

Q&A series

Coronavirus (COVID-19) Questions and Answers for Individuals Affected by Rare Neuroimmune Disorders Part II with Dr. Michael Levy



Dr. Michael Levy, Associate Professor of Neurology at Massachusetts General Hospital and Harvard Medical School, answers some of our community's most frequently asked questions surrounding the COVID-19 pandemic in the context of rare neuroimmune disorders.

Do we know if taking long-term treatments, like Rituxan or mycophenolate mofetil, azathioprine, or repeated IVIG infusions, increase the chance of infection with COVID-19? Or does it increase the risk of a severe case?

I think there are actually three questions in there, and I'll break them down. One is, do immune suppressive medications make it more likely that one will contract the infection? The second is, does it prolong the illness? And then the third is, does it make the illness more severe? And they're separate issues.

So, the first question: do immune suppressive medications make it more likely for you to be infected? The answer is, we think yes. We think so. If you compromise the immune system, it should make it more likely that an infection could take hold. Now, rituximab does not suppress the entire immune system, it just removes B cells from the blood. But patients who use **rituximab** based on B cells in their mucosa, in their sinuses, and their lungs, and the B cells are doing their job there. So, it's not clear if **rituximab** predisposes to infections as maybe other medications do.

Imuran, which is **azathioprine**, **Cellcept**, which is **mycophenolate**, and **methotrexate**, they all impair metabolic function of white blood cells. And that occurs systemically. Therefore, it's certainly possible that there are some medications that can predispose to infections, and some that maybe don't.

We don't have data yet coming out of China, or Italy, or Spain, or any other hotspots that suggest that this is the case. But

I would caution you that a lot of these hotspots are basically like war zones, where they're not collecting all the data. So, maybe some of those patients who are dying in the street in Spain, maybe some of them are on immune suppression. We just don't have that data yet.

The second question is, does immune suppressive medication prolong the illness? Possibly, again, yes. We, we've seen that with **mycophenolate** and the standard flu. Instead of a two-week infection, and staying home for two weeks, a lot of my patients stay home for three weeks when they get the flu. That's entirely observational. There's been no blinded studies to prove that. But those two things certainly make sense. And that's how we've been warning our patients. But we have not seen data to support either one of those yet. So, we're not too worried about it right now.

The third question is, does it make the outcome more severe if you're on immune suppressive medication? The answer to that is, probably no. Because what we're seeing across the world is that the best outcomes are those who suppress the immune system in the severe stage. To prevent that overwhelming immune response, we know that steroids are being tested.

Eculizumab, which is **Soliris**, a drug used for NMO, that's being tested. **Tocilizumab**, which is a drug used in NMO, and sepsis, and cytokine storms. That's being tested. So, if you're on any of those medications, maybe you're more likely to get the infection, maybe it's more likely to be prolonged, but it's not more likely



to result in a bad outcome, in terms of the rationale of using these medications.

If someone is on Rituxan, on rituximab, how often should they have their CBC, liver tests, and other things tested during this outbreak? Does it differ from normal?

It all depends on the access to the lab. I tell my patients: if you have to come into the hospital to get your labs tested, try to find somewhere else to go. There are local laboratories, Quest, LabCorp, and local doctor offices where they don't have 150 COVID-19 patients coughing and sneezing in one building with everything circulating around. And I know these hospitals are doing their absolute best to keep everything clean and sterile, but if you can avoid the hospital setting, then that would be ideal. That goes for lab testing as well as infusions. If you can get your infusions at an infusion center where there are no COVID-19 patients, or where they take special precautions to keep COVID-19 patients out or in a different section of the building, that would be ideal. Try to avoid the infection at all times, but don't compromise your healthcare. Try to find a way around it.

There are a couple of exceptions. If you use IVIG, or if you use eculizumab, those two are safe to use at home. There are very few infusion related reactions with these medications, and they're safe to use at home. That would be our preference. Rituximab and other B cell depleting therapies, we still prefer that you get it in a supervised, nursing supervised setting.

Are hospitals and centers taking precautions schedule things a little bit differently, so that there are fewer patients at a time? Have you heard anything about that happening?

Yes. I've heard of some really clever ways of infusion centers doing this. I don't know that they all do it. One of the ways is: you call the infusion center when you arrive so that you stay in your car until they're ready for you. That avoids the waiting room. In waiting rooms, you have to sit next to people or sit in the seat where they sat and touch the arm rest. You want to try to avoid touching anything in an infusion center as much as possible, unless you're sitting in your chair that's just been cleaned.

Other precautions include using a mask. I think that, at first, people frowned upon masks as not being effective. The idea is now slowly gaining some steam that, if anything, it might help

prevent the spread of illness if you're infected and you don't know it. Then we think masks for our patients are good. Use gloves, if you have them.

The most important thing, and I have a very hard time with this, is avoiding touching your face. Because, remember, whatever you touch in that infusion center that is dirty, touches your hands. You still have an opportunity to wash it off. If you can do that before touching your face, you're very likely to avoid the virus. If you touch your face, scratch your nose, rub your eye, do something like that, that's the most likely transmission and mechanism for the virus to get in.

What if someone uses a mobility device, like a wheelchair or walker, when going to this setting. How do you disinfect or sanitize that?

As much as possible. And you can't wash your hands enough. If you're going to be using a wheelchair, then gloves are a good idea. Get your gloves dirty instead of your hands. When you get home, take off your gloves, wash them and you can keep your hands clean.

It seems like people should be continuing their infusions. If someone's physician wants to extend the time longer than scheduled, is this something that they should do? Should these infusions happen on their regular schedule?

We're not recommending any changes to treatment. So, imagine if you put yourself at risk for relapse, and you end up having to go to a hospital where there are 150 COVID patients all coughing and sneezing in your building. And then you're there, paralyzed or blind from a relapse, plus breathing in all of that potential virus. You don't want that to happen. You have to take care of yourself first. So, we are not recommending any changes to your treatment course.

If you're using an oral medicine, try to call the pharmacy, get an extra 30 day-supply, in case your state shuts down. I don't think they're shutting pharmacies down anywhere, but if you're having a hard time getting out and getting to your pharmacy, that might be something you can do.

Infusion schedules, if you can get them at home, that would be ideal. Rituximab, B cell therapies, you have to go to an infusion center, but try to go to one that's offsite. If you have to end up in the hospital, then take maximum precautions.



There's one exception to this general rule that I've made for rituximab. If you're on a schedule, you're getting two infusions, two weeks apart, and you get that every six months. And for this round, you can suffice with a single infusion, skip the second one or cancel it altogether. You'll get adequate B cell depletion. It may not last as long, and so you'll need to start checking your B cell counts at month five and six to make sure that they're still depleted. Or, you can go ahead and just schedule your next pair of infusions at month five or six to make sure you remain B cell depleted. That way, the point of getting that second infusion is to provide some durability to that B cell depletion that could last eight or nine months, instead of five or six.

If someone is either newly diagnosed or have an existing diagnosis and have a relapse, are they considered to be at risk if they get any of these acute treatments like steroids, IVIG, or plasma exchange? If so, how long does this last?

If you end up at the hospital and you require acute treatment, that will certainly suppress your immune system. And it does put you at risk for infections acquired in the hospital. We want to try to avoid that as much as possible. If you end up with a relapse, you have to go get treated. There's no way around that. At the hospital, I'm sure, they'll take every precaution necessary. The nurses will avoid going from room to room with the same gown, and they'll do everything they can to avoid transmitting the virus around. But, yes, when you get a high dose of steroids, you're suppressing your immune system, making you more vulnerable to the virus. And we want to try and avoid that as much as possible.

Plasma exchange probably suppresses it as well, but maybe not to the same degree. In the case of IVIG, it may actually boost your immune response. Not specifically to the coronavirus, because the general population has never been exposed to the coronavirus. We don't, as a population, make antibodies to coronavirus, they won't be there to help you.

One of the things we have seen is that maybe 40 to 60% of cases of coronavirus have a super-infection. Which is why people are being prescribed Z-Pack, azithromycin, on top of their treatment. That is because there's a bacterial super-infection that can complicate things. We want to try to avoid that as much as possible as well. And IVIG may help that. Steroids may make that more likely. And plasma exchange is probably somewhere in the middle.

As a general rule, should someone avoid an upcoming monitoring and check-up test (such as an MRI) in a healthcare facility or hospital?

That's a great question. That's what we call non-essential testing and non-essential treatments, we advise deferring those. Just wait. Every two weeks check in with your doctor and figure out if you should be rescheduling it. And again, keep pushing it out - as much as you can. If you're getting physical therapy and it's not essential, it helps, but it's not absolutely essential, that might be something to defer.

If it's a safety lab and the doctor is particularly concerned about you, you may have to get it. That would be classified as essential. So, the question for your doctor is not, should I go get it? The question is, is this really essential? Is this a safety issue? Could this really get me in trouble if I skip it. Or, if I skip it, am I going to feel a little bit worse, but then I can make up for it later on when everything opens up?

What about physical and occupational therapy appointments or ongoing appointments such as, for example, a baclofen pump refill. Should those be stopped?

Yes. Those should be classified as well. Physical therapy and occupational therapy are generally not considered essential, but the baclofen pump would be. Because if you suddenly stopped using baclofen in your pump, you might have a seizure, and that would be a medical emergency. So, whatever you're thinking about, the question to ask the doctor is, is this essential? Do I need this? Should I risk the infection to get this? Or, should I put it off and wait until the virus blows over. That's the important question for you to pose to your doctor about it.

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