it it's going to be a very small one. thank you that was very helpful.

The last specific vaccination that we've gotten questions about is pneumonia vaccinations or the adult Pneumovax. Anything you've heard any research that suggests one shouldn't get the adult Pneumovax vaccination? I think I'll defer that one to you.

Dr. Greenberg Yeah we've been using the pneumonia vaccination which is actually a combination of different types of the Streptococcus pneumoniae
bacteria which can cause significant pneumonia or even meningitis. And folks it
doesn't prevent all pneumonia is that specific to certain organisms. I am not
aware of cases of transverse myelitis associate with the Pneumovax I don't think
there have been reports of events following Pneumovax I don't think it would be
at a higher disproportionate rate than we've seen with any other vaccination
frankly and probably falls within the category of just what we would see by
coincidence.

48:37 The specific safety record of Pneumovax I think has been one that's been
extremely good thank you.

48:49 And so now I was sort of left to sort of change gears and talk about you know
research and study so you know are there any studies that are being done to
even show or are there any correlations between vaccinations and rare
neuroimmune diseases. You know where are we understanding and increasing
awareness about you know a link or no link you know getting some clarity on
these issues.

49:18 Well if I can make a plug for two things at this point around that issue and then
also get your input on different research going on all jump out. So, one plug I'm
going to make is there is a currently enrolling study for transverse pediatric
transverse myelitis patients called the CAPTURE study which the TMA has been
a lead advocate for. And what we're looking at is outcomes in children with
transverse myelitis we're specifically looking for kids with in the first few
months of their illness. So, if you hear if anyone on the call hears of families or
friends while we hope that's not the case if that does occur. Please get them to
the TMA to get signed on to the CAPTURE study part of the data we are
collecting is about recent vaccination or infection and just we can keep track
and it's one of the ways return to collect data.

50:08 The second plug I'll make is here at UT Southwestern we do have a longitudinal
study going for both transverse myelitis and Neuromyelitis Optica where we are
collecting vaccination data in trying to get a sense as to the relative rates of
post-vaccination events and is it higher than expected or is it typically what we
would expect. One of the national approaches to this and I can with Dr.
Schreiner talk about this is not a great one. It's called the VAERS system a
Vaccine Adverse Event Reporting System and Terri is this something you can
speak to it and give an explanation of yeah, I can I can talk to that.

50:52 So the VAERS Vaccine Adverse Event Reporting System is a monitoring system
established by the Centers for Disease Control and Prevention as a repository
for anyone to report any occurrence any health issue happening within a time
period surrounding vaccination. So, it is a self-reporting database so to speak.
So, the data is only as good as what people report but it is a means of bringing
to a national body attention of something that may have had may have been influenced by having a vaccine. So, this is publicly available data I looked at it last night. You can you know query I think there are 15,000 events in the last year most of which were you know rash and skin type reactions but I could tell that. But it is it is publicly available but it's also reviewed by the CDC to see if there are any trends in what is being reported.

52:19 So this is something that I would encourage. If you or someone you know you think has had an event that could be related doesn't you know obviously, we've discuss the difficulty and causation. But if there is something that has happened in proximity to a vaccination this would be one way of reporting it but bringing it to a national, to a body to a governing body. The other thing I will say about research in this area is that it's very difficult because we're looking for occurrences that are already very rare. So, we have you know millions of people getting vaccinated. We're looking for a very rare occurrence like transverse myelitis optic neuritis whatever. And so, what we so the studies that have the most robust data are studies that have been done in countries like Denmark or Sweden or even Canada where they have 100 percent catchment.

53:25 So they don't have an Aetna and Blue Cross and you know care is provided within a national network so everything can be collected and reviewed in large numbers and so the data that we have that we feel pretty confident about when we look at the potential impact of vaccinations comes from those very large systems. You know an entire country of people being vaccinated. The most recent of which was a study that just came out about the HPV human papilloma virus that we haven't talked about yet but this particular study was done in Denmark and Sweden over let's see a seven-year period and they looked that all everybody that was vaccinated and everybody that was unvaccinated.

54:21 And then whether or not there was any difference in the number of people who developed multiple sclerosis or any other demyelinating disease between those populations. And they found that there really was not any difference and so, this is a study that involved. Oh, gosh a million over about approximately four million people. And this is the kind of data that we feel good about when we know that we have looked at that many individuals being vaccinated and we have some and we don't see any indication that there is a link between a disease and the vaccination.

55:05 Great thank you. Thank you for also covering the HPV vaccine question that we know we do get asked often about sort of in the last couple of minutes that we have during this podcast you know would you would you each be able to give us sort of take home messages that we should be thinking about and be aware of. Can I start with you Dr. Greenberg?
55:30 Yeah I think the take home message is based on my reading of the data and the experience is that the mainly online very strong I dare I say opinionated concerns over vaccines. The I think has crept into our mindset. And I think exaggerating the issue that is while potentially possible much smaller in existence and in than anyone suggests. And one of the things I'll remind people is when you think anything has caused a bad harm whether it be a procedure or a car accident or a vaccine or a bad piece of sushi you are twenty times more likely to post about it online or write about it or get involved in an action about it than for people who just have an event with no identifiable cause. And so, we don't hear from the masses of people who just had transverse myelitis with no vaccination beforehand because they have no reason to post.

56:42 And that's the overwhelming majority of patients. And so, while I think as a scientist I have to absolutely concede the biologic possibility of a link. The practical implications of that based on the data is say while there is risk the benefits of vaccination far outweigh and are quite quantifiable the potential risk both to ourselves our families and loved ones in the greater community as well as individuals who've already had an event. I think the safety continuing with vaccination and the benefits that are achieved far outweigh the risk.

57:19 So we are not blind or ignoring the potential link but I think the data gives us a very reassuring place to be

57:29 And I would agree I think as we look at any medicine to start any action to take any anything in our lives we always have to balance the risks and the benefits and without causing alarm I would I would like to remind everyone to think about the risk that does come with infections with primary infections of these diseases for which we now have vaccines. So, there is there is a risk of not vaccinating. It is it can be severe whereas we have a preponderance of evidence that shows that the risk of ill effect after vaccination is really quite small compared to the benefit. And so, I would I would encourage a weighing of those options not only with vaccinations but truly with everything in life we have we have choices.

58:33 But in this instance, I would recommend vaccination and I guess I'll throw in one caveat as well which is that we are doctors but we are not your doctors. And so, having a discussion with your care provider about this as well would be something I would recommend so that you have a partner in the decision making about the risks and the benefits. I hope this has been helpful to you.

59:09 This has been fantastic thank you both. You've been really really helpful. And thank you for tackling what is clearly a very controversial and very difficult issue as you said you need a partner in making these decisions. You know this podcast will be recorded and made available for those who haven't been able to listen in
live to this conversation. And it also downloadable on iTunes. And thank you both. Thank you, Dr. Greenberg. Thank you, Dr. Schreiner, for giving us your time and for making this a very interesting.

59:44 Thank you. Thank you.