



Speaker 1-Moderator ([00:00](#)):

So, the first topic of conversation will be around optic neuritis. So, this question is for Dr. Chen and Dr. Chitnis. What is the difference between CRION versus recurring optic neuritis? What are the MOGAD patients more likely to present with?

Speaker 2-- John Chen ([00:15](#)):

That's a very good question. So, CRION stands for chronic relapsing inflammatory optic neuropathy. Essentially there you've got an optic neuritis that will present like any other optic neuritis, but it's very steroid dependent and often very, uh, where, when you come off the steroid you have a relapse. So again, it's steroid dependent. With relapsing optic neuritis, you can have an optic neuritis attack and then you can come off the steroids and you actually can do well for a while and maybe one or two years later you've got another optic neuritis. So that's where I put relapsing optic neuritis as opposed to CRION where you're steroid dependent, you essentially have an optic neuritis, you treat with steroids, it goes away, the second you come off steroids, it comes back. That's where I kind of make that distinction. And in terms of MOGAD patients, you know, they can present with relapsing optic neuritis where you have an attack one year and an attack three years later. But some patients can be steroid dependent where you have an attack, you treat with steroids, they get back to 20/20, they come off steroids and boom, it's back again. And then they kind of fall in that CRION category. It can go either way for those patients.

Speaker 3-Tanuja Chitnis ([01:20](#)):

So, I would absolutely agree, I think that MOGAD patients can have either form, but we know that MOGAD is very steroid sensitive. And so that's something that as a practitioner I've seen, especially in children with MOGAD, that as you start to taper down off the steroids, there might be a worsening of their optic neuritis or even a recurrence. And so, I think these terminologies, they probably need a little bit more fine tuning and especially as definitions are being developed for MOGAD, this is where I think we need to continue to do some work.

([01:20](#)):

Speaker 2-- John Chen ([01:53](#)):

Yeah, it's actually very interesting, because CRION is this kind of umbrella term and we didn't know about MOGAD before and now we're realizing that about half of CRION is actually MOGAD. And so, you know, we're still chipping away at this kind of umbrella term of CRION and we know that MOGAD is a very common cause of it.

Speaker 1-Moderator ([02:11](#)):

Great. And Dr. Chen, oh, go ahead Dr. Banwell

Speaker 4 -Brenda Banwell ([02:14](#)):

I'm sorry. I just wanted to make a comment because I think as a pediatric provider, we think very seriously about steroids and children as we do in adults. But, you know, chronic exposure to corticosteroids influences your growth, bone health, muscle health, body habitus, skin integrity. And so I



think a very important future research question is, in those children or adults that appear to be steroid responsive, can we actually intervene earlier with something else that would supplant the steroids and get them in a situation where they're not having relapses, but they're also not on chronic steroids? I just wanna emphasize the importance of that, particularly for pediatric health.

Speaker 1-Moderator ([02:55](#)):

Dr. Chen. One more for you. For patients who have had multiple attacks of ON and RNFL thinning, is OCT a good option for doctors to verify a relapse of ON? And how does the RNFL react during a relapse and how is it affected over time?

Speaker 2-- John Chen ([03:11](#)):

That's a very good question as well. So, with MOG optic neuritis, it tends to cause more disc swelling than other forms of optic neuritis, like multiple sclerosis and NMO. And so, with OCT in the acute phase, we can often get thickening of that nerve fiber, and that can be a helpful confirmatory sign that there's optic neuritis. The drawback is after you have an attack of optic neuritis, the thickness and nerve tends to get pretty thin and a thin nerve tends to swell less. So it gets, it ends up being a little bit of a less predictive way, but it's still something we look at. Another thing we can do is we kind of, you have your attack and then we can repeat the OCT six weeks later, and if there's a further decline that can help confirm there is an attack as well. But again, you get this floor effect pretty quickly with MOG optic neuritis. You can be 20/20 and have a thickness of 60, which is very, very low. It just hits that floor pretty quickly, even though the, the function tends to respond pretty well to steroids.

Speaker 1-Moderator ([04:08](#)):

So we're gonna switch topics and the next topic is diagnosis and relapses. This question is for Dr. Darshi and Dr. Banwell. What's the latest understanding of titer levels inside of the US and abroad? Is there a consensus on this meaning?

Speaker 5-Sudarshini Ramanathan ([04:25](#)):

So, I can start with that. MOG antibody testing is run in a number of established research laboratories. And the principles and the methodology are very similar between these laboratories, but the way that they identify titers and report them can vary from lab to lab. And each established research laboratory has a particular threshold by which they identify patients as being positive or negative. And their titers help them determine if they're low positives or high positives. So what we do know from multi-center international studies is that those patients who have high positive titers, there's fairly good correlation between the laboratories. What the meaning of a titer: so single titer in a patient who's positive is probably less helpful. What is quite interesting sometimes is looking at serial samples or serial longitudinal titers in a patient. The thought is that patients who have an acute episode at first onset or relapse have generally high titers. And when the patient is well in clinical remission, these titers might reduce. Some studies have shown that when patients become negative or seronegative, their risk of a relapse is lower, but this is not universally identified. I think the real challenge is what you do with those lower titers, those low positive patients, there's less agreement between the laboratories here and that's an area that needs further research.

Speaker 1-Moderator ([05:56](#)):



Dr. Banwell, anything to add?

Speaker 4 -Brenda Banwell ([05:58](#)):

So I think I agree a hundred percent with what was just said. So, the most important MOG test to, in my view at the moment, is the one performed close to the first attack. Done properly in a lab using, a cell-based assay and others on the panel can also speak to the assay biology, and the importance of the correct test is pivotal in the diagnostic phase. Some labs offer spinal fluid MOG testing. That is not the advised way to test from a diagnostics perspective. It may down the road have relevance in terms of severity of MOG or other important findings, but we don't know that yet. What we do know, and by we I mean the whole community, is that there are patients who have clear positive titers in the blood, but are negative in spinal fluid. So if you only tested them in spinal fluid, you would miss the diagnosis. And that has definitely been an issue with patients referred to me who, for example, never had the blood testing done, only had a spinal fluid test sent. So I think it's, you know, testing matters and I, and a blood tested onset is pivotal.

Speaker 1-Moderator ([07:09](#)):

This question is for Dr. Chitnis. Can you speak a little about the difficult cases in diagnosis? For example, MS versus MOG where we understand that with an MS pattern, type II, the MOG antibody is detectable in 90% of patients?

Speaker 3-Tanuja Chitnis ([07:25](#)):

Yes, this is a very good question. It's referring to what was historically known as the MS pathological subsets. And these were subsets one through four in pattern II, had a lot of, had a very clear antibody deposition. And so that deferred from the other MS patterns 1, 3 and 4. And what we now know about MOGAD pathology, and these are, this has been shown in cases of very clearly diagnosed MOGAD patients, is that there's a slight difference in the pathology. There's a very CD4 T-cell deposition and that's different from MS and as well there are antibodies and also complement activation in MOGAD patients. But there are some differences in MS pathology and MOGAD pathology. What we also know is that there are a number of patients with MS who will have typical MS-like lesions and attacks and present with a very MS-like picture but have low titer MOG antibodies. And that is a question that the community is trying to answer now through different case series and studies as to whether those patients really do have MS and respond better to MS treatments or have a form of MOGAD. I tend to think it's probably the first option and they probably have MS with a lot of different antibodies, which we know does occur in MS.

Speaker 1-Moderator ([08:47](#)):

The next question is for Dr. Banwell and Dr. Levy. Are there any new or upcoming diagnostic tools for adults and pediatric patients that can predict a relapse?

Speaker 4 -Brenda Banwell ([09:00](#)):

All right. I thought you were going to talk about diagnostic tools for MOGAD in the first place, which we are actively participating in a new diagnostic criteria format. But in terms of predicting relapses in at the individual person level, no, actually we are not reliably able to do that. If you look at the group level, patients with optic neuritis are more likely to have relapses that, for example, than patients with



myelitis as their first presentation. Children under age 10 with acute disseminated encephalomyelitis, or ADEM, as their first presentation are less likely to relapse than some of the other presentations of MOGAD. But when you look at an individual person, their MOG titer isn't reliably predictive of relapses. If they develop one or two, it's typically a small number of new changes on their MRI in the first three months to six months after their first attack. That has a 20% positive predictive value for relapses. In other words, 80% of the time you'd be wrong. And probably like almost anything in medicine, the most reliable identifier of someone who's going to relapse is time and close clinical observation. But unfortunately, we don't have a biomarker lab test or MRI signature that currently predicts it

Speaker 6-Michael Levy ([10:27](#)):

In the grownup world. I think that adults are a little bit more likely to relapse than children just in general. But as Brenda was saying, there's no individual marker. I think there are a few triggers that are, that have become obvious. First of all, withdrawal of steroids. So, when people come down off of their steroids, I think that that's a major risk for relapse. That requires close observation. And I think any activation of the immune system through vaccines or infection, those are also possible triggers that heighten my awareness that maybe a relapse could be coming. And I would say that the MOG antibody levels, if they remain high are also a little bit more predictive of a future relapse than someone who went from a high level to say a very low level where I would think that the risk of relapse is lower in that person. But as far as a biomarker that is predictive of a relapse, like a monthly blood test, for example, that could tell us when a relapse is going to happen in the next few weeks or so, we don't have something like that yet.

Speaker 4 -Brenda Banwell ([11:36](#)):

Can I make one quick comment, as we're ping-ponging adult to pediatrics, so I'll go back to pediatrics. One really important observation, Canada has a vaccine surveillance program that's quite rigorous that I've been part of for 30 years. And we actually have not linked vaccines specifically to any relapses. And I make that point very explicitly because children have a whole bunch of vaccines given. And it's a major question I get from parents all the time: Is it safe to vaccinate my child? We are facing as a community, an under-vaccinated pediatric population right now partly because of the pandemic and access and also a lot of concern about vaccines. Therefore, the infections we vaccinate against are on the rise. And a patient who's on immune suppression, if they have relapsing MOGAD who then gets chickenpox could end up with chickenpox encephalitis. We are at risk of seeing polio again.

([12:39](#)):

There are other infections that we vaccinate against that our pediatric patients need to be protected against. So, and certainly covid. So because we aren't linking a specific vaccine signature to a relapse risk in multiple sclerosis or MOGAD or Aquaporin-4, I think my advice on vaccines is I never give a vaccine within six months of an attack. Not because I actually think the vaccine's gonna trigger anything, but that's when a second event is most likely. And if a vaccine happened to be given, those two things are gonna look like they were related when they weren't. And then of course there needs to be strategies on when to vaccinate depending which therapy you're on and the type of vaccines you can get. And those, that's not specific to MOGAD that's related to just how to give vaccines if someone's on an immune suppressant. So that is just something I had to say because in children, the bigger risk to their health is not being vaccinated, not the other way around.



Speaker 1-Moderator ([13:33](#)):

The next section is the cognitive and behavioral questions. The first question is for Dr. Chitnis. Can cognitive and behavioral changes be symptoms of new disease activity or only the result of residual damage from past disease activity?

Speaker 3-Tanuja Chitnis ([13:50](#)):

So that's a very good question. And you know, typically cognitive symptoms are not presenting symptoms of MOGAD. I think we know that in, especially in adults, optic neuritis, transverse myelitis are typical presenting symptoms. However, cognitive symptoms are quite prevalent in the presentation of ADEM. So acute disseminated encephalomyelitis, and that occurs in children quite predominantly, but that's also associated with lethargy with what's called encephalopathy or just being very tired and sleepy and even attended. So that's really where we start to see a lot of cognitive issues being one of the first symptoms of a MOGAD relapse, but it's usually associated with lethargy. So that's in the context of ADEM. Now, ADEM can also occur in older people. And so in teenagers, adults we've seen cases of ADEM. And again, that's where cognitive symptoms, lethargy can be a presenting symptom. And I think that's different than, you know, sort of residual symptoms from just generally having MOGAD having brain lesions. And we know that MOG fog or fatigue can also be a result of having MOG lesions and that needs different types of treatments.

Speaker 1-Moderator ([15:04](#)):

This next question is for Dr. Banwell and Dr. Darshi. What common psych overlap is there for adults and pediatric patients? For example, is depression, anxiety, PTSD, bipolar or schizophrenia seen in these patients and are narcolepsy and sexual drive part of this overlap

Speaker 4 -Brenda Banwell ([15:24](#)):

Sure. So, that there's a lot in there. I think my first comment would be that mental health concerns and mental health symptoms are extremely common in the human population. So, no matter what population you have, it's common to have anxiety and depression. Estimates in children have shown that mental health crises have dramatically increased over the last decade and particularly the last couple of years. And the pandemic led to an explosion of mental health to the point that it's recognized as a serious health crisis and suicidality has risen to being one of the top three causes of death in teenagers in this country. So, I say that because that's the stress of being a child and a teenager and in a major component of pediatric health that we need to be aware of. In children who have any chronic health condition there's always the increased risk of reactive depression either with themselves or their families.

([16:25](#)):

In studies in multiple sclerosis, which maybe have gone on a little longer, there's good evidence that the mental health of the family influences the mental health of the child. So if a parent is depressed or anxious, that also leads to a higher rate of anxiety or depression in their child. And anxiety and depression run in families in general, I am not aware of any association between MOGAD and bipolar or early onset psychosis as a disease, as a primary psychiatric disease. The only thing I would add to that is that there are patients who develop NMDA, a receptor encephalitis who have had MOG antibodies or the other way around. And NMDA receptor encephalitis is a separate disease, than MOGAD, but it



presents with psychosis and psychiatric symptoms as a core feature. So, if you saw that in some with MOGAD, I would be looking for NMDA a receptor encephalitis.

Speaker 5-Sudarshini Ramanathan ([17:19](#)):

I would agree with everything Dr. Banwell has mentioned, and my concept with anxiety and depression is either preexisting in a patient or often reactive to a new and significant diagnosis. The implications of losing neurological function or their response to needing treatment for the long term in relapsing cases. And I think it's something that's very important that needs to be recognized and diagnosed and managed proactively, because it really impairs quality of life. I would agree as well with psychosis that it's the autoimmune encephalitis that I would think about. I'm not aware of studies linking MOGAD and narcolepsy. You mentioned sexual drive. I think in patients with myelitis and MOGAD it's often the lower part of the spinal cord that can be affected, which controls also sphincter function, so bladder and bowel and sexual dysfunction. And while lots of patients with myelitis might have motor paralysis that often responds quite well to treatment, whereas the sphincter function is quite slow to recover. So certainly, a lot of adult patients who have myelitis, sexual dysfunction can be a long-term neurological sequela.

Speaker 1-Moderator ([18:34](#)):

This next question is for Dr. Sotirchos. Can sleep difficulty be a symptom of MOGAD?

Speaker 7-Elias Sotirchos ([18:40](#)):

That's a great question. I think that we hear in clinic from patients sleep difficulty and fatigue as a common reported symptom, I have to say, one of the difficulties sometimes interpreting that these are common symptoms just in the general population due to our current lifestyle: people's hectic lifestyle, employment, children responsibilities. So it is sometimes difficult to interpret. However, when we try to look at this and we like actually by leveraging data from a survey administered by The MOG project to people with MOG as well as people from their household who did not have MOG as a kind of control group, we did find that it seemed like patients were with MOGAD were reporting fatigue to a greater extent than their household controls. Although the percentage was quite a bit high in both groups actually. But it was about twofold higher on the MOGAD patients and there was some component of sleep difficulty.

([19:33](#)):

And one thing that we identified was that perhaps people with a history of bilateral optic neuritis were reporting that to a greater extent, which does have some biological rationale since there are cells in the retina that are affected from optic neuritis that may be involved in kind of controlling our body's ability to sense light and daylight cycles. And this is known to be associated with kind of what we call circadian rhythm dysfunction. It's also been described and other things, other conditions that can affect the eyes and people who are blind and also in conditions like multiple sclerosis, which also have optic neuropathy as a frequent manifestation of the disease too.

Speaker 1-Moderator ([20:16](#)):

So, this next section is on ICD 10 and ICD 11 codes. So this is for Dr. Santoro. How will changes to the disease classification to make MOGAD a distinct entity help patients globally?



Speaker 8-Jonathan Santoro ([20:34](#)):

This is an excellent and an important question. So right now there's actually no code for MOGAD and that implicates, you know, or creates some problems for patients because when you go and you receive the diagnosis of MOGAD, the challenge is you have to be phenotyped as ADEM, as transverse myelitis, as optic neuritis, whatever you're presenting symptoms were. Where that becomes a problem is then when a patient is needing additional therapies or preventative therapies, those types of codes can't be used to acquire those therapies. So thankfully with the collaboration of The MOG Project, we were actually able to discuss the importance of this with the CDC just about three weeks ago. And we'll be hearing decision on the ICD 10 coding for MOGAD specifically in the next few months.

Speaker 1-Moderator ([21:26](#)):

The next section we'll be discussing is MOG and aging. This is for Dr. Chitnis. What do we know about the transition from childhood to adulthood, specifically as kids hit puberty? Are they likely to transition away from encephalitis or ADEM to more ON and TM? What else might happen?

Speaker 3-Tanuja Chitnis ([21:46](#)):

Yes, so this is a very important question. So, what we do know is that younger children, so between the ages of typically two and seven years old tend to have ADEM as they're presenting symptom of MOGAD, and these children tend to not relapse. So there's a very low risk of relapsing in the future. There is a present relapse risk, but it's very small. When children are older, so around 10 to 12 or 10 to 15, they're more likely to have optic neuritis as a presenting symptom. And these kids can have a slightly higher risk of relapsing, and this is now being assessed, you know, what exactly is their risk of having a relapse? It's also important to remember that some of these kids can present with bilateral optic neuritis or optic neuritis that starts in one eye and then follows in a second eye.

([22:35](#)):

So it's very important to continue to monitor those young kids. And as children get a little bit older and older kids, we tend to see a bit more transverse myelitis presentations and there's a slight male predominance to that as well. So we start to see some sex differences as well in the presentations in children who are post pubertal. So after age 10 or so, and then in even older teenagers and young adults, then we start to see more NMO presentations. And however, everything I just said, there's always an exception to the rules. So we, you know, I just saw a gentleman with ADEM who is about 35 or so, and so there's many exceptions to these rules, but that's in general what we see. So the phenotype does change with age and also with the transition to puberty or through puberty. And there may be a role of sex hormones here.

([23:29](#)):

And so, there's a lot of work to be done in understanding the role of estrogens, which we know are pro-inflammatory in many cases, and might lead to these different phenotypes. I think another important question that still needs to be answered fully is whether after puberty children who had a maybe ADEM presentation or an early optic neuritis presentation will have more frequent relapses. So that needs to be fully assessed. And just anecdotally, I've seen some kids shortly after puberty will have another attack, and so that might herald or be a sign that they do have relapsing MOGAD. So I think we still need to do a bit more work in this area.





Speaker 1-Moderator ([24:11](#)):

This next question is for Dr. Chen. How can a MOGAD patient distinguish between age related vision problems such as macular degeneration, retinal detachment, glaucoma, cataracts, et cetera, versus a MOG related symptom? Do seniors with MOGAD need to be more proactive in screening for these diseases?

Speaker 2-- John Chen ([24:32](#)):

So, with MOGAD, you know, the, the most common way it relapse is optic neuritis. And with optic neuritis, especially with MOGAD, you tend typically have pain in your eyes, especially when you move your eyes around sometimes that headache behind the eyes, that can be a sign that this is gonna be optic neuritis and not something else, is that pain. But of course, not every patient has pain, someone doesn't read the textbook and then 10% don't have pain. But again, the vision loss tends to drop pretty quickly over a span of, you know, one to three days, one to seven days. So again, pretty quickly. So, some of those other ones, conditions that you talk about tend to cost much more gradual decline in vision like cataracts, macular degeneration, all those are very, very slow decline in vision. And so, you know, the speed of the vision loss can help if you have pain with eye movements that can help.

([25:17](#)):

But of course, anytime you have any decline in vision, you're gonna wanna be seen, especially if it's pretty quick. All those, if it's a quick decline in vision, that could be dangerous. It could be retinal detachment; it could be a stroke to the retina. All those need to be seen, whether it's neuritis, whether it's one of those other things they all require surveillance and to be seen urgently. If it's a very slow decline in vision. It's probably not gonna be MOGAD. In MOGAD there's no progressive phase like in MS. You can actually have just a progressive phase where we just decline without an attack. With MOGAD, we think that you're pretty stable unless you have that attack. So again, acute change in vision - gotta be seen. If it's very slow, it's probably not MOGAD. And obviously you need your annual eye exams to look for cataracts, diabetes, macular degeneration, those kinds of things.

Speaker 1-Moderator ([26:03](#)):

This next question is for Dr. Sotirchos. We know ADEM is more common in children with MOGAD, but are there any relapsing patterns identified for senior adults? What can seniors expect as they age?

Speaker 7-Elias Sotirchos ([26:17](#)):

That's a great question. So, I think that as we mentioned previously, in in adults, the main kinds of relapses that we expect to see are generally transverse myelitis and optic neuritis, especially optic neuritis being the most frequent one. Some studies have suggested that in people with adult onset disease with relapsing disease, that there may be an association of age with the risk of relapse and that older individuals, older adults may be at a lower risk for relapse compared to young adults. However, I think more work needs to be done in terms of following up on those findings in larger cohorts. An additional issue that we don't really know as well also is in as we age, there is a phenomenon called Immunosenescence, where our immune systems become less robust as we age. And it is thought that autoimmune diseases in general may become less active with aging.

([27:07](#)):





So we in MOG antibody disease, I'd say it's a bit less clear because it's a recently discovered disease. Our cohort studies have not followed individuals for many decades in order to see kind of how the disease behaves. People get into an advanced, kind of an advanced age. So that's something that remains to be known. Another feature additionally that is quite important is that the recovery from relapses appears to be highly modified by age. So, children and young adults can often have a very good recovery following attack, whereas older individuals may have a poor recovery following attacks. And this has to do to some extent with just the plasticity of the central nervous system and their resilience to injury that has occurred. And so that's something to be aware of that an attack in somebody of an advanced age or elderly individual may be quite a bit more debilitating than in a younger adult or child.

Speaker 1-Moderator ([28:07](#)):

So the next section we'll talk about treatments. The first question is for Dr. Darshi and Dr. Levy - Levy, sorry, let me say that again. In challenging cases of MOGAD where patients are not responding to therapeutic approaches and are continuing to relapse, what are some of the strategies that doctors can try?

Speaker 5-Sudarshini Ramanathan ([28:29](#)):

So, I think when you have a patient who isn't responding the way that you expect, it's always good to have an open mind and go back to basic principles and make sure this patient has what you think they have. So going back to their initial presentations and examinations and scans and making sure that it is indeed consistent with MOGAD and their laboratory result is from an established laboratory, et cetera. I think once you have confirmed that there aren't any atypical pictures, any atypical features of their condition, then it depends a little bit on what type of treatment they've had. As we've talked about, patients often respond very well acutely to steroids and to slower weaning of steroids, but it's not a acceptable long term solution in patients. So other options that have been considered for relapsing disease include maintenance, intravenous immunoglobulin therapy or oral steroids sparing agents like Mycophenolate.

([29:26](#)):

Some studies have reported maintenance plasma exchange, and of course you have drugs that deplete the cells that produce the antibodies such as rituximab. And studies have shown that all of these agents have an effect in reducing relapse rates compared to no treatment. But these treatments don't invariably work for all patients. So sometimes it is a matter of finding the right treatment or the right combination for a patient. In patients who are chronically relapsing despite escalation of therapy, other treatments with different modes of action have been used with some success. So, there's some agents that target the IL6 pathway and other immune pathways like tocilizumab that have been reported as being successful. And I think one of the very exciting things now is that there are a number of clinical trials for patients with relapsing MOGAD, which have different mechanisms of action that could be used or could be considered for patients who continue to relapse despite current standard of care.

Speaker 6-Michael Levy ([30:28](#)):

The first thing that comes to my mind when I deal with a case that's intractable to treatment is the steroid withdrawal effect. A lot of people will go on steroids to treat the relapse and then start a medication as a preventive and come off of the steroids and then a relapse occurs. And the tendency is to blame the preventive medication that was just started, whereas really sort of triggering a relapse by



withdrawing the steroids maybe too quickly, or there's some people who are just so dependent on the steroids, it's hard to take them off. And my go-to has been intravenous immunoglobulin, as Darshi said. I believe Dr. Chen has a study out that says that with the higher dose there's a response rate of about 80%, but these are biased observational studies, so they're not fixed scientific studies. And for people who, despite my best effort, I cannot get them to stop relapsing, there are these clinical trials and I think that these are sometimes the best options for people who've tried everything and hopefully some of these drugs will become approved later on.

Speaker 1-Moderator ([31:42](#)):

Dr. Levy, can you speak a bit more about these upcoming treatments and clinical trials? Anything else to share?

Speaker 6-Michael Levy ([31:49](#)):

So, two trials have launched worldwide. One is with rozanolixizumab. That's a subcutaneous infusion, a small dose that takes about 15 minutes to infuse. It's every week. And the mechanism is thought to be similar to IVIG. These drugs are going for wherever IG is helpful. The rozanolixizumab and drugs like that are going for those diseases. It has launched in MOG. I believe it's gonna be something like 65 sites worldwide and it's just gotten started. The second is satralizumab. For people who've been in the NMO world, they, that drug has already been approved for the Aquaporin-4 version of NMO disease and now it's being tested in MOG based on some preliminary evidence that the parent compound tocilizumab may be helpful as Darshi mentioned. So that trial has also launched and I believe a patient has already been enrolled in Europe and both I think are expected to read out in sometime around 2025 or so.

Speaker 1-Moderator ([32:56](#)):

This next question is for Dr. Santoro and Dr. Sotirchos. Do doctors ever consider weaning patients off preventatives as an option? Is monophasic or multiphasic a factor? And how long would someone need to be relapse free for it to even be a consideration?

Speaker 8-Jonathan Santoro ([33:17](#)):

So, I think this is a million-dollar question, so to speak. So, with monophasic, you know, processes, I think that there's a lot more flexibility. We typically treat the acute attack and then we're in a phase of monitoring, especially in pediatrics, as most of our patients will not have another attack. When we get into that relapsing group, I think that that becomes a larger problem. So certainly, if a patient becomes seronegative, meaning that they lose their antibody over time, I think that gives us a lot of confidence about coming off therapy. But I don't know if there's necessarily one timeframe that is uniform for all patients. We try to get into that one to two year window before we're coming down on therapy. And ideally, even though we don't have great titer bases to go off, we want to use the other clinical features. So, is the OCT stable or OCT data stable? So, the optical coherence tomography, Is the MRI stable and obviously is the patient not relapsing during that? So if all of these clinical pieces are fitting in to show stability, I think that that gives us better positive predictive value of a patient doing well off therapy. But thus far we've still had a few that we try to come down and we deal with a relapse, which is unfortunate.

Speaker 7-Elias Sotirchos ([34:32](#)):



Yeah, no, I agree completely with everything that Dr. Santoro said. Just to add a couple of points that I try to employ in practice is, so I generally, again, for monophasic disease, generally the treatment is geared towards relapse preventative therapy. I generally institute only for patients who have shown that they have relapsing disease. In patients with relapsing disease. I think there are a number of considerations in order to decide to wean the therapy. And these are, it's always a discussion with the patient of course, because, and I think to some extent an important feature is also the amount of disability that may have been accumulated from prior attacks. So if attacks, if somebody has recovered very well from prior attacks and has been stable on therapy for a number of years, I think that there is a potential rationale to wean provided that the patient is comfortable with that because then there is the likelihood that if another attack occurs, the prior history supports that perhaps the recovery would be good again.

[\(35:24\)](#):

And another feature. Also, it's quite important to bear in mind is also the side effects from these treatments. So, if a patient is experiencing things like recurrent infections due to being on immunosuppressive drugs or if they're intending to become pregnant, which is another thing that happens quite a bit since this is a disease that affects young adults. And so childbearing is another important consideration when we're deciding to continue these therapies. All of these features really need to be taken into account and it's an individualized decision for which I think we need a lot more data to help guide us for what the risk of relapse is and people when we're taking them off treatment to help guide us in this therapeutic decision making.

Speaker 8-Jonathan Santoro [\(35:58\)](#):

We're very highly cognizant of that in pediatrics because of the growing body, growing brain concept as well. So especially with our immunosuppressive or steroid sparing medications, we wanna make that, you know, thread the needle between the balance of immune suppression and prevention of attacks, but also making sure that the body has the best chance to grow and develop as it should.

Speaker 1-Moderator [\(36:20\)](#):

The next question is for Dr. Chen. Can you talk a little bit about the recent study on the efficacy of IVIG?

Speaker 2-- John Chen [\(36:28\)](#):

Absolutely. I think Michael alluded to that earlier in the prior question. So essentially our studies on treatments for MOG all retrospective. We have no prospective trials until these upcoming clinical trials. So really we're kind of dependent on what's been done in the past and how these patients did, again, not randomized clinical data. But there are some prior case studies case series that suggested that IVIG is effective in preventing relapses, but there are predominantly pediatric patients. So most recently we did a large international study looking at MOG centers around the world. And actually, many of the experts here collaborated, provided patients, and what happened with the IVIG. And we found that it did lead to, was associated with a reduction in relapses, a pretty significant reduction in relapses. And what we also found is that the higher dose was actually more effective than a lower dose. So higher dose, more frequent dosing seemed to be more effective in reducing relapses. So again, it suggested probably is effective since there's that dose response curve. The drawback is we don't know how much any given patient needs because there are some patients that did well with a very low dose in



infrequent dosing. Some patients needed more. And that's the hard part in terms of trying to figure out how much a patient needs.

Speaker 1-Moderator ([37:46](#)):

This question is for Dr. Levy of thinking about tolerization options and MOG antibody disease. How real is the possibility of this happening soon?

Speaker 6-Michael Levy ([37:57](#)):

I think this is one of the most exciting research areas and I'm not just saying that because I'm working on it. I'm saying it because there are many companies that are interested in this idea. I would say there are probably at least 10 companies that have tolerization platforms that are looking at MOG. And the reason is that it seems to be one of those diseases where the tolerance to MOG can be broken in almost anyone. But there's so many cases where people get over the disease where the antibody goes away and people can come off of therapy, so called retolerization, natural retolerization seems to be a doable thing in nature. And so, if it happens naturally, maybe we can come up with a therapy that pushes in that direction towards retolerization.

Speaker 1-Moderator ([38:47](#)):

This next question is for Dr. Chen and Dr. Banwell. Can you talk about the likelihood of more IVIG/ SCIG efficacy studies for adults and pediatrics?

Speaker 2-- John Chen ([38:59](#)):

I, again, I think that IVIG does work, and we think that SCIG works as well. Dr. Sotirchos actually led a small case series of about five or six patients that responded very well to SCIG. Obviously, that's convenient because you don't need to have the infusions and you can do it, you know, once a week. There're multiple other studies in other diseases where that has been shown that SCIG is fairly equivalent to IVIG. And so we could probably extend what we found in IVIG and it being fairly effective in MOGAD, likely that SCIG will work. Obviously, the idea would be future randomized clinical trials, IVIG or SCIG compared to placebo. We'll see if that comes around, that'd be wonderful. That would give us the ultimate answer.

Speaker 4 -Brenda Banwell ([39:49](#)):

Yeah, I mean, I think, you know, as someone who treats children and one of the biggest challenges of treating children is they're not particularly fond of needles or infusions. Monthly immunoglobulin at a day medicine center is a day off work for a parent, a day off school for a child almost invariably. And so, you know, that has a significant impact. The plus side of immunoglobulin therapy is it's very safe. It does not compromise their ability to fight infections in the community. And in fact, in actual fact, they get a little bit of community immunity. So, one of the things parents tell me repeatedly is my child hasn't had a serious cough, cold or infection since they started immunoglobulin. And since we think infections may trigger MOGAD relapses, there's a variety of reasons why IVIG has been so popular with families.

([40:36](#)):

The two things that I would comment and many that of the families that I work with have shared and have taught me this one is if I think the patient is going to stay on monthly immunoglobulin as their



strategy, and this is particularly the younger children with relapsing MOGAD for whom subcutaneous isn't necessarily better, it's still a needle under the skin and they're not particularly keen. We do put ports so a secure line access for these children. And you know, I'd initially hesitated to do that, but the psychological impact of a difficult IV access every month for small children is huge. And for families where we have gone with putting in a port line as a secure access, so it's, you know, you put the cream on it, they hardly feel it when the line goes in.

[\(41:26\)](#):

Every single one of those families has told me it's been game changing and the mental health of their child has been significantly better. So I think in the right situation that has gotten around the subcutaneous advantage for the younger children, for my teenagers, they love the subcutaneous option. They do it themselves. They, I mean, I have one patient who starts it on her bus in the morning and finishes it by the time she gets to high school. I mean, it's just literally, she just does not want to miss the bus, so she just does it on her own. So I think, and I think it does work. So, obviously with respect to a trial, my last comment would be, I don't know in relapsing disease that we'll be able to do placebo trials. You know, I think given that the morbidity of MOGAD relates to the attack itself, it's a tough situation. So, I think there'll be comparative trials, which is challenging because that will just be looking at whether something's similar or maybe better, But, you know, having someone experience relapses as a placebo is a really hard thing to do and it's the right study for the best data, but it's a very difficult model to really actually consider for relapsing patients.

Speaker 1-Moderator [\(42:29\)](#):

So just two more questions, general questions. This first one is for Dr. Darshi. Can you tell us a little about known atypical presentations in MOGAD, for example, autoimmune encephalitis, seizures, etcetera?

Speaker 5-Sudarshini Ramanathan [\(42:44\)](#):

As we've heard about in this panel, optic neuritis and transverse myelitis and ADEM are definitely the most common and probably make up over 90% of cases of MOGAD. But it's become increasingly clear over the last few years that there are reproducible clinical patterns that we should be aware of and not miss the diagnosis of MOGAD. Some patients have seizures without clear typical demyelinating presentations like optic neuritis and something, and they go on later to have those more typical presentations. And with the seizures, these patients might get treated with anti-convulsants and this may not be successful. However, when that diagnosis of MOGAD is made and they're treated with immunotherapy, the seizures often respond as well. So, it is an important phenotype for general neurologists and other clinicians to be aware of, to look at MOG in new onset seizures. The other phenotype as we've also alluded to before, is an overlap with autoimmune encephalitis. Patients having autoimmune encephalitis and antibodies associated with that like NMDA receptor antibodies and subsequently or prior to that proceeding having the more typical MOGAD presentations and MOG antibodies.

[\(43:59\)](#):

And, we now think that about five to 7% of patients with a particular type of autoimmune encephalitis have another antibody of which the majority is MOG antibodies. I guess a third phenotype, but it's worth keeping in mind, is patients who present, and clinicians think they have a meningitis, so they might have a bit of a headache, some neck stiffness, some fever, some patients might be a little bit



confused, and when they're investigated and have a lumbar puncture looking at the spinal fluid, they have a lot of inflammatory cells, but the usual diagnostics for looking for a viral or bacterial course are not present. And some of these patients go on to have MOG antibodies and sometimes the lining of the brain or the leptomeninges can be involved on the radiology scan. And sometimes children have been described with having this aseptic meningitis and raised intracranial pressure and having MOGAD so these are important phenotypes to be aware of because they risk being misdiagnosed or undiagnosed.

Speaker 1-Moderator ([44:58](#)):

Thank you. And we'll do one last question. This one is for Dr. Santoro. For kids who had encephalitis or ADEM, what is their long-term seizure risk? Do they eventually outgrow them or is it a lifelong concern?

Speaker 8-Jonathan Santoro ([45:13](#)):

Great question. So, I think when we look at seizures and subsequently epilepsy in individuals who've had MOGAD, we, we kind of see that there's this biphasic pattern, there's seizures at presentation, which do tend to be a little bit higher in prevalence in children. And then we actually see seizures later on once the immunotherapy has actually, if there is a relapsing course, has had an effect. But we've observed several patients who have now gone on to have epilepsy at an unexpected rate later on. When we image some of these patients, we do find some of the classic findings that we'll see in individuals who have epilepsy. So, thinning of the temporal or the medial temporal lobe or the hippocampus is another part of the brain that we see that. The question I think that has come up is, is this sequela of the initial attack because usually these patients will have seizures at presentation and have seizures subsequently, or is this indicative of active inflammation?

([46:10](#)):

When we have done more of the aggressive workup in that latter group, we have not found active inflammation even when patients are having, or children are having the continued seropositivity of the MOG titers. So, the short answer is we don't know, but upfront we see that immunotherapy definitely cleans up the seizure activity and reduces that. But this long-term epilepsy risk is difficult. And we have seen a higher number of individuals who have had these kind of dual antibodies come up where the phenotype is certainly more consistent with MOG, but there are these other antibodies at low levels associated typically with autoimmune encephalitis even though that phenotype is not present.

Speaker 1-Moderator ([46:56](#)):

That's it. Mm-hmm. <affirmative> The end. Thank you so much! This was great!