

How do I know if I am having a relapse?

You can view this presentation at: youtu.be/kjUKMwTMTVI

[00:00:05] **Dr. Benjamin Greenberg:** So, hopefully the breakout sessions were good, and everybody had a chance to focus on different topics. We're bringing everyone back to talk about a topic that comes up for everybody regardless of what your diagnosis is. And this question is, how do I know if I'm having a relapse, how do I know if I'm having a new event? And before I get into the talk, this will go for about 20 minutes and then there'll be a little bit of a break, and then there's gonna be a moderated panel session with several of the providers. And Dr. Levy is going to lead that followed by an open question and answer session where you can ask anything and everything and I encourage you to do so. Unfortunately, I won't be part of that, but I know it's gonna be a great session. So, let's talk about relapses. So, it's important to recognize that definitions matter. I'm not sure how many of you have heard these different words used in different ways: relapse, exacerbation, attack.

[00:01:02] My favorite is event. "I had an event." "Was it a birthday party event or a Bar Mitzvah?" "What was that the event?" "No, I lost feeling on one side, very different event." And the problem is we use these terms very loosely and we really don't do a good job amongst healthcare providers of helping our patients and families understand what these mean, because I may be using this word very differently than you're using this word. And it creates a lot of problems when talking with your health care providers, if you're not speaking the same language. And so, what I wanna do is level set the definitions that we use. So, these terms to me, in the world of neuroimmunology have a very specific meaning and that is a new inflammatory event. So, the immune system going back into the nervous system and causing brand new damage.

[00:02:03] So, if I call Dr. Blackburn up and I say a patient had an event, or a relapse, or an exacerbation, he and I are now speaking the same language. He assumes that what I mean by that is the immune system went back for more. That is not how these terms get used by a lot of folks. A lot of folks will say, "Well, I had symptoms, I had new numbness, or I had new vision changes or new weakness." And what's important to recognize is new symptoms don't always mean that there's a new immune attack. You can have symptoms without new inflammation. And this is where the language is important. So, how do you differentiate recurrent symptoms from a relapse, attack, exacerbation. Again, whatever you wanna call it, it can be very difficult. So, once you've had damage to the nervous system. So, I'm gonna use the optic nerve as an example. So, if I damage my left optic nerve on a Thursday and I lose vision in the eye and I get treated and the vision comes back, there's always some residual damage there.

[00:03:15] Once those neurons are damaged, even if there's a recovery in terms of function, there's always some damage left behind. And from that point on, I can experience the symptom of vision loss again without new damage. Just because the repair that happens is never as good as the original. And in certain circumstances the symptoms may come back without the immune system causing new damage. Now, this was described literally over 100 years ago by a German physician, Wilhelm Uhthoff, who was a German ophthalmologist who had patients who had suffered from optic neuritis, and he noticed that when they would heat them up, when their body temperature would go up, they would lose vision again, and when the patient would cool off, the vision would go back to the new baseline. And what he described was this exacerbation of symptoms that didn't appear to correlate with a new exacerbation from an inflammation point of view. So, we now call this phenomenon Uhthoff's phenomenon, where you can have a recurrence of old symptoms without new inflammation.

[00:04:28] So, how do we differentiate a relapse from a pseudo relapse? From a situation where your symptoms are worsening, but there isn't new inflammation. So, doing this is really important because if you are having new inflammation, you need to be treated for that. If your immune system is actively chewing on wires in the nervous system, again, you need to get steroids or plasmapheresis or some intervention to limit the damage, and very importantly for those of you who suffer from neuromyelitis optica or Anti-MOG associate disorder and you're on a preventative therapy, if you have a relapse on therapy, new inflammation then your therapy isn't working, and I need to talk to you about a switch. But if you come to me saying I had a relapse on mycophenolate, when in reality you had a pseudo exacerbation, I'm gonna switch you from a drug that was working to one that you may not actually respond to. So, getting this correct is very important, both for individuals who aren't on background immunosuppression and those who are on the flip side, accurately identifying a pseudo exacerbation or pseudo relapse is important because they can be managed or prevented and improved quality of life.

[00:05:37] If every time a person gets on a treadmill, they lose vision in their left eye because the old visual symptoms come back that can inhibit their activities. So, if we teach individuals how to manage this, that can improve a person's functioning and quality of life and then confirming that something is a pseudo exacerbation helps to avoid unnecessary treatments for the practitioners in the room. If I went around and asked you, they would all recollect the stories of patients who came to our clinics for second opinions who had gotten six rounds of steroids over two years for their relapses and when we went back and looked at each one, none of them were relapse. None of them was new inflammation. Those steroids were completely unnecessary because we were treating a pseudo-exacerbation and steroids make everybody feel better. So, even if you're having a pseudo exacerbation and you get steroids, you're going to feel better and get better.

[00:06:25] It doesn't mean you had new inflammation, and I might commit a patient to immuno-suppression for the rest of their life based on calling something a relapse that wasn't a relapse. And then finally, the pseudo exacerbations also often have underlying triggers that can be addressed. The most common one we see in our clinic is urinary tract infections. So, either our current urinary tract infection, even a symptomatically can change your body chemistry enough to bring out old symptom. So, you may feel fine, but then when we treat your urinary tract infection, even though you had no bladder symptoms, your vision comes back or your numbness improves or your weakness improves, showing that it was a pseudo exacerbation and not a new inflammation. And so, it's very important to tell the difference between the two. So, what are some triggers of pseudo-exacerbations? What have we learned? So, it was Uhthoff who first described increase in body temperature, and a predecessor of mine at Southwestern did a fascinating experiment where they had volunteers sign a consent form, read the fine print before you sign consent forms because they volunteered to be put in a NASA type space suit, and swallow a capsule that would read their core body temperature.

[00:07:35] That could be read by Bluetooth across the skin. And they would run warm or cold water through this spacesuit and ultimately be able to control a person's body temperature to within 1/10 of a degree. So, we could take somebody from 98/6 to 98/5 to 98/8 and very carefully move them up and down. And they put electrodes over the head and face and other parts of the body. And they measured for every 10th of a degree of body temperature they heated somebody up, what happened to the signal transaction, getting from point A to point B. So, they were looking at the visual pathway, and for a half a degree change. Half a degree, the signal transaction through the visual pathway plummeted in people who had had prior damage to the visual pathway. Absolutely plummeted, half a degree. In Texas, you leave your office and walk to the car, your body temperature changes more than half a degree.

[00:08:28] And during the study, I never saw this data, but I'm told somebody said, "Well, I wonder what happens with a cup of coffee." And they ran down to the Starbucks and they came up and they gave it here drink this and their signals just dropped off the charts, just from one cup of coffee and so increases in body temperature don't have to be extreme. There are some individuals who are susceptible to very small changes in body temperature and get a massive change in function or symptoms. We've also seen in our clinic, and we haven't redone this data probably in in eight or 10 years, the average body temperature of a multiple sclerosis patient who suffers from the same Uthoff's phenomenon on average is a half a degree to full degree lower than the average body temperature of somebody without one of these conditions. So, if I were to ask everyone in Fahrenheit, what's a normal human temperature? What's the number you give? 98.6.

[00:09:19] In our clinic, the average human temperature of an MS patient was about 97.8 just on baseline. And it's as if their body had reset to help protect against some of these Uthoff's phenomena. Although we don't know that to be true. So, what are other triggers of pseudo exacerbations? Infections are very common triggers even without overt symptoms. As your body is fighting an infection, it produces proteins called cytokines, and those cytokines change the way neurons function. And so, if you have a damaged pathway in the setting of an infection, the signal transaction may go down and your neurons may not function as well. So, we always screen for infections when we think somebody is having a recurrence of old symptoms. Lack of sleep is my favorite. No, actually it's my second favorite. We're gonna come up to my favorite at the moment. People get a bad night's sleep even chronically, there are days where your reserve can be lost and you have experience old symptoms again, and it can be an obvious lack of sleep, or it can just be inadequate sleep that you're not aware of.

[00:10:19] We had a great talk from Dr. Van Haren about the importance of sleep studies relative to fatigue. We've cured a lot of walking issues in our clinic by fixing underlying sleep disorders because it really can impact your basic level of functioning, even chronically. This is my favorite. So, lack of sleep is number two. My favorite is stress and arguments. And again, one of my predecessors at UT told me this story and I didn't believe him until he left, and I inherited this patient. Every time she would argue with her spouse, she would go blind in one eye, she would lose vision in one eye. And I said, is it just... He had told me this for years. You know who I'm talking about. He had told me this story for years and I didn't believe him. And then he left, I got the patient and I said, "I've been waiting to meet you. I've heard all about you. I've read the notes. Is it true when you argue with your husband?" She was, "Oh yes, I cannot see out of my left eye." Her adrenaline goes up arguing with her husband. And I said, "Well, I can fix this."

[00:11:19] And I wrote a prescription, and I handed it to her husband, and it said she's always right, just stop. But it is a phenomenon as people and people will describe, if they're in certain stressful situations, their function changes and it isn't just talking about cognition or focus, it can be their walking, their speaking, their vision, whatever the case may be. Nutrition I put a question mark next to because it's not clear to me if it's

a one off like, oh I had a cheeseburger and now I can't see. But chronically I believe based on conversations I have with patients that nutrition makes a difference in a person's reserve level to handle the other things that are going on. And so, I really have become a big proponent of people exploring what are the diets that are gonna serve them the best from a health perspective. And I get this question and I know my colleagues do too every day of the week, what diet should I be on, and I always answer it this way, diet is fundamentally important to your function, your health and well-being.

[00:12:27] Immunologically and neurologically it can make all of the difference. I know it makes a difference, 100% certain makes a difference. And I'm also 100% certain that I don't know which diet you should be on. And so, it turns out it's probably a different diet for each person. That how we interact with our food and how our microbiome changes is gonna be different for all of us. And so, what I encourage people to do is to take 12-week blocks and explore dietary changes in 12-week blocks to see does it make a difference in their functioning or their well-being. And I remind people that if the intersection between nutrition and our health is through the microbiome, the bacteria in our gut and Dr. Yemen can do a better job of talking through this than I can, but if it is indeed the bacteria in our gut you have to commit to the diet for the 12 weeks and you can't cheat.

[00:13:15] So, if you're going low carb to lose weight and six weeks in you have a donut, okay you're not gonna lose weight that day. If you're trying to change your microbiome you just wasted six weeks, because all the bacteria just go right back up, and you're starting over again. And so, if you're ever doing nutritional changes to see if it changes how you feel and function, it's a very different approach than nutritional changes for diet. It's an evolving science and I think we're gonna get better at this year over year, but that's probably the best we have right now. So, I wanted to point out that if you think this is difficult in the setting of your life and your relationship with your neurologist, trying to figure out is it a relapse or not? You're not alone. That even when you get a group of experts internationally to have a clinical trial. And this is from a paper of one of the drugs that was FDA approved for neuromyelitis optica.

[00:14:12] And the way it was approved was by showing people on the drug had fewer relapses than people not on the drug. So, what's the most important thing piece of data to have? Was it a relapse or not? That's the primary outcome. And so, I'm blowing up here some data from this table that looked at the adjudication committee. They got three board certified neuroimmunology trained NMO experts to look at the exact same data. They couldn't talk to each other, but they all had the exact same data, and they looked at whether or not if they called it a relapse. Was it actually a relapse or not. And the two columns one was the placebo arm, one was the inebilizumab on. But if you go to that second line unanimous decisions, there were a lot that weren't unanimous, that were two out of three votes. Even with the same data, couldn't agree if something was a relapse or not. And then if you go down to investigator-determined attacks.

[00:15:19] So, on the left going from 23 to 18, that means 23 times the neurologist on the ground who treated NMO patients said, I think this is a relapse. And in five of those instances, the adjudication committee said you're wrong, it's not a relapse. This is hard, it is not easy to just listen to symptoms or do an exam. There are certain times where we'll look at each other and say could be a relapse. There are certain times I get the phone call, and it's very clear it's a relapse. Certain times where it is very clearly not a new inflammatory event. And then a lot of times where there's a gray area where work needs to be done. So, what are some general guidelines you can live by? How do you know if you're having a relapse or not? And remember the word relapse means new inflammation.

[00:16:07] So, how do you know if you're having new inflammation if experts on an adjudication committee can't agree all the time when they're looking at the new data. So, here are things that make it more or less likely. So, number one, if you're having a new symptom in a new distribution, a symptom you've never had

before affecting a part of your body that was never affected before. And it is consistent with an event meaning vision loss, numbness, weakness, walking changes. So, if your event is ringing in your ear, that's not a typical relapse for these conditions. So, but if it's a new event in a new distribution that lasts for 24 hours or more, that is highly likely to be a new inflammatory event. So, if you've had optic neuritis only in your right eye, and all of a sudden you have blurred vision in your left eye, and the blurred vision is there for 24 hours or more, that is quite definitely quite likely to be a new event. And then we're gonna take away little pieces one at a time as we go to less likely.

[00:17:13] So, the first thing I take away is consistent with an event. So, let's say the symptom you're having is just a little weird. And I said, well that's not a usual symptom, but it fits all the other criteria. I'm still gonna be concerned that you're having a new relapse, a new inflammatory event. But let's take away a little more, the new distribution. So, what do I mean by this? So, let's say you used to have numbness in your right arm, that was your first symptom, but you never had weakness, but now you're having weakness in your right arm. So, it's in the same location but it's a different symptom than the past, lasting 24 hours or more. There's a good chance it's a new inflammatory event. And then we move to the lower side where we're getting to less likely. An old symptom that you had before. You've had this foot drop for years, but it's gotten worse, but it got worse, and it stayed worse for 24 hours. It's not a high probability of being a new inflammatory event. It's on the low side, it's not zero. It's not impossible, but it's definitely getting less likely. And then the old symptom that gets worse but better within 24 hours.

[00:18:22] I used to have a foot drop on my right, it got better and then it was weird all Wednesday afternoon, the foot drop was back. But by Thursday it was better again, it is highly unlikely to be a new inflammatory event. So, does everyone get a sense of that gradation, as you're moving away from the top to the bottom, and I'll encourage any of my colleagues' practitioners who want to edit this. If you feel it needs to be edited, just shout out. But this is more or less a good guideline for how concerned you should be that you're having a new inflammatory event. So, what I tell patients in clinic, if you see me is if you wake up and you've never had vision loss in your left eye, and you now have vision loss in your left eye and it's there all day, call me. If or even for six hours if it's in a new distribution, a new symptom, call me. If you wake up in the morning and your right hand's numb and by the time you brush your teeth, it's feeling fine. Don't call me. I mean you can call me if you want but I'll give you a hug but I'm not giving you an MRI.

[00:19:28] So, it's just what is the probability of it being new inflammation? So, when we think about if you're in the more likely or less likely category, if you're in the more likely category, that's when your practitioner may actually treat empirically while confirming. So, if you've never had vision loss in your left eye, and you are an aquaporin-4 antibody positive neuromyelitis optica patient and you call with new left eye visual changes. We are firing away on the therapy wall getting testing. We're not gonna wait for confirmation if you're in that more likely category. As you move to the less likely category, we may treat empirically while confirming and we may add some tests. We may say, well maybe there is urinary tract infection or something else. We may cover all bases. And then as you move to the less likely is when we hold off on the empiric therapy when we may say, "I'm gonna get the MRI. I'm gonna check your urine. I may check your blood work."

[00:20:25] And then as we get to the least likely, I may just start with the lab work and not even get an MRI. And for the clinics around the country who do this a lot, our nurses on the front line. So, in my pediatric practice is Denise, in my adult practice it's Alyssa. They have trained on this regimen over and over. It's like marine boot camp for a year. They can recite this backwards and forwards so that when our patients call in and Alyssa or Denise answers the call, they know this better than I do. They'll talk, they'll take the history, and they can peg with incredible accuracy where on this spectrum somebody is, and they will get the ball rolling. So, the response I get from Denise because we have standing orders around this is so and so called, the right eye that they always have problems with is blurry again today. They have a little fever. I'm sending

them for labs, but no MRI. Does that sound okay? And I either give a thumbs up or thumbs down or say let me talk to them on the phone.

[00:21:26] And it is remarkably useful and accurate kind of using these guides to determine whether or not somebody needs testing or treatment. But if there's ever a concern and it's going to make a difference in long-term management. We get the imaging because knowing whether something really was no inflammation, or a lot can have lifelong implications around therapies we pick. All right. So, I mentioned Denise and Alyssa, I just give a shout-out to the team at the Southwestern program, the Conquer™ program and Conquer and MO and AM and we have acronyms for all of them. It really does take a village to do this. Hopefully in the breakout sessions as you're able to meet different members of different teams, you realize as you hear from kind of one of us at a time, it's easy to think that there's a single or a few individuals that the institutions who are the reservoirs of knowledge, it's not the case.

[00:22:23] The reason these centers of excellence that have partnered up with the SRNA over the years exist, is the group of people we bring to the table. The central partner in this is you, our patients, and our families, and the more comfortable you are with the language and the vocabulary and why we do the things we do, the better and advocate you'll be for yourself and for your loved ones as you're trying to navigate this path. So, with that, if there are any questions, I'm happy to take a few questions and then we'll give you a little break before we do the last panels of the afternoon. But this was so straightforward, there are no questions because you guys know it. You can spot a relapse a mile away.

[00:23:07] **Audience Member 1:** I felt like I could spot a relapse away until I saw one thing and I just had a question about it. So, with optic neuritis and I happen to have MOG. My experience was that I'd go blind bilaterally get better, and then my relapses were just going blind again. And so would you say that every one of those would have to be confirmed by MRI. Because realistically it was only it was sort of more at the bottom, it was lasting more than 24 hours, an exacerbation of an old symptom.

[00:23:46] **Dr. Benjamin Greenberg:** Lasting more than 24 hours?

[00:23:47] **Audience Member 1:** I'm sorry. Excuse me. Yes, lasting more than 24 hours.

[00:23:50] **Dr. Benjamin Greenberg:** So, you're not at the bottom then.

[00:23:51] **Audience Member 1:** Went from the bottom.

[00:23:52] **Dr. Benjamin Greenberg:** Yeah, but you're not at the bottom and we laugh about it but it's 24 hours turns out to be... It sounds arbitrary, but medically it turns out to be important. So, that's in that middle category where I've seen it go both ways. Where I've seen people who had 24 hours or even 48 hours of symptoms and we found a conclusively they were having a pseudo exacerbation. We found the urinary tract infection, we treated it and their vision got better with no steroids, no plasma exchange, and it was obvious. And then we've had people where we do the MRI, and we see enhancement. I've got a few patients where making that determination is so important to long-term treatment decisions, I make them get an MRI each and every time. And it drives all of us nuts. We hate it, they hate it. Radiology hates it. It's painful but it's our best tool for confirming is it new inflammation or not? And I've had patients where sometimes it was inflammation, and sometimes it wasn't with the exact same symptoms. And so, unfortunately, there are times where we have to jump through those hoops because if you're on background immunotherapy if it's new inflammation then we need to talk about changing your background immunotherapy. It's not just for academic purposes.

[00:25:13] **Audience Member 2:** I had a situation where I was at all at the top of the most likely and everything, and I was treated and I wasn't getting better, and then they did an MRI. And nothing eventually showed up in inflammation. And so, then I was told that this is, and I had to go through plex. All this was like I'd never anything like that in my life. I mean there must have been a pseudo-exacerbation because there was no inflammation, and this is definitely not in my head. How do you as a patient advocate for yourself if you... With all due respect to I am nowhere near as educated on these things. Because maybe it doesn't matter or that's my question, does it matter if I was treated, and I did get better but as they're looking back, they're saying well there was no inflammation. So, it was a pseudo-exacerbation.

[00:26:14] **Dr. Benjamin Greenberg:** So, yeah that makes sense. The timing of the MRI is important. So, if I treat a patient, and then after some amount of time do the MRI after even those first doses, your MRI, the information could be gone because of the treatment, and so it could be a false negative MRI. And so, one of the things we look at is the timing of the MRI relative to the treatment that was given on how trustworthy is that data. And so, what we would do is we put a little asterisk around the MRI and say I can't conclusively prove it, but if you had new symptoms and a new distribution that were consistent with an event lasting more than 24 hours, it's a relapse in our book until proven otherwise. Especially if it responded to immunotherapy. Then we would count it as a relapse in our... Well, I'll say in my clinic I don't want to lump everyone together. I put Kyle and Cindy on the spot and just by thumbs up or thumbs down. It's one of those if it's a consistent event and it's lasting what we'd say it sounds like an exacerbation, especially if the MRI was delayed from the event till after therapy. But those can be tough, those situations come up.

[00:27:30] **Audience Member 3:** I didn't get a mic.

[00:27:32] **Dr. Benjamin Greenberg:** The mic, they can't hear you.

[00:27:35] **Audience Member 3:** They could if I tried. Is it necessary as a patient or was it important to then go back to my physician and say look, I would like to have this classified as a relapse. I know you think it wasn't, but I went to a conference and they... Do you know what I'm saying? Does it matter for my long-term outcome? Does it matter for God forbid this happens something I go through another situation or is it if the doctor thinks it was pseudo, I should just let it stay pseudo? I'm not sure exactly how best to advocate on my behalf in this point moving forward or if it's even necessary.

[00:28:18] **Dr. Benjamin Greenberg:** So, embedded in that question is two parts, one is the retrospective and one's the prospective. So, on the retrospective side, if its classification isn't going to change what's happening from here on, it's probably not important to revisit. If it does have an implication for long-term therapy, then it does need to be a conversation. And all you have to do is say you went to a conference in this physician named Michael Levy from Mass General told you, mlevy4@mgh.edu said it was clearly an exacerbation and where did he go to medical school?

[00:28:59] **Audience Member 3:** Get a selfie of us together.

[00:29:00] **Dr. Benjamin Greenberg:** Yeah, exactly. On the prospective side, it is important. Getting this right matters. It's one of those details, and the question we asked about advocacy in the room with clinicians that you know you like, you trust, where you're not feeling or knowing if the decisions are how you would want them to be or as they should be. It's a delicate conversation to have. My recommendation is if you're ever in a situation with a practitioner where you feel like you're not either receiving the care like you should, or you don't understand the reasoning behind the recommendation, which is another way to say it. I recommend

two things. Number one, the sandwich method of giving the feedback. Dr. Greenberg, thank you so much. I really appreciate your time and everything you said.

[00:29:52] It's clear you invest in my health. I'm not sure I fully understand why we wouldn't do an MRI right now. In my mind if there's new information or not wouldn't it make a difference here, but I definitely want to hear your thought process and trust what you're doing. That sandwich method just to get them to cognitively be receptive to revisiting that issue. And then if you leave still not satisfied, always encourage second opinions, and if you ever have a healthcare provider who is threatened by you getting a second opinion, that is a major red flag about that healthcare provider. That is one of the basics. Even in our program and our clinic and we've done this for a long time, we encourage our patients to get second opinions because you're making very big decisions about your life and your well-being. And I by no means have all the answers. And so, if you get to the end of a visit and you're not feeling it yet, do not be afraid to seek second opinions.

[00:30:55] **Audience Member 4:** We have quite a few questions that are coming in online, and Dr. Greenberg, I'm sure you know that now everyone online is coming up with specific cases so I'm gonna go ahead, and you can feel free.

[00:31:07] **Dr. Benjamin Greenberg:** The first one was a relapse, the second one wasn't, the third one I don't know about.

[00:31:11] **Audience Member 4:** All right. My MRI showed as normal a month after my neuro confirmed a recent attack through neurological observation. The MRI was done after five days of steroid infusions. I'm in Canada, and MRI is difficult to get. Hence why I only had it a month plus after due to symptoms that were not improving. During my attack in June, my brain and spine lesions resolved after infusions and wondering if the same thing happened as the recent one does not seem like a pseudo flare. Is it possible that the lesions resolved?

[00:31:44] **Dr. Benjamin Greenberg:** Yes, it's possible. So, again the tests have a positive and negative predictive value, and the timing of the test makes a difference. So, just to make it simple. So, if you go in with crushing chest pain like an elephant is sitting on your chest, and difficulty breathing, and you're sweating, and you look horrible and you're having trouble breathing. And then a month later I check your troponin and CK blood test, and I tell you well it's normal a month ago you didn't have a heart attack. That doesn't make sense. Certain tests have to be done at the moment in order to be reliable. And so, the MRI in this situation you couldn't hang your hat on it.

[00:32:24] **Audience Member 4:** Okay, thank you. I'm gonna keep going. If a TM patient's MRI reveals that the spinal lesion is enhancing. Is that an indication of a relapse?

[00:32:36] **Dr. Benjamin Greenberg:** It depends. So, we have had patients who have had enhancing lesions and as everyone comfortable with that term. So, what enhancement means is it has to do with the contrast. We put an IV in your vein, we inject the contrast into the vein, and it should stay in your blood vessels. If there is leaky-ness across the blood vessel from inflammation, or anything else creating leaky-ness, the contrast will leave your circulation and go into tissue, and we call that on an MRI, enhancement. So, what it means is contrast got out of the vein whether it was your optic nerve, your brain, or your spinal cord. So, we have had patients who have had NMO, MOGAD, transverse myelitis, optical myelitis, ADEM.

[00:33:20] Any of these diagnoses where the enhancement can linger for a long period of time after the event. So, while most enhancement goes away with therapy in a relatively short amount of time, there are instances where for six months or more, the blood vessel may still be leaky. And so, it really depends on the

timing and the situation as to whether or not persistent enhancement represents new inflammation or old. So, in our practice for example in ADEM, every patient we have with ADEM who gets treated, four months after their treatment no matter how they're doing, we repeat their MRI. To set a new baseline, to see what's going on because if they ever do call us a year later with a symptom, we need to see that things improved during that period of time. So, it really depends on the situation.

[00:34:11] **Audience Member 4:** Thanks. Two more questions and then I'm gonna turn it back over if there's any questions in the room. These are about MOGAD. Is relapse likely if not guaranteed with persistent tires?

[00:34:22] **Dr. Benjamin Greenberg:** Relapse is not guaranteed. The likelihood, some studies will put the likelihood in the 40% range. Some as high as 60-70%. In my practice, I'm quoting 50/50 right now.

[00:34:36] **Audience Member 4:** Thanks, and the final one also, MOGAD. Is a MOG antibody test relevant to determine a relapse? How fast can current technology provide my antibody test results?

[00:34:46] **Dr. Benjamin Greenberg:** Great question. So, we would love to have a blood test to tell me if you're having a relapse or not. And in the NMO trials, they looked at two different blood tests. One was something called serum neural filament and one was called serum GFAP. And in fact, there's some data to suggest that during a NMO relapse, that GFAP level goes up, and it be a game changer for me. Instead of ordering these MRIs to say, well let me just get your blood and tell you if you're having a relapse or not. We don't have that for MOG at this point. It has been validated or explored in MOG but it's an area of research. The antibody titer itself is probably not related to are you having a relapse or not? So, knowing if your titer went up or down doesn't change in my mind, was it a relapse or not. But someday we'll have other blood tests. All right, thank you guys. So, what we're gonna do is let everyone take a 10-minute break to stretch legs. There'll be a panel assembled up here, Mike Levy will be moderating. And the first 30 to 45 minutes of it is gonna be some hot topic areas that they're gonna go through and talk about. And then it's gonna be opened up for open question and answer session. So, anything and everything you have feel free to ask. All right, thank you everyone.