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GG deFiebre: [00:00:00] Hello everyone and welcome to the SRNA Ask The Expert podcast series. Today's podcast is entitled "Latest Updates on COVID-19 and Rare Neuroimmune Disorders." My name is GG deFiebre, and I will be moderating this podcast. SRNA is a nonprofit focused on support, education and research of rare neuroimmune disorders. You can learn more about us on our website at wearesrna.org. This podcast is being recorded and will be made available on the SRNA website and for download via iTunes. During the call, if you have any additional questions, you can send a message through the chat option available with Zoom. Our 2020 Ask the Expert podcast series is sponsored in part by Alexion, Genentech, and Viela Bio.

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[00:02:06] For today's podcast, we are pleased to be joined by Dr. Benjamin Greenberg and Dr. Michael Levy. Dr. Benjamin Greenberg received his Bachelor of Arts degree from Johns Hopkins University and his Master's Degree in Molecular Microbiology and Immunology from the Johns Hopkins School of Public Health in Baltimore, Maryland. He completed his residency in neurology at the Johns Hopkins Hospital and then joined the faculty within the division of neuroimmunology. In January of 2009, he was recruited to the faculty at the University of Texas Southwestern Medical Center where he was named Deputy Director of the Multiple Sclerosis Program and Director of the new Transverse Myelitis and Neuromyelitis Optica Program. Dr. Greenberg is recognized internationally as an expert in rare autoimmune disorders of the central nervous system. His research interests are in both the diagnosis and treatment of transverse myelitis, neuromyelitis optica, encephalitis, multiple sclerosis, and infections of the nervous system. He currently serves as the Director of the Neurosciences Clinical Research Center and is a Cain Denius foundation scholar.

[00:03:12] Dr. Michael Levy is an Associate Professor at Harvard Medical School. He is the Director of the Neuromyelitis Optica Clinic and Research Laboratory and Research Director in the Division of Neuroimmunology and Neuroinfectious Disease at Massachusetts General Hospital. Dr. Levy specializes in taking care of patients with neuroimmunologic diseases including multiple sclerosis,

transverse myelitis, optic neuritis, and neuromyelitis optica. In the laboratory, Dr. Levy's research focus is on the development of neural stems for regenerative therapy in these diseases. He uses rat and mouse models to test the survival, differentiation, and functional capacity of human neural stem cells to improve neurologic function in post-inflammatory conditions. The goal of his laboratory and clinical effort is to translate the basic science stem cell work to a human trial in transverse myelitis and other neuroimmunologic diseases. Welcome and thank you both so much for joining us today.

Benjamin Greenberg: [00:04:10] Pleasure to be here.

Michael Levy: [00:04:11] Thanks.

GG deFiebre: [00:04:13] So we did a Q&A series a few weeks ago about COVID-19 and rare neuroimmune disorders. And so some of these questions may have been asked previously, but we'd like to get an update if possible, if we know any more information. So first off, just kind of generally, are people who are diagnosed with a rare neuroimmune disorder more vulnerable to COVID-19, either getting it or having severe disease? And are any one of the rare neuroimmune disorders more vulnerable than others to COVID-19? So, for example, is someone with AFM more likely to get COVID-19 than someone with TM, or someone with NMO more likely than AFM and so forth? Dr. Greenberg.

Benjamin Greenberg: [00:05:00] So, first, while it may be a subtle point, I think it's important to differentiate risk factors for becoming infected with the coronavirus associated with COVID-19 versus risk factors that would lead to complications if one were infected. So, first, relative to becoming infected, other than exposure, duration of exposure, type of exposure, environments of the exposure, I am unaware of any conditions that would make somebody more likely to get infected versus another individual. The real issue is if infected, is there anything about someone that would lead them to have a complicated course or be at risk for admissions, needing a ventilator, or passing away because of coronavirus.

[00:05:54] And in general, from what we understand about our conditions, we have not seen, repeat, we have not seen, data to suggest that individuals who have had an autoimmune disease are at higher risk of complications from the illness. So the diagnosis doesn't change risk. But if somebody is on an immunosuppressant medication as one of the management strategies of their condition, the medication may increase the risk of complications. So I think it's early, statistically, to know if that's true, but it's definitely a theoretical concern. So if you’ve had one of these conditions and are not on a long-term immunosuppressive regimen, the diagnosis in and of itself doesn't change your risk.

[00:06:45] Now, there's one caveat to that, and that is if as part of damage to the nervous system, whether it be the brain or spinal cord, there was impairment of breathing function. So for some of our families who have had loved ones affected by acute flaccid myelitis and there was a resulting, impact on breathing function. If there is underlying pulmonary disease, breathing function issues, that can be an independent risk factor for complications. So, I know it's a long answer, but the diagnoses themselves, we don't think increase the risk, but sequelae of the diagnoses, specifically breathing issues and/or the use of long-term medication may change the risk of a complication.

GG deFiebre: [00:07:30] Great. Thank you. I think that's a really good overview. And then, so if someone's diagnosis of, for example, TM or AFM or ADEM was due to a viral infection, or a post-viral

event, should they be more concerned that their immune system may respond again in the same manner if they get diagnosed with COVID-19? Dr. Levy.

Michael Levy: [00:07:56] I think that generally infections are a risk factor for relapse. But if you're on a medication and you're stable, I don't think there's any additional risk from COVID-19 compared to, say, the flu or any other cold. Having said that, I think any infection, again, can stimulate a relapse and, not only the infectious rate, but the severity of infection from COVID is much, much greater than any of the other viruses we've talked about. So it's just better to be safe than sorry, avoid the infection altogether, so that risk of having any complications from the infection itself, and then after that, no complications from stimulating your immune system and having a relapse.

GG deFiebre: [00:08:47] Okay, thank you. And then if someone with a rare neuroimmune disorder, one of these disorders, is experiencing symptoms of what they think might be COVID-19, is there anything different they need to do outside of their health care provider's protocol or anything specific as someone with one of these disorders? Dr. Greenberg.

Benjamin Greenberg: [00:09:09] No, in general, you definitely want to start with your family practitioner or pediatrician or internist and get assessed for whether or not you need testing or evaluations. If you're having mild symptoms and are eating and drinking and high temperatures aren't an issue and breathing isn't effected, definitely just contact your primary care physician and get advice. Stay home, try not to have contact with other individuals, etc. If you feel as though it is more than mild, seeking care at a doctor's office or a hospital is definitely indicated. But other than just monitoring your health and watching for any new symptoms that would be concerning neurologically speaking, there are no specific interventions that need to happen.

[00:10:06] I will say for individuals who are on the immunosuppression medication, even if you're having mild symptoms, it's worth reaching out to your primary care physician and pushing to get testing if possible. Because it's worth noting that even though we are focused on coronavirus these days, there are other infections that can cause respiratory symptoms. And one of the concerns we've had is people who are getting sick assuming it's coronavirus when indeed they have pneumonia or bronchitis or something that needs antibiotics.

[00:10:41] The latest statistics in Dallas County where I live indicated that of all the swabs being done for individuals for coronavirus, about 10 to 15% come back as positive for coronavirus, which means 85% of people have something else. And so getting tested isn't always just to find coronavirus. Sometimes it's to sort out if there's something else that we need to treat.

GG deFiebre: [00:11:06] Okay. Thank you. And Dr. Greenberg, I know you've done a lot of work with individuals with AFM. Do you anticipate or expect that COVID-19 could lead to something like AFM or potential misdiagnoses of AFM?

Benjamin Greenberg: [00:11:23] Yeah, it's a good question. So there's intersection, there's several intersections. So first, I have not seen any reports, I don't know if Michael has, of flaccid myelitis in the setting of a coronavirus infection. There's at least one report of a Guillain-Barré case. And then as people are aware, this condition referred to as Kawasaki's disease in children, which is very different than acute flaccid myelitis. I am unaware of any reports of AFM in the setting of

coronavirus. So, I am not yet expecting to see acute flaccid myelitis in the aftermath of coronavirus, but we will be on the lookout.

[00:12:09] Now, the other side of things relative to AFM is this is an even year. It's 2020. And so we have been preparing for over a year for a potential outbreak of AFM in the summer through the fall, which would be the typical cycle that we've seen for enterovirus-associated acute flaccid myelitis. One of the questions everybody is asking, and nobody knows the answer to is, will the implementation of social distancing, if people continue with it through the summer, will that actually blunt the numbers of acute flaccid myelitis this year? And we don't know. If we were to maintain the social distancing through the summer and fall, there's a good chance that we will see far less cases of AFM than we had seen in the past. But it's something we're going to be paying very close attention to.

GG deFiebre: [00:13:03] Great. Thank you. And just as a follow-up, what is the difference between coronaviruses and enteroviruses that can cause AFM? If they're both respiratory, is something like a coronavirus, why do we not think that that might lead to something like an AFM presentation?

Benjamin Greenberg: [00:13:23] So this all has to do with the basic biology of what the viruses do. So every virus, because of its genetics, expresses proteins that allow it to enter different cells and replicate in different cells. And the term we use in virology is tropism. So a virus will have a tropism for a certain cell or organ in the body. So some viruses are neurotrophic, meaning they enter the nervous system. Some viruses have a tropism for the lungs or the liver.

[00:14:05] And so there are many viruses that infect our body all day long, every single day. A lot of them are respiratory viruses. But then based on what proteins they express, they have different abilities to replicate and move to different tissues. And so presumably, if it turns out that certain enteroviruses are indeed the cause of acute flaccid myelitis, and that's what all the data suggests, and coronaviruses don't lead to that, it means that their viral protein, their capsids around the virus, led to different cells being infected. So, there are lots of colds we get that never lead to nervous system disease, or highly unlikely to lead to nervous system disease, and it may be that coronaviruses falls into that category.

GG deFiebre: [00:15:04] Okay, great. Thank you. And then, we got a question from someone who is concerned about if they are potentially compromising their own immune system and their ability to build up immunity to just any kind of viruses that are out there with the use of this really aggressive social distancing. This person is afraid that we'll go back to normal and everyone will be sick because they couldn't be out and about and have their immune systems be affected by whatever's out there. Dr. Levy, is there any concern around this, or what are your thoughts?

Michael Levy: [00:15:40] I think in the short term, there's no meaningful harm in socially isolating and staying away from bugs and not getting infected. Maybe, children are supposed to be encountering bugs all the time. So the first five years of their lives, they are supposed to be chronically ill. And having raised three of them, I know that they are germ factories and they bring the stuff home and they make me sick too. But having a short respite from the normal hustle and bustle of this type of immune activity I think would be fine for the short term. But that does raise a bigger issue regarding COVID about whether or not people in the future will all have to be exposed

to it at some point to develop immunity to it, or if we will be able to develop a vaccine or some sort of herd immunity that can protect the vulnerable.

[00:16:27] And we don't know the answer to that yet. And I think, in some populations, for example, there's a part of Boston called Chelsea where close to half of the population has been exposed to the virus and now that the numbers are dropping off, it may be that this community is more or less protected, that there's enough herd immunity that people who are vulnerable can come out and not be too worried about getting infected. And, whether or not this spreads to the rest of the United States in the same way, I think remains to be seen.

GG deFiebre: [00:17:03] Great. Thank you. And then also as a follow up, Dr. Greenberg, about AFM and enteroviruses. So, as you talked about, with all the social distancing, wearing masks, smaller public gatherings, there is the potential that we might not see this spike in the fall. Is this also the case with potentially, for example, the flu, or if it doesn't spike, if these cases don't spike this year, might it happen at a later date? Are there any thoughts about how that might play out?

Benjamin Greenberg: [00:17:37] Yeah, so what's happening right now is triggering a big, a massive virology experiment. So, we don't know what our world is like health-wise when we have social distancing and consciousness around handwashing and mask wearing and all of these things in a widespread fashion. And I think we as human beings just have no understanding, no capacity to understand as humans, the number of viruses that enter our body on a regular basis.

[00:18:28] And so when we adopt these standards that we have, it changes the ecology of viruses in huge ways that it's going to take us months or years to understand. You bring up the example of flu. I think most people can relate to, if you've ever been in a city where they're having a flu outbreak just before Christmas break. So somewhere between November and the end of school, elementary schools, grade schools, for winter breaks. If the winter break hits at the right time, the flu cases disappear because it's schools, elementary schools, that are the root, that social contact that spread flu from family to family, to family to family.

[00:19:14] And so literally the fastest way to stop an epidemic of a virus is to close schools and send everybody home. And essentially, beyond closing schools in this situation, we've done a lot more to isolate people and pursue social distancing. And so I do, depending on how long we do this, and how many people do it, you need a critical mass of individuals following those guidelines, we definitely could see an impact relative to flu rates, common colds, all sorts of things, going down. It's hard, as we can all witness now. Everybody wants to get out and get back to life as usual. So, depending on what we do from this lesson will dictate what happens to us moving forward.

GG deFiebre: [00:20:07] Okay. Thank you. And then I'd like to move on to treatments and then, a big question we've gotten is around vaccines and the use of vaccines in people with rare neuroimmune disorders. So to start, are there any thoughts on the treatments that are currently being used, as well as things like vitamin C, IV vitamin C or zinc treatments, these non-mainstream treatments that have been used. If someone is hospitalized, should they be advocating for these treatments? Dr. Levy.

Michael Levy: [00:20:40] I don't think there's enough data to advocate for things like vitamin C. There's certainly not much harm either. So I think that if you do try to advocate, I don't think your

doctor is going to put up much of a fight for that. The drugs that have been tested like Remdesivir have proven to be effective. It's a mild effect, about 30% or so. It's not a magic bullet. Better done earlier in the course, rather than in patients who are already on ventilators, but it could be helpful in any part of the disease course.

[00:21:15] And then there are others being tested, including some of the medications that we use in NMO. Those are more for the late stage, when you're pretty much unconscious and unable to advocate for yourself. So I think we need to be patient as these trials move forward. I don't think there's any need to go in there and advocate for any particular medication. I think a lot of it is just supportive therapy at this point, other than the Remdesivir, which does have some clinical trial data.

GG deFiebre: [00:21:51] Okay, great. Thank you. And then how close are we to a vaccine being developed and then, beyond being developed, being available to the public? And then what about other treatments like antibody therapies or anything else? Dr. Levy.

Michael Levy: [00:22:08] There are antibody therapies that are being developed at a lot of different centers, places where patients who have recovered are donating their plasma and then that plasma is being used in very sick patients. In that plasma are antibodies that presumably would bind the virus and could potentially be helpful to those people. And those studies are underway. I know Johns Hopkins has a site for that. And as far as a vaccine goes, I only hear on the news what everyone else hears, which is that there are sites, in Oxford, UK for example, that have been working on the other SARS vaccine that could potentially jump straight into a phase three trial and potentially have vaccine ready by September. I don't know if that's going to be efficacious or not. And then other companies have discussed having vaccines ready as early as December, but it really depends on how much trial data the FDA insists on before proving something. So maybe as early as this fall, maybe this winter, and then latest would be next spring.

GG deFiebre: [00:23:20] Okay, great. Thank you. And then, so a question we've gotten many times in various different forms, is that some of our listeners have reported that they were diagnosed with transverse myelitis or another one of the rare neuroimmune disorders after a vaccination. They either were told never to receive another one, or are concerned that they developed their disorder after a vaccination. So, are there any ideas about what might be recommended for people with rare neuroimmune disorders if a vaccine for this coronavirus is eventually developed? Dr. Greenberg.

Benjamin Greenberg: [00:24:06] Yeah. So I think there's two answers to it. So, first is, in general, we would say it would be safe to get the vaccine, and I'll explain why, with the caveat being every vaccine needs to be looked at independently. So, during the testing of vaccines and the exposure, which happens over large numbers of people, we would look for any signs or signals of concern relative to safety for any adverse events, not just inflammatory adverse events. But assuming there aren't unique issues identified during the research and development of a vaccination, why would I say it's safe to do? So in general, you really can't recreate the same immunologic situation twice. So most research studies that have looked at vaccinations and transverse myelitis have not found a conclusive link on a population basis.

[00:25:06] So the overwhelming majority of people who develop transverse myelitis, they've had no association with vaccine, haven't gotten a vaccine, haven't been exposed to vaccine. And so we know in the majority of cases, transverse myelitis is not vaccine related. If there are concerns for an

individual, immunologically, if there was a relationship, it was very specific to something in that vaccine and to what a person's immune system was doing at that moment. And so it's really hard to recreate those two things, and with a coronavirus vaccine, in theory, it would have nothing to do with prior vaccination. So I don't think individuals would have a unique risk, even if they had concerns about their prior myelitis event. Obviously, these are controversial topics. And I know this is a sensitive area for a lot of folks. But when looking at the data, it would say overwhelmingly it would be safe to get a vaccination.

GG deFiebre: [00:26:07] Okay, great. Thank you. And then, I did want to talk a little bit about, we've gotten a lot of questions about the different medications that are typically used usually for neuromyelitis optica or MOG antibody-associated disease. So if we could just go through the main options that are used, and how these treatments may or may not impact someone's risk of getting COVID or having severe disease if they do get COVID-19. Dr. Levy, do you mind running through the different options and how those might impact someone getting COVID-19?

Benjamin Greenberg: [00:26:45] Is that for me or Michael? Sorry.

GG deFiebre: [00:26:47] Oh, Dr. Levy. Sorry.

Benjamin Greenberg: [00:26:48] Okay. Michael, you're up.

GG deFiebre: [00:26:58] Dr. Levy, you might be muted. There you are.

Michael Levy: [00:27:00] Oh, sorry. GG, I think you were asking if you wanted me to run through all the different medications we use for NMO and for MOG?

GG deFiebre: [00:27:07] Yeah. So starting with Rituxan and then going into IVIG, etc. Because we did get questions about each of them, and I know they affect the immune system in varying ways.

Michael Levy: [00:27:19] Yeah. We have rationale to believe that if you suppress the immune system in any way, that you might be more vulnerable to the infection or maybe it would take you longer to clear the infection. But we don't have hard data yet. We don't have enough patients who've been infected on certain medications to know if those medications pose a risk factor. But rationally, we have seen a lot of MS patients, and they have a B cell depleting drug called ocrelizumab, which is comparable to rituximab. And we have data from about a hundred patients or so on ocrelizumab who've all been infected, and they all had pretty good outcomes, no deaths. And so we don't know if the numbers are higher as far as risk factors go for getting infected, but it doesn't seem like it makes it any riskier in terms of outcomes. And that's for B cell depleting drugs.

[00:28:19] For Cellcept, we don't have the data, but my sense is with steroids and other immune suppressing medications, there may be increased risks. We just don't have the numbers yet. IVIG probably does not pose a risk factor because if anything, it could boost immune responses. But because the coronavirus, the COVID-19, is a new virus that's never been in the population before, we don't think that IVIG contains any antibodies against it specifically. So I don't think it would be necessarily helpful for COVID-19, but on the other hand, for MOG patients who are using IVIG, I don't think there's any additional risk. I don't think it suppresses the immune system enough to be a risk factor for COVID.

GG deFiebre: [00:29:07] Okay, great. Thank you. Dr. Greenberg, do you have anything to add to that?

Benjamin Greenberg: [00:29:11] No, I agree with Michael. I think it's also just worth stressing that we are still gathering data on all of this. And one of the things that happens during a pandemic like this are massive efforts to gather detailed data. And depending on locales, ability to support public health efforts and data gathering, depending on how much testing is happening, in the early days and months, we can have only limited views of what's going on. So I think part of these answers are unfortunately going to take a little bit of time to correlate a lot of data from a lot of different locations. But, over time hopefully we'll get a better answer.

GG deFiebre: [00:30:05] Okay, great. Thank you. And then we have heard a bit, with COVID-19, the term of cytokine storm. Dr. Greenberg, so you mind just giving an overview of what cytokines are and what is meant by this storm?

Benjamin Greenberg: [00:30:24] Sure. So cytokines are proteins that play a very important role in normal immune responses. So when your body is fighting off an infection or fighting off cancer, anything that activates the immune system, there are, the cytokines are released from different cells to organize, orchestrate that immune attack. And then some cytokines are released to actually dampen down the immune response. So it's kind of like a gas and a break on the immune system. So a cytokine storm is when you have a severe immune reaction where you release just a massive amount of cytokines into the blood too quickly. And when this occurs, you can get a lot of different symptoms. You can get skin changes, rashes, high fevers, nausea, fatigue. We can see it in a variety of different situations. Sometimes it's a result of certain medications, certain immunotherapies, where you can get cytokine storms.

[00:31:36] And so, one of the concerns in the setting of COVID-19 has been whether or not there is an overreaction of the immune system leading to release of mass amounts of cytokines causing symptoms and damage to the body independent of the actual virus. Now, this will be reminiscent to people who've talked about autoimmune diseases where the immune system gets overactive. But the difference between a cytokine storm and a specific autoimmune disease, like neuromyelitis optica where you have an anti-aquaporin-4 antibody or the anti-MOG antibody, is in autoimmune diseases, the overactive immune system is targeted based on a specific protein that it's confused about, whereas the cytokine storm is nonspecific. You're just dumping cytokines into the blood and getting symptoms based on that level of protein.

GG deFiebre: [00:32:43] Okay. Thank you for that overview. I think that's really helpful. And I know, Dr. Levy, we did talk about this in the Q&A, but is there any kind of idea of how medications that are used for NMO or MOG might be related to a cytokine storm or used to treat that in severe COVID-19?

Michael Levy: [00:33:06] The cytokine storm includes such cytokines as, for example, interleukin-6, and an interleukin-6 blocker is one of the medications that's being developed for NMO - that would be Satralizumab, and the parent compound Tocilizumab or Actemra, we've been using in NMO for years. And this medication is used to block cytokine storms from other conditions too, like sepsis or what's called a CAR T-cell reaction. And so we have some experience using these medications for cytokine storms and other conditions and they would be useful here.

[00:33:48] Now, it would be curious to know how these medications would predispose you to getting the infection or how long it would take you to clear the infection versus preventing you from having a bad outcome. So those are all different aspects of this infection that are different immunological processes. And of course nobody wants a bad outcome, so it may be better to just err on the side of staying on your medication, whether you're on Tocilizumab, Satralizumab, or something else, to prevent the bad outcome and also prevent relapses even if it predisposes you to having the infection or maybe a prolonged infection.

GG deFiebre: [00:34:29] Is this even the case for something like Rituxan as well? I know you mentioned some others.

Michael Levy: [00:34:35] Rituxan is the one that hasn't really been developed to block any... It may be just too specific to block any consequence of a cytokine storm. So that's the one that has not been developed for this indication.

GG deFiebre: [00:34:50] Okay, thank you. And then, are there concerns related to something like AFM or TM and a potential cytokine storm that we should be aware of? So for example, people are told that their diagnoses are an autoimmune condition. Does the chance of someone with a previous history of one of these rare neuroimmune disorders, does that increase the chance of them having a cytokine storm because of this virus? Dr. Greenberg.

Benjamin Greenberg: [00:35:22] Yeah, it's a good question, and I would say not that I know of. In general, for individuals who’ve had idiopathic transverse myelitis, so they don't have an aquaporin-4 antibody or an anti-MOG antibody or multiple sclerosis or systemic autoimmune diseases. We really think of these as one-time events and don't think that a cytokine storm would necessarily lead to a new myelitis event. Now, it can definitely lead to a worsening of prior symptoms. So anytime somebody who has had myelitis in the past becomes systemically ill, then they can definitely experience old symptoms again or a worsening of existing symptoms. But I'm unaware of a link between that and specifically having a new myelitis event. So I'm never going to say zero risks, but I think the risk is exceptionally low.

GG deFiebre: [00:36:23] Dr. Levy, do you have anything to add to that?

Michael Levy: [00:36:26] I agree wholeheartedly.

GG deFiebre: [00:36:30] Okay, perfect. So another issue we've been hearing a lot, and I know Dr. Greenberg, you talked a little bit about this a bit ago, but children were initially thought to not be part of a high-risk group, but now we're hearing about these inflammatory issues. Kawasaki's specifically is coming up in kids around the country. Do you mind, Dr. Greenberg, just talking a little bit about what this is? Is it possible that any of these children might actually be misdiagnosed with that and actually have AFM, because some of the members of our community are seeing how this is happening after an infection and it sounds like it could be similar to AFM? Do you mind just explaining the difference between these disorders and how a diagnosis is made?

Benjamin Greenberg: [00:37:20] Yeah. So, Kawasaki's disease or Kawasaki's syndrome, where you have this profound inflammation throughout the body, is very distinct and different than acute flaccid myelitis. So when we see Kawasaki's disease, often kids will have rash, high fevers, and in the original descriptions, there was significant inflammation of blood vessels and even the heart. And so,

a lot of the concerns in Kawasaki's disease is the implications for long-term heart disease, coronary disease, aneurysms, a variety of things due to damage to blood vessel walls.

[00:38:08] And so, in this syndrome where you have huge amounts of inflammation throughout the body, it is very different than the very targeted damage to the anterior horn cells in the spinal cord that we see in acute flaccid myelitis. And so, I don't expect for the kids who are being diagnosed with Kawasaki to be uniquely at risk for having spinal cord involvement. And likewise, I don't know of acute flaccid myelitis in kids being associated with Kawasaki's. And when the immune system gets activated, it can have a lot of similar features. The fevers, the words we use, inflammation, all sorts of things like that. But in the end, the end organ that gets targeted makes a big difference in the types of symptoms and syndromes that people have.

GG deFiebre: [00:39:11] Okay. Thank you. I think that's a really important overview, because I know hearing the words inflammatory and that it's affecting kids, it can definitely bring up potential comparisons. I think that that's an important distinction. So thank you. And then we do have, we've been hearing about COVID-19 impacting some neurologically, whether that's through strokes or other conditions. How much do we know at this point about COVID-19 and how it might have neurological issues, if at all? Dr. Levy.

Michael Levy: [00:39:47] Yeah. There is some data on strokes. That seems to be the most popular topic in the neurology grand rounds. And that may be related to the effect on blood clotting, especially in young people who don't seem to have other sorts of neurological conditions that may predispose them for a bad outcome. So in the few cases that have had bad outcomes in the young people, I'm talking about 30s and 40s, who would normally tolerate this virus and do very well, there have been a few strokes. And when you look at them histologically, it seems that there are some blood clots that are forming probably as a result of either the cytokine storm or the virus itself. We don't really know.

[00:40:33] Other than that, other than strokes, there're just a few case reports here and there of neurological consequences like Guillain-Barré syndrome and maybe a transverse myelitis. But it doesn't seem to be directly linked. Now, having said that, sometimes these things take time, the immune system sort of has to think about things, and it's possible that after this initial wave of infections that we're going to start to see neurological complications that could come out even six months, twelve months down the line. So we just have to be aware of these things.

GG deFiebre: [00:41:12] Okay. Thank you. And so one of our listeners did have... They were diagnosed with COVID-19 three weeks ago and had all of the symptoms including high fever, shortness of breath. They're feeling better but are always tired. And so they're just worried that their immune system is going to go into overdrive after this experience. They had an episode of idiopathic myelitis in 2018. Are there any thoughts on the timing of when something might happen, or what to be on the lookout for? Dr. Greenberg.

Benjamin Greenberg: [00:41:47] I think in general, this episode and moment in time is no different than any other. This, again, it's really important to stress that we get infected with viruses every single day. And, in the way I think about idiopathic transverse myelitis is the perfect storm, not just being infected with a virus or being stressed or being tired, or the immune system shifting mildly one direction or another. It really requires a lot of different things to align just perfectly, which is why we

see idiopathic transverse myelitis. I mean, the definition of it is that they are one-time events. And so, it means that it wasn't just being run down or getting exposed to a virus, but the combination of a lot of different things.

[00:42:51] And so in general, the same instructions and rules apply now as would at any other time, which is prioritize our individual health and wellbeing, getting exercise, watching our diets, sleeping well, staying hydrated. Snd we always, whether there's a pandemic going on or not, should take reasonable precautions to avoid catching infections. What we're seeing now with a novel virus with no treatment, no vaccine, and a higher rate of morbidity and hospitalization is a recognition that sometimes there are viruses circulating for which our humanity is not prepared, and we take extra precautions while we work to develop the technology to fight the virus. But I don't think we're in a unique situation of concern about rebound disease or new inflammation in the setting of this pandemic.

GG deFiebre: [00:43:44] Okay. Thank you. Good to know. And then, so as states are kind of taking their own lead in terms of whether they're opening up or not, is there any sort of advice you have for people in our community as things kind of slowly open, or for example, a student who's returning to college, just in terms of reducing risk of infection or anything like that? Dr. Levy.

Michael Levy: [00:44:13] It's hard to say. I think that we're going to be more psychologically prepared as the economy reopens and people are getting out and going back to work. But there will be an increased number of infections, and I think we're kind of prepared for that, not only psychologically but in the hospital to manage these cases. And, the sense is, again, that the highest risk folks are the ones who are over 60 and who have an underlying disorder, especially in the lungs, like lung disease like cancers and things like that.

[00:44:49] For patients with NMO and TM and MOG the, there may be a slight increased risk compared to the general population, but none that we could really put our finger on or quantify. And so, beyond just general precautions, wearing a mask, staying six feet away, washing your hands, don't touch your face, I don't know that there's any increase, any additional precautions that I would take. Dr. Greenberg, do you have any increased, any other behavioral things that you recommend to your patients who are going to be going out and about now after this?

Benjamin Greenberg: [00:45:28] No, I agree with you completely. And I think the big question for all of us is how soon and in what circumstances. I am personally encouraging all of my patients who have any risk factors - age, medication, pulmonary disease - to be one of the last ones to venture back out, meaning we really need to see what happens through June and July and even maybe the beginning of August as different states try to reopen to see how much of a rebound there will be. And, the way I think about this is, it's like in a soccer game, shots on goal. Or if we're being morbid, Russian roulette, how many bullets are in the chamber, in the weapon. The more we go out and the more contact we have, it's just a higher, it's a statistically higher chance of just getting exposed.

[00:46:24] When we looked at data from Dallas County of hospitalized patients, not infected but hospitalized patients, 80% of the hospitalized patients had been classified as an essential worker. They were individuals who were, because of their employment, were still out and about during the lockdown. So whether it be healthcare providers, grocery store employees, individuals who could not stay home. So it really says that going out just is the risk factor. It's how many, what are the odds

you're going to walk past an aisle where somebody sneezed three seconds earlier and you walked through the mist. So it's just about the statistical risk.

[00:47:09] And so if individuals are in the high-risk category, I'm urging them to go slower in terms of reentry in the world than others. And we're going to see collectively as a nation and as the world, what is the rate of infection as we get into July, as we start to reopen. Hopefully it will be low. Hopefully with more handwashing and people staying home if ill, it'll get better. And that's where I'd like to end this answer. And that is if you are ill in any way, shape, or form, you need to stay home. You need to distance yourself, and you need to do that for at least a week or two after feeling better. Lots of people feel it's not, heroic, but they're doing everybody a favor by showing up to work despite being sick. If anything, this has taught us we are not doing anybody any favors by showing up sick. And so please, please, please, if you have any symptoms of illness, you should be staying home.

GG deFiebre: [00:48:17] Great. Thank you. And then, just to wrap up a bit, what research is currently being done as it relates to COVID-19 and rare neuroimmune disorders? Is anything currently happening or anything planned that either of you know of?

Benjamin Greenberg: [00:48:37] Michael, do you want to go first? Or I'm happy to chime in on what I'm aware of.

Michael Levy: [00:48:40] Yeah, jump in Ben.

Benjamin Greenberg: [00:48:42] So, in the world of, just if I zoom out the lens to autoimmune diseases in general, there was a partnership between several centers, the National MS Society and others to launch a registry that is collecting data on individuals with MS or individuals on immunosuppressant drugs, and some related diseases like neuromyelitis optica. Likewise, there are groups that have set up registries to keep track of individuals. So, these are at most institutions nationwide. UT Southwestern has one where we are collecting data from individuals who either test positive or have the symptoms related to COVID-19. I think what we're trying to do is to get a uniform collection and a mechanism for data sharing across the nation.

[00:49:39] It's worth noting that I think one of the things this entire pandemic has made extremely clear, that the AFM community was painfully aware over the last six years, is the very haphazard patchwork of public health organizations across the United States. We have an amazing resource with a talented group of clinician scientists and the CDC that have been woefully underfunded and under-resourced for a long period of time. And likewise, the regulations are set up such that we really rely on state and local health departments that may or may not be funded depending on which state or county you live in. And public health is one of those things that you only recognize you need it during a crisis. And when things are going well, there's not that much of an interest in funding public health centers to the degree they need.

[00:50:38] And what AFM families have known for years is there was a slow response at a public health level to the AFM epidemic that was going on in this nation and around the world. Thankfully, it improved, and I think we're in much better shape, great shape relative to the public health response of AFM. And yet we were not prepared for something like a pandemic, to have an infrastructure to collect this data in real time and answer these questions. It shouldn't take six

months to sort out if somebody on Cellcept has a higher risk of a complication, versus somebody not. We don't have an integrated data sharing system within the United States, and it's a major shortcoming for us from a public health perspective. But there are efforts to collect and share the data, it'll just take time.

GG deFiebre: [00:51:31] Dr. Levy, so you have anything to add?

Michael Levy: [00:51:36] No. I mean, I think that that pretty much sums it up. I agree with Dr. Greenberg.

GG deFiebre: [00:51:44] Okay, perfect. And SRNA hopes to collect some information as well from our community about experiences with COVID-19. So stay tuned for that as well. And then how has the present crisis changed research at UT Southwestern, for example, or Mass General and other institutions? Have other research studies been put on hold or resources diverted? Dr. Greenberg, do you want to start?

Benjamin Greenberg: [00:52:14] Well, when it comes to resources, this is, I think everyone needs to be prepared for big issues over the next couple of years. I mean, obviously the personal impact this has had on so many families and individuals of those who have been sick or passed away, the individuals and families of healthcare workers and food industry workers and first responders has been huge, all at the same time of a major economic hit to locale states in the country. I think we're going to be struggling from a budget perspective in a lot of different ways. I can't speak for my colleagues in Boston, but here in the state of Texas, the institutions are already discussing about what are the financial ramifications and what impacts will this have on research projects and clinical care growth and other things.

[00:53:16] And so I think, and I’d be remiss if I didn't mention this is having a major impact on nonprofit groups like the SRNA. As all of us are worried about our own personal finances throughout the world, there is a tendency for there to be less giving, and so nonprofit groups are expected to suffer significantly. And so I think it's going to take about another six months for us fully to quantify and understand the impact of this and then understand how it's going to slow down research efforts or programmatic efforts. But there is a big concern relative to the long-term implications of those changing resources.

GG deFiebre: [00:54:02] Dr. Levy, do you have anything to add?

Michael Levy: [00:54:04] Yeah. Same here. This has been a major financial hit for the whole hospital. There are hiring freezes. We can't spend more than a certain amount of money on large equipment. We can't even hire people that we plan to hire. No pay cuts yet, guaranteed salaries through June. But it's going to be hard for everybody. The labs are all shut down. I'm in the lab right now because I snuck into my office but can't do any experiments. Everything is basically shut down until a phased reopening is implemented that's safe for everyone to come back to work. And I think it's going to go through the summer.

[00:54:45] I think we all just have to be patient through this time, and we'll see what happens with the second surge. So after people are let out, there's certainly going to be more people infected. And how that impacts the environment and the economy and everybody else, we'll just have to wait and see. But it has been hard on the research group here as well.

GG deFiebre: [00:55:13] Got it. Thank you. And then just to wrap up the end of our time, I just wanted to open it up and see if either of you had any thoughts that we didn't discuss or any additional comments about this particular issue. Dr. Levy.

Michael Levy: [00:55:31] I think at first when we didn't know what the risk factors were going to be for COVID and for outcomes, I think we were all worried, particularly for patients who were on immune suppressive medications and who had underlying neurological disease. And I'm just a little bit more reassured now that NMO and MOG and TM patients are doing fairly well. And again, it's a very small patient population so we don't know for sure whether there are risk factors or not, but I'm just feeling a little bit better about it.

[00:56:07] And I hope, I think my patients who ask me these questions, that whether they can return to work or not. Generally I've been advising them that I think it is probably safe. And it depends on of course every individual situation. But I do think that over time we're going to learn more, and so what we're learning so far just seems to be that it's safe for a lot of our patients to go back to work and to go back to life in general. But with all the precautions in place.

GG deFiebre: [00:56:40] Okay. Thank you. And Dr. Greenberg, any last thoughts?

Benjamin Greenberg: [00:56:44] Yeah, if I had to just highlight anything that we haven't had a chance to cover in detail but is worth mentioning is the psychological and emotional impacts of this entire experience, upon everybody. Our patient community, kids, adults, the like. I would encourage everybody to take care of themselves and each other, it sounds cliché, but to be kind to one another. The rates of anxiety and depression and mood disorders is, I think, significantly higher than what we've seen in the past, and this is hard. We are, for the most part, social organisms, whether we're introverts or extroverts. There is a certain amount of interpersonal interaction that is healthy for all of us, and that coming to an end so abruptly and so profoundly along with the stress of everything that comes with it takes a toll.

[00:57:42] So find ways, despite being distanced, to connect with people in safe manners and reach out to others who you might be worried about. It makes a big difference. And even though we focus on the physical in the wellbeing, the mental health is extremely important as well.

GG deFiebre: [00:58:03] Thank you. I think that that's a really good point as well. So thank you both so much for joining us today. I know we got through a lot of questions, and I know this is obviously on everyone's mind, so we really appreciate you taking the time to talk and address our specific community. So thank you both so much.

Benjamin Greenberg: [00:58:21] Our pleasure.

Michael Levy: [00:58:22] Thank you, GG.

GG deFiebre: [00:58:23] Thank you.

