I Have MOGAD. Now What?

You can watch the video of this podcast at: youtu.be/RaSku2l9oTo

[00:00:02] **Announcer:** "ABCs of MOGAD" is an education podcast series to share knowledge about MOG antibody disease or MOGAD. A rare neuroimmune disorder that preferentially causes inflammation in the optic nerves and spinal cord. "ABCs of MOGAD" is hosted by SRNA, the Siegel Rare Neuroimmune Association.

[00:00:25] 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. This series is sponsored in part by Amgen; Alexion, AstraZeneca Rare Disease; and UCB.

[00:00:54] **Krissy Dilger:** Hello and welcome to "ABCs of MOGAD." My name is Krissy Dilger, and I moderated this episode titled, "I Have MOG Antibody Disease. Now What?" For this episode, I was pleased to be joined by Dr. Michael Levy. Dr. Levy is an Associate Professor at Harvard Medical School and Director of the Neuroimmunology Clinic and Research Laboratory at Massachusetts General Hospital. You can view his full bio in the podcast description. Welcome, Dr. Levy, and thank you so much for joining me today.

[00:01:30] **Dr. Michael Levy:** Pleasure to be here.

[00:01:33] **Krissy Dilger:** So, to start us off, can you just tell us what MOG antibody disease is?

[00:01:41] **Dr. Michael Levy:** I don't know what it is. Just teasing. It is an autoimmune disease. It seems to occur when the immune system is triggered to attack the MOG protein. MOG is a protein in your brain, optic nerves, and spinal cord and it has some immunological role that we don't fully understand, but it's not harmful.

[00:02:06] But for some reason in MOG people, the immune system it believes that it is, that it's harmful and initiates an attack and the attack is inflammatory. The immune system goes in and tries to destroy it like it's a bacteria or virus. And as a result of the damage, people can lose vision if it occurs in the optic nerve.

[00:02:27] They can lose strength, sensation, or bladder function if it occurs in the spinal cord. And in the brain, it causes change of consciousness, cognition, and lots of other problems. And these are all lesions that are visible on the MRI they're readily detectable. We have a good MOG antibody test. So, we can determine if this is the diagnosis.

[00:02:47] And we have good clinical criteria now too. So, we have an outline of criteria that are published as an effort led by Dr. Benwell and I think the awareness now is out. So, when people come into the hospital with these symptoms, we can determine pretty effectively now whether people have MOG antibody disease.

[00:03:09] **Krissy Dilger:** Great, and I was just curious about the history of MOG antibody disease. When was this disorder I guess found out about? Has it been matched or linked to any other disorders in the past?

[00:03:25] **Dr. Michael Levy:** The history is a little bit messy because the idea that MOG, that immunity to MOG could trigger inflammation in the brain was first discovered in the mouse. These are in rodents. These were models that were thought to be the basis of multiple sclerosis. So, we actually knew that immunity that inflammation to MOG could cause inflammation, vision loss, bowel bladder dysfunction, and inflammation in the brain.

[00:03:53] We already knew that from mouse models. But the first time that we really identified the MOG antibody in people was in the late 90s and early 2000s and again, it was thought to be in the context of multiple sclerosis. That's how people were studying it. We didn't have NMO at the time, we didn't have aquaporin-4 antibodies.

[00:04:10] Everyone was just in the bucket of MS. And this MOG antibody was found in a small subset less than 5%. And it was thought, well, are these MS patients with MOG antibodies or what are they? As people were trying to sort that out the aquaporin-4 antibody came out and carved out NMO. And we recognize that's a totally different disease.

[00:04:33] Now we have aquaporin-4 NMO, and we have MS. And then there were people who tested negative for the aquaporin-4 antibody, but they kind of had the clinical disease, we knew it wasn't MS and a lot of those people had MOG. So, now we have this mix, this kind of spectrum of disease with MS and we have NMO aquaporin-4 positive and then we have MOG positive.

[00:04:55] And it overlaps a little with MS, it overlaps a little with NMO, but it also has a unique phenotype all of its own. The aquaporin-4 antibody test was developed in 2004, 2005. Then the MOG antibody test has been improved over time. Now, we have a version that was developed in 2015 that's very good. And in 2017, it was adopted in the US.

[00:05:19] So, we've been following patients now for about six or seven years in the US, more like 10 years abroad. And so, we're starting to understand that this disease really is different from both MS and NMO but has clinical overlap. Talking about the history though. When Dr. Devic first described neuromyelitis optica back in the 1890s, there were clearly cases of MOG in that series.

[00:05:44] So, he had his graduate student, Frederick Gold, to review other cases that had been circulating. Some of them were very clearly bilateral optic neuritis, transverse myelitis, got better. These are people that looked a lot more like MOG compared to NMO. And so, we already had a sense that these people were around. We just didn't have good testing for it, clinical criteria, and recognition of it till recently.

[00:06:14] **Krissy Dilger:** So, can you walk us through what the diagnostic process looks like with MOG antibody disease? You mentioned the antibody test for MOG. What other criteria is used to diagnose this disorder?

[00:06:28] **Dr. Michael Levy:** Well, MOG is diagnosed by neuroimmunology experts, and these experts are people who take care of MS (multiple sclerosis), MOG, and NMO. And MS is still 50 times more common than MOG, but in the workup for MS. So, people who have optic neuritis, brain lesions, transverse myelitis, they all get very similar workups.

[00:06:54] We check for NMO aquaporin-4 antibodies, we check for MOG antibodies, we look at MRIs, we probably do CSF analysis to rule out MS, and this whole work up all the clues put together then get processed,

chewed up, thought about by the doctors. And in order to meet the criteria for MOG, there is a set of criteria that is what I consider to be straightforward.

[00:07:20] This requires symptoms of MOG, optic neuritis, transverse myelitis, in kids often ADEM acute disseminated encephalomyelitis or big brain lesions, but really will accept a lot of different brain lesions in the context of a solid MOG antibody test result. What do I mean by solid?

[00:07:43] There's a range of MOG antibody levels people could have in their body from really high concentration to pretty low. And high concentration is a reliable diagnostic marker. If you have high MOG, then even weird brain lesions are still likely MOG even if there's no optic neuritis or transverse myelitis, it's still very likely MOG.

[00:08:07] People who have lower levels of MOG that's where we start rubbing our chins thinking okay could this be MS, what else could this be? And in fact, there are new studies out even in non-neurological diseases like Lou Gehrig's disease, stroke, other conditions where you might detect a little bit of MOG antibody. What does that mean? Could it be the result of something? Could it be just a false positive test? Is it meaningful in any way?

[00:08:34] Is it an immune response? We don't really know. But the lower MOG antibody levels require a higher threshold for the clinician to make the diagnosis. You have to be really sure. So, how am I really sure? Well, if you have bilateral optic neuritis, that's both optic nerves are involved and transverse myelitis and you have MRIs with long lesions, maybe that spares the brain, negative aquaporin-4, no oligoclonal bands from MS, that's MOG even if it's low-level antibodies.

[00:09:08] **Krissy Dilger:** So, after someone receives a diagnosis of MOG antibody disease in the hospital, what happens next? Are they put on acute treatments or what happens next, I guess?

[00:09:22] **Dr. Michael Levy:** Yeah, it depends on the context. If somebody is actively inflamed, they still have optic nerve inflammation or spinal cord or brain inflammation, you have to put out the inflammation. We don't want any inflammatory disease going on in the nervous system. We think of it like a fire. There's a fire burning, it's causing damage you have to put out the fire.

[00:09:42] That's first priority. And you could do that with steroids most commonly, but also, we've been using IVIG and plasma exchange, those put out the fire. Then once the fire is put out, the healing process starts, it could take months, weeks to months, even a couple of years before you are really fully healed. And most people would still have a little bit of residual damage.

[00:10:05] If it's optic neuritis, for example, we have had patients lose vision completely and then regain most of it, but they still can't see subtle things, or they might have light sensitivity or lots of other subtle things in MOG people that's really hard to quantify.

[00:10:22] But if you ask them, they'll tell you what's wrong with their vision. So, these residual problems persist after every attack, but as long as it's not actively inflamed, we can then think about all right next step is how do we prevent any future attacks? We have two clinical trials ongoing. I don't know if that's one of your questions coming up.

[00:10:43] I'd love to expand on those two clinical trials that will hopefully both be successful, and two drugs approved in the near future. But those are approaches to take to prevent the next attack. So, it doesn't do

anything for your old attack. All your old symptoms still have to heal on their own, but these new drugs will hopefully prevent any new damage.

[00:11:07] **Krissy Dilger:** So, yeah, if you would like to tell us more about long-term treatments, what's available right now, and if there's anything in the works you could briefly touch on that.

[00:11:19] **Dr. Michael Levy:** So, not everyone goes on long-term treatment, because we know that about half of people with MOG don't relapse. We just don't know which half. So, when you come with your first MOG antibody test in hand saying, hey, I had MOG, and I just had this really bad optic neuritis, and I don't want another one. I can't tell you for sure if you're going to be in that group that's not going to get another one.

[00:11:42] Or if you're going to be in that group that will get another attack. And the other attack could be in the other optic nerve, the same optic nerve, so we don't know if it's a random attack, but half will get another attack. We can prevent that with medications the most popular ones are IVIG that is intravenous immunoglobulin, mycophenolate which is CellCept, and prednisone steroids.

[00:12:07] I don't like prednisone steroids, but since we have an international audience here, I know most people around the world use them and they work. They just have a lot of side effects that's why I don't like them. And a high enough dose, you will not have any MOG attacks, but every time you come down a little bit on it, then you'll have new symptoms, it might trigger relapses lots of problems with using chronic prednisone.

[00:12:32] IVIG intravenous immunoglobulin has its problems too. It's not the most tolerable medication. It's given intravenously it's every month you might need two or three infusions a month, causes headaches and blood clots and it's very expensive, but it works, works very well.

[00:12:51] Dr. Chen at Mayo Clinic demonstrated that in the retrospective analysis. And then mycophenolate which is CellCept. It's a broad immune suppressant. It's used for a lot of neuroimmunology diseases. We used to use it for aquaporin-4 NMO, it was tested in multiple sclerosis, it was tested in a lot of different conditions. Rheumatoid arthritis. It's a broad immune suppressant that seems to do the trick for MOG.

[00:13:15] It has issues with pregnancy, cannot get pregnant on it. Might cause some increased risk of the skin cancer, not the harmful kind, but the harmless one. And some other issues, gut side effects, and things like that. But we use it in a lot of kids because they don't have any risk of pregnancy. We use it in older folks. It tends to be pretty gentle.

[00:13:37] And then more recently we started using tocilizumab, which is an anti-interleukin-6 monoclonal antibody. The new version is satralizumab which is being tested in trials. But the old version of tocilizumab is already available and being used in the US for rheumatoid arthritis, juvenile rheumatoid arthritis, and vasculitis, we use it for a lot of rheumatologic conditions.

[00:13:59] And most recently in kids, Dr. Benwell showed that you can use it intravenously to get kids out of the ICU in an acute relapse. So, we're also using it on a preventive basis. The shot, the Actemra shot, which is given subcutaneously is every other week.

[00:14:16] And the infusion is given once a month and it's very tolerable, has its side effect issues. And the new version is going to be a shot just given under the skin once per month. That's called satralizumab and we could talk about that in the clinical trial section.

[00:14:31] **Krissy Dilger:** Great, I know it's hard to make this a generalized statement or answer. How do you help your patients choose which treatment to go with or whether or not to go with the treatment at all?

[00:14:55] **Dr. Michael Levy:** The first thing I do is I really put the decision in their hands, and I say this is the data, you have 50/50 chance. Do you want to go on a treatment? People are pretty confident about their decision. If they don't want to go on a treatment and they want to wait to be sure that they actually need the medicine, they'll tell me that.

[00:15:13] And if they're like, well, if I can prevent another attack, even if I'm not sure that I'm going to have another attack, I prefer to do that, they know that. It's pretty rare that I have to give that kind of advice to people. I really just have to give them the information and they make their own decisions. So, that's been pretty easy. But then the next level, if they do take medication, which one we go through efficacy, safety, logistics.

[00:15:39] Sometimes it's decided by insurance, unfortunately. We may want to use one drug, and insurance is like we're not paying for that. Here are your options. And then the patients sometimes have to go with option B which may not be their first option. So, there are a lot of factors that go into that decision-making process.

[00:16:00] **Krissy Dilger:** So, after someone's acute event, what happens next? Are they referred to rehab typically or just go home and what follow-up appointments should they book?

[00:16:13] **Dr. Michael Levy:** If the attack happened in the optic nerve, there's no rehab. We don't have any way to improve the healing process in the optic nerve after an attack. So, they usually go home assuming it's safe. If it's both eyes and they can't see anything they really need to be in a situation that's safe.

[00:16:33] Usually with family that's taking care of them and about two-thirds of attacks are optic nerves. There's less rehab with MOG than with NMO where the attacks in the spinal cord cause really a lot of damage and a lot of need for physical therapy. We do have MOG attacks in the spinal cord and in the brain and they need time to heal and improve and a lot of those people will benefit from physical therapy.

[00:16:58] And it could be a time from like two weeks to four weeks in the acute setting, sometimes subacute maybe a couple more weeks and then home with physical therapy in the outpatient's sake. That may require another few weeks. And then for most people, they get to the point where they can do their exercises at home.

[00:17:19] **Krissy Dilger:** What follow-up appointment should someone book after an acute attack?

[00:17:26] **Dr. Michael Levy:** So, after that situation, you need to see your neurologist. If you were not on a preventive medication, maybe now it's time to be on one depending on whether that was your first attack or relapse. And if you were on a preventive medication and the attack occurred despite that medication then that's a treatment failure.

[00:17:44] You need to have the discussion of, okay, well, if this treatment failed, what's my backup plan? You might not want to switch. Maybe you took a treatment holiday. So, a lot of people will do that where they'll say, okay, I've been on this treatment for a year I have tolerated say IVIG. Boy, all those infusions really messed up my veins. I'm going to take six months off.

[00:18:08] If you had your relapse, then maybe that happened because you came off of the intravenous immunoglobulin and maybe that was really working for you, and coming off of it is what led to the attack.

Same with prednisone. And so, that's the discussion you need to have with your neurologist about whether the drug worked or whether the drug failed and it's time to go to plan B.

[00:18:34] **Krissy Dilger:** So, after someone's diagnosed and they get on long-term treatments or not perhaps, what may be the long-term effects or symptoms that this disorder causes?

[00:18:49] **Dr. Michael Levy:** Well, that's a great question, because as the healing process proceeds, there are changes that occur. So, it doesn't always heal positively meaning things don't always go back to normal. In the healing process, you may end up with muscle spasms, which is better than weakness, but still, it could be painful, limiting your ability to exercise for example.

[00:19:15] If that attack occurred in the spinal cord, same with bladder spasms you may go from retention where you can't pee to incontinence where it comes out because of a bladder spasm without control. And so, that's part of the normal healing process that's expected and hopefully, it'll continue to heal and get back to a point that's more functional.

[00:19:36] But some people are left with residual damage, same with optic neuritis. You may have lost vision completely and then only gotten back 90% of it. And so, you still have that area in your center of vision that's affected, that you can't see so well through. Or you may have light sensitivity, so you're walking through Target and those LCD lights are really bothering you and you have to wear sunglasses indoors. That happens a lot.

[00:20:02] So, these are all expected. It happens, it's part of the natural healing process. It's not a bad outcome. It's just part of the normal healing process. And then we have some people who make really good recoveries, recovery back to normal. Obviously, the younger you are the better your chance of healing in general.

[00:20:27] **Krissy Dilger:** I know that this disorder is somewhat new or newly coined, but what is known about prognosis? Is this going to affect someone's longevity?

[00:20:42] **Dr. Michael Levy:** We don't think it's going to affect mortality. We actually did put out a short review of the mortality in MOG. It seems to be not affecting lifespan, but it can certainly affect long term function. It affects vision we have some people who are blind, we have some people who need assistance with mobility. Most people don't, I would say 90% don't need a cane or walker and they're not permanently visually impaired.

[00:21:16] They can see to a limited extent so that you can function. You might not be able to see as well as you could, but you could still read, for example. So, there are certainly limitations in function that can occur. But in general, the long-term prognosis from MOG is better than MS, better than multiple sclerosis, better than neuromyelitis optica, but still there are some residual effects.

[00:21:44] As far as relapses go, the longer you don't have a relapse we think, the more likely you won't in the future if you come off of treatment. So, we think it's like that there is some process that takes place in re-educating the immune system over time that makes it less and less likely to have a relapse as long as you keep the disease in remission. And that might require medication for a period of time. But then we're thinking that hopefully, you'll be able to come off of that medication and not relapse.

[00:22:18] **Krissy Dilger:** Okay, great. Well, I think that's the rest of all the questions that I have for today. Hopefully, we can continue this conversation throughout the series but thank you so much for joining and for answering our questions.

[00:22:34] **Dr. Michael Levy:** Thank you.

[00:22:38] **Announcer:** Thank you to our "ABCs of MOGAD" sponsors Amgen; Alexion, AstraZeneca Rare Disease; and UCB. Amgen is focused on the discovery, development, and commercialization of medicines that address critical needs for people impacted by rare, autoimmune and severe inflammatory diseases. They apply scientific expertise and courage to bring clinically meaningful therapies to patients. Amgen believes science and compassion must work together to transform lives.

[00:23:12] Alexion, AstraZeneca Rare Disease is a global biopharmaceutical company focused on serving patients with severe and rare disorders through the innovation, development, and commercialization of life-transforming therapeutic products. Their goal is to deliver medical breakthroughs where none currently exist, and they are committed to ensuring that patient perspective and community engagement are always at the forefront of their work.

[00:23:40] UCB innovates and delivers solutions that make real improvements for people living with severe diseases. They partner with and listen to patients, caregivers, and stakeholders across the healthcare system to identify promising innovations that create valuable health solutions.