COVID-19 and Rare Neuroimmune Disorders

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[00:00:00] **Roberta Pesce:** Okay. We have officially reached, I cannot believe it, our final talk of the 2021 RNDS. Thank you for joining us over the course of these 3 days. One of the reasons we're all joining this conference virtually, unfortunately, this weekend is COVID-19, the COVID-19 pandemic, which is also the topic of our next talk. I'm delighted to be joined, again, today, tonight for me, by Dr. Benjamin Greenberg, Dr. Michael Levy, and Dr. Carlos Pardo. Welcome back, and over to you. That's my cat. Over to you.

[00:00:46] **Dr. Benjamin Greenberg:** Thanks, Roberta. Hi, Michael. Hi, Carlos.

[00:00:50] **Dr. Carlos Pardo:** Hi, Ben. Hi, Michael.

[00:00:51] **Dr. Michael Levy:** Hi, Carlos.

[00:00:52] **Dr. Carlos Pardo:** Thank you, Roberta.

[00:00:53] **Dr. Benjamin Greenberg:** So, I know both of you have been giving talks intermittently throughout the symposium to our audience. You guys have been amazing in terms of your staying power. For those of you who have made it through all 3 days, you deserve a prize. And as we're coming to an end, as Roberta mentioned, we're going to be talking about the reason we're virtual and that's COVID-19. I think I can summarize everyone's feelings on COVID-19 by saying, aren't we done with this yet? And the answer is, unfortunately, no. In our community, I've seen a lot of different questions come up and, Mike and Carlos, I think it would help everyone if we walked through a few of the different aspects that impact our patients.

[00:01:40] Let's start with the infection itself, and just ask the broad question of, have you seen any data or had any experiences that would make you think the COVID-19 infection is more dangerous or uniquely problematic for individuals in our community with these rare autoimmune disorders of the central nervous system? Have you seen any outcome studies that say there's a different or scarier impact if this infection occurred, Michael?

[00:02:11] **Dr. Michael Levy:** No. I haven't. I would say that it's fairly equivalent to a severe flu or a little stronger than that, but the concern, of course, is the virulence and how fast this spreads across the community. It

seems like at this point, basically, everyone has either been vaccinated or exposed in some way and that's, of course, different from the flu where you can just try to avoid it.

[00:02:36] **Dr. Benjamin Greenberg:** Yeah. And so, the other aspect that's unique to our community, where many of our patients have had their first events or only event in the setting after an infection is whether or not the natural infection is a risk factor at all for triggering relapses, whether it be in our idiopathic transverse myelitis population or individuals who are already at risk for relapses, specifically neuromyelitis optica. Carlos, I'm sure this question has come up for you in clinic, have you seen or are you aware of patients having relapses triggered by the COVID-19 infection?

[00:03:17] **Dr. Carlos Pardo:** So, it's a very interesting question. The first thing that I need to alert the community is, number one, actually, what we have seen is that the COVID-19 and subsequent coronavirus infection is unmasking some of our neuroimmunological disorders that we follow closely. We have seen in our center and very surely in other centers, that actually we have discovered patients that may have had neuromyelitis optica or optic neuritis in the past and when they got COVID. Actually, many of the symptoms manifested clearly. And retrospectively, when we go and evaluate those patients actually, we found that before they had multiple sclerosis, they had neuromyelitis optica or other autoimmune disorders before based on the clinical and laboratory assessment. So, that's part one. So, it's very clear and actually most of the patients in which we have encountered complications are that type of patient.

[00:04:13] But the second one is complications in patients that have been already diagnosed with a rare neuroimmunological disorders. The fact is a subset of our patients that experienced COVID-19, experienced exacerbation of symptoms. Not necessarily new attacks or not necessarily increased in the rate of immunological damage, but rather an exacerbation of symptoms based on the magnitude of brain or spinal cord damage that they have experienced before, and that's very clear and this is actually one of the rationale for promoting the use of vaccine among our patient population with rare neuroimmunological disorders is that that infection is going to trigger more symptoms and exacerbation of symptoms.

[00:05:05] **Dr. Benjamin Greenberg:** So then, I think we move now in to probably a more complicated questions, and I'll start still with the actual infectious side of things, there have been reports of post SARS-CoV-2 infection, myelitis, or inflammation cases within the central nervous system. And if we look at worldwide the, literally, hundreds of millions of infections that have occurred, the sense I get is that it's still an extremely rare event, but they're out there. I'm curious, Michael, we were talking yesterday about how we study post-vaccination myelitis, and how it's rare to line these up, it's hard with infections as well. From your read of the literature and what you've experienced, do you get the sense that there is an entity of a post-SARS-CoV-2 myelitis or CNS inflammatory event?

[00:06:01] **Dr. Michael Levy:** I think that that there is something there. I will tell you that in my capacity as a journal editor for the field, that we've now summarized about 100 cases reported of either optic neuritis, transverse myelitis, or NMO that's resulted after the infection itself. And so, in my mind, that's not a huge number given the number of people who are infected, but I think what it suggests is that it's similar to other infections when people look back at cases of transverse myelitis, optic neuritis, and NMO, and they look back and say, "How many people had an infection 3 weeks prior?" About half of them do. And I think when you have a really close cohort of people where pretty much the only infection going around is COVID, I think there is a tendency to try to make that link. But I think what we are seeing is more of a general inflammatory reaction which then spurs the rogue element of the immune system to attack itself, rather than something really specific about the coronavirus virus.

[00:07:07] **Dr. Carlos Pardo:** So let me complement that answer, and actually there is already some data, there is a paper that is going to be published in the next few weeks in Neurology that is basically the result of a multi-center worldwide collaborative effort that was led by many neurologists that were part of the WHO task force for coronavirus neurological complications, and many neurologists of the United States were part of that, but there were neurologists in many other areas of the world including China, Russia, India, and Africa, and other countries.

[00:07:45] And the retrospective analysis that we did actually pointed out, that cases of myelitis, encephalitis were really, really not necessarily important as compared with the magnitude of other neurological problems that we saw, or we have seen, in the pandemic with COVID-19 like strokes, encephalopathies, and other type of neurological problems. So, the magnitude of myelitis and the magnitude of encephalitis is really minimal in terms of the expansion of the pandemic.

[00:08:22] The other indirect data that actually we are putting together, in Columbia, South America, we have a study that actually, it was established back in 2016, when Zika infection produced a major outbreak of encephalitis, Guillain-Barré, and myelitis. And actually, we had been observing what is the prevalence, incidence of these disorders in the past 5 years. During 2020, we didn't see any peak of myelitis, any peak of encephalitis, and even our major target, it was Guillain-Barré, actually Guillain-Barré cases went relatively flat as compared with previous years when we have shared more of those cases. So that suggests a strongly supported view that the infection itself is not triggering the disorders that we are looking for. There are, but it's not necessarily, epidemiologically, it's not necessarily a huge peak or a major factor for the causation.

[00:09:24] **Dr. Benjamin Greenberg:** And before we get to the what's, I think, obviously, a question on everyone's mind, the COVID vaccine related side of things, I do want to bring up this issue of long hauler symptoms with post COVID-19 infection. We've sent our share here in Dallas, and we actually have a clinic set up for individuals who feel as though they're having long-term symptoms, fatigue, and a lot of people complaining of cognitive issues after recovering. At least in the very, what I would call, preliminary investigations that have happened here, we have not seen evidence of an ongoing immune mediated brain-based inflammatory disorder post COVID, but that's very preliminary. I'm not sure if either of you are aware of any concerns of this long hauler syndrome being an independent immune mediated entity versus just what we sometimes see after bad viral infections, Epstein-Barr, flu, all sorts of others. Have either of you had experience with this long hauler cohort?

[00:10:26] **Dr. Michael Levy:** I'm involved in the NIH NYU long haul COVID program which seeks to enroll patients in this biorepository and then we'll have access to the data so we can look specifically at that question about whether anti-inflammatories maybe were helpful or if there were any signs of inflammation. My sense is not yet either, but I'll tell you in just listening to different talks on COVID-19, there are a lot of people who think that the ones who lost their sense of smell through invasion of the nerves that go in through the nose to the brain, those people might be more vulnerable to more long-term complications given the proximity of the virus to the brain. I don't know about that, I haven't seen yet anything in my clinic, but there are a lot of concerns across the neurological world and many of them are not inflammatory mediated, but very much neurological.

[00:11:21] **Dr. Carlos Pardo:** So, it's a very interesting, this is going to be very hot topic of research in the next few years, particularly because there are tons of patients coming to our clinics with the question "Is this brain fog this, lack of concentration, is this a sleep disorder? Is this a problem that I have with low blood pressure and the dizziness that I'm experiencing, part of my inflammatory disease?" Actually, we don't have,

we are tracking down also some biomarkers. Particularly we have a lot of interest in spinal fluid. We have interrogated the spinal fluid of some of the patients that come to our clinic for the investigation of this post COVID conditions, and we haven't had any evidence at all that this is an inflammatory-mediated disease. We base our understanding on testing of cytokines, chemokines, even presence of proteins. What we believe that a subset of patient may have experienced actually, is that COVID-19 produce very small, silent, microvascular changes in the brain.

[00:12:32] But again, this is basically still very preliminary, as Michael says, there is a very large group in the country sponsored and funded by the NIH tracking down the post COVID-19 condition, and particularly, probably in the next several months, probably we are going to learn more and more about the physiology of that condition, but the preliminary evidence that there is some inflammatory mechanism behind that is very, very weak. I think it's more other type of conditions like metabolical disturbances, and perhaps in a subset of patients probably some microvascular brain disease.

[00:13:11] **Dr. Benjamin Greenberg:** Yeah, and there is the interesting evidence of possibly a higher rate of diabetes in people post COVID and we know that there are multiple organs being affected. In that case the pancreas, there's a large wealth of data on renal impairment after COVID-19 infection. So, to your point, Carlos, there are multiple systemic possible impacts of the disease that could change how people feel. So, with that behind us, I think we get to probably the topic that's on most people's minds, and that's around COVID-19 vaccination in our patient population. We had a discussion about vaccines in general the other day, but I want to tailor this conversation to the COVID-19 vaccine.

[00:13:54] And if I can, I'd like to start, maybe it would be fun to go around the horn and start with your most favorite myth or disinformation that's out there about the COVID-19 vaccine. And I'm going to start with my favorite one which is the notion that the vaccines' development was rushed and that somehow corners were cut, and we did this faster than ever before, and I'd like to point out that the standards around safety and efficacy for these vaccines to come out were the exact same standards around safety and efficacy for every vaccine that's been used. The difference is how many cases we had and how quickly we were able to see the difference between a vaccinated and unvaccinated population. When you do a meningitis vaccine study, it takes years for enough cases to occur to show that the vaccine made a difference compared to placebo.

[00:14:51] But during a global pandemic, there were so many cases happening in the placebo arm you could see the efficacy of the vaccine so early on because everybody was getting sick. But even with that separation of the curves, the FDA held the exact same standard of how many months of follow-up would patients have to have, how large was the study in order to ultimately say is it approved or not approved. And, in fact, many people in the field feel as though they went too slow with final approval, that they had plenty of data, but they held the exact same strict standard. So, what I'd like to explain about the myth that it was rushed or that corners were cut is nothing went faster, we were just, so many people were getting sick and dying, that it was obvious to show the benefit of the vaccine early on. Michael, do you have a favorite myth, and there are many to pick from. There are all sorts of questions.

[00:15:48] **Dr. Michael Levy:** My favorite is the 5G myth, that there is some 5G chip in the vaccine that makes you an antenna for your phone, and my wife used to joke that whenever I touch her phone, I make it work, and I tell her, "It's the vaccine. I got the vaccine. Now I can touch your phone and it automatically works." But I think that that myth really encompasses all of the craziness. So, I don't think there's probably anybody on this call right now who actually truly believes in these things, but I think it just represents the worry that there's this, that there are people out there who don't want what's best for you and I think that's a very valid concern just in general, but the actual myths themselves are pretty ludicrous.

[00:16:34] **Dr. Benjamin Greenberg:** Carlos, have you been hit with the myth of the question, and I get this all the time now, around fertility and cross reactivity between the vaccine, the spike protein. I don't know if this one comes up in Baltimore or not.

[00:16:50] **Dr. Carlos Pardo:** Occasionally, and actually it's quite a frequent myth. And the reality is that one of the advantages that we have now is that we have really a good accountability for what is going on in many of these vaccines and the data is all there. There is not any documentation at all that, number one, fertility's affected, number two, that there is disruption of any hormonal pathways. And three, the safety of vaccine even for during pregnancy. Actually, the recent studies are quite amazing and actually very important to understand that the vaccine is even safe in a pregnant woman that's ready to deliver a child, and the baby is going to be protected if we receive a vaccination.

[00:17:40] So, I think that those, unfortunately, are very widespread myths. That the most important is that people understand that there is, in the same way, I'm going to use a war example, is that in the United States we are always ready, the Army, Navy, Marines and the Special Forces. We're always ready. And if you're not very close to infectious diseases, probably you ignore what people are doing in the lab, and when we encountered Zika infection in 2016, and I mention Zika because I was involved in the Zika research, in 2016, actually, the same actors that are playing a very important role now for vaccine development, were ready to go. They basically developed very quickly vaccines that were protective for Zika. Zika came and produced a huge peak in Latin America, Central America, and went away. The SWAT team of researchers who was ready there with a vaccine.

[00:18:49] The reality is the pandemic push to a reality that is different to an outbreak like Zika. The pandemic hit the world. The pandemic really produced a significant disruption of the economy and the life of people, and obviously we, that SWAT team, was ready to work and it worked very quickly, and it was very effective. So, the researchers that were working at NIH for many years, just tracking down the viruses, tracking down the immunology, designing the assays to test immunological reaction. Actually, that's exactly where the money of taxpayers of the United States is working. They were ready to go and the same happened with all the countries where researchers were ready to invest in the development of vaccines. So, I think that people need to understand that this didn't go right away. There were people that have been working for several decades in viruses, immunology, and vaccine development for putting together this pipeline that was very effective and it was very quick, and it's quite amazing model of efficiency and production of a vaccine.

[00:20:03] **Dr. Benjamin Greenberg:** Yeah. And along those lines in terms of kind of the differences now between other times and the differences with the pandemic, when talking about safety and I've gotten the question point blank, have there been any COVID-19 vaccine related transverse myelitis or ADEM related events, and we hear about the individual, I say, multi-case report levels where people have had a new diagnosis of a condition in the weeks or months following a vaccination. One of the things I am reassured about is the if, and I'm not convinced yet there actually is an association or not, it's got to be exquisitely small, and my point around this is we have given so many vaccines to so many people in a short period of time and we have been watching. We have been watching very carefully for any adverse events. Everything's getting reported with the COVID-19 vaccines, and the best evidence for this is we were able to pick up on very rare myocarditis, inflammation of the heart, events that's been reported with the vaccines, and it's recognized by the CDC that this is an extremely rare complication. Those numbers are one in the many millions of doses that we see a case, and we're not seeing transverse myelitis, we're not seeing ADEM, even at that level which is already rare.

[00:21:24] And so, what I've been saying to individuals is, I'm unaware of a COVID-19 vaccine triggering a relapse, that's not something I'm aware of in any statistical fashion, that the overwhelming majority, if not all,

of my patients who have gotten the vaccine have been fine, and I'm not aware of any statistical association between the vaccines and new events or new diagnoses. I'm curious for both of you whether or not you approach it the same way of, "Get the vaccine, it's definitely in your favor, it's safer to get the vaccine than to get infected," where if you're carving it out for any sub-populations or giving any different advice? Mike, I know you've spent a lot of time on this. Are we aligned on this?

[00:22:08] **Dr. Michael Levy:** We are. We are totally aligned. I think you said it very well.

[00:22:13] **Dr. Benjamin Greenberg:** Okay. Carlos?

[00:22:15] **Dr. Carlos Pardo:** It's the same. Actually, the advice that we are giving to our patients is to get vaccinated. And I, as we have mentioned in the past several days in our meetings, it's actually, COVID-19 is a serious disease. Infection with coronavirus is not free of potential problems, it is not transverse myelitis, it's not encephalitis, it's that the virus is going to damage the lungs of patients affected, and may produce strokes, and the strokes are devastating. So that is exactly the rationale. We have no concern that we are preventing a neurological disorders or complications or producing a high risk for that. We are basically trying to prevent patients develop this horrible complication such as a strokes or encephalopathies that may have long, long lasting effects.

[00:23:07] **Dr. Benjamin Greenberg:** Well, I thank you both for this time and information, and I'll open things up to Roberta and our audience to see if they have any questions. I'm sure there are. Roberta?

[00:23:20] **Roberta Pesce:** Yes. I think I received close to 10 questions. Let's see how far we get. Alright.

[00:23:28] **Dr. Benjamin Greenberg:** Question number one, did the Patriots win their football game? Michael, the answer is?

[00:23:32] **Dr. Michael Levy:** Woo-hoo. They did.

[00:23:32] **Dr. Benjamin Greenberg:** Yes. Okay. Now, what else we got.

[00:23:36] **Dr. Michael Levy:** Yes, they did 25-point lead in the last 15 seconds.

[00:23:37] **Roberta Pesce:** I'm going to start at the very beginning, "Are there documented cases where pseudo-relapse has been attributed by patients to pseudo-chronicity with vaccination against COVID-19?"

[00:23:50] **Dr. Benjamin Greenberg:** I understand the first part of the question. I'm not sure if I understand the second part. So, have I had patients with a pseudo-relapse after vaccination with COVID-19? Yes. So, and the way I would define that is, for example, somebody with transverse myelitis who had numbness or weakness of their legs recovered and then in the days after the COVID-19 had a transient return of some of their sensory symptoms, and then went back to their baseline. Yes. I've seen that. It's been rare, actually, but I've seen it. I personally don't understand the pseudo-chronicity with vaccination. Michael or Carlos, is this a term you use?

[00:24:25] **Dr. Carlos Pardo:** Actually, I was very curious about the term, no I am not very familiar with pseudo-chronicity term.

[00:24:32] **Roberta Pesce:** Maybe they can get back to us about this.

[00:24:34] **Dr. Michael Levy:** I think maybe just the timing maybe. They're linking the timing of the vaccine to the symptoms of the pseudo-relapse, and I think that that's a fair link.

[00:24:43] **Dr. Benjamin Greenberg:** Yeah.

[00:24:46] **Roberta Pesce:** Okay. I'm going to move on to the next question. They keep coming in, so I'm going to try and please let me know if I'm going too quickly here. I' doing my best to cover them all. "Has there been any research into molecule mimicry in relation to neuroimmune conditions? Specifically, where the immune system attacks proteins or matters of the CNS because they mimic virus particles?"

[00:25:07] **Dr. Benjamin Greenberg:** Yes. I'm going to actually ask Carlos to take the lead on this because I know he's spent time looking at a variety of infections. There's data that goes to campylobacter and other infections relative to mimicry. Carlos, do you want to walk us through that?

[00:25:19] **Dr. Carlos Pardo:** Yeah. That's a very good question, actually. In terms of viral disorders, the molecular mimicry is a very hot topic of research, but the hard data, documented molecular mimicry is very weak. Bacterial diseases are different. One of the classical example of bacterial disease is campylobacter jejuni, that is a bacteria that produces diarrheal disease, has produced major outbreaks of Guillain-Barré in China, has produced major Guillain-Barré outbreaks in Peru in 2018, 2019, and it's a very important problem in Central America, Mexico, and Latin America. And interestingly, we see campylobacter jejuni here in the United States. Sometimes we'll pay attention, and we'll look for that, but that is, so far, one of the best well documented molecular mimicry factor triggering a neurological disease.

[00:26:18] Many decades ago there was a lot of interest in some staphylococcus species producing myelitis. And actually, the first Transverse Myelitis Association Symposium in Baltimore actually, our colleagues from Europe brought cases of a staphylococcus triggering some devastating immunological disorders including myelitis. So, in terms of viral diseases, particularly the concern in coronavirus, actually there is concern, but there has been no proof and there is no data on that. We pay attention to Zika, we are still looking for molecular mimicry in Zika. We haven't found that. The same with other viral disorders. So, it appears that the most important mechanism is, rather than molecular mimicry is the capacity that the virus to trigger in select subjects, a very overwhelming immunological disorder that targets spinal cord, optic nerve, or brain in the case of encephalitis.

[00:27:18] **Roberta Pesce:** Alright. Perfect. Thank you, Dr. Pardo. Next question here, "If an NMO patient on Rituxin has been vaccinated but did not test positive for the spike antibody test, are you seeing them test positive for antibodies after the third vaccine?"

[00:27:33] **Dr. Benjamin Greenberg:** Yeah. This is a great question. We have a study going on this right now at UT. And in our hands, individuals on Rituximab or related medications, the, if you define efficacy of the vaccine by testing positive for these antibodies, at least half of our patients are not testing positive for these antibodies. The majority, I'd say, actually, might be closer to 60 to 70 percent are not testing positive for the antibodies. In our experience so far with our patients who have gotten the third dose, it's still very few of them are converting to a positive antibody.

[00:28:07] We are doing the booster, but when we've looked in small numbers, because we just started doing boosters over the last month in a systematic way, it's a small number. But I will point out there was a publication from colleagues at the University of Pennsylvania just in the last few weeks that looked at individuals on Rituximab who tested negative for the antibody, and a lot of them had antiviral T cells that had

formed with the vaccination. We don't have a good clinical test for this, and so it's only done on a research basis. And the reason I'm saying this is some people have said, "Well, why bother getting the vaccine if I'm on Rituximab?" You still can get an immunologic response that may be beneficial even without the antibody. And so, while it may not be fully effective, it may be partially effective, and the goal would be if you were to get exposed to COVID-19 that even if you got sick, maybe you wouldn't need to be hospitalized or get as sick because of the partial response of the vaccine. So, I think it's an issue that still needs study over this next year, but our rates of getting antibodies are pretty low on Rituximab.

[00:29:14] **Dr. Michael Levy:** Can I add one thing to that? I think it's really important that people understand that the antibody is not equivalent to immunity. If you don't have the antibody, it doesn't mean you're going to get sick, it doesn't mean your vulnerable. If you breakthrough the vaccine, then you are a true COVID vaccine failure case, that's different from just not having the antibody after your vaccination. They're not equivalent. We only check for the antibody because we can, we don't have that T cell test Dr. Greenberg talked about. So, people keep relying on that antibody as if it's the marker of the vaccination, but it's not necessarily.

[00:29:49] **Roberta Pesce:** Nice. Thank you. Maybe a follow-up, slightly follow-up question on, "Your thoughts of the booster vaccine, when should we consider getting it, is 8 months after the initial shots?"

[00:30:04] **Dr. Benjamin Greenberg:** I think it's actually an open topic. There's one piece of data, very small study that looked at, so the Pfizer mRNA vaccine originally was released as your two doses, 3 weeks apart. Moderna was released as 4 weeks apart. There was one small study looking at people who had a delay in their second shot. They didn't get it at the 3-week mark for Pfizer, they got it later, and in that study those people with the delay actually had a better immune response overall than the 3-week mark. And so, I personally have been leaning towards saying that 6-to-8-month range probably makes sense. I wouldn't do it sooner. I wouldn't be rushing out to get one, two, three shots in the first 3 months. So, I think if you're 8 months after initial shot and you have access to a booster, I think it's a perfectly fine time to get it. I personally don't think we have overwhelming data to say is 6 months better, than 7 month better than 8 month or what have you, we just haven't done that study yet.

[00:31:06] **Roberta Pesce:** Okay. Thank you. I'm going to try and keep going because they're very interesting questions, and just going to keep going. So please stop me if you have to leave. Alright. "Do you recommend the COVID vaccine for a child whose MOGAD onset was about 10 days after Hepatitis A and Hepatitis B vaccines once available? She's 2 years old, 1-year post attack and relapse free on monthly IVIG. IG is missing.

[00:31:34] **Dr. Benjamin Greenberg:** Michael, you want to take a first step?

[00:31:36] **Dr. Michael Levy:** Yeah. My first thought is that not every vaccine is going to trigger a relapse. In this child, if the timing was 10 days after those two shots, I think the link is pretty good. And so, I'm tempted to link those two, those hepA/B vaccines to that MOGAD event. Now that she's one year out, it maybe that she was only two years old at the time, maybe that her immunity to MOG has waned. Also, she's on treatment. So, in my experience, people who are on treatment do not react badly to vaccines. I can't even think of a, I do know one MOG patient who was on Rituximab who did relapse after a vaccine, but other than that it's pretty rare. So, I say there is a lot going for this kid, although a two-year-old, I guess, yeah, I think they are about to start getting, I thought it was three to 12.

[00:32:33] **Dr. Carlos Pardo:** Five.

[00:32:34] **Dr. Michael Levy:** Five to 12. So, I think you may have to wait anyway, but yeah. Thanks, Carlos. Five years old.

[00:32:42] **Roberta Pesce:** Maybe a follow-up question to you, Dr. Levy, "What caveats do you place on vaccine recommendations to MOGAD patients who are not Rituxan?"

[00:32:53] **Dr. Michael Levy:** I don't have many additional ones If a patient is on CellCept, I think it's about the same in the sense that they're not going to make a lot of antibody to it, but they're still going to be protected. And a third booster 6 months later, 8 months later, is probably not a bad idea. For people who are on Eculizumab, I think Soliris that's probably the one treatment where I don't think the vaccines have any problem working.

[00:33:19] **Roberta Pesce:** Okay. Thank you. Another question, "Have your patients who tested negative with the spike antibody test still seem to be protected against COVID-19? And if negative, is there any benefit to getting the booster?"

[00:33:37] **Dr. Benjamin Greenberg:** So, at least in our hands, one of the things to remind everybody is, the vaccine is part of your approach to protection. There are other things that at least I feel like my patients have been doing a great job of that make a difference. So, masking in public places, avoiding large congregations, especially with unvaccinated individuals. And so, thankfully, in my patient population, we've had a low rate of infection and I think part of it is vaccine related and part of it is choices that people are making. But I do still think individuals who test negative may have a partial benefit from the vaccine, and I do still recommend the booster for people who have tested negative, even after the first two shots because there is more, as Michael said, there's more than the antibodies that leads to protection.

[00:34:32] **Roberta Pesce:** Perfect. Thank you, Dr. Greenberg. We have another question come in, "A patient test positive for the spike protein test for antibodies and receives a number of with the results. What is a good number to show you you are covered if you are on immune suppression drugs?"

[00:34:53] **Dr. Benjamin Greenberg:** Yeah. If I, Michael, you want to go ahead?

[00:34:55] **Dr. Michael Levy:** Yeah. I'm just going to say any response, I think, indicates that your body, your immune system has reacted and is at least protective on the side of the adaptive immune response, as Dr. Greenberg mentioned, the T cells are reacting. So, if you make an antibody, it's just, it's a good sign and I think it doesn't mean that you're going to necessarily be 100 percent protected, but it means that your immune system reacted, and I think it doesn't really matter what the number is if you're on immune suppression drugs.

[00:35:23] **Dr. Benjamin Greenberg:** And if I can add to that, the way these assays are being set up in multiple labs and certified in multiple labs, the number from one lab to another may not be exactly the same. It's a little hard for me to take data generated in our lab, clinical lab, at UT and take data from Quest Labs, and if somebody was 500 on each is that exactly the same? It probably isn't. So, within one lab we're looking at does the amount of antibody make a difference, but when we have results from different labs it's very hard to crossover.

[00:35:55] **Roberta Pesce:** Yeah. We have closed the questions. We still have three but we're closing the questions that are coming in through the chat so that our speakers can also enjoy their Sunday. So, the last three questions that are coming up, one is, "After both doses of Pfizer, stable MOGAD patient, antibodies are zero. How will the patient be protected from COVID?"

[00:36:17] **Dr. Benjamin Greenberg:** So, I think this is similar in a different kind of context, but similar to the questions we're getting. So to put it simply, a negative antibody test after the vaccine does not mean you're unprotected, but I will tell you in my clinic I give people the advice to continue being extra cautious with masking and deciding what you do socially, because if you are protected it probably, I shouldn't say probably,

I should say possibly isn't to the same degree as somebody who mounted antibodies, but it doesn't mean that you're completely unprotected. And so, I say be careful, but it wasn't a waste of your time or effort to get the vaccine.

[00:37:01] **Roberta Pesce:** Yeah. Last question of the day, I kept this one for last. "How do we debunk that stuff, the myths that you referenced, or others that people claim and believe?"

[00:37:13] **Dr. Benjamin Greenberg:** Carlos, do you have a...

[00:37:16] **Dr. Carlos Pardo:** Believe in science. Believe in science. There are hundreds and thousands of people known in the United States and around the world, in labs, in clinical settings doing research and they're producing reliable information, very important data that allow us to sit down and appreciate and design clinical treatments and approaches. That is basically the most important part of our lives. We are here because we are clinicians interested in science, we love to interact with our patients and families, and what we follow is basically follow the data, follow the science, follow the evidence. We don't go and start doing experiments because we have a possibility that vitamin A is going to be the cure for COVID-19? No. I think that everything that we are designing in terms of medical treatment, intervention, and other types, are really based on science. So, the most important is follow the data, follow the science, and really have a good conversation with your clinician, with your health care provider, and see what is the best choice for difficult situations that you may experience with health problems and complications in the setting of a neuroimmunological disorders.

[00:38:44] **Roberta Pesce:** Yes.

[00:38:45] **Dr. Carlos Pardo:** The basic example that we have is in terms of believing, and trusting, and paying attention to science is the fact that in less than 15 years after neuromyelitis optica antibody was described, there are several treatments. What is that? That is science. You see? Basically, people pay a lot of attention and put things together and produce a product that is benefiting a lot of patients and families. So, that's basically what we should continue doing.

[00:39:20] **Roberta Pesce:** Yeah. Thank you, Dr. Pardo. Any additional remarks or comments, Dr. Greenberg?

[00:39:26] **Dr. Benjamin Greenberg:** I think it's a great question. I think it's hard. I don't know why some of the myths are able to penetrate psychologically into the community and in to our friends and neighbors with ease, and not, as Carlos says, the painstaking data from science that's occurred and I think we need to work on raising the level of trust in the scientific community and the level of understanding what it means to do this work and that the motives, as Carlos referred to, are pure in terms of we do these studies to try and benefit everybody, and there's not an ulterior motive or agenda there. I don't know how we get better at penetrating the psyche of individuals who are mistrustful of science. I'm all ears and open to all suggestions. I think if we just have Michael post everything on his Facebook page that will help, but I'm not sure how to achieve it.

[00:40:40] **Roberta Pesce:** Yes. Okay. Thank you. Thank you. Thank you. We have reached, I believe, the end of this talk and the end of the symposium. Thank you, Dr. Greenberg, Dr. Levy, and Dr. Pardo, for being here with us today, for spending so much time with our community, and for ending the RNDS talking about such an important topic.

[00:41:02] **Dr. Benjamin Greenberg:** Nice job, Roberta. Good work.

[00:41:03] **Dr. Carlos Pardo:** Thank you, Roberta, for all your effort, for keeping us on time, and organizing everything for this RNDS 2021. I know that you've spent a lot of time with this effort, so we appreciate very much that.

[00:41:17] **Roberta Pesce:** Thank you.

[00:41:17] **Dr. Carlos Pardo:** We all appreciate that very much.

[00:41:19] **Dr. Michael Levy:** And your technological prowess.

[00:41:21] **Dr. Benjamin Greenberg:** Yes.

[00:41:23] **Roberta Pesce:** Thank you. Thank you so much.