This Week in Virology

TWiV 1066 Clinical Update

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pdf of this transcript available (link)

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 1066, recorded on November 30, 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: I can't see your tie. Otherwise, I'd try to guess.

DG: It's the clap. What am I doing wearing a sexually transmitted infectious disease bow tie on a Thursday? It's just to remind everyone that STI, sexually transmitted infections, are not just for the weekends. You should be thinking about this all the time.

VR: Gonorrhea, right?

DG: [chuckles] We had an interesting episode this week that a lot of us have talked about and it was where there was a gentleman. He's heterosexual, but he's very sexually active. He had a conversation with his primary care doc about, "I'm pretty sexually active. I've had some other sexually transmitted infections. Maybe I should be on this prep stuff." The doc said, "It's been 40 years and you haven't gotten HIV. What's the chance you're going to get it now?" The gentleman has HIV.

VR: No, that's not good logic. You still see people with gonorrhea, I presume, right?

DG: We see gonorrhea. I think we've talked about the past. Syphilis has quadrupled in the last year, just in my local area.

VR: Are they treatable?

DG: What was that?

VR: Are they treatable?

DG: That's the whole thing. If you diagnose and jump in, they're treatable. Even HIV is treatable, but not curable. The other ones are actually curable if you diagnose and treat them.

VR: Good to hear.

DG: All right. Moving from the bow tie to the quotation, "Let not anyone pacify his conscience by the delusion that he can do no harm if he takes no part and forms no opinion. Bad men need nothing more to compass their ends than that good men should look on and do nothing. He is not a good man who, without a protest, allows wrong to be committed in his name and with the means which he helps to supply because he will not trouble himself to use his mind on the subject." That's John Stuart Mill in his 1867 inaugural address at the University of St. Andrews in Scotland.

I know we've had several quotations along these lines, but this is going to put us right into a *Nature* news piece, "Microbiologist Who Was Harassed During COVID Pandemic Sues University." This article describes the experience of a microbiologist and science communicator who has been a committed science communicator appearing on mainstream media and social media platforms. She has a rather interesting situation, Vincent, where her university pays for 40% of her time to give her the time and space to engage in science communication.

You might want to mention to Columbia that that's something they should be doing. Dr. Wiles - Maybe not after this. They're getting sued. Dr. Wiles was already a seasoned science communicator by the time of the pandemic and had won the Prime Minister's Science Media Communication Prize in 2013. Dr. Wiles shares that when she asked the university in 2020 about how to deal with the harassment, much of the advice she received suggested she just reduce her public commentary.

VR: It sounds typical of what a university would suggest, right?

DG: Yes, it sounds -

VR: At least they were paying her to communicate. That's not a normal situation. It's what it should be. Professors should be paid to do science communication, but they're not. I never was. It was never appreciated. Now it's late to ask them to pay for it. I gave a talk yesterday at Princeton talking about science communication. I said it needs to be recognized by universities that it is something all scientists need to do and they need to be compensated for it. When they come up for tenure, it needs to be taken into consideration what they have done in that field.

DG: It's interesting, right? Because a lot of universities look at what's the amount of grant funding that you're bringing in. Science communication, actually, impacts the whole pie of how much funding opportunity is going to be out there. We're seeing lately some concerns about failure to keep up decreased funding and that's going to impact who's able to bring those funds into the university.

VR: Universities care about you bringing in money because that's their only source of income outside of tuition. They want you to get grants. If you do science communication, it usually doesn't bring in any money, but it's indirect, as you say. You have to be a little creative there.

DG: All right. An issue that a lot of people are asking about reported clusters of respiratory illness in children in northern China. Over the last week or two here, we've been hearing media and other reports of pneumonia in children in northern China. The WHO has been requesting information on this. What we are hearing so far is that they're not identifying any novel pathogen there.

They're seeing a lot of influenza, a lot of SARS-CoV-2, a lot of RSV, a lot of mycoplasm pneumonia, which I just want to mention that about 80% of that is resistant to azithromycin over there in China. We hear from Van Kerkhove, "This is not an indication of a novel pathogen. This is expected. This is what most countries dealt with a year or two ago." I'll leave in some links, but we'll keep our eye on that.

Now, polio and, basically, what I did here is I put in the title and then I'm going to make you do all the heavy lifting here, Vincent. The personal view use of inactivated poliovirus vaccine for poliovirus outbreak response was recently published in *The Lancet Infectious Diseases* by eight authors. Look at that. Eight authors with the same personal view. They agreed on it. Lots of discussion about IPV, inactivated poliovirus vaccine and IPV followed by OPV. I just thought this was really interesting.

It seems like there's been a bit of an evolution here. You've been listening to some of the other deep dives on *TWiV* of people starting to say maybe it's not acceptable to paralyze one in so many kids when we do the oral polio vaccination.

VR: It's not maybe, it's absolutely not acceptable. [chuckles] It's not acceptable to paralyze kids. The Sabin vaccines have been delicensed in the U.S. It is not ethical to use them in other countries, therefore. The nOPV2 was made to try and reduce or eliminate this vaccine-associated paralysis, but it hasn't worked. It's time to acknowledge that nOPV2 is a failure and move on. Kostya Chumakov, in a recent opinion with one other person, the vaccine guy in Philadelphia. What's his name, Daniel?

DG: [chuckles] I'm going to let you hang out there and keep working on it.

VR: He's a very well-known vaccinologist. Anyway, they said it's not ethical to use this vaccine that paralyzes kids. We should switch the IPV or IPV followed by OPV. That's it.

DG: That was a lot of the discussion here. You give IPV. No one ends up getting paralyzed. Then you can jump in afterwards with OPV to get that gut protection. It was interesting, in this article they actually talk about a little bit of gut protection with IPV maybe short-lived. The strategy of IPV, no one you're vaccinating ends up getting paralyzed. Then OPV follow-up to get that gut. The only problem I have with that is you keep putting OPV out in the environment.

VR: It would actually be best to just keep using, just use IPV, right?

DG: Yes.

VR: Some people say that's very difficult to do. I think that's the way to do it. I can't find his name. That's really - Stanley Plotkin. There it is. Do you know Stanley Plotkin?

DG: Yes. I'm wondering if Stanley listens. We know he does because when you made a comment about nOPV being a failure, there was some response. Stanley, we remember you. We know you well. [chuckles] He was actually on a *TWiV*, I think, right?

VR: He was not, but I would like to have him because I think he's in his 90s and I'd like to hear his story before it's not possible to do that anymore. He's in Philadelphia. I plan to go down there in the new year and interview him.

DG: Oh, that's great. Dr. Plotkin, I look forward. That many years of being in this arena, I'm sure you have great stories. RSV, 'tis the season and we have the article, "Safety and Immunogenicity of Bivalent RSVpreF Vaccine Coadministered With Seasonal Inactivated Influenza Vaccine in Older Adults," published in *CID*. I hate the four-letter acronym for this that they use, but let's move past that. Really asking that question. Is it OK? Can I go ahead and get my RSV vaccine at the same time as my flu shot?

Here we have the results of a phase 3, one-to-one randomized double-blind placebo-controlled study in healthy 65 and over adults in Australia looking at immune responses when they do the coadministration. They used a 1.5-fold non-inferiority margin. They looked at safety and tolerability. We end up with 1,403 participants. 1,399 got the vaccines. No vaccine-related serious events were reported. The geometric mean ratios, they give us those, but basically, I'm just going to say all comparisons to achieve the pre-specified 1.5-fold non-inferiority margin. It is OK. It is safe.

It's tolerated to get your yearly flu shot and your RSV vaccine at the same time. Here's something I want to point out too, is maybe my cousin will be listening because he went to go and try to get his flu shot and RSV at the same time. They're like, "Oh, you don't want to do that. That's going to have a really bad reaction." It's not true. Whether you get the flu shot, the RSV shot, or both at the same time, you basically end up with about the same reactogenicity.

VR: I got both. I actually got three at the same time. I went to the CVS website. They let me check off all three and the computer didn't object, so I got all three.

DG: [chuckles] Listen to the computer. Ignore that pharmacist who sends you away and tells you have to come back later. No, we are seeing a lot of RSV.

I was talking to a woman today and now my question comes up. You're here in the hospital. We got RSV. You're here in the hospital because you got RSV. Did you discuss vaccination with your provider? I will point out that most of us have moved from shared decision to millions of doses out there, safe, effective. About 15%, we're really seeing the RSV come up in the percent positive for the RSV data when we're looking at the influenza-like illnesses, those respiratory illnesses.

VR: Daniel, when an adult has RSV, what is it that puts them in the hospital?

DG: I'm glad you asked. I was having this discussion with one of the other providers and like, "If it's a kid, I really want to know." I'm like, "Why do you really want to know?" I tried to make a comparison. I said, "Listen, in adults, we see maybe 100,000 folks end up hospitalized with RSV. RSV, lower respiratory tract infection. They actually develop a pneumonia from the RSV.

Sometimes it's hard to tell. Is it an RSV bronchiolitis, inflammation of the bronchioles, and then they get a second bacterial low-bar pneumonia and that's what puts them in? Is it the RSV itself actually causes the lower respiratory tract disease?

We do see that the virus itself can do that. Then I pointed out, "About 100, 200 children die every winter from RSV." We see over 10,000 adults die every winter, so about 100 times as deadly in the adults. Just not something that we want to not take seriously. We have the tools, right? We have the vaccines out there and we'll just keep talking about them.

Flu activity is continuing to increase. It has crossed the baseline and it's on the way up. We'll probably be seeing that peak in December, January. You still have time.

I have to say some interesting stuff. What type of flu are we seeing? We're mostly seeing influenza type A, right? Of the stuff that we're subtyping, looking at H1N1, but we're starting to see some H3N2. Interesting. We're actually seeing Victoria and Yamagata B lineage because it was this discussion about the Yamagata being gone and maybe not being in our vaccines next year. If anything, of the influenza Bs we're seeing, Yamagata has taken over more than Victoria.

All right, COVID, we are sitting still at about 1,300 deaths each week, still right about that, 200 deaths per day. The concern I think I will raise is that we are seeing all throughout the country, really, particularly, out there in the Midwest Great Lakes area, we're seeing a real rise in the wastewater, SARS-CoV-2 virus concentration. To highlight, the CDC has a new revamped wastewater page where you could go and you could sort of lay things out. I laid it out looking at it going back to January of 2022, and you can actually start to see where all these peaks are. We keep seeing this summer, sort of late summer, fall peak. We see the winter peak and we're already on our way to our next winter peak this year.

VR: The Northeast is going up again, Daniel.

DG: Yes, they are.

VR: Not unexpected. It's the winter, right?

DG: It's true. It's the winter. People are indoors. People are getting together. We just had a holiday with a lot. Yes, this is anticipated for a respiratory transmission virus. All right. Put away the horse deworming paste and brew up some coffee. We have the article, “Coffee as a Dietary Strategy to Prevent SARS-CoV-2 Infection,” recently published in BMC in the BMC journal *Cell & Bioscience*.

Prior to the study, there was actually evidence that drinking one or more cups of coffee per day was related to an approximately 10% lower risk of getting COVID-19 compared to less than one cup of coffee a day. Should you get a coffee break throughout the infection in a human trial data of elderly volunteers? Coffee breakthrough infections. That's my new term for us this week. This is when you're drinking your one to two cups of coffee a day and you still get COVID. If that happens, there's actually a study showing that there was a decrease severity of the COVID-19 that you might get.

Here, the investigators collected commercially available coffee beans produced from different places and measured their effects on the entry of SARS-CoV-2 by using an assay that used 293T ACE2 cell line. These are human embryonic kidney cells transfected with ACE2 expression vector, which are sensitive to test for efficacy through spike and ACE2 interaction.

I'm a bit critical of this model, Vincent, as I would have preferred some lung organoid, some better representative target cell, but because we're talking about coffee, I will continue, they observed the ground coffee at 6 milligrams per ML has the effect of reducing the entry of SARS-CoV-2 into health host cells in this model with an inhibition of about 60% to 81% in a dose-dependent manner. They go on to demonstrate an ability to interrupt the ACE2 spike interaction and that coffee can inhibit spike cleavage by TMPRSS2.

This gets interesting. They go on to identify which components in coffee mediate this and show that decaffeinated coffee works. It's OK to add milk and sugar and all kinds of other stuff. This Omicron pseudovirus entry assay suggested that the optimal timeline for coffee to inhibit was within six hours. If you have that morning cup of coffee, let's say it's eight o'clock starting to get into the afternoon. You still might want to have that second early afternoon coffee. What do you think, Vincent?

VR: This is absurd, 6 milligrams per mil. Where are you going to get that level after drinking? The coffee goes into your stomach, right? It's not going to just saturate your nasal pharynx so you can throw this in a cell culture and show some inhibition. I don't think this makes any sense in a person.

DG: I'm thinking like when I'm drinking the coffee and it goes down the wrong tube that like that, I'd be like, "It's OK." [chuckles] [crosstalk]

VR: If you like coffee, go ahead, keep drinking it, but it's not going to - I don't think it's going to have any effect. I would like to see this in an infection model. Let's have mice drinking coffee and see if it helps them with COVID.

DG: Some of our listeners out there, we've got that wonderful mouse model. If you can do that for us. All right. Children, COVID, other vulnerable populations. We have the research letter, "Enrollment of Pediatric Patients in COVID-19 Interventional Trials," recently published in *JAMA Health Forum*. Here, the authors identified all U.S. interventional trials studying COVID-19 and registered on clinicaltrials.gov from January 1, 2020 to December 31, 2022. Information was extracted on the trial design characteristics and trials were classified as enrolling exclusively children, 0 to 17 years, both children and adults or only adults.

They reported that less than 10% of the COVID-19 interventional trials initiated were open to pediatric enrollment. Only 1.6% were just exclusively enrolling children. They suggest that this likely reflects established practices of delayed study of interventions in children is in line with prior analyses. Just want to point out that we're really underrepresenting children in our clinical trials, even for conditions with large pediatric disease burdens.

All right. The article, "Vaccination, Immunity, and the Changing Impact of COVID-19 on Infant Health," was recently published in *PNAS*. Here, the investigators used linked population-level data on siblings born between 2014 and 2023 in birthing facilities with confirmed universal

testing. They were able to establish that maternal COVID-19 infection during pregnancy causally and substantially increased the risk of preterm birth.

Really interesting how they do this study. They then show that this effect disappeared by 2022 and demonstrate that the disappearance of this effect happened almost a year earlier in places that were early adopters of COVID-19 vaccination. They really have some great figures where you can look at this. Just sort of putting it in context, getting COVID-19 when you're pregnant, increased risk of a preterm birth. Vaccination having prior immunity gets rid of that effect. You can really see here as you move forward with vaccination, the availability of vaccines and the decision to use them correlates with a reduced risk of these preterm births.

All right. Moving on to active vaccination, we actually have a few here today. The article, "COVID-19 Vaccine Effectiveness Against Post-COVID-19 Condition Among 589,722 Individuals in Sweden Population-Based Cohort Study," recently published in the *BMJ*. I know we have some Swedish listeners. These results are from a register-based cohort in Sweden among 299,692 vaccinated individuals with COVID-19; 1,201, 0.4%, had a diagnosis of post-COVID condition during follow-up compared with 1.4% of the unvaccinated individuals.

We always talk about you've got to have a standard definition. It's always good to look within a study comparing apples to apples. COVID-19 vaccination with any number of doses before infection was associated with a reduced risk of post-COVID conditions. They give us an adjusted hazard ratio of 0.42 with a vaccine effectiveness of 48%. Of the vaccinated individuals, 21,111 received one dose only, 205,650 received two doses, 72,931 got three or more doses, and then they break it down by doses. Vaccine effectiveness against post-COVID conditions for one, two, and three doses was 21%, 59%, and 73%.

VR: Daniel, these numbers make a lot of sense now, 0.4% had Long COVID. You look at studies elsewhere, we're getting huge numbers, which has always baffled me. Maybe they're doing the study correctly over there in Sweden.

DG: [chuckles] The Swedes will write in. They'll be happy. It's interesting. I think it's always hard to say when you say post-COVID condition, what are you talking about, right? We all go back and forth on the definition. I really like within the study, the big thing I take away is, wow, vaccines are incredibly effective at preventing post-COVID conditions.

All right. The article, "Repeated Omicron Exposures Override Ancestral SARS-CoV-2 Immune Imprinting," recently published in *Nature*. Perhaps for our regular listeners, no explaining is needed. What is this immune imprinting? For everyone else, and we'll just do a refresher here, what is immune imprinting or so-called original antigenic sin, or as I was taught, the butterfly effect? This is the observation that when our immune system is exposed to a new variant of something it's seen before, it preferentially reinforces the original response. The new variants produce less of a response to what is different and just keep reinforcing what is in common from before.

The idea goes back to an article by Thomas Francis, you ready for this? Published in 1960 in the *Proceedings of the American Philosophical Society*. While people primarily think about B cells and antibodies, this has also been described for T cells for pathogens such as dengue. This is a complicated paper worth a deep dive. The data does suggest that this imprinting can

be overcome, but is best done with updated vaccines without the original variants. It may even be that the Omicron-based vaccines work best with a second booster shot after a prolonged interval.

The article, "Protection Conferred by COVID-19 Vaccination, Prior SARS-CoV-2 Infection, or Hybrid Immunity Against Omicron-associated Severe Outcomes Among Community-Dwelling Adults*,"* published in *CID*. Another test-negative design, looking at protection by vaccines and or prior infection against hospitalization or death among community-dwelling adults, 50 and over in Ontario, Canada. This included 18,526 cases with Omicron-associated severe outcomes and 90,778 test-negative controls.

Now, they reported that vaccine protection was high during the BA.1, BA.2 predominance, but then dropped to less than 50% during periods of BA.4, BA.5, and BQ, XBB predominance without the boosters. Lots of numbers here that reinforce getting that third or fourth dose and transient boosting. Worrisome in this data was their report that prior infection alone did not seem to confer lasting protection. I have to say, I am actually seeing patients on their third infection sick enough to end in the hospital. I worry that this may explain a little bit of what we're seeing.

VR: These people who are on their third infection, they've been vaccinated also, Daniel?

DG: No, unfortunately, there's this sort of perception that, oh, I've already had a couple of infections, that's just like getting vaccinated. Maybe the third infection is just like finishing off your vaccine series and maybe a little nicer to finish off the vaccine series instead of coming into the hospital for your third dose. All right, and a lot of people, they would like an option from those mRNA vaccines. We have the article, "The Novavax Heterologous COVID Booster Demonstrates Lower Reactogenicity Than mRNA: A Targeted Review, published in *JID*."

Now, this isn't new data. This is based on a targeted literature review looking at what's out there. One of the discussions people have is they hear stories about people getting the mRNA vaccines or they got the Moderna or Pfizer themselves. They were down for a day or two and they're interested in vaccines, but they really don't want to pay the price. Here is really a review where they look at pain and tenderness, swelling, erythema, fatigue, malaise, headache, muscle pain, really the whole sort of a list of things, fever, for instance, which is almost non-existent after getting the Novavax shot.

Just another choice for folks out there that are interested in vaccinations. We heard this week that the WHO authorizes emergency use of Novavax's updated COVID shot.

VR: Daniel, is there any association of the Novavax with myocarditis?

DG: Not as much as we see with the mRNA vaccine.

VR: There is some.

DG: Yes. This is one last one on vaccines, which, Vince and I know you will enjoy. It's the article, "T Cell Responses to SARS-CoV-2 Infection and Vaccination are Elevated in B-Cell Deficiency and Reduced Risk of Severe COVID-19*,"* published in *Science Translational Medicine*. Really,

it's all there in the title, but it's this whole idea that comes up in individuals on some sort of therapy and it's impacting their B cells.

The doc says, "I don't know if it's even worth vaccinating you." We want to point out that those vaccines also impact T cell responses. Even in individuals with B cell deficiencies, those vaccines, those prior infections can actually result in a T cell memory response that can protect you against severe disease.

VR: T cells are wonderful.

DG: All right. [chuckles] Moving on to COVID, the early week, right? The viral phase. You tested positive, you got COVID. What do you do? This is a new article, "Oral VV116 versus Placebo in Patients with Mild-to-Moderate COVID-19 in China: A Multicenter, Double-Blind, Phase 3, Randomized Controlled Study," published in *The Lancet Infectious Disease*. As laid out, results of a multicenter double-blind phase 3 randomized control study that enrolled adults in hospitals for infectious diseases and tertiary general hospitals in China.

The patients were randomly assigned in a one-to-one ratio using permuted block randomization to either get this VV116 or placebo. It's five days. The primary endpoint was time to feel and better clinical symptom resolution for two consecutive days. A total of 1,369 patients were randomly assigned to treatment groups, 1,347. 674 of those got the VV116, 673 got placebo. We get both an interim analysis, and we get a final analysis, and VV116 compared with placebo was associated with a statistically significant reduction in time to sustained clinical symptom resolution.

The final analysis showed that the time to sustained clinical symptom resolution for two consecutive days was 10.9 in the drug group versus 12.9 in the placebo group. Not as impressive as I would like. I don't want to be sick for 10.9 versus 12.9 days. I would like to feel better like we've seen with some of our other agents. What is this VV116? Think of it a lot like remdesivir. It targets the SARS-CoV-2 RNA-dependent RNA polymerase and its mechanism action is really similar to remdesivir. The active triphosphate form acts as a nucleoside analog, gets incorporated, and there you go.

VR: Chain terminates, don't forget.

DG: Chain terminates and basically gets peed out in the urine. One big thing is we don't have to worry about the drug-drug interactions.

VR: We don't need any CYP3 inhibitor, right?

DG: Exactly. This is hopefully something that's going to be an easier lift for folks. The question is going to be how effective is this? What we have actually out there with good data, number one, Paxlovid, five days. Number two, remdesivir, three days if we're in that first week. Molnupiravir, convalescent plasma, and yes, an interesting publication, "COVID-19 Convalescent Plasma Therapy Decreases Inflammatory Cytokines: A Randomized Controlled Trial," published in *Microbiology Spectrum*. We read in the abstract that early COVID-19 convalescent plasma transfusion to outpatients with COVID-19 decreases progression to hospitalization, but the mechanism of how CCP reduces severity is unknown.

I'm not sure I agree with that. I've suggested for some time [chuckles] that the mechanism is decreased viral replication during the first week, leading to a blunting of the early inflammatory response during week two. Let's see if that's true. Here, they look at 882 COVID-19 participants transfused with COVID convalescent plasma or control plasma in a randomized control trial, 21 cytokines and chemokines were measured at the day 14 visit. The median IL-6 and IL-16 levels were lower in the CCP group compared to the early control group. IL-6 levels decreased significantly faster in the early CCP group from screening to day 14.

Our statisticians have issues with p-values here as we are doing multiple comparisons. There's a figure we can look at and it's not quite as impressive as I would like. Again, that becomes an issue when you start looking at 20 different things and one of them meets statistical significance, are we data mining? This is consistent with what we think we understand about the mechanisms here.

Week two, this is individuals that progress, end up with oxygen saturation maybe less than 94%, ending up getting them perhaps in the hospital, maybe on steroids, anticoagulation for folks that end up in the hospital. One of the questions about that has come up over time is what's the right dose for which patient? Early on, there were recommendations, still stand, based upon those early studies that patients that were just floor patients laying around, the less critical ones that perhaps therapeutic dose anticoagulation was associated with better outcomes and then folks in the ICU, a prophylactic dosing just because the bleeding risks went up.

We have a bunch of data on the acute outcomes, but what about longer-term outcomes? Now we have this interesting article, “Therapeutic Heparin in Non-ICU Patients Hospitalized for COVID-19 in the ACTIV-4a Trial: Effect on 3 Month Symptoms and Quality of Life,” published in the august journal *CHEST*. These results from an open-label randomized control trial at 34 hospitals in the U.S. and Spain.

In total, 727 non-critically ill patients hospitalized for COVID-19 from September 2020 to June 2021 were randomized to therapeutic dose versus the prophylactic dose heparin. They have 90-day data on symptoms for a number of these patients and looked at the correlation between therapeutic heparin and 90-day symptoms. They reported that therapeutic dose heparin was associated with less moderate severe impairment in all physical functioning domains, mobility, self-care, usual activities.

Sort of interesting, actually, I have to say because I know a lot of us now look back and we say, "Those studies, those were done on different patients." Most of us have dropped down to a prophylactic instead of a full therapeutic dose heparin in our floor patients with COVID-19. It's interesting to see there may be this benefit out at three months. Again, remember, this is looking at those folks that were hospitalized September 2020 to June 2021. The same issue. We're looking not at the patients right now that we're seeing, but we're looking at a historical cohort.

Pulmonary support, remdesivir if we're still in the first 10 days. Immune modulation. Really, tocilizumab seems to be the last one standing here and occasionally we'll consider using that. Then again, this can be associated with immune suppression, so not something we want to

be thinking about if we wait too long or if the patient has an active bacterial or fungal or other non-viral process.

All right. I'm going to wrap it up here. As I prepare to get myself, I guess I'll be in sub-Saharan Africa when this episode drops. I will make the comment that I've been making for a while. No one is safe until everyone is safe. Here we are. We are right at the end of November. This will drop December, right? November, December, and January, we are doing our MicrobeTV fundraiser. Please stop recording right now, go to parasiteswithoutborders.com, click on the 'Donate' button, and we are hoping to double your donations up to a potential maximum donation of $20,000.

VR: Time for your questions for Daniel. You can send them to danielatmicrobe.tv. Mary writes, "Been a regular listener for some time and every so often you mentioned a situation where a patient has acquired COVID-19 while in the hospital. This is disturbing. I don't anticipate needing hospitalization myself in the near future, but I feel that a healthcare setting is one where care should be taken to prevent transmission of COVID or indeed any infection. I recently visited a friend in a hospital and I was one of the few people, including visitors, staff, and other patients who was wearing a proper protective respirator. What are your thoughts on this?"

DG: It's really a challenge. I know we're moving there, but we're certainly not moving there as quickly as I would like. What would be my ideal world? In my ideal world, each individual, particularly individuals who are high-risk, wow, that's pretty much the hospital. Individuals who may come in contact with someone with a respiratory transmitted virus, OK? Any pathogen actually for that matter. The ideal would be single rooms, would be people practicing proper hygiene and other control measures to prevent that from happening.

Unfortunately, a lot of this is financial, right? When I first trained, I remember being in these large wards in the VA system where there were dozens of people in the same room. There weren't even curtains behind, between the different beds. We are moving down to maybe two individuals in the room, maybe one individual in certain rooms. I think really the goal, the safest thing if possible is to really move to a single occupancy room and then really for everyone to do everything to protect our patients.

VR: Laura writes, "I'm 61, currently being treated with prednisone and doxycycline for the past two and a half months. My dose of prednisone ranged from 60 milligrams a day to 20 milligrams a day. I had a negative temporal artery biopsy in September, but my vision loss symptoms continue. I will be tapering off in the coming weeks as part of the treatment plan.

I have two questions. The neuro-ophthalmologist that I'm seeing at Wills Eye recommends that I do not get any vaccines such as flu, RSV, or COVID. I'm very concerned about entering the holidays, working in a school environment, being immunocompromised, and also, not being protected with vaccines. I had four COVID vaccines, including the bivalent in December 2022. I got COVID in January of '23 anyway but was wondering if I can count on any protection from vaccination and infection in spite of my immunosuppression. In addition, I had a splenectomy at age 20 as a result of abdominal trauma." Let's take that one first, Daniel.

DG: There's a lot here. What are the recommendations regarding the vaccine and let's sort of unpack that. I would say, OK, you don't have a spleen, you're on this immunosuppression. The concern would be that if you got a vaccine, you're just not going to have a robust response. You're not going to have the same benefit that a person not on immunosuppression might have. I don't see any harm and I was trying to listen and see, is there any suggestion that there'd be any problem? I don't see a problem.

I do see that you might not get as much protection as one would hope. It might be substantially developed, reduced with the level of immunocompromised. Are you completely unprotected? That's a no. You've had prior vaccines and we've talked about the fact that there is a durability to that. It is being negatively impacted by the steroids. The other thing, actually, which we bring up time and time again, is getting an early diagnosis, jumping in with early therapy. You can think about that as another 80%-90% reduction in your risk of a bad outcome by jumping in with early treatment.

VR: All right, "Secondly, the origin of my eye condition is unknown. Currently, my doctor is hoping that using doxycycline with prednisone is covering the possibility of Lyme disease or cat scratch fever, even though I tested negative for both. At my last visit, my doctor mentioned that the possibility of my condition having a COVID infection or vaccination cause was floated by the other clinicians consulted on my case. Have you heard of any correlation between ophthalmologic conditions and Long COVID?"

DG: As I was thinking about your doctor saying don't get the vaccine and is this what they're thinking? Is there some concern here, as you're bringing forward, that maybe there was some timing issue with a prior vaccination and maybe they're concerned that a vaccination might trigger some ongoing inflammation? A big thing here is to try to understand what exactly is going on. I will say there are a lot of post-COVID neuro-ophthalmological complications.

You're going to have to really have a good discussion with your providers. You don't want it to just be like, "Oh, a few people have brought it up." You really got to pin them down. What are you talking about? Is this really a post-COVID condition? Because then you would be concerned that a repeat COVID infection may lead to an exacerbation. Yes, there certainly are a number of well-identified retinal and thrombotic and other post-COVID eye conditions.

VR: Nancy writes, "My daughter was diagnosed with COVID 10 days ago. She still cannot taste food. Does that mean she is still contagious?"

DG: Fortunately, no. Ongoing loss of taste or smell, those are not what you count when you say a person is symptom-free. It's the fever, it's the cough, it's the other things. The loss of taste and smell, that can actually go on for months and months, and for some folks, even past the one-year point.

VR: Anissa writes, "I'm an OB/GYN in Atlanta. I've been recommending ABRYSVO to my pregnant patients. As RSV season 'ends' in January, should I still recommend it to patients who are due in February? Does RSV season run long some years? Should I recommend vaccination as some will deliver early?"

DG: This is great. I like the fact that you're thinking it through because it shouldn't just be a check-the-box, right? I always leave a link in each time. You can actually track and see what's

going on with RSV activity. Once the RSV comes down, you can pretty much say, "OK, it's over." You're raising some important points. What if someone delivers a little bit early? Maybe their due date is after this is going to end.

The risk of getting the vaccine really isn't one. We're not seeing any problems here. The child might come into this world without the ability to get the nirsevimab, the Beyfortus. Really look at that. Think about where you are in the timing. If you're in the last trimester, missing the vaccination is much more of an issue than giving a vaccine, which it ends up you didn't actually need.

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

DG: Hey, thank you, and everyone, be safe.

[music]

[00:44:00] [END OF AUDIO]