This Week in Virology

TWiV 988 Clinical Update

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Guest: Daniel Griffin

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Vincent Racaniello: *This Week in Virology*, the podcast about viruses, the kind that make you sick.

[music]

VR: From MicrobeTV, this is *TWiV*, *This Week in Virology* Episode 988, recorded on March 2, 2023. I'm Vincent Racaniello, and you're listening to the podcast all about viruses. Joining me today from New York, Daniel Griffin.

Daniel Griffin: Hello, everyone.

VR: Daniel, are you upset at the possibility that Novavax might go out of business?

DG: I am actually, yes. I mean, I am hearing that their stock has fallen off a cliff, right? They are concerned that going forward they might not be able to survive. I'm not so much concerned about the company as I am about the product. It is amazing to me how few people have gone ahead with the Novavax vaccine. Everyone complains, "Oh, the mRNA technology, and this and that." Well, here is a protein-based vaccine. This is the same thing, shingles, no one balks, no one thinks that getting a shingle shot is any sort of odd.

Yes, I don't think we can let this happen. I don't see the product going away but it is a little troubling. Actually, as we get into today, talk about another company that might be going bankrupt.

VR: Well, it seems to me that part of the issue was the adjuvant they used, which was difficult to obtain, I understand and that's too bad, but I do think it offers an alternative for people who would like to try something else, right?

DG: Even for people that can't tolerate and if we are going to be talking about boosting on a regular basis, certain people are going to want another option because they have a PEG allergy or some other issue. Yes, we do need more options. I don't like the idea of there's only one type of vaccine and that's it.

VR: Last week you talked about RS virus vaccines, and one of them was a protein-based vaccine.

DG: Yes. It is interesting, everyone sort of had this idea like, "Oh my gosh, mRNA vaccines, that's the future." It's really just a way of showing the protein to our immune system and getting our immune system to learn. I'm not sure that it is essential that every vaccine in the future be mRNA-based.

VR: No, we can - It's not going to work for everything. We know this already, that there's never a universal solution, right?

DG: Yes. All right, so my quotation right up front. "It is necessary to look at the results of observation objectively because you, the experimenter, might like one result better than another." That is by Richard Feynman. You just have to be careful, like, are you quoting Richard Feynman or you're quoting something attributed to Richard Feynman? Yes, I think this is the thing and we'll get into a little. You go into science, you don't know, you don't just know things. You go into science to take a look, to find out what's true, and often science will break your heart.

Right up front as I was talking about issues with companies going bankrupt, the FDA news release, “FDA Authorizes First Over-the-counter At-home Test to Detect Both Influenza and COVID-19 Viruses.” This Lucira COVID-19 and flu home test is a single-use test for individuals with signs and symptoms consistent with a respiratory tract infection, including COVID-19. The test is approved so that it can be purchased without a prescription and performed completely at home using a nasal swab, self-collected. If you're under 14 have a parent help you.

The test works by swirling the swab in the front of your nose. This is an anterior nares, no deep brain biopsies here. Then you're going to take that swab and you're going to put it in this little tube that sits on top of the unit. You swirl it around, and then you actually push down on this unit. In 30 minutes or less, the test will let you know, are you positive or negative for Influenza A, Influenza B, or COVID-19.

Actually pretty, pretty impressive sensitivity, specificity. This is a molecular test. It fits well, it fits in the palm of even a person with a small hand. It runs on a couple of AA batteries. I'm very excited about this technology, but I don't know if people heard that Lucira just filed for bankruptcy, so.

VR: Yes.

[laughter]

DG: Not sure how that works out. I think in this country, right? You can go bankrupt and then just keep doing business.

VR: Yes. You filed for Chapter 11. Sure.

DG: [laughs]

VR: Is this a nucleic acid test, Daniel?

DG: It is. It's very similar to the Lucira COVID-19 test that has been used for a while. This just now has more targets in there. It's interesting, the price early on - I hate to get quoted on how much money I spent, but we used this test to help with the United Healthcare Medicare Advantage Group, so we could get these high-risk individuals tested at home. We could then get them to monoclonals within 24 hours back when that was still working. They charged us $55 per test and we ordered 500,000. I don't understand what Lucira did with all that money. [laughs]

VR: Oh my gosh. Well, Daniel, if they throw in some RS virus and Metapneumo, then it'd be really talking about something, wouldn't we?

DG: I think we got to just keep expanding. I mean, I really want to know, like when I have a virus, I don't want to hear it's just a virus. I want to know which one.

[laughter]

VR: It's just a virus. [laughs]

DG: All right. RSV and influenza, and actually big news this week in RSV front, RSV vaccines for 60 and older. The U.S. FDA, Vaccine Advisory Group, I think we know some folks on that panel. They recommended approval first of Pfizer's RSV vaccine for use in the age group. Then Wednesday, the next day, they also recommended that the agency approve the GSK RSV vaccine for the same age group. Big news if the FDA accepts the recommendations of this advisory committee, these would be the first vaccines approved for RSV. This isn't like, give to everyone under the sun, they did comment on some safety issues that were noted, so we'll see where that goes.

Vincent, last week you asked about what about the children. It's sort of nice of you. Well, here's an update. We are hearing that the Pfizer RSV vaccine that protects infants could receive FDA approval as early as this summer. The FDA is currently reviewing this on an expedited basis.

We've talked a little bit about the data here. This is that single dose vaccine administered to expectant mothers in late second or third trimester of pregnancy, which then protects the fetus and the infant against RSV. These were the results of the MATISSE or the Maternal Immunization Study for Safety and Efficacy. Here they're reporting vaccine efficacy of 81.8% for severe medically attended lower respiratory tract infection due to RSV in infants from birth through the first 90 days. Then about 69.4% out to six months of life.

VR: Daniel, you have to love a trial called the MATISSE trial. It's great name.

DG: It is a great -- yes, sort of art lover, right?

[laughter]

DG: Now I guess I should also point out our listeners may not actually know. RSV we've talked about a few times how it's really an issue for infants how it's also an issue for older individuals. But what do we do? How do we treat it? Do we have a lot of tools at the

moment? We really don't, actually. It's just supportive care. Standard pulmonary support, oxygen, maybe some bronchodilators.

We do actually have some highly-priced monoclonal antibody treatments. There was an article, “Monoclonal Antibody for the Prevention of Respiratory Syncytial Virus in Infants and Children: A Systematic Review and Network Meta-analysis,” published in *JAMA Network Open*. Here they actually did this review. They looked at 14 randomized clinical trials looking at the safety of four monoclonal antibodies. Really at the end of the day, palivizumab is the only licensed monoclonal in the U.S. and we really don't use it very much, just because of its incredibly high cost. It would be huge to have some movement on the vaccine front, which looks like we're having.

All right, measles. Measles is back in the news. It's interesting, I'm saying it's back in the news because a lot of this data, as I'm going to mention, it's a little bit old. Mentioning that over 700 children have already died in the ongoing outbreak in Zimbabwe. I'm going to leave in a link to *The New York Times* article. This is reportedly driven by a decline in child immunization during the pandemic and the influence of an anti-vaccination evangelical church. Over 6,000 cases, as mentioned, over 700 deaths, but this is old data, so it's really higher by now. I've discussed before this challenge all across sub-Saharan Africa. Here routine immunization dropped significantly in Zimbabwe during the COVID-19 pandemic. Anxious parents stayed away from healthcare centers. Healthcare workers were reassigned from these vaccination programs to respond to COVID-19. There were school closures, lengthy lockdowns thwarted the usual outreach campaigns. They say scuppered, I had to look that word up. [chuckles]

They reported that apostolic and evangelical pastors have long opposed vaccination, saying their prayers and sacred stones are enough to protect the faithful, and have threatened to expel women who take children to clinics. This rhetoric, fueled by social media ramped up in opposition to COVID-19 shots, which some evangelical leaders warned would contain the mark of the beast. Unfortunately, this hesitancy is spilled over into many routine childhood shots.

Before everyone thinks this is just a problem in Africa, we just heard of another confirmed case of measles in a person that attended a Kentucky spiritual revival event. For the international crowd, that's a state here in the United States. On Friday, February 24, the Kentucky Department of Public Health announced a confirmed case of measles in a Jessamine County resident who had not been vaccinated against the disease. This person had attended what was called the Asbury Revival, which took place in southwest Lexington.

For some perspectives on this vaccine-preventable illness. What about measles? Is it something to worry about? If you look at the data from the CDC, about one in five, 20% of unvaccinated people in the U.S., who get measles will end up hospitalized. There's also the risk of pneumonia, encephalitis, that's inflammation of your brain, not something you want, complications during pregnancy. There's death. Two doses of the vaccine are about 97% effective at preventing even clinical recognizable measles. This is the third case of measles we've seen in Kentucky in just the last three months. Just like our bridges and roads, our public health system seems to be eroding before our eyes.

Now, last week you brought up this bill in Idaho, Vincent, that would criminalize giving anything based on mRNA technology. I responded that misinformed individuals have gained political power and are currently trying to use their positions to advance agendas which will limit citizens' choices. That the recent bill introduced in Idaho is another frightening example of politicians and special interest groups trying to take away the rights of individuals and parents to make healthcare decisions.

I have more bad news for you, Vincent. This week, the Ban the Jab resolution passed with a majority vote in the Lee County Republican Party, and, as they say, will now be headed to Governor Ron DeSantis' desk. Joe Sansone, the Lee County Republican Executive Committee member has labeled the COVID vaccines as a bioweapon. I want to note this resolution bans all COVID vaccines, and that would actually include the protein-based Novavax one.

VR: Daniel, if this law passed and the governor signed it, then if a physician gave an mRNA vaccine, they could be arrested. Is that what the upshot of this is?

DG: It would be a criminal offense, yes.

VR: This is ridiculous.

DG: I think it's really important that we keep spreading the word here because I don't know how many people are spreading the word. We really have to fight this misinformation campaign. This is blood money. People are willing to say things that are not true without realizing - they realize they're not true - just to keep listeners, keep people tuned in, keep people sending them what, $100 million a year to read their misinformation newsletters. These are peoples', these are children's lives at stake. I think we need to continue to do our part with education.

VR: Daniel, I don't need $100 million a year to tell the truth. We could use much less. Give it to us.

DG: Speaking of how this situation makes me nauseated, it makes me want to vomit. Let's move on to norovirus.

[laughter]

DG: That is one of the classic things. A gentleman, who hopefully is going to be discharged from the hospital later today, presented - The story was, "I was at work, I was feeling crummy, feeling like I had the chills, thinking I really need to go home, wondering if it's safe for me to drive home," gets in his car, doesn't quite make it home. Pulls off on one of the off-ramps, just starts vomiting - actually vomiting with such vigor that he actually ends up tearing his esophagus. Now he's vomiting blood. That's how this individual ended up in the hospital.

I go and I see him with one of the residents. Then of course I'm at the sink with the soap and water, because what a compelling story from my perspective. They tested positive for norovirus. Norovirus just keeps - It's going up. I think it's going to hit the moon at this rate. We just keep seeing an increase in the percent of our GiPCRs that are coming back positive

for the norovirus. Wash your hands, soap and water, that alcohol stuff, it doesn't actually kill the norovirus. Kill. Can you kill something that's not alive? I don't know.

VR: Inactivate.

DG: That is a better word. Let's get right into COVID now. I want to start this section with the *MMWR*, "Notes from the Field: Epidemiological Characteristics of SARS-CoV-2 Recombinant Variant XBB.1.5 - New York City, November 1, 2022-January 4, 2023." Every time there's a new dominant variant, there seems to be an idea that there will be some dramatic swing in virulence above the improvements we are seeing as a result of survivor immunity and vaccine-induced immunity. I'm replacing that natural immunity term with survivor immunity. I'm not sure how natural it is to get infected with a coronavirus and have all those negative things.

VR: Daniel, it's organic.

DG: [laughs] Yes, it is. Here, they report XBB.1.5 emerged rapidly in New York City during November through December, 2022 and earlier than in the rest of the United States. Preliminary findings from a sample of sequenced isolates in New York City do not suggest more severe disease among patients infected with XBB.1.5 compared with patients infected with BQ.1. The WHO piled on with the same assessment. No early signals of changes or increases in severity have been observed. So much for the Kraken signaling the end of the world and punishing us for how we have mistreated her.

VR: Daniel, can you tell me how sequencing would tell you if severity has increased? I don't get that.

DG: Vincent, if you want to be on a TV show, every time there's a new variant, you get very upset and worried. I'm this new variant. I'm so worried. Or the opposite. If you want to get on the other news stations, you say, "It's not going to be - If anything, now it's gotten milder. This is the vaccine the pharmaceutical companies couldn't make," and everyone runs out and has parties-

VR: Oh my gosh.

DG: - and visits me in the hospital.

VR: I'm doing the wrong thing. We are doing the wrong thing. Oh my gosh.

DG: You're telling the truth. You'll die with your soul intact. All right, children, COVID, and other vulnerable populations. As we like to point out, children are at risk from COVID. As we've just discussed before, the big endpoint here to think about in children is that endpoint of combined hospitalization and death.

Really, the big thing that we're seeing in children is the hospitalization because death, relatively rare, only - Let's put only in front of over 1,000 children have died due to COVID-19. I'm not sure how comfortable I am with "only" in front of over 1,000 children having died. Remember, about half of those children had no underlying issues prior to ending up in

the hospital. Just a reminder of the article, “COVID-19 Vaccines versus Pediatric Hospitalization,” where we saw that dramatic reduction in hospitalizations.

This is great if you're old enough to get a vaccine, and if your parents are educated enough to take advantage of that protection for you. We have a nice bit of news with the article, “Maternal SARS-CoV-2 Vaccination and Infant Protection against SARS-CoV-2 During the First Six Months of Life,” published in *Nature Communications*.

Maybe we're starting to get an idea where this might be going, but here the investigators examine the effectiveness of maternal vaccination against SARS-CoV-2 in 30,311 infants born at Kaiser Permanente, Northern California, from December 15, 2020 to May 31, 2022. They found that the effectiveness of two or more doses of COVID-19 vaccine received during pregnancy was 84%, 62%, and 56% during the first two months, zero to 4 and zero to 6 of a child's life, respectively, during the Delta variant period. Now in the Omicron variant period, that's where we are now, the effectiveness of maternal vaccination in these three age intervals drop to 21%, 14%, and 13%, respectively.

Now, what kind of efficacy are we talking about? This data is for vaccine efficacy for testing positive and this along with symptomatic infection is one thing. In terms of hospitalization over the entire study period, the incidence of hospitalization for COVID-19 was lower during the first six months of life among infants of vaccinated mothers compared with infants of unvaccinated mothers, and 80% reduction, so five-fold reduction.

My takeaways from this: Vaccination protects the pregnant, vaccination protects the unborn, and getting a booster during the last trimester is a great way to protect infants during the period of time prior to when they can get protection from vaccination. Then at 6 months of age, children can get their own protection from vaccinations. Now, people also seem to forget, now is mentioned, but children are at risk for the multi-system inflammatory syndrome. Thousands of children have suffered this.

The article, “Immunoglobulin, Glucocorticoid, or Combination Therapy for Multisystem Inflammatory Syndrome in Children: A Propensity-weighted Cohort Study,” was published in *The Lancet Rheumatology*. Here the investigators evaluated treatments for MIS-C in an international observational cohort. Analysis of the first 614 patients was previously reported. Here we're up to over 2,000 children less than 19 years of age.

Just to point out this is not uncommon. Thousands of children, over 2,000 right here in this study. Some received intravenous immunoglobulins, some got intravenous immunoglobulins plus steroids, glucocorticoids. Some got the steroids alone. Some patients received some other treatments as well. What they reported was no significant differences between treatments for the primary outcomes.

Another, still on the children, how can it be so much disease in children, because there is, and this is the article, “Fatal Fulminant Cerebral Edema in Six Children with SARS-CoV-2 Omicron BA.2 Infection in Taiwan,” published in *JPIDS*. It's really a description of cases of acute fulminant cerebral edema, so brain swelling. There were six fatal cases in children in Taiwan. All patients had shock initially, five showed rapid progression to multi-organ failure

and disseminated intravascular coagulation, three developed acute respiratory distress syndrome.

The inflammatory biomarkers in the first three days, including interleukin 6. ferritin, lactate dehydrogenase, and D-dimer, showed significant elevation in all cases. The findings suggest that a hyperinflammatory response may play a role in the pathophysiology. I want to point out a couple of things. All these children were unvaccinated and these infections and deaths were all due to Omicron. Please don't say it's mild.

A few other things I pulled from the article was actually the majority of deaths in children in Taiwan were due to Omicron and due to cerebral edema. I want to reinforce that, deaths in children are still rare, the burden is mostly hospitalization, ICU admissions, but here we're actually seeing children die a pretty horrible death.

Moving on to that pre-exposure period. I like to say have a plan. Don't scramble. Remember that masks only actually work if you wear them, this big meta-analysis if you tell people to wear masks, and they don't, apparently doesn't do anything. Remember ventilation, outdoors safer than indoors. Let's move on to COVID active vaccination immunity. I'm getting lots of questions now. We heard a bunch about possible timing of boosters in the fall each year but what about multiple boosters, perhaps boosters every six months?

We heard from Sara Oliver, a CDC official who heads the COVID-19 working group of the CDC's Advisory Committee for Immunization Practices, ACIP, that while they support an annual booster campaign, they did not vote on more frequent vaccines, saying that there was no sufficient evidence to recommend more than one COVID-19 booster shot a year for older people and those with weakened immune systems. They did leave a little gray here saying there might be some flexibility with regard to those who are compromised, weakened immune systems. There might be certain situations where you might consider more often, but not as a general, broad recommendation.

Moving on to "I've got COVID. I tested positive what do I do?" Number one, still Paxlovid, net great reduction if given in the first three to five days. Remdesivir if you're lucky enough to be in parts of the country with access, that 87% reduction if given in the first week. Unfortunately, no currently effective monoclonal antibodies available. Molnupiravir, Thor's hammer, convalescent plasma. A plug for *TWiV 987: Convalescing with Casadevall*.,

Now, I just want to point out because Casadevall is a little bullish on this, I just want to just make sure that we are straight with the details here. The current EUA for convalescent COVID plasma is only for immunosuppressed individuals and I'll just read that here. The U.S. FDA has EUA to permit the emergency use of the unapproved product COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment in either the outpatient or inpatient setting. This is available, but this is just for a very select population.

Just to give a sense of how effective is this stuff, there's a history here, which I'm going to talk a little bit about. About 37% reduction in mortality in the immunocompromised based on review of trials. Just put that in our context of some of our other options out there. I will

encourage people to listen to this, *TWiV 987*, because I think there's a lot to learn if you listen closely to that episode. A big issue was the timing of trials, and we screwed up. I'm going to say that straight off the bat.

I think I've shared this story before, but it was an issue with convalescent plasma as well. Very early in the pandemic, this was the first few days of April, Steve Catani and I had a call with the folks at Regeneron just asking this question, "Why are you giving antibodies during the second and third week of COVID when patients are in the ICU? That makes no sense. This is an antiviral. You're going to get efficacy in the first, maybe five days or so that first week. That's when you need to do the trials. If you keep doing these trials in the second and third week, you're going to get negative data, nobody's going to ever end up getting the benefits of monoclonals, the same to be said for convalescent plasma."

What was the answer? "We don't really know how to do trials in the first week. This was that, we're looking under the streetlight because that's where the light is, even though I dropped my keys when I was out on my boat in the bay."

Fortunately, with the monoclonal antibodies, we were able to coordinate, were able to get access to our network of urgent care centers, we were able to do those monoclonal trials in the first week where they were, what, highly effective 80%, 90% reduction in progression. Those trials in the second and third weeks were stopped for futility. If those are the only trials done, the takeaway would have been monoclonals don't work. A lot of the same issues with convalescent plasma.

The most promising trials with convalescent plasma were when it was given within the first three days. You give convalescent plasma, second, third week, people in the ICU, full of clotting factors that I've even described our experience with D-dimers with triple, suddenly a relatively stable patient would become unstable. Timing is critical. This could have been done better. I know a lot of groups really got behind this, the Mayo Clinic was behind this. Hopkins was behind this. Survivor Corps did a lot of work here. Timing is such a critical thing with COVID. Let's not do that, again. What is helpful at the right time is harmful at the wrong time.

COVID, early inflammatory, lower respiratory hypoxic phase. I think we should have just kept calling this the cytokine storm. It was much catchier, because it left open this window for people to start calling this rebound. Please, let's stop calling this rebound. No rebound here, as Vincent and I have discussed repeatedly. The viral RNA level is dropping from the original high. People do start testing that period of negative and positive tests. This is when you're getting down to sort of this level of detection.

We have looked, as we just talked about multiple times, using antivirals during the inflammatory phase. Antivirals are antivirals. This is the time when you think about anti-inflammatory. Number one, steroids right time, right patient, and coagulation in those hospitalized folks, pulmonary support, maybe remdesivir if you're on room air or nasal cannula within the first 10 days. Once you advance, not helpful I think we're on the same page with that across the board, immune modulation made with tocilizumab in certain contexts, not doing things that are unhelpful. The long late COVID phase. Just a couple of things to wrap us up here. One was interesting. New guidance from the CDC as far as who

died of COVID, who gets certified, so updated “Guidance for Certifying Deaths Due to Coronavirus Disease 2019.” I'm just going to read this one sentence. "For decedents who had a previous SARS-CoV-2 infection and were diagnosed with a post-COVID-19 condition, the certifier may consider the possibility that the death was due to long-term complications of COVID-19 even if the original infection occurred months or years before death."

Just recognizing that a lot of these folks with Long COVID, post-acute sequelae of COVID, this disease can actually progress. People can end up dying from it. That's what happens. Recognizing that. Then I think this is something, hopefully we're hammering home as a therapeutic evidence-based here. Two more articles adding to the benefit of vaccination for Long COVID, “Efficacy of First Dose of Covid-19 Vaccine versus No Vaccination on Symptoms of Patients with Long Covid: Target Trial Emulation Based on ComPaRe e-cohort,” interesting name there, and, “Effective COVID-19 Vaccination on Long COVID: A Systemic Review,” both published in *BMJ Medicine*.

Just adding to the growing body of evidence that COVID-19 vaccines, not only have a protective, but also a therapeutic effect on Long COVID. What do we do when a patient sees us with post-acute sequelae of COVID? First, listen and be supportive. This is a thing. Two, discuss vaccination as evidence-based therapy. Three, identify those with post-exertional issues for pacing and careful increase in exercise. Look for any new diagnoses before attributing all issues to PASC, and identify specific issues impacting the patient and address those. Low and middle-income countries, no one is safe until everyone is safe.

This is where I'd like everyone to pause. Go to parasiteswithoutborders.com and click the Donate button. We've been here three years, Vincent. It was three years ago that the first case we diagnosed in a ProHealth patient, the Westchester patient, and we're still here. We're giving you the science, but we need your support. You make this happen. Every small amount helps us do our work. Right now, we are doing our American Society of Tropical Medicine and Hygiene fundraisers. February, March, and April donations will be matched, doubled up to a potential donation of $30,000.

VR: Nobody does what we do, folks, nobody. Every week, 45 minutes of the real deal. No fake news. Please, please support us. It's time for your questions for Daniel. Where else can you get to ask Daniel questions? Nowhere else in the world.

DG: [laughs]

VR: You can send it to daniel@microbe.tv. Jill writes, "I was a little disappointed by your segment on past SARS-CoV-2 infection protection against reinfection. I was very happy to hear that you were going to address the article, as my husband had heard chatter about it at work and online. I think you are understandably frustrated and exhausted by vaccine skeptics, but I think you overlooked the main question.

I think it's clear you should not get COVID to avoid COVID, but the question is, is there a benefit to getting vaccinated or boosted if you already had COVID? My whole family is completely vaccinated and boosted. Luckily, we have not contracted the virus, but our neighbor next door got COVID and then was saying he doesn't need to get the vaccine. It would be nice if you could articulate a clear science-based response to this argument."

DG: [laughs] I was just thinking about different approaches to this. One is how high are you allowed to build a fence in your neighborhood?

VR: [laughs]

DG: If he was texting you, you could block them or something. This is really the issue with the science. What is the science? I'm sure you want your neighbor to get vaccinated. Let's talk about what is the science, why should they get vaccinated, what's going to happen here. The headlines were all basically, I think along these lines, "Hey, no one needs to get vaccinated if they've already had COVID." What was the actual science in this? Remember, it was a review. It was a meta-analysis. Why do people get vaccinated? People still have this idea that they get vaccinated to prevent them from getting infected. Yes, that is a thing, but it's only a thing for three or four months.

Actually, this meta-analysis asked that question, if someone was infected before, what reduction in their risk of getting symptomatic? It was BA.1, so that was even less immune evasive than we've currently got now. They said the protection was about 44% for a period of time. That's one thing.

Now, the other thing, and this is what we always say, this is why we've always been encouraging, focusing on vaccinations because the main thing, the durable thing that a vaccine will give you is protection against severe disease. What about that question? What were the numbers there if you were infected, and what protection did you get against ancestral, Alpha, Delta, and then Omicron BA.1 is what they had, and they were going out to about 40 weeks here. It was about 90% protection against severe disease.

That's the science, break your heart or not. Your neighbor may actually have this 90% reduction in severe disease going out to about 40 weeks for the variants that I mentioned. How does that translate into the current XBB.1.5? I'm not sure. No one is sure yet. We'll have to see what that data shows. What happens past 40 weeks? Is this person going to be someone who wants to get boosted every fall, or is this someone who wants to get infected every fall? That's the science.

VR: Nicki writes, "Should we be assessing patients for quinoa allergy before vaccinating with a saponin adjuvanted vaccine? The FDA lists saponin on the Novavax fact sheet, but most patients and vaccinators will not correlate saponin with quinoa. You also mentioned saponin in a future adjuvanted RSV vaccine."

DG: Yes. Do you know why they're asking, Vincent? It's interesting. I don't know how much quinoa you eat. Maybe, they know I'm a quinoa eater, but there's a little bit of a bitterness to quinoa that some people might not like. Actually, there's saponins in quinoa. If someone has a quinoa allergy, it may be that they have an issue with saponins. I see where they're going with this.

If you've got a quinoa allergy, you may want to talk to someone who maybe knows a little bit more than an infectious disease doc about, is that really an allergy, or is it just what most people when they have a quinoa allergy, is it gives them GI upset, which is transient? This isn't trouble breathing. This isn't an anaphylaxis. I would clarify what is meant there by an allergy. If it's really an anaphylaxis, if it's that kind of a level, then yes, I would actually talk to

an allergist. I have to say, this is something I think most of our listeners are going to say, "Well, I've never even heard of this before," and I think that's because this has never really been a major concern.

VR: Sharron writes, "My fully vaccinated and boosted 78-year-old husband has a mechanical aortic heart valve requiring the use of Coumadin. He is prediabetic on Metformin, along with stable stage 3a kidney disease, and has had a mild heart attack and has a pacemaker. His moderate Parkinson's treated with Rytary. He is a complex patient that is amazingly vigorous in spite of his conditions. What course of treatment would be recommended for him if he catches COVID?"

DG: This is a little challenging, so let's go through this. High risk individual, 78 years old, so we do want to be looking at potential treatment but now, we're going to run into some challenges. Coumadin, we've talked about. Coumadin, warfarin, which is actually a mix of a lot of different enantiomers, and they're metabolized slightly differently. When you start thinking about something like your nirmatrelvir with the ritonavir, you actually will get some sort of an interaction with the Coumadin, and it's hard to predict. It's only for about five days. It's a weak interaction.

With the Coumadin, you're not going to want to stop it when someone has a mechanical aortic valve. You're going to get a little bit of an impact here. This may be something where if you go down that road, you actually want to get the PT/INR checked probably at about day four just to see if you're having any issues. Metformin, that's fine. The Rytary, that's a dopamine, basically like a Synthroid type of thing.

Then the stage 3a kidney disease. That's going to become important for us in that context to ask, "Well, what exactly is the kidney function? Do they actually have adequate treatment for renal dosed Paxlovid, or are they actually dropping below that GFR where you have to go for another?" If you do move past Paxlovid, then next would be potentially the remdesivir.

If you have access, remember this is why it's good to have a plan. Do I have remdesivir in my region? After that, you would be looking at molnupiravir, which doesn't actually have any interactions. Then what about that convalescent plasma? We heard how exciting that was. This individual does not meet the EUA. Not immunocompromised. We saw what, about a 37% protection of the immunocompromised. That's about that 30% protection with molnupiravir. That would be your list of things.

VR: Wow. Finally, Carol writes, ''Remdesivir has been trending on Twitter.'' [laughs].

DG: OK, that's good. #remdesivir.

VR: There are numerous tweets along the lines of, my grandma tested positive for COVID while in the hospital for something else. All she had was cold symptoms or was asymptomatic. The doctor gave her remdesivir, her kidneys shut down and now she's dead. Remdesivir killed my grandma, or they imply she was in the inflammation stage and they gave her remdesivir. I suspect several people are just plain lying. What's actually going on? Are doctors prescribing remdesivir at the wrong time or when it's not needed?

If so, are they doing this for the profit motive? It seems like an awful lot of people are rejecting effective new drugs because they don't trust hospitals, doctors, big pharma, et cetera. I know from too much personal experience that doctors don't always know what they're talking about. [laughs] Hospitals are for-profit institutions that will rip you off if they can and that they make more money from Medicare for COVID. I don't know what to say. Take a look at the top tweets on remdesivir. It's maddening.

DG: Yes, no, there's a lot of truth in what you just said there, right? Even when a hospital is not for profit, there seems to be people getting paid millions of dollars to be part of the organization, so, yes, I hear what you're saying here. I don't think doctors are prescribing remdesivir for profit. Just to be clear on that point, which I can address. If anything, this has been a little bit of an issue with the remdesivir access during that outpatient three days.

A lot of situations, people are paying more for the remdesivir than they would be reimbursed. The organization's like, we're not going to do it. We're not going to lose money trying to do the right thing. Interesting. But yes remdesivir, we've used really, actually for quite a while now, it's fully licensed. If you look at the literature and you look at the science and you've used this thousands of times, I'll comment. People develop renal failure for a lot of different reasons. Remdesivir is unlikely to be the reason that they're developing it.

Yes, this is remdesivir we've talked about, if you get this within that first seven days, 87% reduction in progression, once you get past day 10, I don't think it really makes any sense. I don't know how many doctors are using it outside that window. Boy, if a person's in the hospital you are closely monitoring their kidney function, their liver function, I suspect most of what you're seeing is part of a misinformation campaign.

VR: That's *TWiV* weekly clinical update with Dr. Daniel Griffin. Thank you, Daniel.

DG: Oh, thank you, Vincent. Everyone be safe.

[music]

[00:43:10] [END OF AUDIO]