This Week in Virology

TWiV 1186 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.

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From *MicrobeTV,* this is *TWiV, This Week in Virology*, Episode 1186, recorded on January 23, 2025. 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 feel so casual next to you, Daniel. You've got a nice jacket there.

DG: I'm all fancy. I've got my jacket on and my biohazard bow tie.

VR: Those are biohazard symbols. I see. Very nice.

DG: It seems sort of appropriate for where things might be headed.

VR: Yes, we're in a biohazardous position in this country for sure.

DG: Yes, and we're going to talk a little bit about - I am going to try. Can you imagine this? I am going to try to be apolitical because you can't. You failed, Vincent.

VR: No, you're very good at being restrained.

DG: I will try, but let me start off. We've got a quotation. We've got a lot to talk about today. I will start with a quotation from Thoreau, and I have mixed feelings about Thoreau. Yes, I've been to Walden Pond. I walked around it. It's really nice. It's only about two miles from Concord, so it's not really in the rural wilds that I imagined when I first read the book. It's close enough that you can walk home and have your mother make you lunch every day and do your laundry. Anyway. Thoreau's quotation, "Rather than love, than money, than fame, give me truth."

VR: Oh, yes.

DG: Again, this is like what a contradiction in people in - Anyway. That's one of the tough things, and I remember it was someone who was saying one of the things they really liked about our show was that we are really committed to sharing the truth, whether we like it or

not. We're going to keep that up. No spins, no partisan bents here. I want to start off by Marburg, and I hadn't mentioned this because I was waiting to find out the truth. People were reporting on this. Initially, we were hearing maybe everything's negative, but we finally read in Reuters and the AP that, yes, Marburg, Tanzania confirms outbreak of Marburg virus.

Tanzania's president, Samia Suluhu Hassan, just this past Monday, confirmed that there is an outbreak of the deadly Marburg virus in the northwest of the country, with one confirmed case so far, actually, but a number of deaths. It seemed like it was Marburg, and we read that laboratory tests conducted at Kabaile Mobile Laboratory in Kagera and later confirmed in Dar es Salaam, identified one patient as being infected by Marburg virus. The president said at a press conference that was attended by the World Health Organization Director-General Tedros, and a number of people have already died as I mentioned.

The initial testing had been negative, but then they actually were able to make the diagnosis. Just a little bit, what is Marburg for our listeners? Think of Ebola. It's very similar. It's a filovirus, and it has a fatality rate as high as 88%, so it's a hemorrhagic fever virus that causes this hemorrhagic fever disease. The WHO has already released $3 million from their contingency fund for emergencies to support efforts to contain this outbreak. We'll be talking a little bit about the WHO later.

VR: Daniel, were you just in Tanzania? Was that somewhere?

DG: I was actually. What a coincidence, right? I was in Uganda when the last Ebola outbreak was going on. I had to be cleared by the CDC once I had gotten back because though I try to avoid hanging out with people with hemorrhagic fevers, I ended up in Jinja where there was a couple of brothers who had gotten in the back of a pickup truck and snuck out of the Ebola zone, ended up in Jija where I was with a bunch of Doctors Without Borders. There's Lake Victoria, and this is the other side, the west of Lake Victoria there.

All right. Yes, I was just there. I had nothing to do with this. OK, mpox. New cases of mpox variant clade Ib detected in England. We've been covering this for a while, and the whole sort of silliness, the idea that things like this are just going to stay in Africa, particularly with all the anti-vax sentiment. Now Britain's health secretary, security agency, also on Monday confirmed that there was another case of the variant clade Ib detected in England. This is the sixth case that they've detected so far since October of last year.

Speaking of the WHO, our listeners are likely aware of the executive order, a lot of executive orders, but this one, January 20, 2025, withdrawing the United States from the World Health Organization. This will potentially involve the U.S. leaving the World Health Organization, pausing the future transfer of any United States government funds, support, or resources to the WHO, recalling and reassigning United States government personnel or contractors working in any capacity with the WHO.

I guess here's the part I'm going to go into. I read through the whole executive order, and one of the things in there, after you read all this, is that they are requesting, it's being requested in this executive order, that we, the United States, identify credible and transparent international partners to actually assume the necessary activities previously undertaken by the WHO. There's this idea that the director of the White House Office of Pandemic

Preparedness and Response Policy will basically review what's been going on, and they're going to replace the WHO functions, basically, by a U.S. global health security program.

VR: It doesn't make any sense.

DG: It's an interesting idea. I think that where this is coming from, if you read more, is that our current president really feels like the WHO fell down in the early days of 2020. A lot of discussion about, how early was it - Could it have been known that there was human-to-human transmission? Could things have been done differently? This whole idea that maybe the U.S. takes that 16%, 18% of the WHO budget, which is a lot of money, and they basically just build something here in the United States that answers to the people and the government here and replace a lot of what the WHO was supposed to have been doing. That's the idea.

VR: First of all, this idea that you said WHO screwed up, therefore, we're leaving, that's stupid.

DG: Remember, I didn't say that. Other people said that.

VR: You work with them to fix what the problems are. I just want to remind everyone that in the early months of 2020, Trump said COVID would be over pretty soon. We have 12 cases. They're soon going to be gone, and that's it. Talk about screw-up. Give me a break. Let's get him out of office because he screwed that up. The WHO harvests health data from all over the world. This outbreak in Tanzania, we're not going to know anything about it once we're severed from WHO, and we need that information because travelers are going to be coming back, and we need to know. You could set up anything in the U.S. that you want, but you're not going to get information about infectious diseases and other issues in other countries, and that's the value of the WHO.

DG: Yes. There were some commentators who made some comments. One is that this doesn't just happen overnight. You give notice. You need to get approval from Congress. The U.S. has to see out a one-year notice period before they leave. They need to continue to meet the financial obligations. There was a WHO comment on this announcement, and so I thought I'll share this and leave in a link.

"The WHO regrets the announcement that the U.S. intends to withdraw from the organization. WHO plays a crucial role in protecting the health and security of the world's people, including Americans, by addressing the root causes of disease, building stronger health systems, detecting, preventing, and responding to health emergencies, including disease outbreaks, often in dangerous places where others cannot go. The United States was a founding member of WHO in 1948," emphasis added by me, "and has participated in shaping and governing WHO's work ever since, alongside 193 other Member States, including through its active participation in the World Health Assembly and Executive Board.

"For over seven decades, WHO and the USA have saved countless lives, protected Americans and all people from health threats. Together, we ended smallpox, and together, we have brought polio to the brink of eradication. American institutions have contributed to and benefited from membership in WHO with the participation of United States and other member states, WHO has over the past seven years implemented the largest set of reforms in its history to transform our accountability, cost-effectiveness, and impact in countries. This work continues."

VR: The point here is that the U.S. contribution is not really that much money. Trump says they're ripping us off, but that's nonsense. It helps them do their work. Not all of those 193 member states have the money to make it work, and the U.S. does. By withdrawing, they're going to mess up the whole organization. Why does one person since 1948 think it's a good idea to leave WHO? Someone unhinged, I think.

DG: I think you make a good point with regard to this isn't just about the 16-18% of the budgets and just the money. This is also an organization that our CDC, our agencies, coordinate with. When there are these responses, when we're trying to find out what's going on in Tanzania and how to respond, when we're worried about mpox in Africa, which we really don't want spreading all around the U.S., even if you don't care about what's going on in Africa, these coordinated efforts help keep everyone safe.

All right, moving on to the next one. Actually, this next headline had me quite concerned. "Trump Officials Pause Health Agencies' Communications, Citing Review." I actually was able to see some of these communications directly shared with me by some of the folks that received them. "The Trump administration has instructed federal health agencies to pause all external communications, such as health advisories, weekly scientific reports, updates to websites, and social media posts." I'm now realizing, Vince, I'm going to get someone in trouble because they're going to call me up. "Who are these people that shared this stuff with you," because you weren't supposed to do that.

They're just looking over their shoulder. The pause on communication includes scientific reports issued by the CDC, known as the *Morbidity and Mortality Weekly Report,* the *MMWR.* We talk about those all the time. Advisory sent out to clinicians on CDC's health alert network, which we rely on to real-time updates on what we need to worry about. Data updates to the CDC website and public health data releases from the National Center for Health Statistics. I want to point out, the CDC was scheduled to publish several *MMWR* reports this week, including three about the H5N1 avian influenza virus outbreak. In the article, they do give a little bit, I could say.

They point out that under the Biden administration, the White House and HHS officials extensively reviewed material related to the coronavirus before it was released, but not to the point where we're hearing that scientific meetings have been canceled without being rescheduled. The end of February meeting of the National Vaccine Advisory Committee, that was canceled without being rescheduled. The Presidential Advisory Council for Combating Antibiotic Resistance Bacteria was scheduled for the end of this month. It's been canceled without rescheduling. Yes, a lot of really important communications that I know we share and our listeners like to hear about are basically not going to be shared.

VR: Yes, *MMWR* and emerging infectious diseases, that's terrible if they don't resume. I just suspect that they're going to resume with some censorship in place and we're not going to be sure of getting accurate information anymore because they're going to have administration lackeys pouring over and I doubt there's anyone that understands any of it.

DG: We've heard that it's at least until the end of next week that everything is on hold, at least until the end of next week, we'll see what happens. In the meantime, avian flu, I'm going to share a link to what to know about protecting your cat from bird flu. The bird flu issue is

continuing. The tally is up to 70 cats so far infected with H5N1, so that's quite a bit. I guess I'm also going to not be able to talk much about other updates. The avian flu outbreaks in Georgia, Virginia, Maryland, Oregon, Missouri, additional detections in six more domestic cats, the harbor seal with H5N1 in Illinois.

The cervil. What is a cervil? A serval apparently in Michigan, detection in another herd in California. We're up to a national total of 930. In the future, we'll be allowed to hear about such things. Yes, I think there was some discussion about the price of eggs, getting those prices of eggs down, but with the culling of millions and millions of chickens, we're now below the number of chickens needed to meet the demand and so price of egg is two to three times what it was a year ago today. All right. You did a reasonable job there of staying bipartisan, Vincent.

VR: Oh no. If you go back and listen to what I said. Daniel, all these things that we do from CDC like the flu view and I don't know about wastewater, is all that information going to stop?

DG: That's what we're going to find out. I'm going to give people information this week and then next week, we're going to see. We may just be on pause. We may just be sharing what we're seeing locally on the ground, doctors communicating among ourselves. We are probably, at least this is, we're not going to get updates on the data we're about to talk about. Let's talk about the data that we still have. I grabbed this stuff before the communication blackout, before the web went dark in more than one way. Influenza A, we are still at high levels of influenza A. If you look at the map, basically, we're high across most of the country.

I'm hoping when you follow a little bit of the curve that we might have crested that peak of influenza A. We'll see next week if I can give any updates there. A lot of interest actually, Vincent, on baloxavir, XOFLUZA. I want to share an article, and this is the article, "Comparative Effectiveness of Baloxavir Marboxil and Oseltamivir Treatment in Reducing Household Transmission of Influenza: A Post Hoc Analysis of the BLOCKSTONE Trial." This came out a few months ago but it was in May. It was not during the flu season. Maybe those flu publications, you want to save them for October when we care. We don't care in May. I was talking to a patient earlier this week and he said that if he got the flu, he wants the good stuff. Now what is the good stuff?

VR: Is that the 25-year-old?

DG: No, this was an older individual.

VR: No, I'm talking about the 25-year-old Scotch, you know.

DG: Oh, yes. He wants the good stuff. The 25-year-old. The aged XOFLUZA. I think all our listeners after I discuss this article, my wife, his wife, his daughter, they're all going to want him to get the good stuff too and maybe they're even going to be willing to search around for the good stuff because this article doesn't just talk about the advantage of baloxavir, XOFLUZA, for the index patient but for people potentially exposed. We know from a prior *New England Journal of Medicine* article that if you give baloxavir to folks who are exposed, that it actually can protect those household contacts.

It was about 86% reduction in getting the flu if the people exposed got it. That's better than Tamiflu. Here in this post-hoc analysis, they're actually saying, "What if we treat the index patient? What if we treat that guy who wants the good stuff with baloxavir versus Tamiflu? How good are we going to be at reducing the household contacts getting flu?" What they actually found here was that you actually get a better reduction in the relative risk of these secondary attack rate cases by using baloxavir versus Tamiflu.

If you looked at the household contacts of the index case treated with baloxavir, 10.8% versus about twice that when you looked at treating the index person with Tamiflu, and that was 18.5%. Relative reduction of about 42%. I'm going to quote a fellow, Robert Krug. I don't know if our listeners are familiar with Dr. Krug. "NIAID has spent large amounts of money to develop an influenza antiviral to replace the weak oseltamivir antiviral paradoxically now that the better baloxavir," I appreciate the alliteration, "antiviral is available. It is not widely used in the United States."

VR: Last year, Dr. Krug wrote us a letter praising baloxavir, saying it's basically better than Tamiflu. That got the conversation going. Recently, he sent us another letter because we've been talking about it. People should really ask for it because it is better than Tamiflu. I think it's one dose, right, Daniel?

DG: Yes. It's one dose. You just take one pill and you're good. Sara Dong, and I talked about this on the *ID Puscast* and why there's an issue with the art of medicine. This was the, why is a Z-Pak five days? Because you don't need to do that. In the hospital, we're just like take one dose a day for three days. It's in your system for two weeks. By the time someone sees a doctor, they've been sick for a day or two. They see the doctor. Now a lot of telehealth, they see the doctor on a computer even.

They get their prescription. It's three days later, four days later. They're still not better, but they're taking like a five-day medicine like a Z-Pak or Tamiflu. You could just be like, "Just finish your medicine. It's going to take you time to get better." Now, the baloxavir, they took one pill. They're like, "Doc, I took that one pill. It's the next day. I'm not better. I need more."

VR: Oh, boy.

DG: Yes. Maybe there's a couple of things. Yes. Catch your name. XOFLUZA sounds like the girl that you don't want to bring home to mom, I was thinking. Don't bring her home. She's a XOFLUZA. Give it a better name, guys. It's got an X, but just after that, it falls apart. Then maybe there's some way to, like, microdose it over time. Now I feel like someone else. Yes. There's a little bit of a marketing issue here. All right. That's XOFLUZA and baloxavir. Moving on to RSV. Again, we're still at a high level with RSV, really similar to where we were last week.

VR: This map, the surveillance map is from CDC. We'll see if that continues.

DG: Yes. Probably the same map next week if even there's even a map, if they even allow the websites to just stay static versus go dark. Then again, COVID. We look at these CDC maps, but we also fortunately have a wastewaterscan.org map. That should be up and running still, fingers crossed, keeping us at high levels with SARS-CoV-2 virus detections in the wastewater. Unfortunately, we are starting to see more states where that mortality 2% to 4%, about one in every 25 people who died this last week, died due to COVID.

I think that's very sobering. People think, "Oh, COVID, it's just a cold." We're talking about 1,000 folks a week dying from, "just a cold." If you follow the wastewater trends that we've done over time, it looks like we may have hit the peak. Again, we had a winter peak. Sort of been following this over, going all the way back to early 2022. We seem to be falling into this cycle of a summer peak, a winter peak, summer peak, a winter peak, and then just varying. If the summer peak's not so bad, the winter peak seems worse. If the summer peak is pretty bad, maybe the winter peak isn't quite as bad.

VR: It seems lower if this is the peak that we're going to have. It seems lower than our summer peak so far.

DG: Yes. Then, last year, we had a small summer peak and a much higher winter peak. We'll see where this goes. We'll also see, again, that's CDC data. That's the national trend data from the CDC. I'm hoping we keep getting that. All right. We will still get publications in the ID journals. I wasn't sure where to put this paper in, but I discussed it on *ID Puscast*. I thought I'd put it in here as well. This is the article, "Host-microbe Multiomic Profiling Identifies Distinct COVID-19 Immune Dysregulation in Solid Organ Transplant Recipients," published in *Nature Communications.*

This was sent in by one of our listeners. I understand the senior author, Chaz Langelier, is not only a *TWiV* fan, but he's also a fellow windsurfer. He's got a 2-year-old he's hoping to get into the sport. That might be a little bit young. Wait till she's 4, Chaz. This study looks at solid organ transplant recipients with acute SARS-CoV-2 and does all this profiling. Basically, what they're going to see is you end up with higher levels of the SARS-CoV-2 RNA. You end up with this sort of delayed impaired viral clearance.

The most interesting finding, I think, in the paper was that the solid organ transplant recipients. You're thinking these people are immunosuppressed. They actually have this hyper-inflammatory innate immune signaling at the transcriptional and protein level. Really the opposite. You're thinking immunocompromised. In the discussion, I tried to pick up what in this article is most relevant to our practicing clinicians. Our listeners may remember our discussions of toci, tocilizumab, and the targeting of IL-6.

In the discussion, they point out that in the non-solid organ transplant control patients, you do see that high IL-6 that we've seen before. The solid organ transplant recipients, they have this early innate elevation, but they don't really have as high an IL-6 level. Things like tocilizumab, JAK inhibitors may not really apply, may not have the same impact on these folks. We tend not to use them anyway because they're already, the immune suppression. Just thought that was interesting.

VR: What immunosuppressants do the solid organ transplant recipients get?

DG: A lot of those, I'm remembering the pronunciation of these last time. They might end up with mycophenolate. They might end up with - A lot of it is T cell focused. tacrolimus, things like that.

VR: It's not surprising that they still have an inflammatory response because that's not being targeted, right?

DG: It almost makes sense when you think it through, because they're mainly trying to target T cells in the adaptive response. They're not really targeting the neutrophils, the innate part of. Maybe it makes sense. Then, yes, I think the implications for treatment.

Talking about treatment, we just shared that we're seeing mortality across the country and COVID early viral phase. This is really our opportunity when we can have the biggest impact. In the U.S., number one, based on our society recommendations, is Paxlovid. We've talked about the reductions there in the RCT and the growing number of real-world efficacy studies.

Here is actually an open-access article published in *Signal Transduction and Targeted Therapy*, and it is entitled "Real-world Effectiveness and Safety of Oral Azvudine Versus Nirmatrelvir–ritonavir (Paxlovid) in Hospitalized Patients with COVID-19: A Multicenter, Retrospective, Cohort Study."

What is azvudine? It's a broad-spectrum RNA virus inhibitor that is metabolized intracellularly into an active 5'-triphosphate metabolite, which specifically targets the RNA-dependent RNA preliminaries of SARS-CoV-2, let me say specifically, but it becomes incorporated during viral RNA synthesis, and it's going to interfere with viral replication. Actually, this drug was initially looked at as an HIV therapeutic, as an anti-cancer drug. Now, this drug, azvudine, is actually approved. It, along with Paxlovid, was widely used to treat patients with COVID-19 in China. Here, what the investigators are going to do is they're going to compare what's the efficacy, what's the safety, these two medications.

They initially start, they look at 40,876 hospitalized patients with COVID-19 from 11 hospitals in a couple of provinces in China. You start off with this big number. As you can see, as you go through, most of the folks get excluded because either they're pregnant or they didn't receive either of the treatments or they had severe liver or kidney disease. Ultimately, you end up with about 7,000 getting the azvudine. You end up with 1,202 getting Paxlovid. They do this matching. They look at a couple of endpoints. One is composite disease progression.

You can follow the curve. The curves look really pretty similar over time. A little bit of separation here and there, but really doesn't separate much out. Then if you look at Figure 2A, I believe it is, they look at all-cause death and we actually start to see some separation between the azvudine and the Paxlovid groups over time. The separation really starts after the third week, so it's kind of a late. Then just a couple of things about this. In this cohort, the vaccination coverage was about 70%.

All right, so about 32% of the folks are unvaccinated, and they're going to conclude that the azvudine is non-inferior to Paxlovid. Actually, there's about an 18% lower risk of all-cause mortality for the azvudine. The interesting thing is when you look at the subgroup, a lot of these folks that ended up getting treated also had cancer, malignant tumors. If you look specifically at that subgroup, it was about a 70% hazard ratio reduction if you were jumping in and a composite disease progression reduction of about 46%. I don't know if this is ever going to make it into the U.S. market. It's a once a day. It's got some benefits, but.

VR: This is not licensed in the U.S., right?

DG: True. In China, it's actually still under an emergency use access. I understand it hasn't gotten the full licensing there yet.

VR: It's an oral drug, right?

DG: It's an oral drug, yes.

VR: Based on these data, would you use it in your patients?

DG: It looks like a great alternative. Yes. It seems like it was very well tolerated. Seems like it was tolerated maybe even better than - because everyone always complains about that taste in their mouth with the Paxlovid.

VR: Then this one does not have a CYP3A inhibitor in it, right?

DG: I was trying to look to find that. I do not think it has the same drug-drug interaction issues. It seems like it wouldn't, if you just think about the mechanism or anything else. It should be nice, right? Number two, we still have remdesivir. Everybody got comments like, "Why do you still talk about remdesivir?" Remdesivir in the PINETREE study, that was the first week, it's a pretty similar efficacy that we see with Paxlovid. It's, again, you don't have that CYP3A, so the cytochrome interaction issues.

It is an oral. It is IV. It's three days. Still a role there. Molnupiravir, convalescent plasma, but really just only in certain contexts. As far as the second early inflammatory phase, we're still seeing folks get admitted during that second week with hypoxemia. Got consulted on another not-so-young lady today. This is where we consider steroids for folks that are hypoxemic, anticoagulation, pulmonary support. Some benefit if you're still within the first 10 days with remdesivir, and then immune modulation in certain contexts with toci and the IL-6 blockers.

All right, late phase, a couple of things to talk about here. I continue to leave a link into the "Postacute Sequelae of COVID (PASC or Long COVID): An Evidenced-Based Approach," in *Open Forum Infectious Diseases*. There are a number of centers that folks with Long COVID can reach out to. We've got one at Columbia, Mount Sinai, NYU. I also want to leave in a link to a website that a number of us have volunteered our time to help with, *Long COVID the Answers*, like we've discussed this before. David Putrino just did a couple of episodes.

I think I may have been one of the first ones to post these freely accessible videos that people can listen to, try to get a better sense. Also, a plug for this Long COVID recovery program that you can sign up for. It's done by Zara Dureno. She's a licensed occupational therapist specializing in Long COVID. There is a minimal fee. I'm hoping it's not a barrier to people. If it is, let me know because we should try reducing. I think it's like $39 for these five-and-a-half hours of content. She herself has recovered from ME-CFS. She's a very, I think, caring and knowledgeable individual. For a lot of folks, this is a nice resource to help you after you've been gaslit and all the other things that unfortunately folks that have experienced.

I will finish off this section with, maybe more important now than ever. No one is safe until everyone is safe. Our organization Parasites Without Borders just points out that really diseases do not respect borders. You can't just sit in your one country and think that you're going to be safe behind your wall. No one's safe until everyone is safe. We're going to need your help more now than ever, because it looks like a lot of us are going to have to pick up the slack if the government is going to step away from these things. Go to parasiteswithoutborders.com, click Donate. Every small amount helps. The large amounts

help too. We are still in our *MicrobeTV* fundraiser, November, December, January, where we'll double your donations, trying to get a donation of up to $20,000 for *MicrobeTV*.

VR: It's time for your questions for Daniel. You can send them to Daniel@microbe.tv. Amy writes, "I've referenced your article, 'Postacute Sequelae of COVID: An Evidence-Based Approach,' multiple times because it provides such useful and practical information. I'm particularly interested in the use of these Bifidobacteria-containing probiotics for treating fatigue. The article you referenced in your review highlights a gut microbiota-derived synbiotic formula, SIMO1."

"However, it seems this formula was developed as an experimental treatment for a clinical trial and isn't currently available on the consumer market. What do you recommend for individuals suffering from Long COVID fatigue? I'm looking to increase my intake of probiotics through supplements and probiotic-rich foods like kefir and kimchi. By the way, I even made my own kimchi. It was a fun experience." Let's take that part first.

DG: Yes. The first thing, it's reminding me of is my daughter Daisy when she went on her make her own kimchi odyssey, and all the bottles of stuff around the house. OK, PTSD from that. The SIMO1 is an interesting product. It is available in Hong Kong and it's a pro- and prebiotic. In the dosing, you get about 10 billion bifidobacterium, colony-forming units twice a day. Then you're also getting certain things in there that are going to help promote the growth of the Bifidobacterium.

How do we do that here in the U.S.? There is a company, Align. I don't get any money from them, but they could send me money. I'd be OK with that. They make a product called 5X. It's a Bifidobacterium. Each pill has five billion of the Bifidobacterium colony-forming units. What you do is you take two pills twice a day. Then we'll talk in a second about modifying your diet or get that prebiotic approach. A lot of folks, what you're doing is it actually matters. It's not just here's like good bacteria. You want the right bacteria. The studies that I reference, people end up with a depletion of this particular bacteria, the Bifidobacteria. You don't want to just give lactobacillus, not just anything.

Sometimes, when you start this, you may actually get bloating as you're taking over the gut microbiome with this versus the other. You might start off with a five billion, one pill once a day, one pill twice a day. You're going to get up to two pills twice a day. Then a lot of modification in the diet as well, because this is a bacteria that will do well in what we really think of as a healthy diet. A diet that's low in saturated animal fats, low in simple sugars, low in all these ultra-processed foods, and the like. A combination of the Align 5X, two pills twice a day, and then some of the dietary adjustments.

VR: Her second question is about vaccinations, "because I'm keen to avoid reinfection. I've opted to get vaccinated twice per year. Until my last dose I stuck with mRNA vaccines. Last fall I got Novavax. Given its potential for longer durability, would you recommend continuing with Novavax for future doses? Thanks for all you do. I'll definitely need *TWiV* more than ever in the next four years."

DG: I ended up with Novavax this fall, as did my family members. There were certain advantages, one is no reactogenicity. I joked about the problem is I used to be able to say,

"Oh, I got my Moderna shot. I need to lay low this weekend." My wife knew better. When I tried that, she's like, "You're fine." I'm like, "All right, you're right." No, we've talked about some of the data either side. If you tolerated Novavax and did well with that, it's an excellent choice for you to think about going forward.

VR: Remember, Amy, vaccines don't prevent infection, they prevent moderate to severe disease. Rich writes, "What percent of unvaccinated individuals contracting poliovirus will actually develop poliomyelitis?"

DG: This is a great question, and I appreciate you threw some numbers at me for it, Vincent, because it actually it matters what type of polio you're talking about. Is it type 1? Is it type 2? Is it type 3? The number of cases, and even the percent of paralytic cases, depends which type you're talking about. We'll start with type 1. Type 1, we say it's about one in 200 infections you'll end up with a symptomatic case. Most of those are going to be paralytic, Vincent, is that fair?

VR: The 0.5 to 0.6 is the paralytic cases that per 100 infections.

DG: Yes. Then when you move to type 2, it's about one in 2,000. It's less. It was here in the in the U.S., in New York. It's actually in other parts of the world. The issue is that so if you see one paralytic case, you're saying there's 2,000 other infections out there that didn't. Then when you end up with type 3, it falls one in 1,500 or so. Doing the math in my head.

VR: Len writes, "Just listened to your recent podcast covering norovirus spread. Thank you. Your weekly updates are extremely helpful. Given the challenges of preventing the spread of the Ferrari of viruses, is it possible or is there any interest in a vaccine? I would certainly be willing to pay for such a vaccine before taking a cruise."

DG: Yes. Let's talk about norovirus again. I like norovirus. Yes, I don't like having it, I don't like people getting it, but it's an interesting virus. Yes, there there's definitely interest and there actually are ongoing trials. All the approaches you would think about. MRNA, attenuated, so they're looking at a number of different vaccinations. One of the interesting things, is how long are you protected? Because we always sort of look at people get infected, what immunity do you generate? There's about 30 different types of norovirus.

Initially, we said, "Oh, you're some degree of immunity for a year or so," but actually it looks like it's somewhere five to eight years, but it also depends upon age. Kids don't seem to get as long-lasting immunity. People in that 20-to-60 probably get like eight years after one of the 30. Remember, you got 30 choices to pick from. There's some cross-reactivity, some protection between the different. Then as we get older, we don't really have as robust or long-lived. Yes, miserable disease and they are working on some vaccines.

VR: Roberta writes, she sends a link to a wonderful letter by Senator Elizabeth Warren to RFK Jr. in which she says, "You basically are not qualified to head HHS and provides incredible referenced statements to counter all the anti-vax nonsense that he has promulgated in the past years." I was very impressed with this letter, Daniel.

DG: I read this letter, and I'm going to say this: I'm glad we're leaving a link and our listeners should go and follow this link. It's really well written. Elizabeth Warren gets all the credit, but

you know she's got some staffer there who's like a superstar because it really did a great job of point-by-point going through so many of these issues. It really is a letter basically, "Hey, we're going to ask you these questions and we're going to expect some answers." You can say, "Oh, I'm not really anti-vaccine," but he's really made it very clear. This document really lays out his public positions over time.

VR: They can't let him take that road and say, "Oh, I'm not really in." No, you said this. You need to tell us why. Right now, provide us -" They have to be tough. Republicans are not going to be tough. People like Elizabeth Warren will be.

DG: Yes, we'll see what happens. Yes, this, as I think as we've shared, it's concerning and it'll be interesting to see, not only how does he answer, but should he move forward in the process, what he actually does.

VR: Daniel writes, "As discussed on a recent clinical update, Paxlovid may be up to 60% effective at preventing Long COVID. Are we at the point where the young and healthy people under 20, 30, and 40 without serious comorbidities should consider Paxlovid for the sole purpose of preventing Long COVID?"

DG: It's a challenge, actually. This would clearly be off-label. Paxlovid is licensed. It's approved for prevention of progression to moderate severe COVID, reducing your risk of death. It's really targeted to high-risk individuals. Actually, one of the things we worry about is, oh, drug-drug interactions when a young, healthy individual won't necessarily have those drug-drug interactions, won't necessarily have any renal issues to worry about.

I think this is definitely something where some providers are talking with patients. If a person maybe has a higher risk, that's one of the challenges. Not sure who is the highest risk for going on. Definitely seen family members where maybe dad has Long COVID and now the daughter ends up getting Long COVID. Now, the sister is like, "What about me?" Yes, I think we're still trying to sort this out.

VR: Dorothy writes, "I'm an enthusiastic listener to *TWiV.* I appreciate all the work you do, in particular when you call a spade a spade. Vincent is good at that. We have some unpleasant anti-science and anti-vax people here in Ontario, but so far, they are not likely to be in decision-making positions in the Canadian government. I wish you luck over the next four years. Two questions. One, is there any protective immunity or resistance to norovirus? There's a sizable outbreak in residents at a nearby university. How many of the mostly healthy young people exposed to 100-plus virions might not get sick?"

DG: We'll start with that. Actually, I touched on this a little, which is great. If you've had norovirus before, I mentioned there's 30 different types and it's a surface protein that is variable between them. There's some cross-reactivity. If we're saying, university age, you're probably at that time where if you get one particular type of norovirus, six to eight years is a good time when you're going to have some lasting immunity. A lot of what's going to happen here is folks who have had prior norovirus, particularly this type of norovirus, but there is some cross-protection, it doesn't take a lot to get sick, actually. Yes. These 100-plus virions, I shared that story of everyone who shook the hand of the maitre d' at this one point. Everyone got it. Yes, very contagious.

VR: I just looked it up and it says the asymptomatic rate, it varies by age, location, outbreak, but it can range from 1% to over 30%. Over 30% of infected people can be asymptomatic. That's a problem for transmission. If you're a food handler and you're infected and you don't know it, you're going to contaminate food.

DG: The maitre d' had no symptoms, right?

VR: Yes.

DG: That was like the classic thing. He was fine. He's like, "What are you talking about?" I wonder that the asymptomatic folks, these people that previously had an infection, again, they're not protected against getting infected. They're not failing to transmit to others, but they themselves are protected against disease. That would be one of the issues. We start vaccinating everyone. You have all these folks. I would love to have a vaccination and not have to worry about winter vomiting.

VR: "Two, a recent topic of discussion was comparing the efficacy of protein-based Novavax with mRNA vaccines for SARS-CoV-2. Would the comparator for efficacy be best an actual infection rather than immunity assessed with in vitro assays always somewhat limited from the vaccines?"

DG: Dorothy, remember, the purpose of vaccines is to protect you against disease, not infection.

VR: Yes. Dorothy is right. It would be actual infection in people.

DG: Yes. Actual infection, actual people getting sick, not just the in vitro assays.

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

DG: Thank you. Everyone be safe.

[music]

VR: You got to be safe from not just the microbes, but from crazy politicians.

[00:47:05] [END OF AUDIO]