

COVID-19 and NMOSD

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Intro: [00:00:00] ABCs of NMOSD is an education podcast series to share knowledge about neuromyelitis optica spectrum disorder, or NMOSD, a rare relapsing autoimmune disorder that preferentially causes inflammation in the optic nerves and spinal cord.

[00:00:22] ABCs of NMOSD podcast series is hosted by SRNA, the Siegel Rare Neuroimmune Association and in collaboration with the Sumaira Foundation for NMO, The Connor B. Judge Foundation and Guthy Jackson Charitable Foundation. This education series is made possible through a patient education grant from Horizon Therapeutics.

GG deFiebre: [00:00:59] Hello everyone and welcome to the ABCs of NMOSD podcast series. Today's podcast is entitled "COVID-19 and NMOSD." My name is GG deFiebre from the Siegel Rare Neuroimmune Association. ABCs of NMOSD is made possible through a patient education grant from Horizon Therapeutics.

[00:01:20] Horizon is focused on the discovery, development, and commercialization of medicines that address critical needs for people impacted by rare, autoimmune, and severe inflammatory diseases. We apply scientific expertise and courage to bring clinically meaningful therapies to patients. We believe science and compassion must work together to transform lives.

[00:01:40] Today, I was joined by Dr. Michael Levy. Dr. Levy specializes in taking care of patients with neuroimmunologic diseases, including multiple sclerosis, transverse myelitis, optic neuritis, and neuromyelitis optica. In 2009, Dr. Levy was appointed to the faculty as Assistant Professor at Johns Hopkins, where he started the Neuromyelitis Optica Clinic and Research Laboratory. And in 2019, he moved to the Massachusetts General Hospital and Harvard Medical School to develop the research program in immunology.

[00:02:14] Thank you so much, Dr. Levy, for joining us today to talk about COVID-19 and NMOSD, or neuromyelitis optica spectrum disorder. So, to start are people who have been diagnosed with NMOSD more vulnerable to COVID or to more severe COVID?

Dr. Michael Levy: [00:02:33] Well, this was certainly a consideration when the pandemic first started last year. The concern was that people with NMOSD have an aberrant immune response to something in the environment and that maybe their immune systems would not be capable of fighting off COVID-19 or would make them more susceptible to the infection or could lead to a bad outcome. And that rationale is really what prompted all of us to be concerned and, and recommend really strict distancing guide-, social distancing, and handwashing, and all the other guidelines for preventing contact with, with COVID-19.

[00:03:17] However, what has emerged over time is that it doesn't appear that autoimmunity, per se, predisposes to autoimmune disease. There are certainly patients who are more vulnerable, but it appears to be due to

age and underlying disability. So those who have very severe mobility issues and those older age or nursing homes, which in areas of high prevalence for COVID-19, those people appear to be the most vulnerable. So there have been some NMO deaths and in that specific patient population. But otherwise, it doesn't appear that the vast majority of NMO patients or MOG patients and TM patients were more vulnerable to COVID-19.

GG deFiebre: [00:04:07] Got it. And so, you know, someone who has NMOSD or has been diagnosed with it might be on long-term immunosuppression, or also if they're having a relapse, might receive acute treatments, you know, like steroids or plasma exchange or IVIG. How, how might these kind of impact someone's experience with COVID-19 if they have NMOSD?

Dr. Michael Levy: [00:04:29] That's a great question because the expectation is that if you suppress the immune system with these drugs, like steroids, that that should make you more vulnerable because your immune system is not able to fight the COVID-19 virus. It seems though that that does not seem to be correct. That basically people on immunosuppression maybe have a slightly higher risk for infection, but their outcomes seem to be fairly similar.

[00:05:00] And what's emerged over time is that now healthy people who get the COVID-19 infection and end up in the hospital, they are started on immunosuppression. So, steroids are our first line treatment now for COVID. And so, it seems to be that the immune system is more dangerous than the virus itself in terms of bad outcomes for COVID.

[00:05:21] And so that's why we use those kinds of medications in, in anybody who's infected. So, if you're already on those drugs and then you get the infection, it seems to be that maybe you have sort of already a, a better outcome if you're on those treatments. And one thing that is interesting are those people who, who have NMO ended up with the infection and, and were in the hospital or with MS on immunosuppression drugs.

[00:05:52] And then those drugs were withdrawn because the thinking was, we want the immune system to be able to fight, to be able to fight the virus. And many of those patients did worse when they came off of their immunosuppression. Not worse only in their underlying disease, but also worse in treating their COVID-19.

[00:06:12] So it really seems like keeping the immune system in check during the infection seems to be the, the best way to ensure a good outcome.

GG deFiebre: [00:06:23] Right. So, I know early on there were concerns, people were asking if they should kind of prolong the time between their infusions and all of that, but that seems to not be, you know, a recommend-, recommended course of action. Correct?

Dr. Michael Levy: [00:06:35] Right. You know, for NMO patients, certainly the balance of risks suggests that you should stay on your current treatment schedule. Even now for patients with MS, there was a thinking, well with MS patients, if you skip your, your B-cell depletion dose, the outcome is not going to be that harmful if you miss a dose or two. And maybe in the pandemic, it's worth keeping patients away from infusion centers where they could get infected.

[00:07:02] But even that has probably, probably suggested that MS patients do better if they stay on their treatment. Of course, maintaining all the social distancing guidelines to, to avoid infection as best as they can, but even MS patients do better when they stay on their treatment, NMO for sure, and it appears MOG as well. Everyone should just stay on their treatment and try to avoid COVID altogether.

GG deFiebre: [00:07:26] And are there any differences kind of between, I know that there are three treatments

that are, have been used kind of traditionally in NMO, and then now we have three new medications. Are there any kind of differences between those three in terms of these recommendations or is it all kind of the same...?

Dr. Michael Levy: [00:07:42] Seems to be all the same. There's a difference when it comes to antibody production to the vaccine, which we'll talk about later. But in response to the infection, all of the drugs seem to be fairly similar. There, there are some studies that suggest that rituximab does increase the risk of bad outcomes in some MS patients who have progressive disease.

[00:08:09] And it's unclear if people with bad MS are on rituximab or ocrelizumab because they have bad MS to begin with and that's an aggressive treatment, or if the B-cell depletion itself in a patient who's disabled sort of adds on to the risk. It's not clear at this point. So, we do, we do, we are careful with all of our patients who especially are disabled or over age 50, because we do want to ensure that we're not contributing to a, a higher risk case scenario.

GG deFiebre: [00:08:44] Got it. And then what if just someone by chance, you know, happens to have a relapse, or is newly diagnosed with NMO, kind of, unrelated to COVID-19 but during this pandemic? Is there any sort of issues with these acute treatments like steroids? I know you mentioned that steroids are kind of a first-line treatment now for COVID-19. But are there any kind of increased risks of severe outcomes or anything if someone needs to get these acute treatments for an onset or a relapse?

Dr. Michael Levy: [00:09:12] You know, I think hospitals are doing their best to keep COVID-19 confined to a room and not let other patients get infected. Certainly, at my hospital, every precaution is taken. So, if you have an NMO attack, my recommendation is still to go seek care.

[00:09:31] It might be better to skip the emergency room perhaps, as emergency rooms are full and sometimes chaotic. Might be better to just get directly admitted or to get an MRI done at an outside center to just avoid that chaos. And then if you have a relapse, the treatment is really important to do because you don't want to take any chances with, with an NMO attack.

[00:09:55] So treatment with high dose steroids plus/minus plasma exchange is still the recommended treatment, even through the pandemic. And we're transitioning a lot of patients to home treatment. So oral steroids, a slightly higher dose than the IV, same bioequivalence. It should help, and it keeps the patients out of the hospital.

[00:10:14] Similarly, plasma exchange, we can insert the, the IV catheter for the plasma exchange and then do them on an outpatient basis. So, we're trying to figure out ways to keep patients away from COVID in the hospital, but, and still provide the necessary care for their relapses.

GG deFiebre: [00:10:31] Got it. And do you think any of these kind of protocols will be maintained post pandemic as well? Or is it, do you think it's just kind of as a result of this emergency situation?

Dr. Michael Levy: [00:10:40] That's a good question. I think it really depends, in part, on safety of, of this approach. If it turns out to be just as safe and effective to keep patients at home during their treatment and nobody's falling or falling through the cracks, or has any really bad outcomes, then I think it can be maintained.

[00:10:59] Also, there are payers. If it, certainly, if it's cheaper to do things at home, payers would be keen on that. And then also patient preference. If they like to be home, then that might be the preferred way. If there are problems at home, in terms of mobility, getting around, you know, in the hospital, you have more support to get to the bathroom, things like that. I think for severe attacks, people are going to still have to be in the hospital, but maybe for mild attacks, we'll be doing more at home.

GG deFiebre: [00:11:29] Got it. So, if someone's diagnosis of COVID-19 was due to a viral infection or, you know, occurred after a viral illness before the COVID-19 pandemic, should they be concerned that their immune system may respond in the same sort of way if they got COVID-19?

Dr. Michael Levy: [00:11:48] I, I think that NMO is partly due to genetic predisposition, to something in the environment. And what that is in the environment that triggers disease and then triggers relapses, we don't know. It could be infections, could be viruses, bacteria, gut bacteria. I've seen many, many cases of relapses that were triggered by an infection.

[00:12:13] In fact, one third of our patients who come in with relapses have a urinary tract infection. It could be as simple as that. But we also have about an equal number of patients who have a urinary tract infection with no relapses. So, we're not exactly sure what triggers the disease. We're not exactly sure what triggers the attacks afterwards, the relapses. But we do think that anything that activates the immune system has the potential to, to trigger a relapse.

[00:12:40] COVID-19 is no different. COVID-19 activates the immune system. So does the vaccine. They both probably have a risk of reactivating the immune system and triggering an attack, but we have to consider the context. So, if you're on an immune suppressive treatment, one, that's very good for NMO, like one of the three FDA-approved drugs, it's unlikely that, that either the infection or the vaccines would trigger a relapse because these drugs are very good at keeping the immune system calm, specifically for aquaporin-4 NMO.

GG deFiebre: [00:13:13] Got it. And then have we seen COVID-19 leading to, kind of, new cases of NMO?

Dr. Michael Levy: [00:13:20] I have one, I know of one case where COVID-19 has unmasked NMO, and we call that unmasked because the thinking is that if you have an immunological reaction immediately after the vaccine and it's aquaporin-4 positive, the thinking is that there was always kind of a predisposition for the disease, and it really just took an immunological trigger, like the infection or a vaccine, to unmask the disease.

[00:13:51] So I do have one case I'm aware of where that has happened. I'm also aware of cases of transverse myelitis, as well as seronegative disease. So, there are a handful of cases now that I've heard of where immediately after the vaccine, within days, there's a very potent immunological reaction causing a tax on the optic nerve, spinal cord, and in some cases, the brain.

[00:14:16] And it responds to suppressing the immune system, but they don't test positive for anything - for MOG, for aquaporin-4. And so, we don't know what that disease is and if it's, if that predicts relapsing disease or if it's just a one-time immunological reaction to the COVID vaccine.

GG deFiebre: [00:14:33] Got it. And so, you mentioned that this was after the COVID vaccine. Have you seen NMO occurring after COVID infection itself?

Dr. Michael Levy: [00:14:41] That's, I, I'm aware of about 40 cases of transverse myelitis occurring after the infection itself. These are published cases throughout the world. And the numbers don't necessarily imply that they're directly linked to COVID specifically, because if you just think about how many cases of transverse myelitis occur yearly, many of which occur after the, after an infection of some kind, it may just be within the normal range. But because COVID is so prevalent and so infectious, many people are getting it. Whether COVID is actually contributing to the disease, we're not exactly clear.

GG deFiebre: [00:15:26] Got it. And then if someone is experiencing symptoms of COVID-19 and they have NMOSD, is there anything different that they need to do kind of outside the normal protocol for someone who has COVID-19?

Dr. Michael Levy: [00:15:41] You know, I think there are two issues there. One is treatment for COVID-19. It depends on their immune status. I think just being on immune suppression is helpful, but, depending on other co-morbidities. If, for example, if you limited mobility and you're at high risk for blood clot or something like that, then there may need to be more care for, for you if you get that kind of infection.

[00:16:09] If, but then there's the question of your autoimmune disease. So, if you get infected, I think you do have to be more observant for relapses. And what I say to most of my patients is if you get the infection, and you notice your old symptoms are just flaring, then that's likely to be okay because that's expected that old symptoms can re-emerge in the context of any infection, including COVID. But anything new, any new symptom, new part of the body, or new sensation or new vision loss, new weakness, or new urinary retention, that's always an emergency that needs to be reported right away.

GG deFiebre: [00:16:50] Got it. Okay. And so, we talked a little bit about the COVID vaccines, but if we could talk a little bit in more detail about them. So, I know that there are a few that are currently being used in the United States and then a few more outside of the US. So, what is it that we know so far about NMO and the COVID-19 vaccines?

Dr. Michael Levy: [00:17:11] Nothing specific. There are the, the Pfizer and Moderna vaccines have been used in the US since December. And we have, probably the vast majority of our patients in the US have used one of those two vaccines. And in fact, worldwide, I think most people are still using one of those two vaccines.

[00:17:33] The third would be J and J and the Novavax coming out soon. There are some people in trials using that. It doesn't appear that there is much difference in the NMO patient population in response to those vaccines, either in efficacy or in safety. The numbers of vaccine side effects seems to be about the same. About twenty-five percent of my patients will report worsening neurological symptoms from previous attacks.

[00:18:04] So, let's say you've had pain in your, in your legs since your last transverse myelitis. After the vaccine, you might get pain in your legs that's worse. And in about 10% of those cases, requires more intensive treatment, maybe addition, additional medication, or even hospitalization. Rarely, there have been attacks, relapses. I'm aware of one occurring in the context of MOG antibody disease that occurred shortly after a vaccine.

[00:18:34] So, we do know that that can happen. But for the most part, it does seem to be safe as long as you're on effective treatment for your disease. It seems that other than those side effects occurring, it does seem to be safe and so far effective. We haven't had any breakthrough attacks so far. And what we call a breakthrough attack is one where you've completed your vaccination, and then at least two weeks has elapsed, really giving your immune system time to respond to the vaccine, and then had a COVID infection.

[00:19:08] I have colleagues at my hospital who have, I think now we have two cases of breakthrough disease, and in MS, for example. And we're not sure if that's just kind of within the normal numbers. So, these vaccines are anywhere between 77 and 95 percent effective. So, are these breakthrough attacks really just within that failure rate or is there something specific about their vaccination because of their treatment or their underlying disease? We're not quite sure yet.

GG deFiebre: [00:19:40] Okay. And so, you know, is there... I know that there was, you know, the potential for, for example, those who are on rituximab to maybe not create an antibody, you know, antibody production that is expected from someone from getting one of these vaccines.

[00:19:59] Are we still kind of concerned about that happening? And if so, you know, is there anything that someone should do about it? You know, extra booster doses? What's that kind of conversation been like for those on immunosuppression getting these vaccines?

Dr. Michael Levy: [00:20:14] That's a complicated story because antibody responses to vaccines are the easiest thing to measure. It's a blood test. You can check right away. It gives some reassurance, especially in healthy people, that the vaccine is working. But if you're on a drug that blocks the antibody production, then what does that mean that you don't produce an antibody response? In the data so far, it appears that somewhere between 15 and 35 percent of patients who are on B cell therapy will still make an antibody.

[00:20:47] And maybe it's because they got their vaccine towards the end of their rituximab cycle or ocrelizumab cycle. Or maybe it's because even if they don't have B cells in their blood, they still have B cells other places. So, if you get an injection in your arm and you have B cells in the muscle tissue, that you could still produce an antibody response. The antibody response though, just because it's easy to measure, is not necessarily predictive of response to the vaccine.

[00:21:15] So there are studies even 10 years ago that were done with ocrelizumab as it was being used in MS and response to other vaccines, not COVID, but things like tetanus. And what emerged out of that is, you have these patients do not make an antibody response as, as well as other people do, but it doesn't appear that they're more vulnerable to the infection.

[00:21:44] And so, as long as there's a robust T-cell response - T cells are another cell type in the immune system that are not necessarily inhibited by these B-cell drugs, like rituximab and may be sufficient to provide efficacy from the vaccine. So, what data do we have from the COVID-19 vaccine? Very little. There was a study just released out of Israel, where they lumped in all of their immunosuppressed patients on, on many different treatments for many different causes and found that the Pfizer vaccine was at about 84% effective.

[00:22:24] So that's down from 95%. So clearly less. But they didn't suggest that it was linked necessarily to an antibody response or to any particular disease or to any particular treatment, so we really need to do a lot more work to figure that out. Now I'll mention one more thing. Out of the 88 million or so Americans who've been vaccinated so far, there have only been somewhere on the order of 80 to 90 cases where a vaccine failure has resulted in death.

[00:22:55] So it's about a one in a million death rate in, in patients who've been vaccinated. And these numbers are just too small for us to be able to make any conclusions. And out of those 88, for example, I don't know how many have been on rituximab.

[00:23:10] This is nationwide of all vaccine failures who've passed away. I don't know how many have been rituximab or had an autoimmune disease. Those data are so hard to get. When we queried the CDC for this data, they showed us that the case report forms that they collect this on, they just ask if the patient is immune suppressed, and it doesn't necessarily ask for which, which treatments they were on.

[00:23:35] So I'm afraid this data is going to be very, very hard to come by.

GG deFiebre: [00:23:39] Got it. And then, so are there, we talked about rituximab. Are there any kind of other considerations for any of the other medications or is it kind of all the same for, for them all in terms of response to the COVID-19 vaccines?

Dr. Michael Levy: [00:23:54] Yeah, that's a good question. There are some studies showing that of all the treatments, including for MS, the ones that seem to be the most suppressive in terms of antibody response is fingolimod, which is used for multiple sclerosis. And that doesn't necessarily target B-cells. So, it's not, it's not, I mean, it's clearly immune suppressive, but not specifically against the cells that are producing antibodies.

[00:24:21] And then there were treatments that did not, that were quite immune suppressive, but did not appear to suppress antibody response, like Cladribine, which again, is used for multiple sclerosis. And so, it, it's a mix. It's certainly a mix. And again, one of the things I really want to emphasize is just because the antibodies are not produced, it doesn't mean the vaccine is not effective.

[00:24:43] So I have lots of patients asking me for, for a blood test to see if they responded to the vaccine. And I send it to them because they really want to know, and that's fine, and I'm interested too. But again, none of them have, have had a breakthrough infection. And so even if they test negative, I say, "Don't worry. If you're on a B cell drug, especially, or if you're on fingolimod, I expect you to test negative, but I don't expect you to break through the vaccine."

GG deFiebre: [00:25:10] Got it. And then there has also been a lot of discussion about the timing of, you know, when should you get your infusion or, you know, do your medication in relation to the vaccine. Are there any sort of recommendations to kind of get the optimal response to these vaccines?

Dr. Michael Levy: [00:25:25] Yeah, it depends on what you're trying to optimize.

[00:25:29] If you want to optimize the response to the vaccine, then the best course is to wait until the end of your B-cell treatment cycle, because then you have some B cells coming back, and it provides the most likely scenario that you'll get to that 95% efficacy that Pfizer and Moderna promise you. However, if you allow your B cells to recover to any degree in, especially with NMO, you're putting yourself at risk for relapse.

[00:26:00] So it's a balance of risk. Which one do you want to try to optimize? Do you want to try to optimize response to the vaccine? Or do you want to try to kind of get the best of both where you're getting a decent response to the vaccine, but not putting yourself at risk for an NMO attack? It's not clear how to do that.

[00:26:18] And because it's not clear how to do that, I've just been advising my patients, "Don't change your NMO treatment. If it's working for you and you're not relapsing, you're stable, and you're in remission, don't mess with that. That is going to cause a lot more trouble than it's worth. So, stay on your treatment. And as soon as the vaccine becomes available to you, take it. And even if you get a partial response, like what they found in Israel, where there's a slightly reduced efficacy in patients who are immune suppressed, take it anyway. 80 something percent efficacy is not bad, especially for a vaccine, when you consider flu is in the 30, 40, 50 percent efficacy, 80% is still wonderful.

[00:26:57] You're still providing some protection to yourself and, and, and stopping the infection from spreading to others and contributing to, to global herd immunity. And in the future, if you didn't get that perfect response, maybe by either antibody production or otherwise, if we, if we can demonstrate other, using other assays that you, you did not respond well to the vaccine, you can always take a booster later."

[00:27:26] Boosters are something that have been tested and considered. Again, appear to be safe, maybe six months out, maybe 12 months out. We're not quite sure. And we're also not quite sure how to tell if you, if you need a booster. Again, antibody response is the easiest to check, but again, not always the most predictive.

GG deFiebre: [00:27:46] Got it. And then, in terms of, I know we talked a bit about the different types of the vaccines. So, there's the mRNA vaccines - the Pfizer and Moderna - and then Johnson and Johnson in the US. Are there any kind of differences in these types of vaccines in terms of response and NMO, or outcomes in those with NMO?

Dr. Michael Levy: [00:28:05] Not that we've seen yet. It, it, the numbers are too small to compare Pfizer, Moderna, versus J&J or an adenovirus that AstraZeneca makes. So, J&J and AstraZeneca share a common adenoviral vector. They're slightly different. One is human, one is chimpanzee based. But they both use an adenovirus to deliver the COVID-19 DNA to, to the human tissue.

[00:28:34] I have patients who've received any of these, and they all seem to be efficacious at this point. Again, we don't have enough time and real close monitoring. It's not like I, I check my patients for nasal swabs. So even if they got, you know, there was some concern that the adenoviral ones like AstraZeneca or J&J are not as effective.

[00:28:57] It, maybe it's because they only need one shot for that protocol, or maybe it's because the mechanism is just different. But in my patients who've received those adenoviral vaccines, they seem to be fine. Now I don't go to their house and check their nasal swab every week to see if they've, you know, truly had a, a perfect response. But in my experience so far, they seem to be okay.

GG deFiebre: [00:29:20] Okay. And then moving on to the potential for a relapse. So, if someone, you know, have you seen kind of relapses occurring post, you know, after COVID-19 vaccine, vaccination? And then also, how can someone determine whether what they're experiencing is just a worsening of symptoms versus a true relapse?

Dr. Michael Levy: [00:29:43] Yeah. So, we've had a lot of concern about this, after the COVID vaccine, when people do have symptoms that flare. Again, it's really very rare that we've seen a COVID-vaccine-induced relapse. I've heard some reports. MRIs seem to be negative so far. So, fingers crossed that everything is, is okay. But they're clearly worsening symptoms, and that still requires some treatment in some cases.

[00:30:16] The ones that seem to be the most common are flares of previous symptoms: more pain, more tingling, more discomfort of whatever, slightly blurring of vision, feeling tired and ill and feverish in that context as well, and having multiple symptoms. Because it's like all of your previous attacks are coming back, feeling, making you feel much, much worse.

[00:30:46] That is actually reassuring. Those situations are the ones where the MRIs tend to be negative and responsive to just supportive care, Advil, you know, rest and that seem to respond and resolve over time. It could take a week, 10 days, or even more in some cases. The ones that I'd be particularly worried about are new symptoms that come out immediately after the vaccine or the, especially the second one.

[00:31:17] And then I mentioned, I am aware of one case with MOG antibody disease where 10 days after the second dose of Pfizer, the patient presented with new and worsening symptoms and obtained an MRI that showed a contrast-enhancing lesion in the spinal cord. So that was a true relapse. Because it followed

10 days after the second dose of the Pfizer vaccine, the implication was that it was probably linked, most likely, just based on the timing and not having any other trigger for that attack. I think it's likely. But so far, otherwise, I haven't seen any other cases.

GG deFiebre: [00:31:52] Got it. And then is there any research being done on COVID-19 and NMO or the vaccines and NMO?

Dr. Michael Levy: [00:32:00] There is. So, if you, if you've surfed Facebook and found my, our Facebook group that we started back in 2013. We now have over, I think, 3,500 followers. And this is a, an amazing source of information. So, we tapped all of our followers. If they could please report any symptoms that occurred after the COVID vaccine. Because we really want to know, number one, is it safe? And number two, how do you feel afterwards? What can we advise our patients to, to be aware of?

[00:32:31] And it does appear right now that about 25% will experience some significant side effects, enough to report to us, and that they are neurologically based, and again, mostly due to previous attacks.

[00:32:48] So we have that on our Facebook page, and we have about 500 injections so far reported. And I think that we're going to be publishing it very soon in order to get the word out to other people that, again, it does appear to be safe. However, this is what to watch out for. These are the symptoms that commonly occur following a, an injection.

GG deFiebre: [00:33:08] Got it. And then, is there anything else you want to mention that we haven't talked about today about COVID-19 and NMO?

Dr. Michael Levy: [00:33:15] I, I'm, I'm keeping an eye on the antibody data. There is also now a test offered by Quest to interrogate your T-cell reaction to the COVID vaccine. This is a new test. There are several others available throughout the country.

[00:33:32] And it's not clear to me if that's also going to be useful or predictive. We need to, we need to start a study in a cohort of NMO patients with MOG and TM and see if that is helpful. But again, in the end, what really matters is does the vaccine prevent the illness? And so, as long as that data remains small - one in the million - that you might die after, despite the COVID vaccine, that you might die from COVID, I'm encouraged that the, that the vaccine is probably working.

GG deFiebre: [00:34:10] Great. Thank you. Thank you so much for taking the time today to talk to us about this.

Dr. Michael Levy: [00:34:14] Thank you for having me.