This Week in Virology

TWiV 1122 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.

Amy Rosenfeld: From MicrobeTV, this is *TWiV. This Week in Virology*, Episode 1122, recorded on Thursday, June 13, 2024. You're listening to the podcast all about viruses. Joining me today from New York, Daniel Griffin. Hello, Daniel.

Daniel Griffin: Hello, everyone, including you, mystery Vincent replacement for the night. I have to say for our listeners that Vincent has not missed one of these recordings since February of 2020. I know he's doing something important. He is texting me, for whatever that's worth.

AR: Well, that's great. What's your bow tie today, Daniel? We got to have the bow tie conversation.

DG: Oh, yes, I got to do it. If you look closely, now people have to go to YouTube, you'll see this very bright red bow tie. Actually it's a disease instead of a particular pathogen. It's hepatitis. These are inflamed hepatocytes.

AR: Any hepatitis A, B or C, E, D.

DG: It can even be toxic. It could even be non-pathogen-related.

AR: I'm sorry, what?

DG: It could be non-pathogen related, dare I say that. It could be a toxin ingestion. It could be one of those *Herpesviridae.* It doesn't have to even -

AR: Again, I hear this - I hear the noninfectious. I'm like, "What?"

DG: Yes, it can be everything. This is just good. For me, it's always about pathogens.

AR: Well, that's good because we're here at *TWiV.* The podcast all about viruses, the kind that makes you sick.

DG: The kind that make you and your liver sick.

AR: Exactly.

DG: All right. Well, I notice sometimes in the comments, people say they enjoy my quotations or my song lyrics, or what I start with. Sometimes they don't really, necessarily catch this. I will say there's always a particular reason why I pick a particular quotation or song lyric. If you go through the show, you'll see, "OK, I see why he picked that." Two challenges for our listeners.

One is, figure out why am I sharing these particular song lyrics that we're going to share tonight. Then, also, you can list every single pathogen that causes inflammation of those hepatocytes. All right. This week, I want to start with the song lyrics from one of my favorite songs by Peter Gabriel. Yes, I am a Peter Gabriel fan.

AR: Is this before Genesis or after?

DG: I like it all. I also love Peter Collins. I'm watching some of the old *Miami Vice* episodes, so-

AR: Of course.

DG: - a fan all the way through the career. Here we go. “In this proud land, we grow up strong. We were wanted all along. I was taught to fight, taught to win. I never thought I could fail. No fight left or so it seems. I am a man whose dreams have all deserted. I've changed my face, I've changed my name, but no one wants you when you lose. Don't give up because you have friends. Don't give up, you're not beaten yet. Don't give up, I know you can make it good.”

When we get to our Long COVID part, I think maybe people will understand why I'm bringing that up today. All right. Let's start today with RSV. We have a couple studies today. First one highlighting the seriousness of RSV. Then one addressing the effectiveness of the monoclonal nirsevimab or Beyfortus for protecting our infants from RSV. Now, I was very troubled to hear that the baby of one of our immune hosts was not able to navigate the access, and this infant ended up last winter in the hospital with RSV.

In the journal *Pediatrics*, we have the article, “Respiratory Syncytial Virus-Associated Hospitalizations in Children Less Than 5 Years: 2016–2022.” Open access, so everyone can take a look. Prospective surveillance for acute respiratory illness during 2016-2022 at seven pediatric hospitals. They estimated annual RSV-associated hospitalization rates in children aged less than 5, and compared hospitalization rates and characteristics of RSV-positive hospitalized children over four pre-pandemic seasons.

Now, the RSV-associated hospitalization rates were higher in 2021 and 2022 than the pre-pandemic average across age groups. We've taken those four pre-pandemic seasons, 2016-2022, and then we're looking at 2021-2022 when we get these results. Now, compared to 2021-2022, RSV-associated hospitalizations were similar among children less than 2 years of age. However, children aged 24 to 59 months had significantly higher rates of RSV-associated hospitalization in 2022. That's a rate ratio of 1.68.

More RSV-positive hospitalized children received supplemental oxygen and there were more respiratory virus co-detections in 2022 than in pre-pandemic seasons. A little bit of a pause there. Why is that happening? Why are we getting more viral co-detections in 2022? I'm hoping it's because everyone's listening to *TWiV* and they're remembering the dictum, they're

remembering that Occam was not a doctor. You can have more than one thing at the same time. Yes, if you look, you will see a lot of respiratory virus co-infections.

All right. Now, the second article is, “Nirsevimab Effectiveness Against Cases of Respiratory Syncytial Virus Bronchiolitis Hospitalized in Pediatric Intensive Care Units in France, September 2023-January 2024,” published in the journal *Influenza and Other Respiratory Viruses*. Now, why France? Well, first, kudos to France as we read that in September 2023, France was one of the first countries to start a national immunization campaign with nirsevimab, the new monoclonal against RSV.

We read that using data from a network of pediatric intensive care units, PICUs, the authors estimated the nirsevimab effectiveness against severe cases of RSV bronchiolitis in France. They conducted a case-control study based on the test-negative design and included 288 infants reported by 20 PICUs. Ready for this? They estimated nirsevimab effectiveness at 75.9% in the main analysis, 80.6%, and 80.4% in two sensitivity analyses. These are real-world estimates confirming the efficacy that we saw in those clinical studies.

Very powerful tool, but I wanted to wrap up this little section with a quotation that I read in the CIDRAP analysis of these studies. The authors tell us, "RSV prevention products have demonstrated efficacy against RSV disease, not infection." I'm going to leave a link into *TWiV* 695, where we talk about the important concept that our goal with vaccines is to prevent disease. Some very smart people missed this section in med school, vaccines prevent disease, not infection.

There's actually been a little bit of retweeting of this in defense when people have been beating up one of our leaders, poor Anthony, who's been up on Capitol Hill and people have been berating him. "You said, you said these vaccines work, but people are still getting infected." You can watch *TWiV* 695 and you can understand why vaccines do work. We also heard this week that the FDA expanded the age indication for GSK's Arexvy, respiratory syncytial virus vaccine, to include adults aged 50 to 59.

With the qualification at increased risk for complications from the virus, I was ready to rush out. No, this is targeting the higher-risk folks in their 50s. I am in my 50s. In a press release, GSK said that more than 13 million Americans fall into this category. The vaccine was initially approved last fall for use in all adults 60 and older. Now if you're in your 50s and at higher risk, you can be included.

All right, our COVID update, a little bit of a surprise this week when I was looking at this, I noticed that, the entire country is this - what would you call this?

It's like a greenish turquoise or something. Some areas are thatched, some areas are not. Sort of everywhere is in the either less than one or the less than 2%. Then there's this yellow square. Looks to me like Puerto Rico. What is going on in Puerto Rico where 4-to-6% of all deaths in the past week were due to COVID? Pretty significant. I just want to put that on people's radar. I always follow the Wastewater Viral Activity Level, and thanks for the emailer who helped us figure out what are those numbers on the y-axis.

We are starting to see a rise, well, really in the West. We'll see what happens. Really a lot of what I'm curious about is, here we are. The data is always a little bit old. We're dealing with

data from early June. We're getting into mid-June. We're seeing a little bit of a rise. Are we going to see what we saw last summer, right, where we see a little bit of a peak as we get into August, then our drop before our major winter surge? We'll keep track of that. COVID is not gone. Had a patient that we discharged from the hospital today, came in hypoxic.

We're still seeing COVID. We're still seeing severe COVID. All right, children, other vulnerable populations. The article, "Neurodevelopmental Delay in Children Exposed to Maternal SARS-CoV-2 In-utero," recently published in *Scientific Reports*. Always reminds me of that day when I'm on *CNN Live* messing with my bow tie, getting it all messed up, worse than when I started. Sometimes you're better off just doing nothing. Being asked about, what should we be thinking about with pregnant individuals and SARS-CoV-2 infection, COVID-19?

Well, here, these investigators assessed pediatric neurodevelopmental outcomes in children born to mothers with laboratory-confirmed SARS-CoV-2 infection during pregnancy. Neurodevelopmental outcomes of in-utero exposed children were compared to that of pre-pandemic control children in LA, that's in California, USA, and Rio de Janeiro, Brazil. Neurodevelopmental testing was performed in 300 children total, 172 COVID-19-exposed, really SARS-CoV-2-exposed children, just between 5 to 30 months of age, 128 controlled children.

They found that children exposed to, I guess we'll call it an antenatal mom COVID-19 infection, had a tenfold higher frequency of developmental delays as compared to controls. Let's dig a little bit deeper because that is not good news, that's not encouraging. I was a little curious if I could tease out any potential benefit for vaccination of the mothers in terms of protecting the kids. Now we read that no participants in Rio were vaccinated before COVID-19, while 30.4% of the LA women had received COVID-19 vaccination before infection.

Not surprising based on this, 8.8% of mothers in LA had severe COVID-19 versus 34.6% of moms in Rio. Just doing that math quickly in your head, it's like quadruple. A four-fold reduction. Now be honest. These are not exactly matched populations. In Rio, 12% of the children were delayed in the COVID-19 cohort, 2.6% in the control group. In LA, we had 5.7% delayed compared to none in the control group. Trying to sort of tease that out.

Just to get on that soapbox here, we already have compelling data that we discussed before that vaccination protects pregnant individuals from the tenfold higher risk of bad outcomes with getting COVID-19 during pregnancy. Here we see in this cohort with 30% vaccination versus 0%, a difference in developmental delay for the kids, 12% compared to 5.7. All kinds of limitations. We're looking at two different populations, lots of confounders. Just wanted to put this out there.

For all those OBs, we're still recommending against vaccination for their pregnant patients. All right. Well, so what about the risk to pregnant individuals themselves? We have the article, "COVID-19 is Associated with Early Emergence of Preeclampsia: Results from a Large Regional Collaborative." published in *The Journal of Maternal-Fetal & Neonatal Medicine*. It's a retrospective cohort study, pregnant women between March and October 2020.

Pregnant patients admitted to 14 obstetrical centers in Michigan, it's here in the U.S. They formed the study population. Of the 1,458 participants, 369 had SARS-CoV-2 infection, these

are the cases. Controls were uninfected pregnancies that were delivered in the same obstetric unit within 30 days of the index case. We read that SARS-CoV-2 infection during pregnancy increased the risk of preeclampsia, adjusted relative risk 1.69, so almost doubling there.

Preeclampsia involving placental lesions, adjusted relative risk 1.97, so about doubling there. Preterm eclampsia 2.48, so more than doubling. Now, they comment that the highest rate of preeclampsia was observed in patients infected with SARS-CoV-2 that were symptomatic, that's 18.4%. There was increased risk even in asymptomatic, about 14.2% relative to non-infected controls, that was 8.7. If you got symptomatic SARS-CoV-2 during that pregnancy, 18.4%. If you were asymptomatic, still 14.2 compared to a background risk in our controls of 8.7.

So the association with symptomatology was also noted with preterm eclampsia for which the rate doubled from 2.7 to 5.2 in asymptomatic and reached 11.8% among symptomatic cases. Getting COVID-19 when you're pregnant, not good, being symptomatic, even more not good.

All right, so right in this section, I'm going to share a study that could have gone in some of the other sections. “Effectiveness of Nirmatrelvir/ritonavir in Children and Adolescents” - so Paxlovid – “In Children and Adolescents Aged 12-17 Years Following SARS-CoV-2 Omicron Infection: A Target Trial Emulation.” It's published in *Nature Communications*. I actually have a paper sitting out there at the moment, getting ready to send back with the reviewer revisions that just when you read those, just make you feel so good about yourself and your study. In this study, the primary outcome was 28-day, all-cause mortality or all-cause hospitalization. Yes, children and adolescents end up in the hospital with COVID.

Nirmatrelvir/ritonavir treatment was associated with reduced 28-day, all-cause hospitalization. Absolute risk reduction, 0.23, so about 23% reduction. What I think is really nice, and I'm going to suggest that people take a look at the figure - actually, Figure 2 here, because it's interesting to look at people that get nirmatrelvir. You see within the first seven days, there's a certain percent. It's about half a percent, less than half a percent that end up in the hospital. Then you look at the folks that didn't get Paxlovid, and you see well, not much happens during that first week.

Well, of course, you're sort of trying to prevent that inflammatory post-first week viral replication phase, and you start to see this rise from day seven to 14. The interesting thing is it keeps going, 14 to 21, we're seeing more, 21 to 28, it's still rising when they finally stop looking. Really something going on, that you're not sort of putting your foot on during that first week. Really interesting. I want people to sort of think about what we might be doing. Boy, what if we kept following those kids out to 60 days, 90 days, et cetera. We'll talk a little bit about Long COVID later.

All right, moving to COVID active vaccination. We've heard that the vaccine advisors are recommending switching to a new vaccine formulation for the fall. We'll see how closely that ends up actually matching the currently circulating variants at the time. Just a little discussion, I want people to sort of be thinking about this. You got a little time, to boost or not to boost this fall. We'll be coming back to that as we get a little bit closer to the fall and when decision time is in front of you. All right, passive vaccination.

Successfully actually getting Pemgarda to our patients. This is a passive vaccination. I should say there might be some other options on the horizons. We've got some interesting results that are coming out. We'll keep everyone up to date on options there. Then COVID, early viral phase, we always keep the guidelines out there. If your doctor is not following them, feel free to share the links. Number one, Paxlovid, number two, remdesivir, three, molnupiravir, convalescent plasma is a treatment option for some immunosuppressed COVID-19 patients.

Then, guess what? When you're sick, you can be contagious. We've got our isolation guidance. COVID during that second week, the early inflammatory week, still steroids at the right time in the right patient, anticoagulation, pulmonary support. Remdesivir if you're still in the first 10 days, and in some cases, immune modulation. All right, moving to COVID, the late phase, PASC, Long COVID. Many of us have been waiting a really long time for the results of this study.

We now have the article, “Nirmatrelvir-Ritonavir and Symptoms in Adults with Postacute Sequelae of SARS-CoV-2 Infection.” These are the “STOP-PASC Randomized Clinical Trial,” published in *JAMA Internal Medicine*. Now, this is, does Paxlovid not prevent Long COVID? Instead the question, what is the efficacy of 15 days of Paxlovid for improving select symptoms of post-acute sequelae in folks with PASC? Post-acute sequelae of SARS-CoV-2 infection.

These are the results of a 15-week blinded, placebo-controlled randomized clinical trial conducted from November 2022 to September 2023 at Stanford University out there in California. The participants were adults with moderate to severe PASC, symptoms of three months or longer duration. Participants were randomized two-to-one to treatment with oral nirmatrelvir, 30 milligrams, 100 milligrams, or, this is a little interesting, placebo-ritonavir. They weren't just getting placebo, they were getting ritonavir, which it's that booster.

Also one of the side effects that maybe people don't know, it gives you a little bit of that dysgeusia, that metallic bad taste in your mouth. Because people are like, "Everyone's going to know." This was sort of that idea, but we'll talk about was that such a good idea. They're going to get this twice daily for 15 days, either basically Paxlovid or just the ritonavir. Primary outcome was a pooled severity of six PASC symptoms, fatigue, brain fog, shortness of breath, body aches, gastrointestinal symptoms, and cardiovascular symptoms based on a Likert Scale score at 10 weeks.

Saying Likert Score is really just a fancy way of saying on a zero-to-10 scale, on a numbered scale, but it sounds so cool. In your grant proposal, make sure you use a Likert Scale. Don't just say, I'm going to rate this zero to 10. Secondary outcomes included symptoms severity at different time points, symptom burden, and release, relief, patient global measures, patient-reported outcomes, measurement information system, PROMIS measures, orthostatic vital signs, sit to stand test change from baseline. We're going to get a lot of information here.

Of the 155 participants, we have 102 randomized to the Paxlovid, 53 to the placebo-ritonavir group. Nearly all the participants had received the primary series of the COVID-19 vaccination. The median time between the index SARS-CoV-2 infection and randomization was about 17.5 with a range of 9.1 months. This is really far out. We've got severe people well past three months still suffering. Now, unfortunately, this is where we get to the results. There was no

statistically significant difference at 10 weeks between the Paxlovid-treated and the placebo ritonavir groups.

No statistically significant between-group differences were found at 10 weeks in the patient global impression of severity or patient global impression of change scores. Summative symptom scores changed from baseline at 10 weeks in the PROMIS, fatigue, dyspnea, cognitive function and physical function measures. Now, adverse event rates were similar. Mostly low grade. In short, we're not getting any indication here that Paxlovid at this dose for this duration was an effective treatment of Long COVID in this patient population.

Now, there's an interesting discussion section where the authors make a few comments that are worth discussing. The authors write, "This trial's results do not reject the hypothesis that viral persistence may lead to PASC, but they will help inform further studies in this area. None of the participant baseline stool samples specimens had detectable SARS-CoV-2 RNA, other tissues were not assessed." They point out as assays to dissect SARS-CoV-2 reservoirs become optimized and validated, they could help identify individuals who may benefit from antiviral therapy.

They go on with sort of the usual longer treatment durations, dose variations, optimal timing, different phenotypes of PASC should be investigated in larger studies. A lot of passion in this area, a lot I've seen on social media, and I know people are worried that we're making a Type 2 error here. Type 1, Type 2. Just a reminder, I saw this recent cartoon that's going to help us keep straight. What's a Type 1? What's a Type 2 error? What's Dr. Griffin talking about?

This cartoon shows a man in a bed with the doctor telling the man that according to his blood work, he is pregnant. This is an example of a Type 1, so a false positive. Come on, the guy's got a bit of a beer belly, that's a little bit too much beer drinking, that's not a baby in there. That's a Type 1 error. That's when you think something is true, a false positive. Now, there's another, obviously, gravid pregnant woman with a stethoscope on the protuberant gravid belly. The clinician is unable to hear the heartbeat with the cheap stethoscope and proclaims that the lady is not pregnant.

This is an example of a Type 2 error. A false negative. Something's actually true. She, by the way, is pregnant. I'm sure now this provider is going to start fat-shaming the lady and trying to get her started on Ozempic. Now, lots of people are disappointed that these 15 days of Paxlovid did not work. To put these results in context, we have here the results of a well-designed, well-conducted study that provided not a suggestion that antiviral therapy was an effective approach to the treatment of Long COVID in this context. Now, there might be viral remnants such as RNA.

We've seen some evidence for that. There may even be antigen that's associated with Long COVID. We keep looking. I have to say what we're not finding. We're not finding replication-competent virus. There are a few other ongoing studies looking at different doses of Paxlovid, different durations of antiviral therapy, and we'll see if these provide any further insight. As upset as people are either side, we're still not done investigating this. All right. I will wrap this up with, as I have for a while now, no one is safe until everyone is safe.

I do want everyone to pause the recording right here and go to parasiteswithoutborders.com and click on the Donate button. Every amount helps, even those small amounts. The small amounts, we love to see those. We'd love to see people sort of joining us in this effort. We are now doing our Floating Doctors fundraiser, where for May, June, and July, we double your donations up to a potential maximum donation of $20,000. You got to go and help us because otherwise, we're not going to make it. Yes.

AR: All right. It's time for your questions for Daniel. You can send your questions to daniel@microbe.tv. Theodore writes, are you ready, Daniel?

DG: I am ready.

AR: (Chuckling) My parents say that until their glasses are on their face, they can't hear, see, or think. Just to demonstrate, are you ready?

DG: I am. It is interesting, as we get older and our hearing fails us, a lot of people actually are partially lip reading. Now that my glasses are back on, I hear what you got to say.

AR: All right. We're ready for Theodore. She writes, "Dear, TWiV Team, Kalispera from flaming Athens, Greece, 38°C, that's about 100-plus Fahrenheit. I'll be short and sweet. I am 46 years old, under secukinumab, the anti-IL-17 antibody therapy for psoriasis. Major pertussis outbreak in Europe this year. As a child, I had been vaccinated with the bivalent vaccine, diphtheria, and tetanus, but not a DTaP, and never had pertussis. I am a smoker. Vaccination for pertussis is required by the Lung Association guidelines.

I know that adults do the TDaP formulation, but not the DTaP. In Greece, I have found that TDaP plus IPV formulation, (already had six doses of Sabin's OPV as a child, last in 1989). My question is, as I haven't had a previous exposure to pertussis, will I be covered with one dose of TDaP, or is more than one required in order to be considered fully vaccinated? In case only the TDaP+IPV formulation available, please verify if there's no contraindications for IPV and secukinumab. Yours, Theodore."

DG: OK. I feel like for our people that are listening, the capital and the small letters are a little bit lost. Just give some context here. I don't want to try to make this not a particular person, clinical consult, but just general knowledge for folks. Yes, secukinumab. That's also known as Cosentyx. Actually, it is immune suppressive. Anyone on a medication that's going to impact their immune system like that, don't just go out get your vaccines, and make sure you speak to your provider.

Ideally, the person who's prescribing and putting you on that Cosentyx because there are certain replication, competent, attenuated viral vaccines that can get you in trouble. Make sure you force your doctor to earn their pay by looking at the options that you're considering and moving forward. Fortunately, IPV. We're not worried about a replication-competent. We would be worried maybe if you were doing one of those oral attenuated replicating things.

Now the other, which is interesting, and this is kind of what are all these crazy letters. There's a capital D capital T, which really means you're getting a large dose of the diphtheria vaccine. The large T meaning you're getting a large dose of the tetanus vaccine, and then the little A's just a cellular pertussis. Then the capital P is you're getting a lot of pertussis. Now there's also

something that folks get in the U.S. called a Tdap, and that's a capital T, little D, little A, little P.

What that is, is our tetanus booster every 10 years. We're getting a pretty hefty dose with that. Once we've gotten up front, then you end up with the little D and the little P. Just sort of a booster versus that high thing. Yes, just sort of bring people up to speed on this. Yes, if you've got a doc, in your case, Theodore, talk to the provider who's given you the second tune about your different vaccine options.

AR: All right. Lisa writes, "Hi, *TWiV*, you have helped keep me sane during the pandemic with your information and expertise. I am a 65-year-old retired cardiac anesthesiologist and PhD biochemist. I have had breast cancer twice. The first time in 2011, left lumpectomy and radiation. Then again in 2017 with a bilateral mastectomy and reconstruction. Incidentally, left arm lymphedema, occasionally MTHFR deficiency heterozygous.

I have been swelling in the left posterior triangle, then to the left face and left arm. All of my doctors were perplexed. The US and CT scan showed lymph nodes less than a centimeter, which they considered non-neoplastic. Many other studies were done to rule out gyn-leaking breast implants, et cetera. Lymphedema is resolving with lymphatic massage. I had my last COVID vaccine, Pfizer, in my left arm.

The question is then how to proceed with next COVID vaccination. My decision is confounded by upcoming trip to France in the fall. I would like to get flu and COVID vaccines prior to the trip. My thought is that lymphadenopathy is normal occurrence after vaccination. I would proceed again with Pfizer vaccination, but get shot in right arm, right or left leg. I'm interested in your thoughts on the situation. Thanks again, Lisa Dodson, MD, PhD."

DG: OK. Lisa, this is a great scenario. I actually have a gal in the hospital at the moment who's developed a left upper arm cellulitis after she had sort of a similar history to what you're describing here. When you go ahead and have these interventions, so you're describing here a bilateral mastectomy and reconstruction, and particularly that left lumpectomy and radiation, the left arm lymphedema. In a context like that, we really want to think about avoiding that left deltoid for our immunizations, usually recommending the right deltoid.

What you bring up is also another great option. A lot of people in the history like this get a little unsettled if they start having adenopathy. Let's say you did right deltoid, ended up with the not unexpected, not unsurprising adenopathy right axilla, right armpit there. You do have, as you bring up, the option of a right lateral thigh injection for your vaccines. Plenty of muscle there. Nothing to worry about there. That's definitely an option.

Now, a lot of times, unfortunately, you might have to go to a provider's office, a lot of the pharmacies, they're not necessarily trained. If you do, you probably want to wear a pair of shorts, otherwise, you're dropping your drawers. No, this is a great situation that brings up some of these other options. In a situation like this, I would tend to avoid the left deltoid. I would tend to favor the right lateral thigh. Right deltoid is also an option, but keep in mind the possible adenopathy.

AR: All right. Becky writes, "As always, your episodes are full of useful information. I was disappointed that KN95 masks weren't as great as I had hoped. I relied on them and still do

when needed. Do you think KN95 masks will be effective against H5N1 if this virus becomes more widespread? If not, what type? N95? I know why many wear surgical masks. It is easier to breathe but therein is the problem.

I had hoped with all the money the government gave to local and state governments and private businesses that decent air filtration systems would have been installed. This hasn't happened as far as I know. Thanks to *TWiV* team for all your efforts to get the word out about COVID and other issues. We could not have survived without you. Becky."

DG: All right. Thank you, Becky. I like the fact that you're bringing up what I think are important topics to talk about. I was a little surprised in that site we talked about last week, just about how the KN95s just were not as effective as we had hoped. It was sort of nice to see in that study how well the duckbill N95s did, even in people without training, just put this on, sort of make a seal, go right ahead. That was good to see.

Now, the other thing that I really like is that we are moving from terminology that was 100 years old, this whole obsession that we've got to move away from the miasma. We've got to make sure everyone believes in germ theory. The whole idea that we took transmission of respiratory pathogens and we somehow cut in the middle and said, "Oh, no, what's happening is you're getting sprayed in the face with droplets."

You're really being contacted, taking forever to admit that measles and tuberculosis is something you could breathe in after the person has already left the room. We see in a medical center, particularly one with good ventilation, we've got these air exchanges, sort of a different scenario. The suburban home, where we don't have great air exchanges, and unfortunately, all these governments, schools, et cetera.

Where all this money was made available and no one upgraded their air filtration systems. I think the HVAC lobby should have worked a little harder because it would be nice to have that updated. Now, H5N1, in general, the influenza viruses, we're seeing less transmission, even in those situations where you have poor ventilation, but it's relative. Again, the N95, particularly with a virus, if we have the high mortality that we might see should this jump over.

That's going to weigh in a little bit with the precautions that we talk about because we talk not about protecting people from just infection, but we really don't want severe outcomes. What are going to be the recommendations as far as vaccination, as far as therapeutics, as far as protective equipment? No, I appreciate you bringing all this up, and hopefully, people are putting decent air filtration systems in their homes as well.

AR: All right. The last one is from Susan. Susan writes, "Dear Dr. Griffin, my virologist daughter turned me on to *TWiV* in early 2020, and I have been listening and learning ever since. Thank you. In trying to figure out a now seven-month-long diagnosis of Meniere's disease syndrome. I have been wandering through countless academic papers. I've come across a series of citations for papers exploring viral links to MD, and among such viruses, SARS-CoV-2, and COVID-19.

I'm wondering whether you have treated patients with Long COVID who have MD-like symptoms, tinnitus, hearing loss, vertigo, vomiting. If so, can you describe this subset of patients and your approach to treatment? Thank you so much. Susan."

DG: All right, thank you, Susan, for bringing this up. This is really challenging. I'm thinking of a particular patient who went to an audiologist who claimed to be a specialist in tinnitus and gave them all kinds of hope. They came and saw me, and they were just all excited because now they're going to get better, and here's like a bunch of cards, and I can refer patients to them. A couple months go by, and I check it, and I'm like, "Hey, how's that going?"

Basically, months later, the tinnitus was just as bad as before, and yes, so tinnitus is really tough. We certainly see a lot of tinnitus post-SARS-CoV-2, and that's just what is tinnitus. That's just ringing in your ears that will drive you mad. Actually, there was a rather successful individual, who owned a chain of steakhouses, actually committed suicide. Just the tinnitus drove him to that extreme.

This is not just, oh, some ringing in your ears, put on some background music. This is horrible, debilitating stuff. It can be associated with hearing loss. There can be issues with vertigo to the point where people have issues with vomiting. Yes, we do take care of folks with these issues and it's not an easy fix, it's tough. Sometimes we're trying to do things, autonomic focus, or trying to do things to improve vagal tone.

A lot of the other things that just are really not as effective as we would like the background noise and things like that. There are some excellent centers, here in the New York area, Mount Sinai, Columbia, NYU. Really going to a large center like that where they have a lot of people to help with the management is really the best thing to do in a situation like this.

AR: All right, that's *TWiV* weekly clinical update with Dr. Daniel Griffin. Thank you, Daniel.

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

[END OF AUDIO]