COVID-19 Vaccines with Dr. Benjamin Greenberg

Part III

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GG deFiebre: [00:00:07] Hi everyone. I'm GG deFiebre from the Siegel Rare Neuroimmune Association. I'm joined today again with Dr. Benjamin Greenberg for our third part in this COVID-19 vaccines and rare neuroimmune disorders series. We have some additional questions for the, from the community about these vaccines. [00:00:24] So to start, Dr. Greenberg, for patients with MS or any of the rare neuroimmune disorders who were infected by COVID-19 and who received a monoclonal antibody treatment, how long should they wait after getting this treatment to get an mRNA vaccine for COVID-19?

Dr. Benjamin Greenberg: [00:00:44] Yeah, GG. So this is a very specific question. And let me just delve into some of the aspects of it so people in the community understand what, what's being asked. So there is available, through an emergency use authorization, a cocktail of what are called antibodies, which were artificially generated against the COVID vaccine. And the indication for them right now is, if you have mild to moderate symptoms but have not been hospitalized yet, and you're in a high-risk group of having complications from COVID, you can receive these antibodies. And what the data suggests is that it would help prevent hospitalization. But once you're in the hospital or really sick, the data suggests that it didn't change the outcome.

[00:01:28] And it's very important to recognize that the data for this is early and the recommendations are being based on the early data, and we may see changes in those recommendations. That said, at the heart of the question is if somebody has received these antibodies, would the antibodies prevent the person from mounting a response to the vaccine? And the answer is possibly, and it depends on which type of vaccine you're getting generated.

[00:01:57] In general, these antibodies should be out of your system in a, in a significant way in about two to three months. And so in general, I'd say it's worth waiting at least let's say 90 days from when you received the monoclonal antibody to receiving the vaccine. That is not based on any studies. It's not based on any published data. It's just based on the average lifespan of an antibody circulating in a human.

GG deFiebre: [00:02:25] Okay, great. Thank you. And then many members of our community are on long-term medications like Rituxan, for example, that, or rituximab, that they get infusions for periodically. Is there timing considerations that one should take if they are on these medications and, you know, in terms of when they should get the vaccine in relation to an infusion?

Dr. Benjamin Greenberg: [00:02:48] Yeah. This is a hot topic right now in our community with a lot of our patients on immunosuppressant medications. And I'm, I'm getting this question probably three to five times a day. And I'll, I'll tell you where we are with the understanding. So for certain medications that deplete B cells - Rituximab is the most common one in our community. It's an infusion that patients who are at risk of having recurrent disease over time, for example, neuromyelitis optica patients will receive an infusion

every six months to kill off their B cells in efforts to prevent relapses from their disease. So while it is safe to receive the COVID-19 vaccine while on these medications, there is no increased risk of an adverse event.

[00:03:33] The concern is the lack of B cells will reduce the efficacy of the vaccine. So let me say that one more time. It is safe to get the vaccine at any point, relative to the right fusion, but without B cells, our best estimate - and it's an estimate - is that the vaccine will have about 50% efficacy compared to the general population.

[00:03:56] That number comes from studies done for the influenza vaccine in patients who were on B-cell depleting therapy. They had about a 50% response rate compared to the general population. So this has triggered a lot of different recommendations relative to timing. Should you get the vaccine three months after your infusion, right before the next infusion? And it's it's... or I've been asked, should we delay an infusion to allow B cells to come back and then get the vaccine?

[00:04:28] This is a very personalized decision that needs careful discussion with your treating physicians. Because, in general for our neuromyelitis optica patients in my clinic, I am not recommending a delay of your rituximab infusion. I'm recommending taking the vaccine anywhere from two to three months after your infusion up until the next infusion.

[00:04:52] And it's not because of the rituximab. It's because with the infusion, we also usually give a dose of steroid, and I think the additional steroid may impact the efficacy of the vaccine. Frankly, if Rituximab is doing its job, your B cell count the day before your next infusion is the same as the day after - it's zero.

[00:05:12] So I don't think delaying your vaccination until the weeks before the next infusion is going to change the efficacy. But what I'll remind our community about is after you do get vaccinated and you get your second dose, you can talk to your clinician about six weeks later about checking for anti-COVID-19 antibodies. You can measure to see was the vaccine effective in you or not.

[00:05:41] So you can at least get a sense of whether or not you mounted a response. So to simplify it, for my patients on Rituximab, I am not delaying the infusion, for the most part, and I'm recommending they get the vaccine at any point in between the two infusions, but not in the first month after the infusion.

[00:06:01] And then six weeks after their second shot, I am checking for anti-COVID antibodies so I can at least inform them whether or not they mounted a response.

GG deFiebre: [00:06:10] Great. Thank you. And then what about any of the other medications other than rituximab? Any kind of specific consideration for those as well?

Dr. Benjamin Greenberg: [00:06:17] Yeah, so the most common other medications we use are things like mycophenolate, which is sold as CellCept in the United States, azathioprine, which is sold as Imuran, and steroids.

[00:06:28] For those, those medications reach a steady state in the system. And so, and they're usually administered daily. So you just take the vaccine when, whenever it's offered to you. And again, you can check for an anti-COVID antibody response to see if you mounted a response. We don't have the same data for those medications relative to efficacy of the vaccines, but we think it's better than the B-cell depleters. So my, my concerns about efficacy for medications like CellCept, Imuran, prednisone are less than my concerns about efficacy in the B cell depleting therapies.

GG deFiebre: [00:07:07] Great. Thank you. And then I have some questions kind of more generally about the immune system and, and how it might respond. So for COVID-19, immunity is not expected - at this point, we don't know - but it's not expected to be life long, potentially. So for those who've already had COVID who have one of these rare neuroimmune disorders, if they got through that infection without any sort of weird, you know, new attacks or any sort of other immune system issues, does this mean anything potentially in terms of how they might react to a vaccine for COVID-19?

Dr. Benjamin Greenberg: [00:07:41] Yeah, so if you have had COVID-19, the actual infection, the recommendation right now is that you should still be offered the vaccine. We do not know of any increased risk to getting the vaccine if you've already had the illness. In, in theory, it would be similar to getting exposed to the virus again. Your body's going to react in a similar or identical fashion. And to your point, since we don't know the duration of immunity that's elicited by a natural infection, you can think of the vaccine as a booster dose of protection against the virus. So in our clinic, regardless, I've had patients say, "Listen, I was sick in February or March, I'm sure it was COVID." I say, "Great. You should still get the vaccine because it is trying to add layers of protection."

GG deFiebre: [00:08:35] Okay. And then, should people with rare neuroimmune disorders be concerned about an overactive immune response to these vaccines, and does this differ based on the disorder? You know, I know we say rare neuroimmune disorders, but that covers kind of a range of disorders within that.

Dr. Benjamin Greenberg: [00:08:53] Yeah. So in general, no, we are collecting data prospectively on individuals with autoimmune disorders relative to these vaccines. And it's been a cause of much discussion in the community because there was what I consider some conflicting sound bites in the media relative to people with autoimmune diseases and getting these vaccines. And in general, what the recommendation has been is talk to your physician and make a decision. When we look at our patient population, and so for people who've had transverse myelitis, neuromyelitis optica, acute disseminated encephalomyelitis, the rates of having documented relapses after a whole host of different vaccines is exceedingly low or zero, depending on how you look at data.

[00:09:45] I am, I have not had a patient in my clinic where immediately after a vaccine, they had a documented inflammatory relapse. I've had people have returnable symptoms, but when I do an MRI, I can't find new inflammation. So I think it's an exceedingly rare event. And one of the things to remember is when we give a vaccine, it's essentially, and depends on the vaccine we're talking about, but for the COVID vaccines, we're ramping up the immune system against a specific protein.

[00:10:15] We're not inciting a global immune response. So, which is the same as when you get the natural infection. People are separating out a immune response to the vaccine, as somehow being different than the immune response to the actual infection. And in fact, they're, they're pretty similar, but there are more breaks on what happens when you get the vaccine, because you don't have a replicating virus all over your body. So when people talk about the relative safety, it is many fold, thousandfold, dramatically fold safer to get vaccinated than to risk exposure to the virus. And we do have data on it. So this isn't a made-up statistic.

[00:11:03] If you look at, for every hundred people who get COVID-19, how many wind up in the hospital, how many wind up in an ICU, and how many people die, and the fatality rate still hovers in that 1%, one to 2% rate. And then you look at the now millions of people who have gotten the vaccine, and we haven't had people in ICUs or developing strokes or clots or lung disease or heart disease or dying. It gives us the data to say the vaccine is infinitely more safe than the actual virus that's out there, even among people with autoimmune diseases. And when we've looked at multiple sclerosis, and the only reason I mention this is we just have more data there, we are not seeing the natural virus trigger relapses in those patients.

[00:11:54] And so I, what it says to me is the proteins that are being expressed by this virus, one of which forms the basis of the vaccine, is not somehow triggering people with autoimmune diseases, at least the ones we treat, to have recurrences of those autoimmune diseases. So I am not worried in terms of triggering the immune system with this vaccine relative to relapses.

GG deFiebre: [00:12:15] Okay. And then, what if someone was told that their rare neuroimmune disorder attack was as a result of getting a vaccine, should they avoid getting one of the COVID-19 vaccines?

Dr. Benjamin Greenberg: [00:12:25] Yeah, it's a great question. I get it all the time. And the answer is no, they should not avoid getting it. The positive way of saying that is roll up your sleeves, go get your COVID-19 vaccine, and do it with confidence.

[00:12:36] Why, why do I say that confidently? So if, and, and the data on vaccine-related transverse myelitis, neuromyelitis optica is thin at best, but because, and the data assumes a temporal relationship. So if somebody says to me, I got vaccine 'X' on the first of the month, and on the 30th of the month, I got my transverse myelitis. What we have proven is A proceeded B. We haven't proven causation. But if, hypothetically, there was a link and a causation that was specific to whatever protein was in that vaccine, which has nothing to do with the proteins in the COVID-19 vaccine. So if hypothetically, somebody has a negative response to one vaccine, it does not overlap to other vaccinations.

[00:13:24] And again, we have experience in our population where a sizeable number, the majority of my patients who have had one of these conditions have gone on to get vaccines, including the same vaccine that may have proceeded their illness. And again, as I said, I've not seen a recurrence in my population. So if it's a risk, it's an exceedingly small one and much smaller than the risk of the actual infection.

GG deFiebre: [00:13:48] Okay. And then obviously those who are older are at increased risk of severe outcomes with COVID-19. Are there any kind of known risks with a COVID-19 vaccine for someone who's older, who also has something like transverse myelitis, or one of the other rare neuroimmune disorders? So is age kind of coupled with an autoimmune disorder more of a concern than not?

Dr. Benjamin Greenberg: [00:14:11] Yeah, it's an interesting question. Obviously, we don't have data from a thousand transverse myelitis patients getting the COVID-19 vaccine and looking at outcomes. In fact, as we have this conversation, GG, offline we can talk about the SRNA collecting that data prospectively.

[00:14:27] And I encourage everybody who's getting the COVID-19 vaccine in our community, you can register for free with the CDC. They have an app where they'll track your daily symptoms. Do you have a sore arm? Do you have a fever? And that, that data is incredibly valuable. And we can talk about setting up something with the SRNA to collect the same data, and next time we do the podcast, share it. That said, age when in the vaccine trials, when it was looked at relative to adverse events was not associated with people having more fevers or headaches or sore arms. And so I wouldn't expect for it to be a covariate of risk in our population. And so, if you're 35 and have had transverse myelitis or 75 and had transverse myelitis, I view your risk as the same relative to the vaccine and low.

GG deFiebre: [00:15:18] Okay. Thank you. And then, if someone receives one of these mRNA vaccines, can they still transmit the virus even if they aren't infected?

Dr. Benjamin Greenberg: [00:15:27] Yeah, that, that's, that's a, I was going to say million-dollar question, but it's probably multi-billion or trillion, the entire economy of the world rests on that scientific question.

[00:15:38] It wasn't studied in the trials. And so everybody, the FDA, the NIH, the CDC, the World Health Organization, everyone's being very cautious with our answer to this question. And the answer goes something like this. We don't know. We think the vaccine will reduce, but potentially not eliminate, the chances of spread.

[00:15:59] What does that mean practically for the time being? Even after you get a vaccine, keep wearing your mask, keep physical distancing. We're going to need about six to nine more months to really understand that question. In my gut, I think it's going to reduce the chances significantly, but we, we don't want to trust our gut on this one. We really want data because it has massive implications for the recommendations we make in the community around the precautions people are taking.

GG deFiebre: [00:16:31] Got it. And so we've talked a bit in previous videos as well about the mRNA vaccines, which are the ones that are available currently from Pfizer and Moderna. There are other types of vaccines that are being studied, and then I believe in the UK some are available as well, other than the mRNA vaccines, or have been started to be distributed. So, you know, the types of, so if you could just talk, I guess, a little bit about, for example, the AstraZeneca vaccine, I think that's the one that's next in line. Just to explain that a little bit, and then, you know, if there's any issues with someone with a rare neuroimmune disorder potentially taking that vaccine, when it, if and when it becomes available in the US or if it's available elsewhere at the moment.

Dr. Benjamin Greenberg: [00:17:16] Yeah. So this is going to be a cause of much discussion going forward. And, and as you noted, it's important for our community to understand that today, as of January I think sixth is where we're at, the two available vaccines in the United States are mRNA vaccines - the Moderna and the Pfizer vaccine - and everything I have been talking about applies to them. As we move forward, this conversation could change as we get other types of vaccines available.

[00:17:44] So when, when, and it's been confusing for everyone to keep track of these different vaccines. So, depending on how you categorize things, you can talk about four or eight different types of vaccines. And the mRNA... So if you categorize them by four, there are viral vaccines, viral vector vaccines, nucleic acid vaccines, and protein-based vaccines.

[00:18:12] And within those four categories, there's two types of each. So within the nucleic acid, for example, there is DNA and RNA vaccines. So the Moderna and the Pfizer are the RNA vaccine. So what we have is one out of these eight possibilities available to us now. The AstraZeneca vaccine, and then in the United States, one being produced by Johnson and Johnson fall into the second category, which is the viral vector vaccine. And let me explain what the technology is, because it, it is a fascinating technology. So, the whole point of a vaccine is to put some portion of a virus, in this case a virus, into the human body, let human cells process that protein, present it to the immune system, and allow your immune system to start generating a response to that virus without having the dangerous version of the virus in your body.

[00:19:14] That's the whole point of it. So it's, it's to say, let's get your body ready for when and if it ever sees that dangerous virus so that your army is ready to protect your, your body against it. So as you can imagine, there's lots of ways to get your body primed. So with the mRNA vaccines, the mRNA goes into the human cell, the cell makes one of the virus proteins, not the whole virus,

[00:19:42] just one of the proteins. So it can't do anything bad to you, it's just that one protein. The, the virus isn't being grown, you can't get the virus from the vaccine, you can't get COVID from the vaccine. All you're doing is using your cellular machinery to produce, transiently, some of the protein so it can show it to your immune system and get your immune system to say, "Oh, well, if I ever see that again, I'm going to go on the attack and attack the actual virus."

[00:20:11] So a viral vector vaccine, like the AstraZeneca or the Johnson and Johnson, takes an innocuous virus, a common cold virus called an adenovirus, it takes out several genes from the adenovirus so it can't replicate. It can't make you sick, but it puts in one of the genes into the virus for a COVID protein.

[00:20:37] So it's a delivery vehicle for getting that genetic material into the cell so that your cell will make the one protein for COVID, but the virus, the adenovirus, can't replicate. It's not going to cause or make you sick or anything like that because we've taken out the parts that would lead the virus to replicating.

[00:20:59] And so it's a delivery vehicle for getting that protein to express transiently. Not forever, it doesn't integrate into your genetic material or anything like that. And so it's a delivery vehicle for getting your body to make the protein and then get an immune response. So, one of the differences between the mRNA vaccines and the viral vector vaccines is there are some, whatever adenovirus is used, there are some people who have been infected with that adenovirus before, because it's a common cold. So one of the issues with the viral vector vaccines that we're waiting to see on the efficacy side is some people's body may fight off the vector so that you never mount a response, never has a chance to generate the COVID particle and mount a response.

[00:21:49] So on the efficacy side, we don't know where it's going to wind up. On the safety side, so far from what's been publicly available, which is not all of the data, the safety appears in line with what we would want in, in any type of vaccine. As everyone in this community I'm sure knows, in the AstraZeneca trial, there was one case of transverse myelitis that occurred during the course of the trial. They placed the trial on hold, then they opened it back up again. And to my knowledge, they have not seen other cases. And so we're watching, we're watching the UK experience. We're watching to see if there are any unique aspects relative to using the viral vector for our community. So it's, it's early for me to make a recommendation for my transverse myelitis patients on if that vaccine were available, is it safe to take. I think it will be, but the data so far on the mRNA vaccines is very clean.

[00:22:46] And so it's, it's easier for me to say I believe in and have confidence in the safety there. While I expect to have confidence in the safety of the Johnson and Johnson and AstraZeneca vaccines, we want to see the final data. So practically speaking, to our population, when your time comes to be offered a vaccine, you want to know which one it is.

[00:23:08] If it's one of the RNA vaccines, in my opinion, it is safe to go ahead and take it. If it is not, you need to check back in. If it's not one of the RNA vaccines, check with your clinician to make sure there isn't any new data to suggest holding off.

GG deFiebre: [00:23:24] Okay, thank you. And then, so there are some folks in our community that have more than one autoimmune condition. You know, they might have transverse myelitis and something else. So as you said, there's kind of been some mixed information or some soundbites that have come out about autoimmune conditions and getting vaccines, and that people have been told that those with autoimmune conditions should avoid all live vaccines, but that none of the COVID vaccines are live ones, and so that there's no special need for concern for them. So if these viral vector vaccines use, you know, as you explained, use the virus to get the COVID virus into the cells, should they then not be counted as a live virus vaccine? And if, if so, should they be avoided in those with other autoimmune conditions as well?

Dr. Benjamin Greenberg: [00:24:14] Yeah, so the viral vector vaccines that we just talked about are not considered live virus vaccines in, in the same way as what's being generated by some groups, which is a, what's called an attenuated COVID virus. So a live virus is when you take the actual virus you want to immunize

against. So the best example that some people may have had is, there are two types of influenza vaccines in certain years. One is a shot, which is the inactivated or killed virus, but another is the nasal spray. And that's one of them, that's an example of a live attenuated virus. So it's the actual flu virus, but it's been grown in such a way that it's a really weak virus.

[00:24:56] It's not going to really make anyone sick who has a normal immune system. If your immune system has been suppressed by medication, maybe you're on one of the drugs we spoke about, we avoid live attenuated viruses. But those are specific types that are not available yet and are further back in development.

[00:25:18] And so in the next six months, I - or I should say three months, things move quickly - I don't expect for us to have a live attenuated vaccine even available yet. So we have time to sort that out.

GG deFiebre: [00:25:31] Okay. And then just briefly, if you could just talk a little bit about, I know that there's been a lot of news about the mutation, the mutations, the UK variant, and then the South African variant that have been spreading and potential implications for our community as well.

Dr. Benjamin Greenberg: [00:25:50] Yeah. So the implications of those mutations are the same for our community and in the world, unfortunately. So, so what's happened is, first in the UK, but it's in the US, it's been documented now in at least four states. There have been mutations in a protein of the virus that seems to make it more transmissible.

[00:26:08] So if you're in a room with somebody who has COVID and there's 10 people in the room, a few months ago some number of people would have gotten sick. Now it's a bigger number because it's easier to transmit. So far, as researchers have been looking at the implications of those mutations for vaccine efficacy, so far, we have not seen a mutation that would change the efficacy of the vaccine. Now, they're still working on it. There were eight different mutations found. They've moved through several of them to show that there doesn't seem to be an impact on the vaccine-elicited response and the ability to protect against the virus.

[00:26:49] But it's something we're watching closely. And, and let me zoom out the lens and just put my public health hat on for a second and just remind everyone, it's these type of events that remind us why it's important to stop the spread of these viruses early on. If we had done a better job as a world, as a country, of wearing masks and physical distancing, there wouldn't be as many opportunities for the virus to mutate. If we do a good job of everybody taking the vaccine and shutting down the transmission, there wouldn't be a chance for the virus to mutate. So if people are worried about the virus mutating into a form that is not vaccine-preventable, that is more dangerous or transmissible, then we all have a job to do.

[00:27:35] The more virus that's out there, it's, it's like bets at a roulette table. Imagine a roulette table with a billion different spots to bet on. If you come to the table with one bet, it's never going to win. But if you, if you come to the table with 900 million bets, at some point, it's going to hit the jackpot. That's what the virus is doing.

[00:27:55] It's looking to hit the jackpot. So the more virus that's out there, the more chances there are to mutate in such a way that it can hit the jackpot of avoiding the vaccine. So we actually all have an obligation here to take precautions as best we can, as safe as we can, based on our own histories, so that the chances of the virus hitting the jackpot go down significantly.

GG deFiebre: [00:28:22] Right. Yep. And as you said, viruses need hosts to replicate and mutate, so the more hosts, the more mutations. So yeah, we have to continue this physical distancing, mask wearing, et cetera. And we've also heard in the news about the UK trying to kind of spread out the vaccination program by pausing or spacing out the second dose for these mRNA vaccines. Is there any talk about doing that here in the US?

Dr. Benjamin Greenberg: [00:28:50] So there's talk, but it's been shut down by FDA, NIH, CDC. There is not data to indicate that a single dose of the Pfizer or Moderna vaccine would be protective or the spacing out would work. It doesn't mean spacing out won't work, it's just we have no data. And so, what would be a real tragedy would be to start implementing a strategy that we have no data to support only to find out in retrospect that we literally wasted millions of vaccine doses because now we have to do it all over again because people didn't mount immunity. So I understand the public health reasons and the mathematical reasons to want to do that.

[00:29:30] You get more people vaccinated sooner. But just as important as the number of people who get vaccinated is making sure that the people who get the vaccine have a benefit, because their benefit provides you and me safety. The less people, the less hosts - you said it perfectly - that are available in the community, the better it is for all of us.

[00:29:52] So we are invested in trying to make sure that every shot that goes into an arm and every series of two shots that goes into an arm actually works, because otherwise we're going through these efforts, and it's an act of futility. So until there's a study that shows a different timeline has equal efficacy or a different approach, I think what you're going to see in the United States is a recommendation to stick with what we know works so that we can just chip away at this problem.

GG deFiebre: [00:30:21] Great. And then any final thoughts before we end today?

Dr. Benjamin Greenberg: [00:30:26] You know, I think where we've ended each podcast, in terms of reminding people what we need to do, I do want to say that we're, we're going to turn a corner on this. It's, it's a little interesting in my mind that the vaccine roll outs are happening right at a time that we're having the worst numbers we've seen in the country throughout this whole endeavor. Now is not a time for complacency. And as we talked about, the number of hosts out there put us all at risk.

[00:30:53] We still have to wear masks, we still have to distance, we still should not do gatherings, et cetera. I've received my vaccine. I got my first dose a few weeks ago. My second dose is tomorrow. I can share I had a sore arm and that was it. And as I've talked to colleagues, overwhelmingly, that's what we've seen.

[00:31:11] A few people have had headaches or felt chills, but at least in our experience, things have gone extremely well. And I share that only to say that we're practicing what we preach. It's important if you're in a position to get the vaccine when it's offered, to go ahead and do it.

GG deFiebre: [00:31:31] Great. Thank you so much.

Dr. Benjamin Greenberg: [00:31:33] My pleasure.