MOG Antibody Disease
Diagnosis and Treatment Guidelines

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[00:00:00] **Krissy Dilger:** Hello, and welcome to the SRNA Ask the Expert podcast series. This podcast is titled, "MOG Antibody Disease: Diagnosis and Treatment Guidelines." My name is Krissy Dilger, and I will be moderating this podcast. SRNA is a nonprofit focused on support, education, and research of rare neuroimmune disorders. You can learn more about us on our website at wearesrna.org. Our 2021 Ask the Expert podcast series is sponsored in part by Alexion - AstraZeneca Rare Disease, Genentech, and Horizon Therapeutics.

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[00:01:36] Horizon 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. Horizon believes science and compassion must work together to transform lives.

[00:02:01] For today's podcast, we are pleased to be joined by Dr. Eoin Flanagan and Dr. Rohini Samudralwar.

[00:02:08] Dr. Eoin Flanagan is a Professor of Neurology and Consultant in the departments of Neurology and Laboratory Medicine and Pathology at the Mayo Clinic in Rochester, Minnesota. He completed his medical school training at University College Dublin in Ireland in 2005.

[00:02:26] He did a medical residency in Ireland and then completed neurology residency fellowships in neuroimmunology and a master’s in clinical and translational science at Mayo Clinic. He works in the Autoimmune Neurology and Multiple Sclerosis Clinics and the Neuroimmunology Laboratory at the Mayo Clinic. His clinical expertise and research is focused on inflammatory myelopathies and their imaging patterns, Myelin Oligodendrocyte Glycoprotein - or MOG - antibody associated disorder, neuromyelitis optica spectrum disorders, autoimmune encephalitis, paraneoplastic neurologic disorders, and multiple sclerosis. He is principal investigator on an NIH R01 grant studying MOG antibody associated disorder.

[00:03:16] Dr. Rohini Samudralwar is an Assistant Professor in the Division of Multiple Sclerosis and Neuroimmunology, part of the Department of Neurology at the University of Texas Health Science Center at Houston. She received her medical degree in Philadelphia at Drexel University College of Medicine and Neurology training at Baylor College of Medicine. Her sub-specialty training in Neuroimmunology was at Washington University in St. Louis where she developed her expertise in multiple sclerosis, neurosarcoidosis, and Neuro-infectious Diseases. She currently works both in the Texas Medical Center as well as in the Harris Health System. Her clinical efforts extend to all forms of neuroimmunological diseases and has a special interest in neurosarcoidosis.

[00:04:04] Her current research focuses on the relationship between inflammatory markers and hormonal changes in multiple sclerosis as well as system-based studies in autoimmune encephalitis and neurosarcoidosis. She is the designated neurologist, part of a multidisciplinary group of physicians, that make up the UT Sarcoidosis Clinic recognized by WASOG.

[00:04:27] Welcome, and thank you for joining us today. We can start off by just a brief overview of what MOG antibody disease, or sometimes referred to as MOGAD, is. Dr. Flanagan, if you want to start us off?

[00:04:45] **Dr. Eoin Flanagan:** Yeah. So, the way I think about MOG antibody disease, or probably we'll just call it MOG for this talk is that it's part of the CNS, or central nervous system, demyelinating diseases. So, they are diseases that are immune-mediated, and the immune system remove the myelin or the insulation around the nerves. So, other examples of those diseases would be multiple sclerosis and neuromyelitis optica spectrum disorder, or NMOSD as we term it. And I think they're the three main central nervous system demyelinating diseases.

[00:05:19] And the disease, with MOG antibody disease, tends to come in the form of attacks. So, patients might have episodes where their vision gets affected, where they have optic nerve involvement that we term 'optic neuritis' or 'optic nerve inflammation.' They may have other episodes where the brain or spinal cord gets inflamed. That's what we call acute disseminated encephalomyelitis, or ADEM.

[00:05:43] Or they might have other episodes where just the spinal cord is involved with inflammation that we call transverse myelitis. So, that's the way it tends to come with these episodes or attacks. And then, you know, our goal when those attacks come is to treat them and then also to try and prevent those attacks in patients who have relapsing disease.

[00:06:05] **Krissy Dilger:** Thank you so much. That's a great overview. Our next question is, what are the signs and symptoms of MOGAD in the acute stage? Dr. Rohini?

[00:06:14] **Dr. Rohini Samudralwar:** Yeah, I think Dr. Flanagan mentioned a little bit of this. What makes it so challenging is that a lot of the symptoms can be similar to our other diseases like multiple sclerosis and neuromyelitis optica syndrome.

[00:06:27] Many times people can, adults mainly, will have involvement of their optic nerve. So, can present with an optic neuritis. Many times can also involve both eyes at the same time. Also, a transverse myelitis, where you have inflammation of the spinal cord. Or a presentation called ADEM, which is an acronym that essentially can cause inflammation in more of the cortical areas or the higher-level areas in the, in the brain itself.

[00:06:57] So, that can present with weakness, sometimes confusion. Many times, in children we'll have this sort of presentation focusing on, specifically, the brain.

[00:07:06] **Krissy Dilger:** Great. Thank you. And Dr. Flanagan, this is a question we do get a lot, and I know it might be kind of an ambiguous answer, but what is considered the cause of MOGAD?

[00:07:18] **Dr. Eoin Flanagan:** Yeah. That's a good question. And unfortunately, we don't know really the full cause. What we do know is that sometimes, very rarely, or sometimes it can be triggered by infections.

[00:07:30] So, a lot of patients will report that they have a prodrome, or just before they develop their neurologic symptoms they might have a flu-like illness or a diarrheal illness or some sort of illness. And very, very rarely we've seen vaccinations as a potential trigger. But really, we don't know the exact cause of this disease, just like with multiple sclerosis and NMOSD.

[00:07:52] We know that the MOG antibody seems to be quite important in it, but we really don't know what triggers it in the first place. And I think that's something we need to study more and see if there are genetic causes or risks there and other things. But it's early in the stage of our understanding of MOG antibody disease, so we're not fully sure at this time.

[00:08:13] **Krissy Dilger:** Thank you. And Dr. Samudralwar, what are the demographics for people who have MOG antibody disease? For example, is it more likely to occur in children rather than adults or in a certain demographic?

[00:08:29] **Dr. Rohini Samudralwar:** Well, MOG antibody disease is an autoimmune condition. So, like many autoimmune conditions, it tends to, it can affect women more than men. We, the numbers right now are quite small, and I think we need more dedicated large-scale studies to better understand the true demographics of this disease. And we tend to see it more in Caucasian, perhaps more female, more than men. And then, we used to think it was a disease that was primarily in children actually, but have come to realize that it can very much affect adults as well. And that's truly a benefit from all the testing that we have available now.

[00:09:07] **Krissy Dilger:** Great. Thank you. Our next question is, how is MOGAD diagnosed, i.e., the diagnostic tests used, clinical characteristics, et cetera? Dr. Flanagan?

[00:09:21] **Dr. Eoin Flanagan:** Yeah. So, the way we diagnose MOG antibody disease is based on the patient's symptoms and signs. And we, an MRI scan or imaging of the brain plays an important role. So, we usually look at that and see if it looks like this demyelinating disease and the particular features that might look like MOG antibody disease. And then the second component, in addition to how the patient's symptoms and signs are when the neurologist examines them or ophthalmologist, and then, and what the MRI looks like.

[00:09:50] And then the third component is the antibody test. So, this is best tested in blood. And the MOG antibody is a very reliable test, really a good test. And we look at those findings and put them all together. We'll talk a little bit later. Sometimes the MOG antibody seems to be a little bit sticky. So, sometimes people will have a low level of MOG antibody where they might have another cause for their symptoms. So, we can perhaps come back to that later but that's how we diagnose it, based on the symptoms and the findings on examination, the MRI findings, and the antibody test.

[00:10:29] **Krissy Dilger:** Great. Thank you. And Dr. Samudralwar, how is MOG antibody disease differentiated from neuromyelitis optica spectrum disorder, and especially in people who are negative for both antibodies?

[00:10:44] **Dr. Rohini Samudralwar:** Yeah. I mean, at the, at the more superficial level, it's really the testing that helps differentiate. But as far as the symptoms are concerned, even there, even then there can be a lot of overlap. So, as I mentioned before, both entities can have optic neuritis, many times involving both eyes

at the same time, can also present with the transverse myelitis. But what's interesting about MOG antibody disease is that we tend to, we can see more involvement of the brain, less so in NMO spectrum disorder.

[00:11:15] And so, many times we rely on the clinical symptoms in that way and at the MRI distribution to help differentiate, especially when the patients might be seronegative. The other way that we can help is, is also looking at other subtle clues. So, for example, MOG antibody overall may tend to be more steroid responsive than something like NMO spectrum disorder, which many times can actually require the use of additional therapy like plasmapheresis. So, that even then can be clues as well.

[00:11:51] And even with NMO spectrum disorder, we tend to see more severe disability after steroids compared to MOG. Again, the numbers are on the lower end for MOG antibody disease. It is, it is more rare overall. So, further studies looking into this, and larger population observations could be helpful in differentiating further.

[00:12:14] **Krissy Dilger:** Great. Thank you. And we did get a question from someone in the community. Dr. Flanagan, can a person be positive for MOG antibodies but have a different diagnosis than MOG antibody disease?

[00:12:28] **Dr. Eoin Flanagan:** Yeah, unfortunately, the antibody, with the MOG antibody, we use this technique called the cell-based assay. And the glycoprotein, which is part of the MOG, might be a little bit sticky. And sometimes other patients with other diseases like multiple sclerosis, strokes, or tumors, kind of have some low-level binding and that results in a low, positive level of the MOG antibody.

[00:12:51] So, it's always important when, when I see the patient in the clinic, that I put together what their patient symptoms are, what their MRI looks like, and, you know, sometimes we'll also analyze the spinal fluid as well and make sure that everything fits well with MOG antibody disease and that there's not a better different diagnosis, because obviously we want to treat the underlying disease. So, it gets a bit confusing, but at the low level of the antibody, there can be some false positives.

[00:13:19] We're kind of aware of the risk of false positives from COVID and different things. It's more out there in the community. So, I think people have some understanding. So, it's important for everything to fit well together. But most of the time, it's still a very good test. So, in most patients, it will be the correct answer, but sometimes we can see it low positive with other diseases.

[00:13:39] **Krissy Dilger:** Great, thank you. Dr. Samudralwar, why do people test positive for the MOG antibody in the CSF as well as serum? Is it rare to test positive in the CSF, and does this tell us anything about the presentation or disease?

[00:13:58] **Dr. Rohini Samudralwar:** This may actually be a better question for Dr. Flanagan. I'll probably defer to him, and in the specificities beyond that. We usually test in the serum because the sensitivity and specificity of the testing is much better, and I haven't found that it's been too useful in the CSF.

[00:14:16] **Dr. Eoin Flanagan:** Yeah, I think that's a, it's a good question. I think there have been some studies coming out showing that, you know, there may be some use in the spinal fluid where some patients were positive only in the spinal fluid, but we need more studies of the spinal fluid to see, is it really that useful? I think, initially, the disease was described by the blood test, and the blood test really picks up more, much more cases.

[00:14:40] So, you may miss a case if you only test the spinal fluid. So, we're still recommending everybody be tested in blood. But the spinal fluid analysis is something that we're looking at and I think is an area of

active study to see both are those patients more likely to have a severe course, or is there something different about those patients? Because we can pick it up in the spinal fluid. So, that's kind of an area of active study. But for now, really, it's best considered as a blood test.

[00:15:07] **Dr. Rohini Samudralwar:** I think there was a similar kind of story behind NMO spectrum disorder as well. Is that right, Dr. Flanigan?

[00:15:13] **Dr. Eoin Flanagan:** Yeah. It's similar. Yep. Yeah. It's better tested in the blood with the aquaporin-4 antibody, and we don't tend to pick it up as much in the spinal fluid. So, if you only test the spinal fluid, that can be a problem. So, you really want to test the blood. But we, we are looking at the spinal fluid. We're interested in studying it more and seeing if it is useful.

[00:15:34] **Krissy Dilger:** Okay, thank you. And what are the acute treatments used for MOG antibody disease? And what is the timeframe for receiving these treatments? For example, how long after symptom onset can they be administered? Dr. Samudralwar?

[00:15:53] **Dr. Rohini Samudralwar:** In the acute setting, meaning pretty soon after symptom onset and we're pretty certain this is some sort of demyelinating entity - probably MOG antibody disease, we want to start off with high-dose steroids. Again, very similar to the other demyelinating conditions like MS or NMO spectrum disorder. And many times, practitioners will do three to five days, a thousand milligrams, high doses to really help with minimizing the active inflammation that's there.

[00:16:25] And like any other disease, it's important to treat as soon as you have an understanding that this might be MOG antibody disease. Sometimes, initially, it can be tough, especially in the first 24 hours. So, we want to make sure that there are symptoms that would make sense with correlating with brain or spinal cord disease, and they're constant, lasting at least 24 hours, to be more certain that it would fall within this category.

[00:16:52] And then I think you also asked if there's any other treatments after this as well. So, you know, steroids tend to be the, what we give in the acute setting. And, rarely, but we can also use plasmapheresis, which is something that can remove any pathogenic antibodies or antibodies that are causing the problems and the symptoms that we're seeing.

[00:17:15] Usually with MOG antibody, it doesn't, we don't really need to rely on that so much, and steroids can be quite effective. But we think that it's a relapsing condition, and so we have to then talk about immunotherapy - ways to prevent further relapses or further symptoms of this disease down the line.

[00:17:36] **Krissy Dilger:** Okay, great. Thank you. And Dr. Flanagan, can you explain why you might use one treatment over another or why some people might receive multiple treatments and others only receive one? Also, are there any side effects for any of the treatments or risk factors one should be aware of?

[00:17:54] **Dr. Eoin Flanagan:** Yeah. So, that's a good question and covers a number of different things. So, firstly, the way we think about treatment is treatment of the attack, of the acute attack. And, as Dr. Samudralwar mentioned, the, the steroids are really the mainstay of treatment. Steroids can cause some side effects, because we give pretty high doses. So, sometimes in elderly patients, they can develop some confusion.

[00:18:19] Sometimes people have a hard time sleeping for those few days when they take the steroids. And if the steroids don't work, or if the patient is not fully recovered, sometimes we'll use plasma exchange. The plasma exchange is a, is a treatment where we put a, a line in, into the neck oftentimes, and we remove all of the antibodies in the system, in the body.

[00:18:41] And sometimes that can cause some complications from placing that line, that's what we call a central line, into the neck. Or sometimes can reduce some blood counts when you take that treatment. And then a third treatment is IVIG, which is kind of trying to pull antibodies into the system to neutralize all the bad antibodies, is the way I think about it.

[00:19:04] And that treatment can be given just through a regular IV, and so it's a little bit easier. And sometimes that's used commonly in children with the acute episodes. It's a pretty safe treatment. Rarely we can see people who get, sometimes people get headaches with that. Rarely, blood clots can be a side effect of that acute treatment.

[00:19:25] For the chronic treatment, I don't know if we want to talk about that now or come back to it later. The chronic treatments can have other side effects. They're more for preventing future attacks and the side effects, a lot of those relate to dampening down the immune system and an increased risk of infection. But one thing I will mention is that for the chronic treatments, is that in some people, up to 50% of patients, they just have a one-off episode.

[00:19:52] So, we don't want to put them on a long-term treatment and put them at risk of those side effects if they're not going to have another episode. So, in general, a lot of times we will wait and see if the patient develops a further relapse, and at that point we'll initiate more of those long-term treatments. But we make exceptions, and we treat it on a case-by-case basis, but that's a general approach that we have used, too.

[00:20:15] **Krissy Dilger:** Okay, great. Thank you. And you mentioned waiting to see about relapses. So, Dr. Samudralwar, how likely is it that someone with MOG antibody disease will experience a relapse?

[00:20:30] **Dr. Rohini Samudralwar:** Yeah, I think this is one of the unique features of MOG antibody disease compared to some of the other disorders where, like Dr. Flanagan mentioned, up to 50% might actually just have one event and that's it. And so, we don't want to commit someone to lifelong therapy unnecessarily. And so, it, many times it involves close monitoring.

[00:20:54] So, it's, it's pretty common to just have follow-up and do clinical monitoring, perhaps even reviewing MRIs to see if there's anything showing up under the surface on the, on the MRIs, even if the patient isn't having symptoms. And so, that can sometimes help us and guide us in whether or not that person might need long-term therapy with an immunosuppressant.

[00:21:18] **Krissy Dilger:** Okay. Thank you. Our next question is, is it possible to have another rare neuroimmune disorder in addition to MOGAD, such as acute disseminated encephalomyelitis or transverse myelitis? Dr. Flanagan?

[00:21:34] **Dr. Eoin Flanagan:** Yeah. I can explain that. I think sometimes people can, the, the terminology of these conditions can be a little bit confusing. Because the way I think about it is that those syndromes that were mentioned, the acute disseminated encephalomyelitis or transverse myelitis, are kind of, they're the types of attacks that patients can have, and they can occur with many different diseases, while the disease itself is kind of its own entity.

[00:22:01] So, we have three different demyelinating diseases. One is MOG antibody disease, one is the NMOSD with the positive aquaporin-4 antibody, and the third one is multiple sclerosis. And those other episodes, like transverse myelitis, acute disseminated encephalomyelitis, are more what we use to describe the attacks. But sometimes patients will receive a diagnosis of ADEM, or acute disseminated encephalomyelitis, or transverse myelitis, and when we test for all those antibodies, everything is negative, and they're left with that diagnosis.

[00:22:33] But if the MOG antibody comes back positive, then we would move those patients and describe them as now having MOG antibody disease. Or if the aquaporin-4 antibody was positive, then they would move to having the aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder.

[00:22:49] So, it can get a little bit confusing, but once you have the MOG antibody, you really enter the MOG antibody disease. And if you're negative for all the antibodies, then we really can't categorize you as having the antibody-positive disease. So, it gets a little, it's a little bit confusing, some of the terminology, but hopefully that clarifies a little bit.

[00:23:10] **Krissy Dilger:** It does. It does. Thank you. Dr. Samudralwar, what does the recovery process involve following a MOGAD diagnosis? Do people typically fully recover, or can there be lasting damage? Also, is there a difference in prognosis for children who are diagnosed versus adults?

[00:23:28] **Dr. Rohini Samudralwar:** Yeah, the recovery process might be variable, and it depends on a couple of factors. One is how soon someone might be able to get therapy and an effective dose of steroids or plasmapheresis or IVIG that was mentioned before. The sooner therapy can be started, in general, tends to portend better recovery as well, and hopefully minimize any permanent damage. The other factor is what areas of the brain might be involved.

[00:23:59] So, for example, if you develop inflammation from MOGAD in an area of the brain that has a lot of redundant or backup pathways, many times you can have minimal symptoms to no symptoms. Whereas if it's somewhere in the spinal cord, where we call, it's part of some of what we call eloquent structures, there's not too many backup pathways, so you can have pretty severe and debilitating symptoms from that.

[00:24:26] And again, recovery will many times depend on how long you've had the symptoms and how quickly you can start therapy with the acute treatments. And then, as far as the differences in children versus adults, there were a couple of studies in the past few years that looked into this. And it seems that although at onset, disability might be about the same in children and adults, later on down the line it seems like children do tend to have a more substantial recovery.

[00:24:57] We see this in many different diseases. Children tend to be more resilient in that way. We hear terms like neuroplasticity and things like that, that might play a role here in their recovery versus adults. But at the same time, the importance of starting treatment as soon as one has a relapse or symptoms still is very, very important, whether they're children or adults.

[00:25:24] **Dr. Eoin Flanagan:** Right. I might make a quick comment as well, just to mention that, you know, with multiple sclerosis, we can sometimes see this delayed, slow, gradual progression that we call secondary progressive disease, and we don't tend to see that with the MOG antibody. So, they tend to have a better long-term outcome in that way. And then, they do tend to recover a bit better with the treatment than with the aquaporin-4 antibody-positive NMOSD. So, there is, there does tend to be a little bit better recovery from the attacks than the aquaporin-4 antibody, and then they don't have, patients don't usually develop that secondary progressive course, which is useful.

[00:26:03] **Krissy Dilger:** Okay, great. Thank you so much. And, Dr. Flanagan, is rehabilitation recommended following a MOGAD diagnosis? How long should the rehabilitation process last?

[00:26:15] **Dr. Eoin Flanagan:** Yeah, that's a good question, and it might depend a little bit on the type of attack. You know, if the patient has just an optic neuritis, then rehabilitation, depending, may be more in the realm of visual and ensuring that patients can see and get therapy in that way. While with transverse myelitis or

with acute disseminated encephalomyelitis, or ADEM, patients will often be hospitalized for longer and may require additional rehabilitation, like rehabilitation in the hospital for a few weeks to recover from the episode might be necessary. So, sometimes it depends on the, the type of attack. And then, you know, when you have involvement of the spinal cord, sometimes the bladder and the bowel can be affected. And oftentimes we need to help manage those conditions with additional medications and other things in conjunction with our rehab physicians.

[00:27:09] **Krissy Dilger:** Okay. Great. Thank you. And Dr. Flannigan mentioned maintenance therapies earlier. So, Dr. Samudralwar, what maintenance therapies are recommended for someone with MOG antibody disease, and how can someone decide which one to choose?

[00:27:24] **Dr. Rohini Samudralwar:** Yeah, in reference to the maintenance therapies, we're talking about immunosuppressive or immunomodulatory therapies that are meant to prevent relapses or further disability with this disease. So, would really, like Dr. Flanagan mentioned earlier, would be started in, in situations where we suspect there might be recurrence of the disease.

[00:27:48] Some options... Unfortunately, you know, there are, there isn't an FDA-approved option at the moment, but what has typically been used in the past are things like rituximab, which is an infusion or IV medication that's given every six months and the immune target being a CD20 cell or CD19 inhibitors. These are all B cells sort of therapies, and that has seemed to be somewhat effective in preventing disease and MOG antibody disease. Other types of oral medications that have been used in the past are some older immunosuppressants like Imuran or azathioprine and methotrexate, also mycophenolate, and mofetil.

[00:28:32] Unfortunately, there aren't large-scale studies on this, hopefully coming soon, looking at what might be better. And at the moment, what we really do is individualize it to the patient, what is tolerable, where we can minimize side effects, and what might have the best efficacy in that individual.

[00:28:51] **Krissy Dilger:** Okay. Great. Thank you so much. Dr. Flanagan, what type of doctors should a MOGAD patient see on an ongoing basis? If you have no major problems or concerns, do you still need periodic checkups with a neurologist and other specialists from time to time?

[00:29:09] **Dr. Eoin Flanagan:** I think initially, certainly after the first episode, it's probably worth following up. You know, the main doctors who look after patients would be a neurologist, ophthalmologist, neuro-ophthalmologist, would often be closely involved, and then sometimes our rehab physicians or urology to manage the bladder symptoms. You know, if a patient has a one-off episode and they're stable with their neurologist over a few years, and some of those patients will only need to follow up if they develop new symptoms, and they may not need ongoing follow-up.

[00:29:40] On the country, if a patient is, you know, has relapsing disease, has had more than two episodes, then a lot of times those patients are on treatment, and we do like to follow them closely to make sure that they're tolerating the treatment, that there is no active changes. The MRIs are not really as useful in follow-up as they are in multiple sclerosis. We do sometimes repeat the MRIs, but we don't tend to see as much. When the patient is not having symptoms, we don't tend to see as much active lesions on the MRI at that time.

[00:30:12] **Krissy Dilger:** Okay, thank you. Doctor Samudralwar, does the titer level for the MOG antibody indicate anything such as the severity of the disease or the likelihood of relapse?

[00:30:26] **Dr. Rohini Samudralwar:** So, when we're talking about the titer, that's the number that comes along with the positive or negative test. And so, we have a positive test that tells us how much of the antibody

might be in, in the blood or the CSF that we're testing. And, although I wish it could be as reliable to tell us, you know, if someone is developing a relapse or a severity of disease, I don't know that we have enough data for that yet, but I think that is something that folks are looking into and, and hoping that we can rely on that a little bit more beyond just a diagnosis of the disease itself.

[00:31:04] And then I think Dr. Flanagan had mentioned earlier about the lower titers being sometimes, can be a little bit challenging because it may suggest a false positive and may suggest actually another entity. And I think Dr. Flanagan, you wanted to actually come back on just this area about the titer.

[00:31:23] **Dr. Eoin Flanagan:** Yeah, and that the titer, this is an excellent point, and I agree completely. The titer, when the titer is very high, it does give you a lot more confidence in the diagnosis. So, we can generally be much surer at higher titers. You know, when the titer is low, we did a study at Mayo Clinic, and sometimes it can be as low as a 50/50 chance that you really truly have MOGAD disease.

[00:31:45] The problem is, is if we were to raise our cutoff a little bit higher, then we would miss a lot of patients who really have MOGAD. So, you really want your neurologist, a neurologist who's clued in, who maybe has experience with MS to be able to be sure you have the right diagnosis. But, and when the antibody is high, then it gives you more confidence, and there is probably a little bit higher risk of relapse.

[00:32:09] We tend to follow the patients though more from how they're doing clinically. Are they having any attacks? Rather than sometimes we repeat the antibody tests down the line, but we don't really know yet what that means. Because in some patients who have a one-off episode, the antibodies go away and, you know, they never have another episode, while other patients, the antibody stays around and they might be at higher risk, if the antibody stays around, of a relapse. But we mostly base our decisions around if a patient has new symptoms or new symptoms of another attack down the line.

[00:32:41] **Krissy Dilger:** Okay. Great. Thanks. And, as a quick follow-up question, you mentioned you may retest someone's antibody levels. Do you know how often someone should get their levels tested?

[00:32:54] **Dr. Eoin Flanagan:** There's not a definite answer for this. I think sometimes, you know, we do that, we collect the samples to learn more. So, at the moment, part of the, the NIH grant that I have on MOG is to follow these patients and see what happens the level over time.

[00:33:11] But in some patients, we don't do it at all, and we just follow the patient and see how they're doing. So, it's very variable. Or if they've had a long period of remission and then they come back and have a new attack, sometimes we'll repeat the antibody test. So, sometimes we repeat it at six or 12 months. But again, most of the decisions should be based on if you're having more attacks, that's what's really the most important thing.

[00:33:35] **Krissy Dilger:** Okay, thank you. Dr. Samudralwar, a member of our community asked a great question. If someone was diagnosed with transverse myelitis or seronegative NMOSD, perhaps years ago before the MOG test was discovered, should they get tested for MOG antibody disease? Or what are the circumstances in which they should be tested, and how would they go about doing so?

[00:34:03] **Dr. Rohini Samudralwar:** Oh, that is a really good question. Yeah, if... You know, our testing has improved dramatically over the years. And in fact, you know, in the past, we didn't really have this available commercially outside of research studies. And so, many folks who unfortunately had transverse myelitis or optic neuritis or, or ADEM may have just gotten the, that, that title rather than the ultimate diagnosis of MOG antibody disease.

[00:34:31] So, I would say if, you know, you had a one-off event in the past and recovered and have not since had any further disease or any other disability, it may not be quite as important to get tested for it, especially if you've been completely stable without any, anything else new or different in your, in your medical condition.

[00:34:54] However, if you continue to have symptoms or hadn't, hadn't recovered from that previous episode, it may be worth checking and talking to your neurologist or a neuroimmunologist or MOG specialist who, and discussing getting tested for this and seeing if it can give you clarity on the overarching disease, because then it might help inform whether or not you need to be on long-term therapy or not.

[00:35:21] But it would probably, like you're mentioning before, it, the test is really most useful when you're having active symptoms and we have the clinical symptoms to really correlate with the actual test itself.

[00:35:38] **Krissy Dilger:** Okay, thank you. And then we did get another question from the community. Are there similarities or differences in demyelination on an MRI of an MS patient versus a MOG patient? For example, the lesion size or the number of lesions. Do active MOG lesions light up, so to speak, in a contrasted MRI in the way MS lesions can? Dr. Flanagan?

[00:36:02] **Dr. Eoin Flanagan:** Yep. Happy to answer that. So, yeah, the MRI can look a little bit different with the MOG antibody. There is some overlap. So, what patients will recognize is when the doctor shows them the MRI, we see kind of white spots within the brain with both disorders. But sometimes the ones with multiple sclerosis are, are quite round, and they're kind of clearly defined.

[00:36:23] You can see the borders very nicely. With the MOG antibodies, they tend to be a bit more fluffy or what we call ill-defined. And sometimes, they're a little bit larger, and they don't tend to have as intense a contrast enhancement as the MS. And we don't tend to see, sometimes with the MS we see nice rings of, of enhancement.

[00:36:43] We don't send to see that as much with the MOG antibody. And then in the spinal cord, the lesions tend to be a little bit longer with the MOG antibody. So, they often extend beyond three vertebral segments, which is a cutoff that we use. But with MS, they tend to be shorter. They extend about the length of one vertebrae of your back.

[00:37:00] And, the other thing I'll mention is that, which is quite interesting and something that we've, we've done some recent studies on, is that when you look and follow up, when you follow up patients and you repeat the MRI down the line, a lot of the MOG antibody, those white spots go away completely. Most or all of them often go away completely, and that suggests that the MOG antibody recovers better.

[00:37:22] While with MS, we often see scars left on the brain where we see some white spots that stay there. And that might be part of the reason, those, there's some differences in the long-term where those MS patients develop more progression. We don't know for sure, but that's just something we're interested in. So, a lot of times, the MOG antibodies will disappear or vanish, you know, in an MRI a year or two years down the line.

[00:37:48] **Dr. Rohini Samudralwar:** I've noticed that in my patients actually. And so, I was really excited to see that study, Dr. Flanagan. And it hopefully suggests something really good for these MOG patients.

[00:38:00] **Krissy Dilger:** Great. Thank you so much. Yeah, that is great, great news. We also got a question from someone asking about a study. So, if you have heard of it, there was a study: Selective Depletion of Antigen-Specific Antibodies for the Treatment of Demyelinating Disease. This person was just wondering if this was planned for commercialization and if it would possibly lead to a treatment for MOG.

[00:38:24] Dr. Samudralwar?

[00:38:27] **Dr. Rohini Samudralwar:** Could you repeat that first part? What was that?

[00:38:29] **Krissy Dilger:** So, the paper is called Selective Depletion of Antigen-Specific Antibodies for the Treatment of Demyelinating Disease. And the author has created agents that selectively eliminate the antigen MOG-specific antibodies without affecting the levels of antibodies of other specificities. And this person just wants to know if this is something that's planned for commercialization or will possibly lead to a treatment for MOG?

[00:38:56] **Dr. Rohini Samudralwar:** I don't know that I'm familiar with that study, but based on that description, shows some, some interesting... or sounds like something interesting that for MOG antibody disease. I'm not aware of anything getting commercialized from this aspect. I'm not sure if Dr. Flanagan might be more familiar with that.

[00:39:16] **Dr. Eoin Flanagan:** Yeah. I, I don't, I don't, I don't know the particular study, but I know that, that, you know, people are looking at, you know, how could we deplete, you know, how could we get kind of more targeted treatments so that we could just target the MOG antibody and not target the whole immune system and maybe have less side effects of infection.

[00:39:34] So, I think that's going to be the future, you know, that will be, but we're not there yet. I do think there's going to be some clinical trials probably coming in the next few years for medications to try and prevent attacks. So, we know with the aquaporin-4 antibody that in the last two or three years, there's been three new proven treatments in clinical trials.

[00:39:54] So, we really need to do the same thing with the MOG antibody and figure out some treatments that work for our patients. So, we're very hopeful that we'll be able to bring more, more treatments that can work better for our patients with MOG.

[00:40:08] **Krissy Dilger:** Okay great, thank you. We also got another question that came in just now. Dr. Samudralwar, what is the difference between lesions and demyelination? The lesions seem to respond to steroid treatment and may go away over time, but does demyelination disappear or reduce over time?

[00:40:29] **Dr. Rohini Samudralwar:** Yeah, this is a good question. I think sometimes as physicians or folks in the medical community, we, we tend to use words interchangeably and maybe could spend more time explaining it a little bit. When we refer to lesions and demyelination, we're many times actually saying the same thing. Lesions are usually what, when we're, when we mention that, we're mentioning the inflammation that we're seeing in the brain or spinal cord on the MRI. And demyelination is the description of what, what's kind of happening at the cellular level.

[00:41:02] So, the myelin sheath that is kind of like the insulation that covers all of the nerves is being, kind of, is being destroyed and peeled away when we're talking about diseases like MOG or NMO spectrum disorder or, or multiple sclerosis. And that, in that process, there's a ton of inflammatory cells that start to attack and try to repair, and sometimes also exacerbate the, the destruction of the myelin, and that results in a lesion or the inflammation that we see in the brain.

[00:41:34] So, really, we're, we're kind of saying this, usually both words interchangeably. So, whenever we're giving steroids, we're trying to minimize the inflammation, minimize the inflammatory response from the demyelination that's happening at the cellular level. I hope that helps and describes that a little bit better.

[00:41:56] **Krissy Dilger:** Yeah, that's great. Thank you. And as kind of a follow-up, Dr. Flanagan, is there anything that can be done to repair that demyelination, either on the optic nerve or the spinal cord or wherever it may be?

[00:42:11] **Dr. Eoin Flanagan:** Yeah, that's an excellent question. And I think, you know, the body itself is good in that when the inflammation happens and we lose all this myelin, your body does try to remyelinate and put the covering back on the nerves. And actually, with the MOG antibody disease, we think it probably does that a little bit better in that some of these areas of that we presume are demyelination on the MRI then will eventually go away.

[00:42:36] You know, it would be nice also in these diseases if we could develop a treatment that would put the myelin or help put the myelin back on the nerves. But we're not quite there yet with those kinds of treatments, but I think there's going to be more studies in that regard. But right now, I think, you know, the main thing, like Dr. Samudralwar mentioned earlier, is getting in for early treatment with the steroid treatments to try and really treat the attacks as quick as possible to help them recover and help that, you know, remyelination take place.

[00:43:11] **Krissy Dilger:** Okay, great. Thank you so much. Dr. Samudralwar, we got a question from someone who is receiving rituximab. They want to know, why would someone have a relapse who is on rituximab when it's supposed to deplete 98% of your B cells?

[00:43:31] **Dr. Rohini Samudralwar:** Yeah, this is a great question. And it really, it is... the answer is really because of what rituximab specifically targets. It's important to note that we have multiple different types of B cells in our body, not just... B cells aren't just kind of a monolithic entity. So, rituximab affects the CD20 B cells, which means, when we say any term with a CD in front of it, it usually is an indication of a marker on some of the immune cells.

[00:44:06] So, the B cells that have the CD20 marker are the ones that are specifically affected with rituximab. However, there's several other types of B cells that have different CD markers that are not necessarily affected with rituximab and therefore may still be able to cause some trouble resulting in relapses.

[00:44:28] So, although it, it can be quite effective and quite helpful in MOG antibody disease and other conditions, it's not going to be perfect, because it's not fully affecting every single cell that might be causing trouble in the brain or spinal cord.

[00:44:44] **Krissy Dilger:** Okay. Thank you for that explanation. Is there any research currently being done on MOG antibody disease right now? Dr. Flanagan?

[00:44:53] **Dr. Eoin Flanagan:** Yeah. Yeah, there's a lot of people very interested in this disease, which is great news for our patients. And I have to say, thank you to all the patients, because without patients participating, being willing to be involved in research, we wouldn't be able to learn quite as much. But we're learning a lot about this disease.

[00:45:10] And there's many different studies, both looking at, you know, how do we make sure we have the correct diagnosis? How common is the MOG antibody disease? And then I think really the next. Types of research are going to be, how can we better treat the disease and prevent those attacks that can happen? I see many patients commenting that they've had multiple relapses, and we really want to be able to get a treatment that we can prevent those relapses from happening and keep patients stable.

[00:45:38] So, I think there's lots happening in the field, there's lots of people out there who are interested. We're, and we appreciate everyone's involvement. We have a lot of patients who give us samples, where we retest the antibodies, and we're looking in the laboratory to see if we can see, are there any pathways that look elevated with the MOG antibody that we could target with the treatment?

[00:45:58] Because that's how we figured out some treatments for the aquaporin-4 antibody neuromyelitis optica spectrum disorder. So, if we can do the same thing with the MOG antibody, that'll be really successful. So, thanks again to all people participating in research.

[00:46:14] **Krissy Dilger:** Yes, that's a great point. and, yeah, that's very important for people to participate when they can. It helps the future of, of medicine. This next question comes from the community as well. This person was diagnosed with MOG antibody in February. They have, they have tested negative for the antibody currently and their MRIs for their cervical, lumbar, and thoracic areas show no additional lesions. They are told everything looks good. However, this person experienced a slowly increasing numbness below the waist, and they're just wondering if this is something seen as a result of MOG antibody disease, and if so, is it treatable? Dr. Samudralwar?

[00:47:00] **Dr. Rohini Samudralwar:** Yeah, this can be really challenging sometimes where, you know, MRIs may not be as helpful in explaining some of the symptoms one might be experiencing. And there can be a whole host of reasons for why that is. And it's really important to get a good clinical examination from your doctor, and that can many times help figure out if it's coming from the spinal cord or perhaps coming from the nerves outside of the spinal cord that might be causing the symptoms that you're experiencing and maybe related to something else.

[00:47:32] And so, it might be that what's necessary is not directly treating the MOG antibody, but treat symptomatic therapies that can help with the, the symptoms directly rather than changing or altering anything with the MOG antibody itself. So, it would really depend on the examination findings that your physician sees and, and going from there.

[00:47:59] **Dr. Eoin Flanagan:** And I can jump in there just for a second. I think, you know, when you might be suspicious for an attack, it's always important to, you know, to talk to your doctor and, you know, at that time, they may want to consider an MRI to confirm that. Because we don't like... These medications have side effects. So, we don't like to give patients lots and lots of steroids for symptoms that are just from the prior damage rather than from active inflammation right there. So, it's quite important that an MRI would confirm that, you know, that a patient has a relapse.

[00:48:30] **Krissy Dilger:** Okay, great. Thank you. We got another question from the community about stress. So, is there anything known about if stress can either cause MOG antibody disease or possibly exacerbate the condition once you already have it? Dr. Flanagan.

[00:48:49] **Dr. Eoin Flanagan:** Yeah. I'm not aware of any studies on that, I suppose. You know, we, we know that stress can cause problems in other parts of the body, just as physicians, with stress ulcers, people will be aware of. So, we don't know. It's good always to try and limit stress. But we don't really know how much it plays a role in the disease, I think at this stage.

[00:49:12] **Dr. Rohini Samudralwar:** What you might see is the stress can sometimes cause worsening of previous symptoms or sometimes feel like your old symptoms might be exacerbated, so it might not

show something on the MRI as a, as a relapse necessarily, but can, can feel like you're having some sort of symptoms and really just be triggered from stressful, stressful factors in your environment or something else going on. So, it can affect you in that way, but a bit indirectly than, than direct impacts on, on new relapses or new, new lesions on the MRI.

[00:49:54] **Dr. Eoin Flanagan:** That's an excellent point, yeah.

[00:49:55] **Krissy Dilger:** Okay, great. Thank you. We just got another question about rituximab. So, a person wants to know if rituximab can be taken for someone's whole life or if it has kind of a, only a timeline by which you should stop taking it after a certain point? Dr. Samudralwar?

[00:50:16] **Dr. Rohini Samudralwar:** Good question, and one that comes up with a lot of my patients. We always get the question of, you know, when can I stop the medication? How long do I need to be on it? And I think this question is sort of in line with that. We don't really have end dates for many of these medications. I think that might be a bit practitioner dependent or perhaps even dependent on the symptomatology of, of the individual. So, ideally, we don't want to commit someone for lifelong therapy unnecessarily, all the more reason to be absolutely sure about the diagnosis.

[00:50:51] But as far as we can tell, you know, long-term therapy when it's necessary is, is helpful. And we do our best to minimize any side effects through regular blood checks and examinations and MRIs. But I don't know that we have enough data to look at a full lifespan in, in many, in several different people to know ultimately what might happen with medications like rituximab.

[00:51:19] **Krissy Dilger:** Okay, great. Thank you. We also got a question from the community. Do you know what causes fatigue in these disorders? And even when you're not having a relapse or an episode, so to speak, the fatigue still seems to be there. Dr. Flanagan?

[00:51:38] **Dr. Eoin Flanagan:** Yeah, we don't know. That is, that can be common, particularly actually with multiple sclerosis where it's most common. And we don't really have a good understanding why that is. It might be, you know, from that background, ongoing inflammation that just at a low level, you know, contributes to people being fatigued.

[00:51:57] We, we see it probably, I would say, less with the MOG antibody disease than we do with multiple sclerosis, but it can be an issue for patients. And sometimes, you know, having a timed nap, or sometimes we can use some medications that can help increase energy. Or, you know, we, we do recommend people exercise if they can to try and build up their stamina and fitness, and sometimes that can help, too.

[00:52:20] **Krissy Dilger:** Great. Thank you. We're almost at the end of our time, but we did get one more question. Dr. Samudralwar, this person wants to know if they, they keep getting a belly button infection and are on Actemra. Is there anything they can do? This person says that they've tried some meds and they have all failed so far.

[00:52:44] **Dr. Rohini Samudralwar:** I'm sorry. Yeah, that's probably best discussed with the physician seeing you and figuring out where the source of that infection is and what that organism might be, and if it is actually related to something like Actemra, the medication that you're on. It, it would really depend on the source and the cause of that infection.

[00:53:08] **Krissy Dilger:** Okay. Thank you so much. Real quick again, we are getting a few last-minute questions here. Dr. Flanagan, is there any treatment to recover loss of vision due to optic neuritis? This

person had an acute attack almost a year ago and lost all of the bottom field of their vision and just wants to know if there's anything they can do.

[00:53:28] **Dr. Eoin Flanagan:** Yeah, I don't think at this point, it's just about still waiting and seeing. Sometimes people can recover beyond one year. Most people, most of the recovery happens in the weeks and months after the episode. The important things really are to be on the lookout and to try and get early treatment when you do have the attack, because early on is when it can be most reversible and that steroid treatment can be quite important.

[00:53:53] And I know Dr. Chen, one of our ophthalmologists here at Mayo Clinic, has a study looking at what he calls steroid in the pocket, which is getting patients to have steroids at home. And if they did develop an episode of optic neuritis, they're not able to get in to see the doctor that, they could consider having some on hand to get them treated as early as possible, and looking to see if that might be useful.

[00:54:15] So, earlier treater treatment better, it's a little bit difficult beyond one year. There's not much else we can do at that point, other than watch and wait and hope, hope that we still get some ongoing improvement.

[00:54:27] **Krissy Dilger:** Great. Thank you so much. We are close to the end of our time here. I just wanted to give both of you the opportunity to add any last-minute thoughts if you have any. Dr. Flanagan, if you'd like to go first, anything we didn't cover that you'd like to mention?

[00:54:44] **Dr. Eoin Flanagan:** No, I just like to, you know, thank everyone out there with MOG antibody disease. We really appreciate, you know, all our patients. We, that's where we learned the most, from patients, reviewing their MRIs, them telling us their stories, and, you know, their involvement in research. And I'm really hopeful for the future, that we can develop more treatments to help patients, patients along the way. So, just a final thanks to everybody.

[00:55:08] **Dr. Rohini Samudralwar:** Yeah, thank you so much for having us. And, I have to echo a lot of the same sentiments. I, I think it's a privilege to be able to treat folks with rare conditions and have them trust us knowing that we're sort of learning about these diseases together. So, really, really grateful to, to our patient population. Thank you.

[00:55:29] **Krissy Dilger:** Thank you both so much. We really appreciate your time, and I'm excited to be able to offer this resource to our community because I think it's really important.

[00:55:38] **Dr. Rohini Samudralwar:** Thank you.

[00:55:39] **Dr. Eoin Flanagan:** Thanks again. Thanks everybody.