Open Q&A on MOG Antibody Disease (MOGAD)

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[00:00:00] **Krissy Dilger:** Hello, and welcome to the Siegel Rare Neuroimmune Association's "Ask the Expert" podcast series. This episode is titled, "Open Q&A on MOG Antibody Disease [MOGAD]." My name is Krissy Dilger, and I moderated this episode. Today I am pleased to be joined by Dr. John Chen. Dr. Chen serves as a consultant and professor of ophthalmology and neurology and neuro-ophthalmology fellowship director at the Mayo Clinic.

[00:00:33] You can find his full bio in the podcast description. SRNA is a non-profit focused on support, education, and research of rare neuroimmune disorders. You can learn more about us on our website at wearesrna.org. This episode is made possible in part by the generous support of Amgen, Alexion, AstraZeneca Rare Disease, Genentech, and UCB. Thank you so much for joining us, Dr. Chen.

[00:01:03] **Dr. John Chen:** Yeah, thanks so much for inviting me to join you all today.

[00:01:07] **Krissy Dilger:** Great. So, can you begin by briefly explaining what MOG antibody disease is?

[00:01:15] **Dr. John Chen:** Yeah, so MOG antibody disease, or MOGAD, is essentially a disease where you have inflammation of various parts of the brain, including the optic nerve, the brain, or the spinal cord. And it's associated with antibodies against MOG—myelin oligodendrocyte glycoprotein—which is essentially this protein found on the myelin.

[00:01:38] It again can cause inflammation of any part of the central nervous system. It can mimic multiple sclerosis, which we've known about for over a century. And then after multiple sclerosis, we realized that this other condition called neuromyelitis optica, NMO, was a separate disease, which is antibodies against aquaporin-4.

[00:02:00] And then now, just more recently, since around 2015 or so, we recognized that there's a separate entity, MOGAD, with these antibodies against MOG. And what's important about differentiating these different conditions is it's a different pathophysiology; it is acting through the MOG antibody.

[00:02:19] And it's important because the prognosis is different between these three entities and, even more importantly, the treatments are different. So, it's important for us to understand when you have a patient with transverse myelitis or a patient with optic neuritis, we want to look for these conditions because it allows us to dictate how we're going to treat patients.

[00:02:41] **Krissy Dilger:** Great, thank you. So, what causes MOG antibody disease?

[00:02:47] **Dr. John Chen:** To be honest, we actually still don't know. It's an autoimmune process, and about a third of patients have a prior infection of some kind, like a viral illness. And the thought is that the immune system revs up to fight off infections and things like that.

[00:03:04] And for some patients—we don't know the trigger or the reason—but these antibodies against MOG get developed, and then their own immune system is attacking parts of the brain, the optic nerve, or the spinal cord in that way. We don't know the exact reason or why it happens.

[00:03:22] **Krissy Dilger:** Great, thank you. So how is MOGAD diagnosed?

[00:03:27] **Dr. John Chen:** Essentially, you have to have inflammation of parts of the brain. Most commonly optic nerve with optic neuritis. Especially in children, you get inflammation in the brain called ADEM. Transverse myelitis is another common way; cortical encephalitis as well. So, you have these ways that MOG can cause inflammation in various parts of the brain, spinal cord, and optic nerves.

[00:03:51] You have to have the antibodies against MOG present in the blood or, in a small subset of patients, just in the cerebrospinal fluid on a spinal tap, but usually in the blood. By definition, it is MOG antibody-associated disease. You have to have the MOG antibodies present to have that diagnosis of MOGAD.

[00:04:13] **Krissy Dilger:** Got it. So, what acute treatments are used during a MOGAD attack?

[00:04:20] **Dr. John Chen:** Early steroids. High dose is certainly thought to be very beneficial, and the earlier the better. And the high-dose steroids usually are in the form of IV methylprednisolone. So essentially, getting these infusions of high doses of IV steroids for three to five days.

[00:04:36] You can also do very high doses of oral prednisone pills, but the bioequivalent is 1,250 milligrams of prednisone. Since the biggest prednisone tablet we can have is 50 milligrams, it's actually 25 tablets all at once, which you can do for three to five days. And then with MOG, it's important because sometimes it's not only steroid-responsive but steroid-dependent.

[00:05:02] And so we tend to do an oral prednisone taper over one to two months because sometimes if you just treat them with steroids and then stop the steroids, they can have a relapse because, again, the inflammation just hadn't fully been controlled with the steroids. So, essentially, high-dose steroids for three to five days, and then an oral prednisone taper over one to two months.

[00:05:22] There are some patients with really severe attacks where the steroids actually doesn't lead to enough recovery. And then we'll do this extra treatment called plasma exchange, where oftentimes it requires a central line where they actually get a line into their vein, and we actually can take the blood, wash out the pathologic antibodies and inflammation, and then give back plasma. So essentially to wash out the pathologic antibodies. But that's a little bit more of an involved treatment. Only about 10% up to 20% of attacks from MOG need that plasma exchange, but it's something that certainly is an option if they don't respond to steroids.

[00:06:06] And in terms of the timing of that, it's hard to know exactly when to "pull the trigger" in terms of giving more days of steroids to see if it's going to recover or when we switch over to plasma exchange. And that part is still getting worked out, and there's actually a randomized clinical trial called Timely-Plex that we're co-leading with Johns Hopkins to try and answer that question. If we have time we can even chat about that clinical trial some in the future too.

[00:06:34] **Krissy Dilger:** Definitely. Someone just put in the chat—and I think this is a common concern with steroids—is possible weight gain. Can you talk a little bit about that and if it's usually temporary or what can be done about that?

[00:06:55] **Dr. John Chen:** Yeah, steroids have a lot of side effects. In the acute setting, they're not too bad. That five days or three days of high-dose steroids is not going to cause weight gain. But it's the long-term steroid use that causes weight gain. It causes thinning of the bones. It can often cause diabetes. And these are drawbacks, and that's why we look for if a patient is steroid-dependent.

[00:07:21] Like every time we come off steroids, they have a relapse. That's why we tend to switch over to other medications to get patients off the steroids because, again, steroids have lots of side effects. In the acute setting, it's not so bad. Again, it's going to cause acid reflux, difficulty sleeping, and mood changes.

[00:07:39] Very rarely, it can cause even strokes to the bone called avascular necrosis, which we can't predict. But usually, in the acute setting—five days of steroids, two weeks of steroids—it's not too bad. But long-term... MOG responds very well to steroids, but we can't just put patients on steroids for three years. It just causes too many side effects. So, that's why we switch over to more chronic immunotherapy if they continue to have relapses every time we taper off the steroids.

[00:08:13] **Krissy Dilger:** Will MOGAD testing results be affected by concurrent IV steroids being administered, or any other of the acute therapies that you mentioned?

[00:08:24] **Dr. John Chen:** Potentially a little bit. The steroids probably not as much, but the plasma exchange certainly probably can for at least about a month. Essentially, we're washing out the pathologic antibodies, including the MOG antibodies, and all the cytokines and inflammatory markers.

[00:08:39] So I do think plasma exchange can certainly influence it. Sometimes acute treatments can also include IVIG, even though that's more commonly used for chronic immunotherapy. Sometimes we use it for acute treatment – that may not have as much of an influence on the MOG antibodies. But the thought is that any acute treatment and any potential chronic treatment can influence it; plasma exchange would probably be your biggest one.

[00:09:07] **Krissy Dilger:** Got it. So, what are the—I know we touched on this a little bit—but what are the currently available long-term therapies for MOGAD? And does this differ by location, for example, the United States versus Europe or Asia?

[00:09:22] **Dr. John Chen:** That's certainly still evolving. What we know is some of the traditional medications for MS are not effective. And when we first knew about MOGAD, we essentially took all the treatments we used for NMO and essentially used them for MOGAD. And so, we were using CellCept, Azathioprine, and Rituximab; those are some of the traditional medications used for NMO.

[00:09:45] Those all probably kind of work for MOGAD, but not as well. Rituximab, which depletes these B cells in your immune system, is very effective for NMO but just doesn't seem to work quite as well for MOGAD. And again, the thought is it's just a different pathophysiology, a different disease process. So, some treatments that we think may work a little better are IVIG or SCIG [subcutaneous IG], and the dosing actually matters. We essentially found with these multicenter studies is that IVIG, if given at a very high dose or high frequency, is very effective. But given at a low dose or low frequency, it doesn't seem to work as well.

[00:10:26] Subcutaneous IG—essentially, you take your IG and you put it through the skin via infusions that can take two to three hours a week. It can be very effective because you're getting it every week instead of every month. So, with IVIG, you get these kinds of spikes in your IG levels, but then they can taper down and it goes up and down. With SCIG every week, it tends to be very effective because you have that more stable level.

[00:10:51] So, those are some treatments that, again, we don't use for MS or NMO, but they seem to be effective for MOGAD. The other pathway that seems to be effective is blocking this IL-6 pathway. And so, there's satralizumab and tocilizumab, both shown to be effective for NMO, and they seem to be quite effective for MOGAD, as well.

[00:11:12] There's currently a clinical trial on satralizumab, again an IL-6 blocker, and the results will be officially released at the American Academy of Neurology very very soon in the next couple of weeks, but it looks very promising. And then there's another ongoing clinical trial blocking the Fc receptor. It's an Fc receptor inhibitor. Essentially, it's again trying to remove pathologic antibodies, and we don't know the results of that clinical trial, but we hope that'll be effective and then give us FDA-approved medications. So, we're learning a lot about treatments for MOGAD. Our knowledge for MOGAD is about 10 years behind NMO, but we're catching up, and hopefully in the next couple of years, we'll have FDA-approved medications and more clinical trials.

[00:12:02] **Krissy Dilger:** Yeah, we're looking forward to learning what the research will show and hopefully, as you mentioned, new therapies in the near future. We have a question—and this is a specific case, but also I think it can be applicable more broadly—this person was diagnosed with idiopathic TM in 2019. They've had slight relapses, but yearly MRIs showed no brain involvement and no optic nerve involvement. They have never tested positive for MOG or aquaporin-4.

[00:12:42] But in 2025, they had antibodies that apparently triggered spinal lesions; once they had their labs done again, MOG was positive. Their question is: with no optic nerve, no brain, and only spinal cord lesions, but a MOG-positive test, is that enough to diagnose MOG versus TM? And I guess also more broadly, how do these shifts in MOG levels correlate to diagnosis?

[00:13:21] **Dr. John Chen:** Yeah, with any case, let's say you have an attack initially and you are MOG antibody negative; if you have a new attack, it's important to check again for MOG or aquaporin-4 antibodies, especially if it's transverse myelitis. Again, for the first attack, perhaps the blood draw would've been done later after the attack.

[00:13:46] And we know MOG antibody levels can slightly decline over time. It could have been after steroids, plasma exchange—all these things that can wash out the antibodies. If you have a new attack, again, it's important to check again. If it's aquaporin-4 positive on the cell-based assay, that's your diagnosis of NMO.

[00:14:02] The NMO antibody against aquaporin-4 is essentially perfect if it's a cell-based live assay. The problem about the MOG antibody is they're not perfect. They're pretty good—they're 98% specific when done with a live cell-based assay.

[00:14:17] That's really good compared to, say, we have this marker against Lupus called an ANA. It's only 80% specific, so 20% of normal people actually just have this antibody floating around or antibodies against ANA. So that's not helpful. But MOG is 98% specific. Pretty good. The drawback is MOG is pretty rare relative to MS and other diseases.

[00:14:41] And so, if you've got a disease that's relatively uncommon and you have a test that's not 100% perfect, you can get false positives. And so I would say with that patient, I would look at the MOG antibody

titer and make sure it's done on a cell-based assay, ideally a live cell-based assay rather than these fixed dead cells. The "live" part actually makes the assay a little bit better, and if it's a high titer, even though it's just transverse myelitis, that makes your diagnosis of MOGAD.

[00:15:13] If it's, let's say, a very low titer, typically what we want to confirm a diagnosis of MOGAD is these clinical features or radiologic features that help you say it's MOGAD as opposed to MS or something else. For MOGAD, in terms of the transverse myelitis, it tends to be longer segments of inflammation of the spinal cord than multiple sclerosis, where the lesions are much smaller.

[00:15:36] So that's something that can help. With MOGAD, it tends to affect this central gray of the spinal cord. And so, if you look at the spinal cord in an axial cut, it'll actually look like an "H" in terms of the inflammation. So that's something we look for.

[00:15:51] And then lastly, one way to help differentiate MS from MOGAD is MS stands for "multiple sclerosis" or "multiple scars." And with MS, it's interesting—when you get this inflammation, you get these little scars, and then they persist on the MRI that you do later. And then you get a new lesion, and then you get a new scar, and you get multiple scars that just keep persisting.

[00:16:13] With MOGAD, during the inflammatory attacks, you get a lot of inflammation, but about 80% of the lesions actually shrink and sometimes even disappear. And so, repeat MRIs to show that these lesions you get in these acute attacks are disappearing—that's another sign that it's MOGAD. So, I know it's a long answer for this particular question, but there's a lot of nuances, and very well—just because it's transverse myelitis—it very well could be MOGAD. It just depends on the titer and what it looked like on radiology.

[00:16:48] **Krissy Dilger:** Thank you. Another question came in. Could MOGAD cause one of your eyes to have trouble opening after being asleep, either lying down or sitting up, or is this condition more dry eye related? This person says, "My MOGAD diagnosis came from optic neuritis in the right eye with temporary loss of vision."

[00:17:15] **Dr. John Chen:** Yeah. MOGAD itself wouldn't cause an inability to open one eye, and so that's going to be something else if it's only upon awakening. There's a very interesting condition called apraxia of eyelid opening upon awakening, where essentially patients wake up and are unable to open one eye.

[00:17:34] Fortunately, it's not a dangerous condition, and we don't know the exact cause for it. One thought is it's actually dry eye; it's difficult to open a peanut butter jar if you're trying while it's dry, and then you pop it open and it stays open. That's the thought—the eye is just dry, and it's crusted shut and you just have difficulty opening it. And once you get it up, it's okay.

[00:17:57] The other thought is when we're asleep, our brain activity is essentially paralyzed. We don't want us running around and enacting our dreams. And the thought is that the eyelid itself is still essentially asleep for five minutes or so, and it just requires some time to wake up, but it's not going to be MOGAD. But again, if it's only upon awakening, it's probably this condition called apraxia of eyelid opening upon awakening.

[00:18:30] **Krissy Dilger:** It's really interesting, and thank you for sharing. I hope that person's able to look into that. Is having vision coming and going normal while on IVIG and IV steroids?

[00:18:50] **Dr. John Chen:** Not from the treatment itself. "Coming and going" can mean a lot of different things. I'm not entirely sure how fast it's coming and going. Sometimes with MOG, you can get a pretty swollen optic nerve, and if you get a swollen optic nerve, sometimes if it's swollen enough, if you stand up too quickly, your vision will actually black out for a second or two.

[00:19:14] So it could be from a lot of optic nerve swelling. If it's a much slower process, it could be inflammation that's being controlled or not being controlled, but that's talking about days and weeks as opposed to minutes and hours.

[00:19:35] If it's heat-induced or exercise-induced, there's a condition called Uhthoff's phenomenon where essentially if you have a prior optic neuritis, if you get too hot or if you exercise, it actually slows the signal down along the optic nerve and you'll get transient blurring of your vision in the affected eye with prior optic neuritis. Again, not related to treatment or IVIG. I think I just have to have a little more details in terms of how fast the vision's kind of coming and going. But the treatment itself shouldn't cause the vision to go in and out.

[00:20:12] **Krissy Dilger:** Does the amount of MOG antibody found on testing correlate to the severity of an attack or of the long-term course of the disease?

[00:20:24] **Dr. John Chen:** Oh, that's a good question. Right now, the titer most importantly is to help confirm the diagnosis. If you have a very high titer of, say, 1:1,000, that's probably going to be MOGAD. There are very few false positives there. And then if you've got a low titer—at 1:20 or 1:40, at least on the Mayo titer scale [all titers are a little bit different]—then you could certainly have false positives there.

[00:20:49] So that's where it's most important. Some studies have suggested that higher titers are associated with more severe attacks, but most studies have not found them to be associated with future risk of relapse or permanent disability. So, I think clinically it's probably the most important in terms of helping confirm the attack, but not quite as much for what's going to happen in the future.

[00:21:19] **Krissy Dilger:** Got it. We got a question, and this kind of correlates to something I was also going to ask about. This person asks, "Following the first attack and steroid treatment of optic neuritis, what are the chances of relapse after the step-down process with the steroids?" And I guess more broadly, are there any factors that help predict whether a person is likely to relapse or not following diagnosis?

[00:21:45] **Dr. John Chen:** That's the million-dollar question, actually. Can we predict who's going to have a future relapse? Unfortunately, we haven't had a perfect test or perfect way of knowing who's going to relapse in the future. Overall, we think that about 50% of patients will relapse over time, but that means 50% of patients won't relapse over time. And so essentially, we do a slow prednisone taper, and then if they have a relapse when they come off, then they've got relapsing disease. I'd say the one predictive factor that's shared across all of them is that if you have a relapsing disease, you're more likely to have another relapse.

[00:22:24] So if you've had two attacks, you're more likely to have a third or fourth attack. Whereas that first time, it's really hard. Some studies suggest all these various factors, but there hasn't been anything that's been consistent to say, "Okay, if you are a 45-year-old female and you have this kind of attack and you have this titer, you're going to relapse." We haven't found that consistently across studies.

[00:22:49] Again, each one kind of shows different things, but nothing as consistent. I would say though, if you are a patient with relapsing disease—if you've had two attacks—it's a higher chance you're going to have a third attack, as opposed to if you've had one attack; the risk of that second attack is still about 50%.

[00:23:07] **Krissy Dilger:** Someone wrote in and asked: do people with MOGAD have non-epileptic seizures?

[00:23:17] **Dr. John Chen:** MOGAD itself doesn't cause non-epileptic seizures, but it can cause seizures, especially if you've got ADEM or cortical encephalitis [inflammation in the brain]. It can cause seizures and it can cause epilepsy [recurrent seizures].

[00:23:32] But the non-epileptic seizures it doesn't cause by itself. Non-epileptic seizures are thought to be a functional neurologic condition where essentially it's not driven by abnormalities in the CNS signaling but is sometimes driven by stress or other things like that.

[00:23:52] And I think for some patients who have had seizures from MOGAD, it's possible they've had the "real" seizures, and sometimes that can lead to these pseudoseizures or non-epileptic seizures that we call them. But MOGAD itself doesn't drive non-epileptic seizures.

[00:24:14] **Krissy Dilger:** Got it. Thank you. Can vision be improved or even fully restored after damage caused from a MOGAD attack?

[00:24:26] **Dr. John Chen:** With a MOGAD attack, again we're going to treat it aggressively with steroids, and then we may add on plasma exchange. Then after that attack, the majority of the recovery happens in the first three months, and then there can be some further recovery for a full year out. After a year after the attack, that's going to be your new baseline.

[00:24:44] And then, so if the question is "Can it improve after the attack initially?", the answer is definitely yes. The majority of attacks do improve. Now, if you're sitting at a year out and you still have a lot of damage in terms of function for that eye at that point, we don't have good treatments. Sometimes my patients ask, "We did steroids, we did plasma exchange three months in, and my vision's still pretty bad. Can we just do plasma exchange again, or IV steroids again?"

[00:25:11] And that, unfortunately, doesn't help. All those treatments are in that first acute phase, the first two to four weeks, that we're really trying to treat things and calm down the inflammation.

[00:25:23] Again, whatever we have at one month... currently, we don't have a way of regrowing the optic nerve, unfortunately. I think in the future there will be treatments like stem cells and other things to regenerate the optic nerve, but we're not there yet. If we have time, we can talk about where we're at in terms of that technology, but I think the future will be regeneration of the optic nerve. We're just not there yet right now.

[00:25:49] **Krissy Dilger:** I would love to talk about that some more. Maybe if we have time at the end, we can chat about it. Is MOGAD hereditary, and is there a chance I will pass on the MOGAD gene to future children?

[00:26:04] **Dr. John Chen:** Yeah, we don't think it's hereditary. There's been really not much of a signal of that right now, fortunately. It's an autoimmune process, and there can be slightly higher tendencies toward autoimmune disease in patients with MOGAD, but it's not a strong correlation with autoimmune disease. So really not very hereditary. Not really going to be passed on, or we don't see large families with MOGAD.

[00:26:33] **Krissy Dilger:** Got it. This person asks: "I was diagnosed with MOG antibody disease and acute TM in November 2015. Their last blood test showed MOG antibody was negative. This person's neurologist suggested that they wean off of Azathioprine. But their pain levels and their legs and feet have been quite bad, especially at night. They were wondering: is weaning off the medication causing their pain to worsen? What's the correlation there?"

[00:27:14] **Dr. John Chen:** Yeah, I think residual pain and residual lack of function, things like that, are from the actual prior transverse myelitis attack. The Azathioprine's job is to prevent new attacks, and so coming off those treatments doesn't worsen old symptoms. Really, their job is to prevent new attacks. If any of these symptoms are new, you'd want to get some imaging in the spine to make sure you don't have a new transverse myelitis attack but if it's just the old symptoms, coming off the Azathioprine isn't going to worsen them.

[00:27:50] And so that's important. And in terms of the decision to come off or not, that's a good one too. And again, there are a lot of different ways to do it, but certainly, we do try to often come off treatment if patients have been quiet for three years or five years, especially if the antibody titers go to negative.

[00:28:15] In about 75% of patients, the MOG antibody titers will stay positive consistently. 25% will go to a level where they're not detectable. That doesn't mean they're not going to relapse again. Overall, again, we think that about 50% of patients will relapse, but if the antibody titers go to undetectable, we think the risk of relapse is about 10% to 20%.

[00:28:40] And so I think again, if you've been on Azathioprine and no new attacks for five years, it'd be quite reasonable to try coming off and seeing how you do. And then again, if you have a new attack, essentially it's very early steroids. And again, you have plasma exchange as your backup plan, but very early steroids.

[00:28:59] So patients tend to do pretty well, actually, if they were to have a relapse the second time around because you know what you're looking for. You're looking for optic neuritis, transverse myelitis, anything neurologic, and you can get those steroids right away. The first attack is the one that tends to cause the most disability because no one's thinking about optic neuritis or transverse myelitis.

[00:29:17] It often takes one or two or three weeks to even figure out that this is an inflammation in the brain. The steroids are delayed by two weeks. It's a little bit different where you know you've got MOGAD and you're coming off the Azathioprine; so there's that potential risk of a relapse—let's say it's 50%. If you have a new relapse, you treat right away, and then you do have to be on chronic immunotherapy for another five or ten years, or just depends on how aggressive the disease process is.

[00:29:49] **Krissy Dilger:** Got it. And that person then could potentially try to treat the pain separately?

[00:29:55] **Dr. John Chen:** Right. Yeah. So, the pain separately—again, pain can happen after, especially after transverse myelitis and MOGAD. And you can treat it with things like Lyrica, gabapentin, and other things to calm down nerves.

[00:30:11] **Krissy Dilger:** Yeah. Great. Related to what you were just speaking about, someone asked: how long should someone be on IVIG before they try Plex to get better?

[00:30:26] **Dr. John Chen:** So, this goes back to... this is now an acute attack. In an acute attack, essentially we try the steroids first, and then usually we go to plasma exchange if they don't respond to steroids. Especially in children, though, we'll sometimes try IVIG. We try to do that probably all in that first month.

[00:30:49] And again, the timing of when to go to these more aggressive treatments is quite unknown and unclear. But certainly, if it's a very severe attack, we'll probably start with five days of steroids. And then if they don't start turning the corner, we'll probably add on plasma exchange shortly after.

[00:31:05] That's typically how we do it here at the Mayo Clinic. It's reasonable to start with IV and steroids and then give it two weeks, and then if you don't respond, then do plasma exchange but in terms of these rescue treatments like plasma exchange or IVIG, they don't really help too much if they're three months out.

[00:31:25] These are all treatments we're doing in that first one to two months, ideally within the first month if we're going to do it. The problem is we don't know who's going to recover on the steroids alone. And that's what makes it very difficult. If we had a crystal ball saying, "If we give you steroids, you're going to get back to 20/20 without plasma exchange," obviously we would just watch and wait.

[00:31:46] And if we knew that person was destined to do poorly, we would do plasma exchange right away. That's the hard part, and that's why, again, we're doing that Timely-Plex randomized clinical trial to look at the Timely-Plex. But it's tough. But again, if you're going to pull the trigger on one of these other treatments, usually in that first four to six weeks we're doing it.

[00:32:06] **Krissy Dilger:** Got it. Someone just asked if it's possible that a COVID infection could be tied to an acute attack of either MOGAD or acute optic neuritis?

[00:32:22] **Dr. John Chen:** Yeah, we think so. Not COVID-specific, but again, about a third of patients have some kind of a viral prodrome or some kind of infection that again ramps up the immune system. And with COVID being so common, that is a trigger.

[00:32:39] But we haven't seen... with COVID coming in 2020, we didn't see this gigantic, huge peak in MOGAD. So, it's clearly not 100% tied by any means. But again, any kind of infection that can ramp up the immune system can potentially trigger MOGAD. So, we do see some.

[00:32:59] **Krissy Dilger:** Got it. This person... I know we briefly mentioned the potential tie between MOG antibody disease and acute disseminated encephalomyelitis, or ADEM. If MOG was not present at the time of an ADEM attack, is it possible that it could be present in the future? And is it worthwhile to monitor MOG levels via blood tests going forward?

[00:33:28] **Dr. John Chen:** That's a good question. Again, during that acute attack of any kind, sometimes you're getting steroids or plasma exchange, and that could potentially influence things. So, it's definitely worth checking at least one more time.

[00:33:41] Beyond that, it's probably not worth checking MOG antibodies every year to see if you're going to become MOG positive. The rate of that is quite low. So, I would say check during the acute attack, check again maybe one more time if this clinical picture was suspicious for MOG and you were negative.

[00:33:58] And then what I would do is essentially if you have any new attacks of any kind—whether it's ADEM, transverse myelitis, optic neuritis, anything inflammatory in the brain—then check for the MOG antibody.

[00:34:11] And then lastly, if you have recurrent attacks and the blood keeps being negative, the last thing that you could check is actually check for MOG antibodies in the spinal fluid by doing a spinal tap or lumbar puncture.

[00:34:25] At the Mayo Clinic, we can check for MOG antibodies in spinal fluid under research purposes. But there have been studies around the world, including the Mayo Clinic, where we think that up to 10% of patients who are negative in the blood for MOG can actually be positive for MOG antibodies in the spinal fluid and help clinch a diagnosis of MOGAD, but always start with the blood first. Much easier to do; much more established. But this spinal fluid is something... if a patient has recurrent attacks that look like MOG and they're negative in the blood, that's something that could be considered.

[00:34:58] **Krissy Dilger:** Got it. Thank you. Someone wrote in that their fatigue seems to be one of their most debilitating issues. Is there anything you can speak on to treatment for fatigue? Is this known to be related to MOG antibody disease? And is there any research going on in terms of the connection?

[00:35:24] **Dr. John Chen:** I think there is an association with fatigue and prior inflammation, especially if MOGAD involved the brain. So, ADEM or cortical encephalitis shows definitely an association with fatigue.

[00:35:39] It's hard, though, to quantify, which makes it hard to study. I think that a couple things that would be important to do if fatigue is actually one of the largest factors is to make sure that there's nothing else also contributing to the fatigue. So that'd be checking for sleep apnea, checking thyroid levels—other things that can cause fatigue too—and not just automatically blame it on the MOGAD.

[00:36:03] Obviously, if those were all normal and you had a prior episode of ADEM or cortical encephalitis [inflammation in the brain], it probably is tied in. But I'd say that's one of the harder parts of research in MOGAD for sure—the fatigue—just because it's hard to quantify and define.

[00:36:21] **Krissy Dilger:** Thank you. Someone asked: can a diagnosis of MOGAD affect life expectancy? What is the prognosis for someone with MOGAD?

[00:36:33] **Dr. John Chen:** Yeah, we don't currently think it will affect life expectancy. But it really depends on the type of attack and how much disability is remaining from the attack. So, the good part is, unlike multiple sclerosis... With MS, you can get these recurrent attacks where you're symptomatic, but also even when you're not symptomatic, you can get this progressive phase where essentially patients can have this steady decline even though they're not having discrete attacks.

[00:37:02] With MOG, there is... we don't think they're these "invisible" attacks. So, all the disability is driven by symptomatic attacks that you notice, and so that allows you to escalate therapy and prevent new attacks. There's not this invisible progressive phase for MOGAD. So, we don't think it'll affect life expectancy overall.

[00:37:23] But of course, if you had a very severe transverse myelitis attack and you're wheelchair-bound or things are tough, then you might be more prone to infections, that kind of thing. But just the disease itself—let's say you had an optic neuritis with it—it shouldn't affect life expectancy.

[00:37:42] **Krissy Dilger:** Got it. Thank you. Someone asked: "When I have a flare or a relapse, I usually get inflammation in my ears. Tinnitus, such as whooshing noises and then beeping noises that block my ear. Can this be related to MOG?"

[00:38:00] **Dr. John Chen:** That's interesting. It's not a common symptom that I've heard of very much. Sometimes with MOG attacks, you can get raised pressure in the brain, and a symptom of raised pressure in the brain can be this whooshing noise that syncs up with your heartbeat. It's called pulsatile tinnitus. Maybe that's how it could be connected, but otherwise, we don't tend to think of it causing any pulsatile hearing changes.

[00:38:31] But again, if there's raised intracranial pressure [raised pressure in the brain], it can cause pulsatile tinnitus. So maybe it's driving it through that. Again, the important part is if you have new symptoms, you'd want to have some kind of way of objectively showing that there's inflammation. That's usually an MRI or, if it's optic neuritis, it's an OCT image or seeing that the pupils don't respond as well to light, those kinds of things.

[00:39:02] **Krissy Dilger:** Got it. I'm going to ask: getting MOGAD as a child, are there any special concerns, like maybe puberty or anything that pediatric MOGAD is specific to?

[00:39:23] **Dr. John Chen:** MOGAD does explain a good amount of inflammation in children. Fortunately, the attacks tend to recover a little bit better than adults, and we do think the relapse rate in children is lower than in adults.

[00:39:39] It shouldn't affect puberty or any of those kinds of things unless the patient had inflammation of the hypothalamus. The hypothalamus is the part of the brain that's involved in hormone function. It secretes

hormones and growth hormones that allow you to grow, those kinds of things. So, if you had inflammation of the hypothalamus or parts of that system, then it could be involved. But otherwise, if it's, let's say, an isolated optic neuritis attack, there should be no problems with just normal development and growth.

[00:40:15] **Krissy Dilger:** I'm going to ask, for family planning purposes, are there any special concerns for pregnancy if I have had MOGAD in the past? Are there concerns with being on IVIG while trying to get pregnant?

[00:40:31] **Dr. John Chen:** No, that's a good question. In terms of pregnancy, the pregnancy itself is thought to actually potentially decrease the risk of relapse in MOGAD while you're pregnant. Essentially, you have the fetus that's growing, and your body does not want to reject the fetus. And so, it actually suppresses the immune system somewhat. And so that's something to keep in mind; that part's okay.

[00:41:02] After delivery, there's always the potential for relapse at that point. That's something to look for. I'd say the biggest thing, though, is treatments—some treatments you can't do during pregnancy. For IVIG specifically, that one you are probably safe to use during pregnancy, so that part's okay. It all just depends. The biggest impact in terms of pregnancy is what treatments we can do. Some we can't do and some we can do.

[00:41:35] **Krissy Dilger:** Got it. Thank you. So, I... we mentioned earlier about the research. I think we do have some time if you want to talk more about that and what to look forward to in the future.

[00:41:48] **Dr. John Chen:** Maybe we can talk about the randomized clinical trial for plasma exchange. It's called Timely-Plex, and essentially, we're taking any patient with severe optic neuritis or severe transverse myelitis. And right now, the big question is: does plasma exchange work, and if so, when do we do it? Do we do it right away, or do we do it only if they don't respond to steroids?

[00:42:11] And so essentially, if you've got severe optic neuritis or severe transverse myelitis and you're part of the clinical trial, you get randomized to either getting steroids alone or steroids and plasma exchanges at the exact same time. And then we can look at the outcomes. If you were randomized to steroids alone and you don't recover in one to two weeks, then you get this delayed rescue Plex. And so hopefully that'll help inform us in terms of when we should be doing this treatment.

[00:42:42] If plasma exchange was as easy as taking a pill of aspirin, we would just do it right off the bat. But it's pretty involved—it requires a central line oftentimes, and five treatments every other day. So again, it's pretty involved, but if early treatment is pivotal to leading to better outcomes, we would do it right away.

[00:43:03] If we can wait one to two weeks, we would probably delay. And so, this will inform how we move going forward, because right now every center does it differently. Some do very early plasma exchange; some don't use it much at all. And so it's really a hodgepodge in terms of what we do.

[00:43:20] This will help consolidate and guide us with actual clinical data. We have 31 sites enrolling or soon to be enrolling around the US. Again, John Hopkins—Laster Toco, he's an immunologist there—we're co-leading it together. And then we have... eventually by August we'll have 31 sites recruiting for this.

[00:43:43] So hopefully this will really help us in terms of helping gauge treatments. And this will be for MOG patients, NMO, MS... really any patient with kind of severe attacks will be eligible for this trial. So that's one avenue of research.

[00:44:02] There was a question about: is there anything we can do to recover vision after these attacks? And I do think the future will be stem cells. Right now, we can actually take skin and grow optic nerves in a

dish. So, we can do what we call "in vitro." The problem is we don't know how to make these optic nerve stem cells grow to where they're supposed to grow. So essentially, the very first connection for the optic nerve is actually from your eyeball to the middle of your brain, the very first connection actually has to go that far before it makes its first connection.

[00:44:35] And we don't know how to make those nerves grow to where they're supposed to grow. And so that's the barrier right now. But there's a lot of animal studies trying to figure that out. I know at UC Irvine and Stanford, they're doing studies to try and get the axons of the optic nerve to go in actually the correct direction.

[00:44:56] Some are using electromagnetic waves to try and get them to go where they're supposed to go. So again, the hope is to direct them in an animal model. And then once we have it working in animals, then, you know, it's something that we'll apply to humans.

[00:45:11] I maybe want to caution some of the audience: there are stem cell clinics out there where they will inject optic nerve stem cells into your eye. But there hasn't been any great data on how that's going to work because then we don't know how to make those optic nerves go to where they're supposed to go.

[00:45:30] The drawback of that kind of therapy right now is, one, there's not great evidence that it would work. And then two, there have been reports of patients developing a lot of inflammation in the eye from the injections and actually even going blind from the injections. So, I wouldn't—even if you had a billion dollars, I wouldn't recommend that treatment right now until we get it working in animals and then clinical trials in humans. But right now, I wouldn't recommend any of those stem cell clinics right now, unfortunately.

[00:46:04] **Krissy Dilger:** Very interesting. Thank you for sharing, and we are excited to hear about the results when they come in, especially about the study that you and Dr. Toco are conducting. And we can also put information about that study, if you'd like, on our clinical trials and studies pages on our website.

[00:46:29] Also, I would just recommend anyone interested in getting involved in research can always check—if you're located in the US—clinicaltrials.gov and just search "MOG antibody disease" or whatever you are interested in research on. But thank you so much for sharing, and I hope to have you on in the future to talk about the developments from your findings.

[00:46:59] **Dr. John Chen:** Oh, absolutely. It was a lot of fun having a chance to chat with all of you, especially with MOG Awareness Month in April.

[00:47:07] **Krissy Dilger:** Yes. Yes, we are having a few MOG awareness month events. And we've partnered with the MOG Project as well to put together some resources and other events. So look out for that the rest of this month. I... we don't have any more questions, so I think we can probably end early unless anyone else has any questions in the chat—I'll give it a minute. But thank you so much Dr. Chen, and we really appreciate you volunteering to come on and to share your expertise.

[00:47:45] **Dr. John Chen:** I really enjoyed it, and if any questions come up later, I'm sure you can reach out to SRNA and I'd be happy to answer them.

[00:47:56] **Krissy Dilger:** Awesome. Yes, you can always email us; we're at info@wearesrna.org. You can find more information on our website, wearesrna.org. Happy to try and help answer any questions anyone might have now and in the future. Great. Thank you so much, and enjoy the rest of your day.

[00:48:20] **Dr. John Chen:** Great. Thank you, everyone. Have a wonderful day.

[00:48:26] **Krissy Dilger:** Thank you to our "Ask the Expert" sponsors: Amgen, Alexion, AstraZeneca Rare Disease, Genentech, and UCB. Amgen is focused on the discovery, development, and commercialization of medicines that address critical needs for people impacted by rare autoimmune and severe inflammatory diseases. They apply scientific expertise and courage to bring clinically meaningful therapies to patients. Amgen believes science and compassion must work together to transform lives.

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