This Week in Virology

TWiV 1176 Clinical Update

Host: Vincent Racaniello

Guest: Daniel Griffin

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VR: *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 1176, recorded on December 19, 2024. 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: What's on your tie, Daniel?

DG: Let's see. It's this virus with these spikes, the spike proteins all sticking out. Looks like a corona. If I was going to name it, I would probably call it a coronavirus.

VR: I heard you bought it before the pandemic. It's not SARS-CoV-2, right?

DG: Hey, it depends if you're a conspiracy theorist or not.

VR: You bought it in Wuhan, China?

DG: [laughs] Let's jump right in. I will start with a Yogi Berra quote. I used to really enjoy Yogi Berra. Some of the stuff, so entertaining. I'll start off with, "It ain't the heat. It's the humility." That's by Yogi Berra.

VR: Did he say that? I thought he said was, really? That's good. I like it.

DG: "Half the lies you heard about me are not true." That's another good one. We're back into another holiday gathering time. Instead of talking about the current news, why don't people just trade around some Yogi Berra quotes?

VR: Here's one that I really like. "Nobody goes to that restaurant anymore. It's too crowded."

[laughter]

DG: I love that. Yes. "Nobody goes there. It's too crowded."

VR: "When you reach a fork in the road, take it."

DG: Take it. All right. Hardest thing to predict? The future.

VR: The future.

DG: All right. Mystery disease in the DRC, and we read the headline, mysterious disease in DRC is severe malaria health authorities say. We've been following this for about a month now. Earlier this month, local authorities said that there was this disease. It killed 143 people in the DRC, the country's Panzi health zone. This actually went back into November when we first started hearing about this. Here we read that they feel like, and this is from the Ministry of Public Health, the mystery has finally been solved. It's a case of severe malaria in the form of a respiratory illness.

A big issue here is malnutrition. You really got a weakened, vulnerable population. In the statement we read, there are almost 600 cases reported since October. Fatality rate was about 6.2%. They've got some anti-malaria medicine that's been provided by the WHO. It's being distributed. Just to give everyone an update on that.

VR: Daniel, this is still transmitted by mosquitoes, right?

DG: Yes, it's the same thing. I don't want anyone to think suddenly malaria became a respiratory, transmitted pathogen. It's not born by the air. It's not born by respiratory particles. What are those? PRIs or something they call them respiratory particles. This is you get bitten by a female Anopheles mosquito. That's how you get malaria.

VR: Then in this case, they have respiratory syndrome symptoms, which is not usually the case of malaria?

DG: Malaria can present in a myriad of ways. We always think about fever. That's always key. Sometimes people present with respiratory distress. Sometimes they present with abdominal pain. I remember seeing a case in India. It's everything malaria. This person is here with abdominal pain. I'm like, "Yes, could certainly be malaria." It presents with a myriad of different.

All right. Bird flu. The U.S. Centers for Disease Control and Prevention on 12/18, so this is a day before recording, a few days before this drops, they announced that they had confirmed the nation's first severe H5N1 avian flu case, which involved a patient in Louisiana who required hospitalization. The CDC said the illness marks the nation's avian flu infection, the first link to backyard poultry. We get partial genetic sequencing of the virus from the patient.

This is going to be important. Just to go through this slowly. This virus belongs to the D1.1 genotype, and that's different from the B3.13 genotype circulating in dairy cattle. This is avian

from avian, not avian flu from cattle, not the cattle. That genotype, the cattle one, has mainly caused mild symptoms, such as conjunctivitis in infected dairy workers. The D1.1 genotype is known to circulate in wild birds and has recently implicated in severe illness in a British Columbian teen, poultry cullers in Washington. The last update, I heard this individual is actually in the hospital in critical condition in the ICU.

Also, because bird flu is – I think they want to be hot for the holidays, California just declared an emergency. We read in Reuters, California, the most populous state, declared an emergency over the H5N1 virus as it spread more widely in dairy herds and after it has infected dozens of farm workers this year. Federal and state officials have failed to control the nation's outbreak, which infected dairy cattle for the first time in 2024.

We hear that some farmers have resisted testing and containment measures. The CDC has confirmed 61 human cases nationally since April. We mentioned some serology that maybe we're missing even more, but mostly in workers on dairy farms where the virus infected cattle. Workers culling infected poultry also have tested positive. Bird flu has infected more than 860 dairy herds in 16 states since March and killed 123 million poultry since the outbreak began in 2022.

In California, the top U.S. milk-producing state, didn't know that, 649 herds have tested positive since late August, roughly 60% of its herds. It's the majority of those herds out in California. Four Southern California dairies tested positive on December 12, and here we get this quotation, "Necessitating a shift from regional containment to statewide monitoring and response." That's from California Governor Gavin Newsom. Earlier cases had been centered in the Central Valley in the middle of the state. Now, what's the point of all this? The declaration aims to streamline and expedite California's response by allowing more flexibility for staffing, contracting, and other rules.

VR: I just want to make a comment on the earlier case you mentioned in the U.S., the more severe case which originated in poultry. This is not uncommon. This has happened many hundreds of times globally, maybe the first in the U.S. to be severe. It's not surprising given the more widespread distribution of avian H5N1 influenza viruses, but this virus has been jumping from poultry into humans for decades and causing severe disease but never transmitting. That's the key.

DG: I think those are, we'll say, a couple key. One is that it tends to go from poultry to people. People get super sick, but then we really haven't seen onward transmission from people. This is different, and this is severe. This is different from the dairy, the cow avian flu, where the cases are all mild, unless you're a cat. If you're a cat or if you're a bird, not so mild.

VR: That's correct. The ones from cows are mild, which further emphasizes that cows are nice animals.

DG: All right. Now polio. I'm excited to hear your take on this because there was even like a recent update, which was sent out by she who will remain nameless. Let us start with this section with the news that “Kennedy's Lawyer Has Asked the FDA to Revoke Approval of the Polio Vaccine.” All right. That's the title. For background, Aaron Siri, a lawyer helping Robert

F. Kennedy Jr. pick federal health officials for the incoming Trump administration. That's who this guy is.

We read that this lawyer, the lawyer helping RFK Jr. pick federal health officials for the incoming Trump administration, has petitioned the government to revoke its approval of the polio vaccine. It's really going to be some of the polio vaccine formulations, which for decades have protected millions of people from a virus that can because paralysis or death. Mr. Siri has also filed a petition seeking to pause the distribution of 13 other vaccines and these vaccines targeted cover tetanus, diphtheria, hepatitis A.

I just wanted to contrast this with a few others. We'll mention that Mitch McConnell is a polio survivor. We have a quotation from incoming President Trump. You ready for this? "The polio vaccine is the greatest thing. If someone told me, get rid of the polio vaccine, they're going to have to work really hard to convince me."

VR: Can't believe we're using Trump.

DG: To counter RFK Jr. and Aaron Siri.

VR: The point is that Trump appointed, he nominated RFK Jr.

DG: He nominated him. It may have been.

VR: First of all, there are two polio vaccines. There's an activated or Salk IPV, and then there's oral polio vaccine made by Sabin. We no longer use OPV. It's no longer licensed in the U.S. because it causes polio in a certain fraction of kids who get it. We only use IPV, with which there are no adverse events, as far as I can tell. It just prevents you from developing poliomyelitis. It was first licensed in 1955, and it brought the number of cases of polio in the U.S. from the tens of thousands down to a few thousand. Now we have no more poliomyelitis. We've been using IPV since 2000. It's an amazingly effective vaccine. There's nothing wrong with it. It doesn't do anything to you. I don't understand why you would want to eliminate it. Anyone with some modicum of sanity would say this is ridiculous. There's no basis behind this.

DG: All right, we'll just make sure we keep mentioning, because we certainly get a lot of questions about this, and I guess we're on the topic of vaccines. I'm going to leave in a link to an article, also WHO comments on this, but this is one of those articles that really found upsetting, but it's the article, “Tiny Coffins: Measles Is Killing Thousands of Children in Congo.” Maybe this is a reminder of just what a horrible disease measles can actually be.

The measles vaccine has been in use since 1963 and is believed to have saved more lives than any other childhood immunization. There were more than 311,000 reported cases of measles in Congo last year. Isn't that crazy? Over a quarter million cases of measles in Congo last year. We used to see about 500,000 in the U.S. per year prior to vaccines. Now, some 6,000 of them ended up with a child buried in a small coffin days after first running a fever and breaking out in a red rash. This year, cases have been fewer, about 97,000, but a higher case fatality rate killing over a thousand of these children.

Globally, there were 20% more measles cases in 2023 than the year before for a total of over 10 million, with over 107,000 people dying from measles. Just the importance of staying on top of these vaccine-preventable diseases, and we've talked about in the U.S. and it is a little bit controversial, but I'm going to go there, anyway. We used to see over 500,000 cases. The measles cases we're seeing in the U.S., the majority of the ones that we saw this last year, ended up requiring hospitalization. We're now dropping to dangerously low vaccination levels. This is not just an individual issue. This is a community public health issue.

All right, so right here, I also wanted to talk about the news piece in *Nature*. “Wuhan Lab Samples Hold No Close Relatives to Virus Behind COVID.” Now, while multiple independent lines of evidence indicate that the COVID-19 pandemic likely began with at least two zoonotic spillovers to humans from one or more mammalian species being sold at the Hunan market in Wuhan, the early epicenter of the outbreak, some continue to speculate about whether this virus or a closely related virus was present in the samples at the Wuhan laboratory. How do I pronounce this? Shi Zhengli.

VR: Shi Zhengli.

DG: Shi Zhengli, who was leading coronavirus research at the Wuhan Institute of Virology, promised to sequence the genomes of the coronaviruses in her lab and release the data, because once she does this, everyone's going to say, "OK, great. Now we know the truth. We can move forward." The latest analysis, which has not been peer reviewed, but was presented at a conference, includes data from the whole genomes of 56 new beta coronaviruses, the broad group to which SARS-CoV-2 belongs, as well as some partial sequences.

All the, say, the viruses, the viral sequences were collected between 2004 and 2021. They didn't find any new sequences which were more closely related to SARS-CoV and SARS-CoV-2. The closest known viruses to SARS-CoV-2 to date were found in bats in Laos and Yunnan in southern China. Years, if not decades, have passed since those split from their common ancestor with the virus that causes COVID-19, SARS-CoV-2.

VR: No evidence that this virus originated in a lab, as we have said many times. Someone posted somewhere on one of our sites that scientists are divided about the origin of SARS-CoV-2. No, they are not. The scientists who are divided are not virologists and don't know what they're talking about. There are a few virologists who are suspicious, but most virologists understand the data. The scientists are not divided. Bret Weinstein may be, but he's not a virologist."

DG: Oh, is that who said that "My son's friend's dad is still thinking it might have been from aliens or from the lab"?

VR: Yes, that's right.

DG: It's hard for us as scientists. How do you communicate? Are we divided about climate change? No, we are not. Are we divided about gravity or tectonic plates? No.

VR: How about the flatness of the earth?

DG: Yes. Are we divided? Are there a few people out there? Can you prove the overwhelming evidence? Yes. Always a challenge for us as scientists to communicate these things. We will try. Right now, we also have the article, “Controversial COVID Study that Promoted Unproven Treatment Retracted after Four-Year Saga.” Finally, this paper's withdrawal on the grounds of concerns over ethical approval and doubts about the conduct of the research marks the 28th retraction for co-author Didier Raoult, a French microbiologist formerly at Marseilles Hospital University Institute Mediterranean Infection.

This was the paper that led to all the hype around hydroxychloroquine. I think he had already written like a book, before he even published this, glorifying himself. A number of the study's co-authors had asked to have their names removed from the paper, saying they had doubts about its methods. This is a problem when you've got someone like this who just keeps publishing stuff that's not true. You've got 28 retractions now. It's really a problem. Should we mention hydroxychloroquine and ivermectin do not cure all ills? Actually, hydroxychloroquine probably increased mortality about 20%. This bit of unethical behavior had pretty significant consequences. There was a there was a death toll.

All right. Moving on to flu. I follow the map over time. You can start to see - that we're starting to see the activity come up in parts of the country. This data is always a little bit behind. We're starting to enter the 2024-2025 influenza season. Then we'll all get together for these December holidays and then it'll spread all across the country. If you're feeling like things are pretty good in Minnesota, just you wait.

RSV activity, it's really high in most of the country. We're really also going to get the flu and RSV at the same time.

Unfortunately, Vincent, I wish that your optimism had held, but you can actually see the wastewater levels are really starting to shoot up. I've had some people ask, what do you talk about with wastewater? I'm going to just explain what is going on here. What they do is there are these wastewater treatment plants and when we use the toilet, and we send our waste off to the treatment plants where it can be turned into water that we will then drink and shower ourselves with after being cleaned, they actually have the ability to test and see if there's levels of different pathogens.

I say pathogens pretty broadly, but we're particularly excited about viruses, but I know people have looked for other pathogens, even *Candida auris*, they look in and even parasites. When people, the community, start to get ill with a certain infection, they'll actually shed that in the urine, in the feces, depending on which pathogen, and then you can actually start to pick up activity. What's good about this, it doesn't rely on clinicians catching the diagnosis. It doesn't necessarily rely on people testing it to let you know what's going on. It's a non-biased exploratory thing.

Nobody's there at the sewage treatment plant getting SARS-CoV-2. They've gotten SARS-CoV-2 from breathing. Then this is ending up in the water. All across the country, not only are we seeing this exponential rise trajectory, but we're actually seeing activity go up. I have to say, I was in the hospital this week, and we're starting to see a number of folks getting hospitalized with COVID.

VR: At least it's later than it was last year.

DG: It's a little later, so maybe that's good, but we'll see what happens with the holidays.

VR: I should mention that this presence of flu or RSV, SARS-CoV-2, any of these respiratory viruses, they're present in your mucus, which you swallow. That brings it into the intestinal tract. That's why it's there. Flu does not replicate in the intestinal tract. I don't think SARS-CoV-2 does either, but many people do, good for them. That's how it's there. This is an indicator. For other viruses, the presence in the intestinal tract is an indication of they're infecting it like norovirus or rotavirus or poliovirus.

DG: Actually, yes, norovirus, winter vomiting diseases is also a very high activity throughout the country. I know I've enjoyed that over the Christmas holidays while visiting the in-laws, which not a good combination. Just the norovirus. I love visiting the in-laws. I don't want anyone to take that wrong, but OK.

SARS-CoV-2 variants, we still have KP3.1.1, but we've also got this other variant there creeping up, but sort of taken over there. The XEC is now about 44% nationally, the KP.3.1.1 is about 39% nationally. Those look like they're the dominant variants.

All right. Let's talk a bit more about vaccines today. Are vaccines and boosters for everyone? We have the article, "BNT162b2 XBB Vaccine for COVID-19 Among Children 5-17 Years of Age," published in *JAMA Network Open* as a research letter. We have lots of information on boosters in adults, but what about kids? Here they evaluated the Pfizer-BioNTech vaccine effectiveness in children age 5 to 17 years during the 2023-2024 respiratory virus season in a large integrated U.S. health system.

To look into this issue, they conducted a test-negative case-control analysis to look at this vaccine that is the XBB vaccine effectiveness against acute respiratory infection associated hospital admission and emergency department or urgent care visits among these kids aged 5 to 11 and 12 to 17. They're doing this out at Kaiser Permanente. Cases had a positive SARS-CoV-2 PCR or antigen test during a hospital admission or ED or urgent care visit and controls tested negative had no evidence of a positive SARS-CoV-2 test in the past 90 days.

Of 15,233 ARI, that's the acute respiratory infection visits here, children age 5 to 17 meeting eligibility criteria, 7.2% tested SARS-CoV-2 positive. In the full cohort, 1,125, so 7.4% of the kids, received an XBB vaccine by the end of April 2024. Among those aged 5 to 11 and 12 to 17, the estimated effectiveness of the vaccine, we're going to break this down against what, so was 68% and 63% against hospitalization, COVID-19 associated hospitalization admission or ED or urgent care visits. With an overall estimated vaccine effectiveness for all 5-to-17-year-olds of 65%, no COVID-19 associated hospitalizations occurred among those who received the XBB Pfizer vaccine, so zero hospitalizations.

With the lower number of hospitalizations, this age group, is this really important? They're going to do this calculation and try to figure like, does this make a difference? Hospitalizations are really low, so if you lower a lower number, is it really important? The U.S. rate of COVID-19-associated hospitalizations during this period was roughly 10.5 per 100,000 among 5-to-17-year-olds from October 2023 through April 2024.

With this 65% vaccine effectiveness, vaccinating this roughly 54.3 million 5-to-17-year-olds in the U.S. would have averted approximately 3,700 hospitalizations and they calculate 111,000 ED or urgent care visits during the respiratory virus season. It's actually quite a bit. You would have avoided almost 4,000 hospitalizations and you would have gotten rid of over 100,000 ED or urgent care visits for these kids. Giving you that numbers to do your calculation. In the U.S., we do not see a great uptake in this age group, but these are the numbers. This is the impact we could have with those vaccines.

Now the most current recommendations were out in the *MMWR* just this last week: Use of additional doses of 2024-2025 COVID-19 vaccine for adults aged the other end of the spectrum 65 or older years and persons aged greater than six months with moderate or severe immunocompromised. Recommendations of the Advisory Committee on Immunization Practices, United States 2024. In October 2024, the ACIP recommended that all persons aged 65 and over and persons aged 6 months to 64 with moderate or severe immunocompromised receive a second 2024-2025 COVID-19 vaccine dose six months after their last dose.

Furthermore, ACIP recommended that persons aged greater than 6 months with moderate or severe immunocompromised may receive additional doses based on shared clinical decision-making. Basically, they're saying for everyone in general, get a yearly shot. For some of these folks 65 and over with immunocompromised, the recommendation is get two shots a year.

VR: Now we need a COVID, a flu and an RSV shot every year.

DG: Flu shot every year, COVID shot every year. Now the RSV, we think, lasts at least two years. If you got your RSV, you're good for a little. Everyone over 50 should get that conjugate pneumococcal shot. Everyone over 50 should get a shingles shot. Talk to your doctor and make sure you're up to date with your vaccines because hey, vaccines, they actually work.

All right. Just a little thing in testing here. I'm going to tell a little bit of a story. Then my point is, people should probably have their own tests. We had a little bit of a discussion right before we started, but if you are feeling crummy, a lot of times your physician won't necessarily be thinking about COVID. They may actually not have a setup in their office to test you for COVID or the flu. We still have a lot of availability of these tests out there that test for COVID, they test for flu. Go ahead, test yourself, because if you are a high-risk individual, as we'll discuss, there are therapies that potentially would benefit you. If you don't know you have COVID until it's too late, you're not going to get that early first week treatment.

What is the early first week treatment? Number one, Paxlovid, initially based on that randomized control trial with what is it, 86% reduction in progression in unvaccinated individuals?

VR: EPIC-HR.

DG: In EPIC-HR. Now supported by over 800 real-world efficacy studies, about an 80% reduction in vaccinated individuals during Omicron. Still works. Still makes a difference. With over 50,000 people dying last year from COVID-19, with an average of over 1,000 deaths and

tens of thousands of hospitalizations, yes, we can reduce that all by, let's say, 80% if we can get folks treated in that first week.

We also have remdesivir if there's an issue, but that is IV; molnupiravir, in some contexts, convalescent plasma. Remember, yes, particularly with the holidays, if you've got COVID, I know it's inconvenient, but you're contagious. For some people who are at high risk, getting infected with SARS-CoV-2, getting COVID-19 is a little more than inconvenient. A patient in the hospital today, I really feel for this man. In his 90s, he was actually tearful when I was seeing him because this is his first infection. This is his first episode with COVID-19. His live-in aid was sick, probably with COVID. He got sick, saw the doc, thought it was bronchitis, got what you get for bronchitis these days.

He wasn't tested, so they didn't know it was COVID at that point. Got a Z-Pak, got an inhaler, got some steroids. Now in the hospital on oxygen support, oxygen was down in the 70s when I saw him in the emergency room. It's tough. Test yourself because then you can tell the doctor, "Hey, I don't feel well, and my COVID test is positive." Then you end up like this gentleman in the hospital, and that's often when people feel rotten, they get that low oxygen level. I've been saying steroids at the right time in the right patient at the right dose, so that still continues to be a little bit of a challenge, not during the first week. We have anticoagulation guidelines and pulmonary support, still is a role of remdesivir. We're using five days if we're in this zone versus three for the first week, and in some cases, immune modulation.

VR: Daniel, I think any elderly individual that presents with some kind of respiratory symptoms should be tested for COVID.

DG: That's the tough thing with viral syndromes. You really don't know whether it's COVID or RSV or influenza until you do a test. I just don't think we're smart enough to know the difference. Clinically, you can't tell them apart. The way you tell them apart is you do a test. If someone could benefit from treatment, it's ideal to get that testing done. If it's flu and you're past 48 hours, I'm not sure Tamiflu is going to make a big difference. If it's COVID and you're still in the first five days, then yes, as we've said, even in vaccinated, even in the time of Omicron, about 80% reduction in a person.

VR: For flu, there's that other antiviral.

DG: Oh, yes. What is that other one that we always forget about?

VR: The endonuclease inhibitor, which does work past 48 hours.

DG: Yes.

VR: There's no treatment for RSV, right?

DG: At this point, unfortunately, yes, you want to get that vaccine. You want to do active or passive. Passive in the young folks, active for pregnancy and older folks. Once you end up in the hospital, it's just supportive care.

All right. Long COVID, just a couple here to round it out before we get to emails. I'll continue to leave a link into the post-acute sequelae of COVID, PASC/Long COVID and evidence-based approach. There still are things that we can try. I don't feel like this is something where you just throw up your hands.

If people have noticed, life is really not fair. We have the article, "Post-acute Sequelae of COVID-19 in Cancer Patients: Two Cohorts in UK and Hong Kong," recently published in *Cancer Medicine*. Here they looked at PASC in cancer patients, and they found that cancer patients with COVID-19 consistently showed significant higher risk of major cardiovascular diseases in the UK and the Hong Kong cohort. They're a little bit different. It's about twice the risk, so it has a ratio of 1.8 in the UK. It's 1.4 in the Hong Kong.

Death due to cardiovascular was more than fourfold increased in the UK cohort, about doubled in the Hong Kong. All-cause mortality we see similar, almost fivefold increase in the UK and almost doubled in the Hong Kong. Cancer patients at advanced ages or severely infected had higher all-cause mortality risk. You're ready for this? Associations between COVID-19 and cardiovascular disease became insignificant for fully vaccinated patients.

VR: It's good news.

DG: The vaccines really, really made a difference here. All right. This is an opinion piece, "Skeletal Muscle Adaptations and Post-exertional Malaise in Long COVID," published in *Trends in Endocrinology & Metabolism*. I will say a well-referenced opinion piece. As excited as I am, I want to point that out. Now the most prevalent Long COVID symptoms are fatigue, brain fog, cognitive impairments, muscle pain, and post-exertional malaise.

In this article, they highlight intrinsic mitochondrial dysfunction, endothelial abnormalities, and a muscle fiber type shift toward a more glycolytic phenotype as main contributors to the reduced exercise capacity of Long COVID. Now, the mechanistic trigger for physical exercise to induce post-exertional malaise is not known, but rapid skeletal muscle tissue damage and intramuscular infiltration of immune cells contribute to the PEM-related symptoms.

Going a little bit more into what we read here, patients with Long COVID exhibit a reduced aerobic capacity and earlier onset of lactate accumulation during exercise. This is not in their head. This is really going on. The reduced exercise capacity in patients with Long COVID has most often been attributed to alterations in skeletal muscle, with really only minor impairments of the pulmonary and cardiac systems. In this article, they point out that dysregulated breathing and improper heart rate responses indicate that a dysfunctional autonomic nervous system might be a contributor. Again, its alterations in skeletal muscle structure and function in Long COVID, such as mitochondrial function and content, capillarization, and muscle fiber size and type, seem to really contribute to this reduced exercise capacity.

It's really a challenge. We have ongoing trials, but it's really a challenge where you're trying to avoid triggering post-exertional malaise, but at the same time, you want to avoid deconditioning. You do want to find whether it's low-impact yoga, whether it's walking. A lot of times, this takes a lot of back and forth with patients to really find what amount of exercise they can safely do. As we learn more and more, just growing parallels with all we've learned

from ME/CFS. All right, I will close it out there. No one is safe until everyone is safe. We are right in the middle of - what are we in the middle of, Vincent?

VR: Our fundraiser for *MicrobeTV*.

DG: Where for November, December, January, we double your donations up to a potential maximum donation of $20,000 to support the great work of *MicrobeTV*.

VR: As you know science is under siege in the U.S., and if you want to get real science, you need us, *MicrobeTV*, and all our science podcasts. Please support us. It's time for your questions for Daniel. You can send yours to Daniel@microbe.tv. Portia writes, "I want to thank you for telling us about PAXCESS, which came in handy this week. My 93-year-old mother, who managed to not get COVID all this time, tested positive this week. She just had a sore throat and cough. I did not think to test her for COVID until my husband asked. We were surprised she tested positive. We did the test twice. We were able to get a video appointment with her doctor's office and get the Paxlovid prescription.

However, our first visit to the pharmacy, we were told her Medicare did not cover prescriptions. It was going to cost $1,726. Luckily, my husband came to the rescue, remembering what was mentioned on *TWiV* clinical update, the PAXCESS program. Good to the end of 2024. It turned out it was very easy to enroll online. After answering a few questions, they emailed the voucher immediately. We were able to get her Paxlovid, and hopefully all will be well. Thank you, Dr. Griffin and *TWiV*."

DG: Oh, no, this is great. For several reasons. One, most importantly, the access to the Paxlovid and shining a light on this PAXCESS program. Also, actually, that the husband was useful, right?

VR: Yes, highly unusual. Do you have any idea whether there's going to be a continuation of the PAXCESS program?

DG: I believe there will be a renewal. We'll keep people updated. I'll keep an eye on that.

VR: Bob writes, "I'm concerned that under the new administration, the federal government may become an untrustworthy source of infectious disease and vaccine information. What alternative sources would you recommend?"

DG: I wish, Vincent, that there was some organization that maybe they could produce, like YouTube videos or podcasts on like a regular basis, maybe like weekly, and they could just keep people updated on all this important stuff. What do you think?

VR: I know one is *MicrobeTV*.

DG: Yes.

VR: Bob, you wrote to us. If anything, this clinical update it will keep you up to date on infectious diseases of all kinds.

DG: Yes, we will. We'll keep up to date. Send us your questions, and we'll continue to answer them.

VR: It's a good point. Maybe compile a list of trustworthy podcasts about infectious diseases. We have a bunch here at *MicrobeTV*. We have *Puscast*, for example. There may be some others that are useful.

DG: Febrile. I was listening to *Febrile* by Sara Dong earlier today. There's a number.

VR: Hailey writes, "It's my understanding that the U.S. stopped OPV use in the year 2000." That's correct. "I'm pretty sure I got OPV in the early '90s and my mother confirmed I got some vaccine by mouth." That's the only one that you would get by mouth, right? OPV.

DG: Yes.

VR: "Should those of us who got OPV consider getting IPV as a booster?"

DG: This is a good one, Vincent. You and I should talk about this. We covered the data last week, and I really liked that. I actually got some feedback from some listeners. They really felt that was the first time they really understood what was going on with polio and the different vaccine options. In Europe right now that they're seeing it in the wastewater and they're realizing it's circulating but at a low level. We talked a little bit about when we said, "Oh, once you get your vaccine, you're good for life." Part of the background was that there was probably constant boosting in the environment. Now it's at a low level. In Europe, they're actually going to start in certain countries, recommending every 10 years getting an IPV booster.

VR I got IPV in 1955 and then I got OPV in 1962 when it was licensed and nothing since. However, I did work with polio virus for many years. I probably boosted myself. I'm not a good case for this. I think it's a good point of whether, of how long the protection lasts. I'm not sure we really know. Certainly, if you go to a polio endemic country, you should get boosted.

DG: That's definitely the recommendation. I think that's fair is that I don't know if we really know. I don't think there's much of a downside to the strategy of once every 10 years. We're going to have to see. The thing I will say is we're not seeing, we really haven't seen polio, the disease in people that get IPV, even as far back as the '50s and '60s. It may still be lifelong.

VR: When you go to Africa, you don't get polio vaccines, do you?

DG: I don't, actually. No.

VR: The last one you got was as a baby, right? Your first years of life.

DG: Back in the early '90s, I got oral too. Because that was back then, that was one of the recommendations.

VR: Toni writes, "Your appearance on TWiV is my go-to for the latest, most reliable information on COVID. It's been immensely helpful to me in navigating the pandemic. Many thanks to you and Vincent for your mission and the work you do. Here's my question. My

husband and I are both taking immunosuppressants for autoimmune diseases. We are trying to pin down best practices to find the sweet spot between avoiding exposure and still seeing family and friends. On rare occasions, we might meet a friend for a meal in a less than fully occupied restaurant. How likely are we to become infected from a person across the table? Should the friend pass a COVID test beforehand?" Why don't you answer that one first?

DG: This is a good question. I think part of what makes it good is things have changed over time. Let's go through what's changed over time. First is early on in the pandemic, some of the models were estimating that somewhere close to half of the transmissions were occurring from asymptomatic and pre-symptomatic individuals. Also, early on, we probably saw in some of the estimates that I've seen recently, maybe a third of patients that were testing positive never had any symptoms. We were seeing a lot of pre-symptomatic transmission. We were also seeing folks who were completely asymptomatic the whole time and participating in the transmission chain.

Nowadays, with immunity, with vaccinations, we're actually seeing that less than 10%. Single digit individuals remain completely asymptomatic despite testing positive. Also, what we're seeing is people tend to get symptomatic before they're infectious to others. This is encouraging. It used to be you're sitting there at a restaurant. The person across the table feels fine. The next day, they get symptoms, and then you were there during this high period of transmission. We're seeing a lot less asymptomatic transmitters out there.

That's helpful. That's one thing. If you're sitting across from someone, they feel fine, your chances is much lower. The other is, of course, this timing of - you don't go out when it's raining. It's starting to rain. COVID numbers are starting to shoot up. Last couple months, it really was a great time to get out there with friends and family and enjoy these things. Next month or two, we're going to have really high rates, so balancing all these things.

VR: All right. Next question. If we have a houseguest who has traveled to join us, should that guest take a COVID test every day of their visit? Even if they pass a test on their arrival and do not mix with others, is it possible they could carry an infection in subsequent days?

DG: Yes. There still is an incubation period. There still is a time from when you're exposed to when you actually become symptomatic, when you become infectious to others. That actually has changed over time. Based on the contact tracing early on, it was about six days. Now, the latest estimates, it's down to about three or four days from exposure. Then we see something like 98% of folks will get symptomatic within, I think, it's 11 days was when I was reviewing the data on this. Yes, it is possible they travel; they get exposed; they start to get symptoms. Then, as I talked about, with a much lower incidence of asymptomatic transmission and staying asymptomatic, it's a reasonable strategy to just have them see how they do. If they feel that scratchy throat, anything like that, yes, go ahead and get that morning test.

VR: Finally, Vincent writes, "Norovirus levels on the Wastewater SCAN Dashboard appear high compared with the past two years. We are nearing the peak of last year and it's not even January yet. Can you think of any reasons why this might be the case and if you've seen a lot of it in the clinic?" This is not me, by the way.

DG: [laughs] Different Vincent. I mentioned just a little bit earlier. Yes, we're actually at really high levels with norovirus at the moment. I don't know if the timing had anything to do with our recent giving of thanks and eating of turkeys. We've got folks in the hospital. We're really at pretty high levels with norovirus.

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

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

[music]

[00:48:24] [END OF AUDIO]