Q&A and Closing Remarks

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[00:00:04] **Dr. Carlos A. Pardo:** We have approximately 35 minutes, and in the next 35 minutes, what we are going to do is, we are going to wrap up with questions and answers. And first, this is one important part of our activity and symposium, is we like to make sure that when you go home all your questions are answered. If we don't answer that, you will come next year for the next symposium, and we will try to have another answer. All right. Remember ACTG, write down that, because I will disclose what means ACTG for myelitis. ACTG, those are the four magic letters of the genetic code, so our DNA is a combination of ACTG, but you will learn about ACTG later. All right. Roberta, do we have any equation from our virtual audience?

[00:01:15] **Audience Member:** Yes. We actually got one for you, Dr. Pardo. They're asking if you could please elaborate on the TM change to just myelitis which is also a broad term. If there is any additional explanation, for example, saying something about diagnosis, viral infection, spinal cord stroke.

[00:01:39] **Dr. Carlos A. Pardo:** Yeah. So, the first day I mentioned that the term transverse myelitis is extremely misleading, because it's taking away the opportunity to do a very thorough assessment of the cause of the myelitis. So, what we are going to be proposing for the future is to keep the term transverse, I'm sorry to keep the terms myelitis and get the term transverse ditched in the trash can, so in other words we are going to keep the terminology myelitis. What we need to do as clinicians is we need to understand what the cause of myelitis was. It was MOG, is NMO, is an idiopathic myelitis, we don't understand what is going on, it's a genetic myelitis. So, after myelitis we are going to insert the last name of the myelitis, is supposed infectious myelitis, is a myelitis associated with a viral infection, is a myelitis associated with autoimmune disorder, like MOG or NMO, is a myelitis associated with a demyelinating disorder like multiple sclerosis or it's a myelitis that is coming from a genetic disorder like was described before.

[00:02:55]: So, in other words, we are moving from a very generic term like transverse myelitis to a more precise definition of the cause of the myelitis, that's basically the purpose. We are trying to wrap up a discussion that we had in the past few years for redefining the criteria, the diagnostic criteria for myelitis. For example, there are a group of myelitis that are mostly autoimmune and that's the most frequent group at this moment. But there are other spinal cord disorders that look like myelitis, like a stroke of the spinal cord and the term that

we are going to use for those are vascular myelopathies. So, that's basically the generalization and trying to have a better definition of myelitis. Great. Question from the audience here.

[00:03:50] **Audience Member:** So, by doing that, will that not cause more barriers to access to treatments?

[00:03:55] **Dr. Carlos A. Pardo:** Actually, the answer to that is no, because if I do and sign in my clinical report transverse myelitis and I asked for a specific treatment for NMO, what is going to be the answer from the insurance company? Is no, this is no indication for specific treatment. So, if we tell in our diagnosis, you have neuromyelitis optica, is a better chance to get basically approval for the medication that we have for neuromyelitis optica and the same for other type of myelopathies. So, I don't believe we are going to create barriers, I think that we are going to be more precise and facilitate a better treatment of our patients. Any comment, Melissa, about this in pediatric neurology for example?

[00:04:45] **Dr. Melissa Hutchinson:** I have recently noticed in the last year that I have an option to choose MOGAD as a diagnostic code. And so, I think this has to be a discussion across the insurance companies, across the people who build our electronic medical records, across our community. And honestly, it can be really confusing to read the literature as well if people are using different definitions of different neuron inflammatory diseases. And you're like, "Well, how do I apply this to myself? I don't know, I have a patient in front of me, but which category are these researchers using?" So, I think having a standardized definition improves access in those ways as well so that we can all be speaking the same language when we're doing our research studies, when we're coding our patient charts and talking with insurance companies as well and talking with each other.

[00:05:32] **Dr. Carlos A. Pardo:** One of the examples for being very precise is acute flaccid myelitis. Until a year ago we didn't have a code for acute flaccid myelitis. And parents of patients with acute flaccid myelitis were denied care because there was no diagnosis of acute flaccid myelitis, so that's the reason. Great. Any other question from the audience here.

[00:05:56] **Audience Member:** So, does that mean those of us with idiopathic myelopathies have to go form our own group?

[00:06:02] **Dr. Carlos A. Pardo:** The answer is no, and Kyle is answering the difficult questions. Kyle.

[00:06:10] **Dr. Kyle Blackburn:** No. So, I think the ultimate goal of all of this, and periodically definitions need to change in medicine as things become updated. So, I like to tell a lot of people when we start this discussion, we last updated the criteria and defined the term idiopathic transverse myelitis, which when most people say they have transverse myelitis, that's actually what they mean, we just make it shorter, we just say transverse myelitis. That was defined in 2002 and we discovered the aquaporin-4 antibody about two years after that. The MOG antibody, we really kind of recognized its importance 10 years after that. Acute flaccid myelitis emerged as an infectious disease, and we want to create an environment where the definitions are updated and also recreate the criteria to include these disorders that weren't around in 2002, so to make sure that clinicians are also doing the appropriate assessments, to make sure people get the treatment they need in the time that they need. So, if your diagnosis was transverse myelitis and that seems to stick and after a thorough evaluation there was no other cause, there's still idiopathic myelitis and I think that's still going to be well covered by the SRNA. That's still a group that requires a lot of investigation.

[00:07:42] **Dr. Carlos A. Pardo:** And actually, I'm going to shoot the ball to the other side. So, Janet is changing the perspective of transverse myelitis to a more precise a theological diagnosis. Is that going to help both of you at the Kennedy Krieger to treat patients?

[00:08:02] **Janet Dean:** Is it on? So, for rehab, I don't use those diagnoses, I use tetraplegia or paraplegia. So, I look at the functional outcomes of those conditions, and so the actual neurologic condition is kind of secondary. And the other thing that I see sometimes is people come and have one diagnosis here and one diagnosis there as neurology is kind of trying to establish new criteria. And what I tell my patients is, "That doesn't really matter to me, I just want to know about your function. If you're having bowel and bladder issues, I'm going to treat that. If you're having a lack of sensation, we're going to make sure you know what to do for that." So, for Kourtney and me in the rehab part, and if you've got paraplegia, she's going to do therapy and it doesn't really matter what caused the condition that affected your spinal cord or your brain

[00:09:04] **Dr. Carlos A. Pardo:** Courtney, did you agree with that?

[00:09:08] **Courtney R. Porter:** I do agree with that. I think that we, from a therapeutic level, I'm going to look at where you are functionally. I'm going to see where you have limitations, where you have strengths and work on you from there. I think that your title of your diagnosis from a medical standpoint is important. But when you come to me for a therapy session, it's not the first thing that I am looking at, it's not the part that is as important to my job. The part that's important to me is where are you functionally and how can we improve that?

[00:09:38] **Dr. Carlos A. Pardo:** Thank you so much. There is another question over there.

[00:09:41] **Audience Member:** Hi, as someone with idiopathic TM, is the goal kind of to whittle down, figure out what the causes of this myelitis for each group to kind of make that idiopathic group smaller and smaller as we figure out more and more?

[00:09:41] **Dr. Carlos A. Pardo:** The answer is, yes. So, actually, I like Cynthia's name, the aperture. So, for people that like photography, if you open the infra too much, you got glory, if you close a little bit, there's a better picture, right? So, in other words, what we are trying to do is to force clinicians and healthcare provider to be more precise, and to be more precise means that instead of giving you a diagnosis of multiple sclerosis, people need to go and check MOG and NMO and make sure that there are no methodological problems, rather than jumping and say the easy way, "You have MS. You have optic neuritis, there are MRI changes." And then, "Go ahead with A, B, and C, and I see you in two years." So, that's basically what we are trying to emphasize, that the clinicians need to be more precise. There is an important thing that is very clear, medicine is advancing constantly. In the past 15 years, we got the more precise diagnosis for myelitis, because we got NMO antibody, we got MOG antibody, we got better techniques in MR Is, we got better techniques and spinal fluid analysis. So, we need to evolve in our diagnosis as well. Eventually this is not going to be a final change in the nomenclature that we are going to use for myelitis. Eventually in 10 years, Kyle is coming and is going to say, "No, 10 years ago we were wrong and then I have now the right definition of what means myelitis, idiopathic myelitis." So, again, we are learning every day in the areas that we are studying. Okay, Sandy.

[00:11:51] **Sandy Siegel:** I have two points that I will try to make quickly. So, first to address Allen's concern about whether you might need to look for a new home. This association from the very beginning has been a home, not just to start as transverse myelitis, but very, very quickly we became an advocate for, as we were getting these new diagnoses for all of these related rare neuroimmune disorders, but it never stopped there. I'm going to tell a quick story, there was a very, very young child who came to our camp one summer, he had received a transverse myelitis diagnosis at six months old. And mom, the family was just so relieved when they came to camp and their child was with other children and she was with all of these other physicians and having that identity and that connection is a really powerful thing if you are part of a rare disease community. So, she had that experience, she left camp and she had an appointment with Dr. Pardo, who is one of the most brilliant diagnosticians around in this area, and he changed the diagnosis. And I got a telephone call

from this mom, and she was unbelievably distraught, because the name of what her child had was different from all of the other listed names under our advocacy umbrella. And what I said to her was, "You have home, you don't have a home anywhere else, this is your home. The things that your child is going to go through is a matter of symptom and treatment from here on in will be no different than what a child with transverse myelitis has or any other children who had an inflammatory attack in their spinal cord. So, everything that is relevant to the children that are a part of our community listed by diagnosis will apply to your child, your home."

[00:14:27]: And I will say there are many other disorders, some of which we don't even know, because we don't have diagnoses for everything that where people present with similar types of-- you've spent a whole weekend hearing about all of what we don't really understand about all of these disorders, and Carlos has made it clear we're going to continue to discover new ones. This is a home for people who have similar conditions. So, we've never turned anybody away, so that's the answer, Allen, for your concern. If you, Carlos, let me anywhere near the room when you all sit down to decide how you're going to deal with the diagnostic criteria in the nomenclature, I am going to beg you folks to stop using the word myelitis as a description of a symptom of inflammation in the context of MS, or NMO, or ADEM, because it confuses, just that nomenclature does not just confuse patients, it confuses physicians. GG and I have dealt with this in the surveys that we've administered. So many people think they have more than one diagnosis, because they've been told by a physician, "You have NMO and transverse myelitis or myelitis." Same with ADEM, over and over again from my kitchen telephone I've been telling people, "You only get to have one of these diseases." So, I think it will help to-- I support the idea of what you're describing in terms of a disease category using the word myelitis but using that term to describe the inflammatory symptom in the context of these other disorders is way too confusing.

[00:16:42] **Dr. Carlos A. Pardo:** Message is very well taken. I actually am very curious, because I am an adult neurologist and I frequently see patients that basically come in the setting of a cute spinal cord disorder. But our colleagues in pediatrics actually have a much better view of the world, because they are seeing our patients from the beginning and early stages of life. So, I'd like to ask Cynthia and also Melissa about what is your view? Because you see a wide spectrum of pediatric problems from infectious disorders to genetic disorders. So, give us your impression about how you think that we should approach the diagnostic criteria when we find problems on the spinal cord. So, Melissa first and Cynthia second.

[00:17:44] **Dr. Melissa Hutchinson:** So, when I sit down with a family or a patient, when they are in the hospital for the 1st 24 hours of their acute onset of their spinal cord problem, that's exactly what I talk about. I say that there's a problem with the spinal cord and we need to figure out what is causing that. And that could be an infection and that could be an autoimmune problem and inflammation related to a dysregulated immune system that could be a vascular problem. Kids also have spinal cord strokes as well that could be a traumatic problem after gymnastics class, for example. And the reality is that has to be an open dialogue from the beginning, is, we're going to do a few different diagnostic tests to try to figure out what's causing that problem. And I think when you kind of take away any of the nomenclature and just kind of get down to the descriptive words is when families really understand, what am I looking at and why am I looking at the MR I, why am I looking at the spinal fluid? Why am I looking at other blood tests? So, I try not to even use nomenclature at all in the first couple of conversations, it is too confusing.

[00:19:02] I'm also a very visual person, and so I like to draw a lot of pictures and discuss with those pictures about kind of ways in which the spinal cord can be affected whether it's because of a vascular problem or because of an autoimmune problem. And the reality is, it depends on the clinical context obviously, but most of the time it is going to be a MOG related encephalomyelitis. And statistically speaking and our data shows

the same as about 50% of patients with ADEM are positive for MOG antibodies. And so, once you can drill down into the cause of it then I think it's more appropriate to add the nomenclature in the actual descriptive words in so that you can choose those words based on where you are with that patient at that time. I think I have a distinct advantage of having these tests available when diagnosing patients for the first time, because certainly patients that have been diagnosed years ago when the tests weren't available, they didn't have the ability to be have an understanding of that autoimmune process at that time and now adding in that piece of science is a little bit more difficult especially if they've built their identity around that for a while.

[00:20:33] **Dr. Carlos A. Pardo:** Thank you, Melissa. Cynthia.

[00:20:37] **Dr. Cynthia Wang:** Thank you. I think it's a great question, I definitely can relate with a lot of things that Dr. Hutchinson said. I think the importance of still keeping some of those terms is that the families will have to see other physicians and that is something that they can understand. And I think it's also important to know that an inflammatory myelitis versus a myelopathy, because it puts us in the framework of what can we do to help improve the condition of this person. I think in some cases where it's idiopathic, but we know it started really quickly. Like Dr. Pardo had mentioned, sometimes the therapies that we would use to treat inflammatory spinal cord disorder can be actually harmful. If we do plasma exchange, we can drop the blood pressures even more when the body is trying to compensate by increasing the blood pressure. So, I think there's still a role for those, and then in the antibody related conditions, again, we might not know if you're a MOG, if you're NMO until after the patient leaves the hospital. So, I think for some purposes, those terminologies have to stick around for now, but it's probably in the setting of seeing in a specialized neurologist that they will do some education to clarify, this meets this syndrome more than the specific symptom.

[00:22:00] **Dr. Carlos A. Pardo:** Thank you, Cynthia. There are some questions from the virtual audience.

[00:22:05] **Audience Member:** Yes, there are quite a few. So, is IVIG worth considering as a treatment for MOG fatigue? In addition to being a preventative treatment, what are the best ways we have found to treat fatigue?

[00:22:05] **Dr. Carlos A. Pardo:** Kyle, difficult questions coming to you.

[00:22:20] **Dr. Kyle Blackburn:** Excellent. So, in general, fatigue and talking about symptoms that overlap among different disorders, if you put 100 people with a rare autoimmune disorder, have different types in a room, probably 95 of them would raise their hand if you ask, "Do you have fatigue?" So, it's a very common symptom. For the vast majority of cases, it is not necessarily an indication that the disease may be active, it can be a consequence of the disease. So, we see people who have, for example, I think Dr. Harder was talking about this, idiopathic transverse myelitis, what we think is a one-time event, but we still have a lot of fatigue. So, unless there is evidence of activity on an MRI or a relapse, we don't necessarily change treatment for fatigue, at least in terms of immunotherapy like an IVIG, for example. Fatigue has a lot of different causes beyond just having a neuroimmune disorders, so I think it's important to screen for those.

[00:22:30]: In many of our patients we're thinking about, we often are asking them about healthy habits, sleep being one of the key ones. I think everybody recognizes your energy levels are different if you haven't been sleeping well. So, sleep is something that we harp on a lot and make sure people are getting adequate sleep. Certainly, making sure there isn't another medical condition like a thyroid condition or anemia causing fatigue or worsening the fatigue is important. So, if all of those things have been ruled out and fatigue is still a bothersome part of someone's life, and certain lifestyle modifications like, kind of using the using the spoon model that was discussed earlier, you're still using your spoons up at the end of the day, in certain

instances, doctors will use certain medications. All of these medications are off label, and those can range from anything from certain supplements to certain medications that are classically stimulants depending upon the type of fatigue.

[00:24:38] **Dr. Carlos A. Pardo:** So, following the question on fatigue, I had one of my patients recently just say, "I don't want to go to physical therapy, because I have too much fatigue." So, Courtney and Janet, how do you deal with fatigue in patients going to rehabilitation?

[00:24:56] **Courtney R. Porter:** Yeah, I mean, like you said, I think it's a common thing. I think a lot of our patients do hit that point of fatigue and that's part of my job at the same time, is to make you fatigued, because part of my job is to work you and exercise you and get those activities in. My goal is not to push you to the point that then you can't do any other activities that day, that week, however long it may last. But my goal is to kind of find that balance and teach you how to find that balance of, I can do these activities, these activities are going to help me get stronger. So, maybe if that fatigue is from a muscular level it sets in later. If that fatigue is from more cognitive things, it's usually handled by our lovely doctors, but if that fatigue is coming from a muscular level where your body is just done, my job is to fatigue you a little bit more and work on those muscles and get you stronger in that sense, so that hopefully that fatigue maybe starts later in the day. Maybe you can learn to do this activity a little bit easier or for longer so that fatigue doesn't hit you quite as hard and quite as quickly

[00:25:59] **Dr. Carlos A. Pardo:** Janet, anything else? Okay, great.

[00:26:04] **Audience Member:** Thank you. We have two questions for Dr. Wang. My daughter was originally diagnosed with leukodystrophy due to extensive symmetric bilateral lesions and multiple cystic prominent perivascular spaces on MRI. She was later found to have MOG antibodies and her genetic testing came back negative for leukodystrophy. She's had significant lesion resolution, but follow MRIs always mentioned the prominent perivascular spaces. Have you seen other MOG patients with these prominent spaces on MRI who don't also have a genetic condition?

[00:26:41] **Dr. Cynthia Wang:** Yeah, thank you for that question. So, are usually the remnants of history of brain inflammation. So, I don't think it would be necessarily specific, there are certain genetic white matter syndromes that have larger cysts, but I think if the person had earlier, with MOG titers were still in that beginning stage, but it does seem to depend how high those titers are. If it's a low titer, it might not be significant, but I think the number that we were giving out is, if it's over 1 to 1,000, that's really highly suggestive and specific. And in the context that it sounds like the lesions improved over time, I think it is most consistent with that diagnosis.

[00:27:30] **Audience Member:** Thank you. And another question that came in for you. My daughter had ADEM when she was 11 turning 12 in the hospital, she's now 21. She started having seizures five years post ADEM. Do you see this often? And if so, what would cause this five years later, she has been taking Lamotrigine for the last three years.

[00:27:50] **Dr. Cynthia Wang:** Yeah, that's a great question. I would be interested if this person's daughter had seizures in this beginning stages during the ADEM and if it was hard to control. Sometimes there can be enough kind of glucose or scarring in the brain that you still can have the risk of seizures, but sometimes we see other conditions, I think it could be something like an epilepsy syndrome. So, I think probably that warrants investigation, hopefully, they've had that. So, I would say, don't expect that those are necessarily related and have a neurologist weigh in.

[00:28:32] **Audience Member:** Thank you. And another question that came in regarding the conversation that was happening earlier. For those of us who were diagnosed a long time ago. Do we need to try to get a "new diagnosis" that is more accurate? I was diagnosed with TM in 2003.

[00:28:50] **Dr. Carlos A. Pardo:** A very good question. So, if this was "TM" that happened in 2003 and after that there has been not any other neurological problem, I think at this moment, probably going and trying to identify more specifically an ethological cause or cause of the problem is going to be challenging. However, if there was an event in 2003 and there are more problems emerging after that, related with neurological symptoms, visual symptoms, optic neuritis, and other things, it's extremely important to reassess what was the original diagnosis. In 2003, we didn't have markers like reporting for neuromyelitis optica, we didn't have MOG, for MOGAD. And again, so, it's important to clarify what is the time profile of whatever is going on neurologically and if there are new symptoms after 2003. Any other questions from the audience.

[00:30:02] **Audience Member:** Yeah, I was wondering if it's some sort of excessive exercise like jumping on the trampoline or long bike rides or things like that could have contributed to the TM or if it's more from like an infection or something like that.

[00:30:25] **Dr. Carlos A. Pardo:** Kyle, do you like to take that challenge?

[00:30:28] **Dr. Kyle Blackburn:** Sure. In many instances when I think of somebody jumping on a trampoline, I always worry about an injury to the spinal cord in a different way. Now, I'm not saying usually that would happen shortly after somebody was jumping on a trampoline, like a fall or in rare cases that could dislodge a disc that could then cause a stroke of the spinal cord, but for the most part that would not be thought to cause inflammation in the spine. I think I want to make sure I got the other part of the question.

[00:31:03] **Audience Member:** No, well, it was just a jogging trampoline and I go jump on that for an hour or something like that or ride a mountain bike for four or 5 hours, just any sort of excessive exercise. I'm just trying to rule out some things that have been suggested to me.

[00:31:31] **Dr. Kyle Blackburn:** I think I understand. While some of those things, certainly if there was, like I said, a fall or trauma or you felt a pop or something like that and that was a very alarming part of the story, those can be clues sometimes that can lead us to start thinking about a vascular cause, blood flow being cut off, but we wouldn't expect those to cause inflammation of the spine. I think you are right; we start to think about possibly signs of an infection in the days before and things like that more so.

[00:32:24] **Audience Member:** Thank you. Also, as far as giving a sample of blood, to get things nailed down closer, I got an arm right here, I'm willing to volunteer some or if there's a place to go to, to go ahead and do that, do I do that to my regular neurologist or something?

[00:32:24] **Dr. Kyle Blackburn:** Well, that's a great question. So, I think giving blood for research is great. Unfortunately, here, I don't think we have a phlebotomist or anybody that can help us with that, but that's gracious. But I do know that some of our organizations in the past have had research studies ongoing where they would collect blood in people. So certainly, if you ever did visit one of our sites, there'd be an opportunity to give blood. But as far as for a routine clinical diagnosis, I agree with what Dr. Pardo was saying earlier, many, many years out of somebody has been neurologically stable, pursuing a workup for secondary causes at that point, if there were an infection that infection has long cleared, I can't detect it at this point. Even in our kids that have a very, very suspicious acute flaccid myelitis and we're looking at it and everything lines

up perfectly, we can still see negative testing for that virus, but with our current techniques and it may just be that the virus is cleared at that point, at least in the ways that we can detect it. So, these things can be hard to nail down, and if you've been stable for a long time, going back and getting a bunch of blood work or spinal fluid testing purely for clinical purposes probably isn't needed. But if you do want to contribute to research, certainly somebody will take you up on that.

[00:33:50] **Audience Member:** Yeah, thanks. I'd just like to ask, it's a bit of an old question. My diagnosis was five years ago, I heard it then, and I still hear it in in chat groups. Is that if you've got TM or IM now, your recovery is pretty much going to be set at a threshold after about 18 months and then that's about it. Even if that was true five years ago, I wasn't inclined to accept it and I still expect to do better from one year to the next, after five years. You did make some comment about the recovery, tending to be thresh holding and I know my gain over the first year is going to greatly exceed my gain in the fourth or fifth year, but is there any absolute threshold?

[00:34:38] **Dr. Carlos A. Pardo:** That's a very interesting question. And again, I have the privilege to have Courtney here who is working in the Kennedy Krieger working with many of our patients that have had problems 10 years ago, 15 years ago. And Courtney has the right answer for that.

[00:34:54] **Courtney R. Porter:** Yeah, like you said, at our clinic, we see people back year after year after year their injury and we still see progress year after year, after year. Sometimes it's lower, sometimes it's smaller progress, but the beauty of coming back and getting check ins is we can really fine tune some of those things and say, "This is the area that I'm still feeling really weakened and this is what I want to work on." We can hone in on that one specific area and then work on that for a while and we do still see that progress many years after injury.

[00:35:25] **Dr. Carlos A. Pardo:** And I will emphasize in that aspect is, we are not able to say that MRI is going to define what is the prognosis. Now, the only thing that is able to say is the way that you are basically going in your recovery and there is recovery even 10 years after the myelopathy. So, in other words, never stopped your plan of rehabilitation and physical therapy, never, because number one, you need to keep going and regenerating nerves and trying to basically get good stamina, and second, you need to sustain the gains that you have acquired in the first few years after the TM.

[00:36:11] **Janet Dean:** The other thing is that activity is important for everything you. And so, whether you're doing rehabilitation, formal rehabilitation, finding ways to be active, because activity is important like there's nothing exercise isn't good for it's good for your brain, it's good for your heart, it's good for diabetes, it's good for everything. So, finding activities that you can do to keep yourself active, keeps your brain healthy, keeps lots of stuff, your bones and all of those things healthy. So, it is really important to not let limitations stop you from being active.

[00:36:55] **Audience Member:** Another question here, are there any common vitamin deficiencies among these disorders?

[00:37:02] **Dr. Carlos A. Pardo:** Very good question. Melissa.

[00:37:09] **Dr. Melissa Hutchinson:** So, when I talk to my patients in the neuroimmunology clinic, I certainly talk about how there are lots of ongoing research and diseases such as MOGAD in terms of vitamin deficiencies, but the most well studied neuroinflammatory condition being multiple sclerosis has an association with low vitamin D. And so, my ask is for my patients to take over the counter vitamin D and to follow those levels, not because they have multiple sclerosis, but because there is some data mostly within multiple sclerosis, but

within the neuroimmunology literature suggesting that vitamin D levels do support the immune system in ways that prevent ongoing neuro-inflammation. To my knowledge, those studies are still being done in MOGAD and other neuroimmune populations, but I don't think that there's anything that's been conclusive so far.

[00:38:08] **Dr. Carlos A. Pardo:** Vitamins are very important in our central nervous system, and actually, there is one important vitamin in our world that is called vitamin B12 that actually is frequently associated with spinal cord disorders that mimic, occasionally, myelitis, and mimic other spinal cord. Vitamin B12 deficiency may produce many things, anemia, may produce other type of disorders, visual changes, optic nerve changes. But among the vitamins in addition to vitamin D, vitamin B12 is the other one that is important. Go ahead.

[00:38:46] **Audience Member:** I had a question about an angiogram that is how my husband's TM. Was diagnosed with a lesion. Would it be too risky, or would you recommend having another angiogram after a year and a half, two years to see where the lesion is or has recovered?

[00:39:08] **Dr. Carlos A. Pardo:** I will take that question, because it's one of the areas that I do work. Angiograms for understanding the blood supply to the spinal cord are very tricky and that is one of the difficult parts of our practice, need to be done by skillful neuro-radiologist or interventional radiologist. And the angiogram needs to be actually very comprehensive, particularly if the clinician is suspicious for a stroke of the spinal cord. The angiogram should be directed to understand if there is any occlusion of small blood vessels or large blood vessels. The problem with acute spinal code strokes is, our blood vessels are very dynamic to the point that sometimes even after after a few hours, few days, a few months the blood vessel reconstitute, and the blood vessels actually may appear to be normal. So, sometimes it's difficult to even identify occlusion in blood vessels. If the cause of the stroke was a large blood vessel like the aorta or there is aortic aneurysm it's very easy for the radiologist to identify that problem. But again, it depends basically, how high the certainty of stroke of the spinal cord is suspected. There is one condition that is dural AV fistula, as the malformation of arterial structure and venous structure, that again, those are sometimes very tricky to detect. So, again the summary is, unfortunately, it depends on the technique and the skills, and unfortunately the MR A, the Magnetic Resonance Angiogram is not going to replace the standard approach at least for evaluating the spinal code. There is one question from the virtual audience.

[00:41:08] **Audience Member:** Yes. Are you seeing a larger amount of patients getting TM after fighting, COVID?

[00:41:15] **Dr. Carlos A. Pardo:** It's a very interesting question. Again, difficult questions go for Kyle.

[00:41:23] **Dr. Kyle Blackburn:** Thank you for that. We certainly have seen reports in the literature and in our experience as well, some people who develop what we would label as a probably a post infectious myelitis after COVID. Whether I have seen convincing data that that seems to be increased compared to what we would consider normal levels of post infectious myelitis, I don't think that I've seen anything that convincing myself. I'd certainly ask Dr. Pardo the same, I'll let him answer some tough questions too. But I haven't seen anything that's had me overly convinced that while COVID is a very prevalent virus and maybe that would tend to put the odds a little higher. I haven't seen anything that would say that there's a higher likelihood of COVID causing this compared to a flu or other viruses?

[00:42:20] **Dr. Carlos A. Pardo:** Cynthia and Melissa, MISC, M-I-S-C, do you mind explaining what is that the meaning of that? And do you mind clarifying if there is any case of myelitis associated with that?

[00:42:35] **Dr. Cynthia Wang:** Yeah. So, in children specifically sometimes they have this kind of over abundant immune activation that has been triggered by COVID usually leads to certain blood tests or blood abnormalities increase inflammatory markers? I personally haven't seen an overlap between that syndrome I've seen and

maybe some of the other your inflammatory disorders in the context of positive COVID. But I think like DR Blackburn was mentioning, it's just been so common to have had COVID or had an immunization to COVID that I think that's more likely explanation.

[00:43:20] **Dr. Carlos A. Pardo:** Melissa, have you seen any spinal cord complication with COVID or MISC?

[00:43:22] **Dr. Melissa Hutchinson:** So, we have seen a lot of MISC after COVID and I personally haven't seen an isolated spinal cord inflammation after COVID. But there is a great paper coming out on the pediatric neural complications after COVID and that's going to be a multicenter group who have pushed their data together, because there are a few number of patients having these neurologic complications. And so, looking across the country at the neurologic complications after COVID, we'll look at that data to help us answer this question that should be coming out in the next couple of weeks, I believe.

[00:44:00] **Dr. Carlos A. Pardo:** And let me answer from the adult point of view, back in 2021, actually, we got together with more than 20 centers around the world to check if there were what was the profile of neurological complications in the setting of COVID 19 and my lightest was nothing, in other words, there was no evidence that the COVID-19 basically triggered myelitis. However, what COVID-19, and this is actually one paper that we are trying to submit, in the experience that we have on COVID-19 vaccinations as complications on spinal cord, the most frequent problem that COVID may trigger in central nervous system is strokes, vascular problems and in the same way that there are strokes in the brain. We have seen few patients with strokes in the spinal cord. So, actually modern myelitis, what we have seen in our experience at least at John Hopkins is a few cases of spinal cord stroke. Again, are those very frequent? The answer is no, those are very rare. Any other questions from the virtual audience?

[00:45:14] **Audience Member:** Yeah, maybe one last question that came in. I have NMO, my B cells are suppressed every six months by rituximab infusion to keep my immune system from attacking my central nervous system. Again, would vitamin B12 be helpful for me or work against me?

[00:45:32] **Dr. Carlos A. Pardo:** Kyle.

[00:45:36] **Dr. Kyle Blackburn:** For this specific instance, I would say, unless there was a low vitamin B12 level requiring supplementation to prevent neurological complications that supplementing B12 probably is not going to affect the neuron myelitis optica itself. Again, if it's low, it could affect the nervous system in another way, but should not affect the disease activity in the NMO.

[00:46:04] **Dr. Melissa Hutchinson:** I just want to ask a clarifying question of that person who asked that question. They mentioned that their B cells were suppressed on purpose, trying to suppress their B cells. So, the B cells themselves, part of the immune system are different than B12 as the vitamin. So, those are two separate one is a vitamin that our body and cells use, and one is the specific immune cell population that you're trying to suppress with rituximab. So, they're different, and I agree with Kyle's answer.

[00:46:39] **Dr. Kyle Blackburn:** Good clarification.

[00:46:40] **Dr. Carlos A. Pardo:** The last question before we go to clarify what ACTG is.

[00:46:48] **Audience Member:** Last question. Well, I think what may have been coming from that question, because we do get a lot of this on our NMO Facebook pages is, if I'm suppressing my immune system, am I fighting that by taking vitamins that boost my immune system. So, your answer to that would be?

[00:47:13] **Dr. Carlos A. Pardo:** It's a very interesting trend, is multivitamins. The answer to that is vitamin B12 is a good vitamin. I need to alert you that, occasionally, an excessive amount of multivitamins maybe also dangerous. Every time that you take multivitamins, pay attention to the composition of the multivitamins. There is one vitamin, particularly vitamin B6, that if you take too much vitamin B6, actually that's toxic to the nervous system and produce a peripheral neuropathy. And patients occasionally come to us and say, "I have a lot of numbness, tingling, and pain." And when we go and check vitamin B6 levels, they're over the roof, and the reason is they are taking too much vitamins. And some of these multivitamins occasionally contain an excessive amount of vitamin B6. So, you need to be careful with what you are taking and how you are taking.

[00:48:21]: All right. It is 4:36, and we are ready to wrap up our symposium. And the first thing that I need to acknowledge, and I always acknowledge is you, because you are taking time for coming here. Our families and patients are taking the time from Saturday and Sunday to be in the virtual meeting, so thank you so much for being in the virtual meeting. But we need also to be very grateful for that gentleman who is sitting over there, who is Sandy, who in the past 25 years has been an advocate for transverse myelitis patients and their families. So, I want to say thank you, Sandy. So, the second thing is I am very grateful with the staff of the SRNA and raise hands who are part of the staff of SRNA here. They are helping us to keep alive the spirit of helping our patients and thank you so much for all what you do for all of the organization of the symposium and making sure they're helping works and the lectures broadcast correctly. Thank you so much for the staff, the men, and the women in black behind, so thank you. All right, and thank you to the faculty of the symposium, thank you so much for being able to take three or four days and coming to Los Angeles and helping with this symposium. All right. ACTG, so is the DNA of what you need to do. ACTG, and this is what I'm going to tell you what ACTG. is A, you need to be alert, and you need to recognize the signs of alarm, and you need to be your own advocate. That is A, in other words, you are the only person who is going to be alert, identify the signs of alarm and be fighting for yourself, and be active. Thank you, I'm going to add that one.

[00:50:58]: C, is for communication, you need to be good communicating with your partner, with your friend with your family, wife, husband, children, and you need to be good communicating with your healthcare providers. Again, because you are your own advocate and communication is the only way to keep moving forward. So, C is for communication. Janet, do you want to order another one? T, you know what is T for? Team, you need to have a good team. The team is not only your primary care doctor, is not only your neurologist, is the rehabilitation specialist, is the therapist, is the pharmacist that is giving you the prescriptions every month and is the social worker that is advocating for you. So, you need to have a team that really is able to fight for you. So, T is for team. And G is the best one, is not for GG, but G is for one thing that is very important, you are great, you are good. So, you need to be fighting to continue being great and good, because that's the only way to keep moving forward. And the best vitamin that you need to take is not vitamin B12, is vitamin P, P as Peter. You know what that is? You need to be positive all the time, so vitamin P is the best vitamin. So, with that the symposium of the Rare Neuroimmunological Disorders is closed. Thank you so much, safe traveling back home, and again, thank you to everybody.