TWiV 1344 Clinical Update

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

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VR: From *MicrobeTV*, this is *TWiV, This Week in Virology*, Episode 1344, recorded on July 30, 2026. 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 am not in New York. I am in Minneapolis, Minnesota.

DG: You got to say that with the Minnesota accent, right?

VR: They're very proud that they stood up to the federal government, by the way. They mention it all the time.

DG: Oh, really? That's great. Let us start off with a quotation, which maybe people can figure out why this quotation is here, and I'm going to claim it's a little more optimistic than maybe I am. “Sometimes reality comes crashing down on you. Other times reality simply waits patiently for you to run out of the energy it takes to deny it.” That's why I think it's optimistic, because I think some people just go to their grave. Somehow they're funneling all their energy into some false narrative, rewrite of history.

VR: All right. I understand it. Yes.

DG: Good. I think our listeners will get it too. I think the people that don't listen to us, well, one, they won't listen to me, so they won't try to get it, but they also won't get it. That's good. We have a number of things to cover. Let's start off with this vaccine news. Probably as our listeners know, this isn't really just a one-person, two-person show. We have other folks that'll sort of nudge things. "Hey, let's talk about this." They'll put things in. This is put in by one of our group, one of our consortium contributors. This is this article in *The New York Times.*

Dozens of states tried to roll back vaccine laws. Here's how they fared. We read, "Lawmakers flooded statehouses this year with bills seeking to dismantle vaccination rules or raise questions about vaccine safety, introducing more than 200 measures in 34 states. The bills challenged every part of the system that states rely on to vaccinate the public, from the pamphlets patients receive before getting a shot to the requirements schools, daycare

centers, and employers can implement. A proposal in Wisconsin would have designated October as Immunization Injury Awareness Month. A bill in Iowa would have eliminated all vaccination requirements for elementary and secondary schools."

VR: What happened with these bills? What was the outcome?

DG: Unfortunately, a lot of this is still in process, so we'll have to see where this is all going to end up. This is concerning, right?

VR: Of course. It's only happening because there's no health leadership in this country. There's just the vaccine denialist who says they cause injuries when they don't. He's a liar. All these bills are based on lies. They're politically motivated, and it's just putting people at risk. Let me tell you an example. Can I have one minute?

DG: Yes, go for it.

VR: Today on *TWiV* here at ASV, I'm in Minneapolis, we talked about SSPE. This is a late sequelae to measles. It is uniformly fatal. It is rare, but these kids who had measles because they weren't vaccinated, they get this disease. It's a neurological degeneration, and they all die. When they're sick, the parents call my host, Roberto Cattaneo, and they say, "What can I do? The doctors tell me there's nothing to do. Can we vaccinate him now?" Parents don't understand. This is rare, but you will lose your child if your child gets SSPE. So get vaccinated.

DG: Yes. What is the incidence? Is it one in 1,000, one in 10,000? What's the -

VR: Oh, it's quite high. It's one in 100,000 or something like that.

DG: When we used to have hundreds of thousands of cases, we had over a million cases, then you would see a few of these.

VR: Yes. Also, if the child gets it in the first year of life, the incidence is one in 600.

DG: Yes.

VR: That's usually when you can get it, especially before you get vaccinated at 12 months of age.

DG: It's crazy if you think about it. Hey, I'm not going to vaccinate, and then I'm going to potentially infect your child. Your child now has a one in 600 chance of dying of a horrible brain inflammatory process. What horrible.. I thought we lived in a society. You don't shoot your gun in your backyard. That's what this is. It's like shooting your gun in the backyard. It's exposing your fellow Americans, fellow individuals, your friends, your neighbors. If you don't like your neighbor, don't kill their child.

VR: You have a choice. You can vaccinate your child against these and other diseases with vaccines that are safe, or you can listen to the liars and then perhaps lose your child one day. It's your choice.

DG: It really is. It's horrible. Another thing to talk about, dengue. We always see dengue cases here in New York. People travel. They end up with dengue. I almost died of dengue. I don't know. I have to tell that story sometime, my second bout of dengue. Dengue cases in

Sri Lanka surged past 80,000. Sri Lanka has recorded a sharp rise in dengue cases this year, with official surveillance data showing 80,114 infections as of July 23. Health officials confirmed 59 dengue-related deaths this year. Case fatality rate is well below 1%, but when you have this many cases, you actually start to see this number of deaths.

VR: It's a lot of dengue.

DG: Yes. Actually, this is one of the most common viral diseases that we see each year. They go to parts of Asia during the right season or the wrong season, however you think about it. There are hospitals just full, like dengue wards. I remember when I was at the Children's Hospital in Siem Reap, the Angkor Wat Children's Hospital. You've got all these open areas. Unfortunately, you end up with people with dengue, and then there's mosquitoes, and then other people get dengue. It's just a bit of a disaster.

VR: Also, there are long-term sequelae. Many patients have pains in their joints for many years.

DG: Yes, the dengue, there's clearly a post-dengue or a long dengue. I guess I'm going to call it a long dengue because it's really, they don't get better. They continue to have issues.

VR: You don't have any joint issues as a consequence of dengue?

DG: Not from dengue, from all my ski accidents.

VR: Well, that's not infectious.

DG: Yes, no. *Cyclospora*, we've got a lot to talk about here. The biggest thing I'd say, this is still ongoing. First, I'm going to discuss a *CIDRAP* piece. That's very appropriate for you out there in Minnesota, right?

VR: That's right.

DG: This is from Megan Holahan. “A Difficult-to-trace Parasite Messaging Missteps Contribute to Summer of Overwhelming *Cyclospora O*utbreaks.” The article does discuss this confusion around the false positive and Taylor Farms. Let's talk, because people are like, "What's going on here?" This, I thought, was a good explanation. They explain that on July 18, the FDA, the U.S. FDA, announced that a sample of iceberg lettuce from Taylor Farms de Mexico tested positive for *Cyclospora*, the microscopic parasite responsible for a nine-state outbreak of foodborne illness. The next day, the agency, they say, noted it was a false positive test.

My understanding is just it came up positive at a high cycle threshold, high CT value. I think our listeners are familiar with that. Then, there was an argument that that was such a high threshold that could be a false positive. They say, "OK, we'll consider it a false positive." Some people thought that this meant that iceberg lettuce did not contribute to the thousands of cases of Cyclosporiasis, this illness caused by *Cyclospora*. Then, a day later, the FDA holds a media briefing, because they're so good at communication here, to explain that the false positive was from lettuce that underwent regular screening at the border, not of the lettuce connected to the outbreak.

Taylor Farms lettuce was still suspected. We've actually discussed, like, the epidemiology is pretty convincing. Then, there's this huge discussion, the *CIDRAP* piece, about the fact that

there's a second outbreak unrelated to Taylor Farms lettuce. They do talk about the huge information vacuum. We read, "While it's believed cases from the large *Cyclospora* outbreak were first reported on May 1, the CDC didn't issue a health alert network advisory about it until July 14, 10 weeks later."

VR: That's not acceptable.

DG: Isn't that crazy?

VR: Crazy.

DG: We got something going on 10 weeks later. "Hey, by the way, something's going on," I commented about when that came out.

VR: I don't know why this would be, Daniel. It can't just be a shortage of personnel. It has to be management.

DG: Yes, and I think it is. You hate to say suppression, but let's talk about it. Nationwide, there were 4,500 cases in 2023, 3,500 cases in 2024. What about this year? You can look at numbers from different sources. Let's go to the CDC. We go to the CDC. I'm going to leave in a link to this. As of July 28, the CDC says we have 6,707 laboratory-confirmed domestic cases, but then we actually go, and we go to the states. I'm going to go to Michigan, and we'll leave a link in here. Michigan tells us they have over 10,000 cases. How can that be? They didn't tell the CDC. The CDC is not looking. Michigan alone has over 10,000 cases; 160 people have been hospitalized. We've talked about that's the tip of the iceberg. There's also something going on in North Carolina, and there's a dashboard; I'll leave a link to that. 718 cases so far down there in North Carolina. We've got a couple dozen hospitalizations.

Then New York City. We're actually over 500 cases in New York City alone, just New York City. You can actually see that this is ongoing.

VR: This is a big nationwide outbreak. There's no question about it.

DG: Yes, big nationwide outbreak, thousands of cases, clearly more than double anything we've seen in recent years. It looks like there are multiple sources. I was talking to my brother-in-law earlier. I was basically saying, once you have over 10,000 cases, you're getting to the point where, OK, maybe it was brought in with the lettuce from Mexico, but now you've got thousands and thousands of people with explosive diarrhea, some of them not diagnosed, so the number's even higher. Some of those people work in the food-preparing industry, and, "Oh, take some time off from work if you have diarrhea."

They're not really necessarily in the economic situation where you could take a week off from work. A lot of folks are living paycheck to paycheck. You're going to start seeing spread in the U.S. as a secondary spread phenomenon.

VR: I wonder how much the reporting is due to shortage of personnel or, as I said, maybe they can't do the tests. It looks like the states are keeping up. I would love to get a nationwide tally based on the individual states.

DG: It seems like the CDC could do that. Somebody at CDC -

VR: Should be.

DG: - say, "Hey, your job is just 50 states, each department of health. Just look at those numbers, add them up." If Michigan's at 10,000, "Why is your number at 6,000?" That doesn't make any sense. Yes, we're actually, not a spoiler alert, maybe a link alert. Our plan, my plan, is when we record our *This Week in Parasitism* tomorrow, is to do a discussion of a review and an update on *Cyclospora.* A really deep dive into understanding Cyclosporiasis, the parasite *Cyclospora*, how it spreads, how it's treated. Give everyone a primer on what's going on here.

Then you know what paper to read for the discussion tomorrow, Vincent. *Legionella*. As of July 28, 90 people have tested positive for Legionnaires' disease, six deaths. Actually, a majority of folks have actually ended up hospitalized with this. I think we're past the outbreak because if you look in the last week or so, we're not seeing any new cases. We did read that 50 buildings in Manhattan outbreak zone test positive for live bacteria. This is interesting. There's an article in *NBC New York* by Jennifer Millman. It has this great map, and hopefully that'll be up on the screen for people that are looking at this on YouTube. You can basically see where it is.

It's basically east of the reservoir, and there's a whole bunch of these buildings that are red. I was looking into the details here. They say for live bacteria. Is this PCR? Is this molecular testing? Is this culture data? I wasn't sure that we actually had the culture data back yet. They even have a nice table where you can actually see the address of every single building where they say tested positive for live *Legionella* bacteria, which really would imply culture results.

VR: One of these streets is where I used to live many years ago, 94th Street.

DG: Wow, yes, Park Avenue. They got it on Park Avenue, Madison Avenue. Wow, and fancy zip codes here.

Screwworm. We've got another case, but only one new animal case of screwworm this last week. We'll keep an eye on the screwworm. The big thing, Ebola. We were talking last time about how the numbers seem to really be rising faster at this early stage than we ever have seen before. It does seem to be mainly confined to the DRC.

Actually, Uganda said, "We don't have any active Ebola in our country as of now," but the DRC confirmed cases, 3,360. It's confirmed, so even more. The mortality is 40%, 50%, confirmed as 1,487. We have some, I'm going to say, some good news. First volunteer vaccinated in the world's first Bundibugyo. [crosstalk]

VR: Bundibugyo.

DG: Bundibugyo, Ebola virus vaccine trial. This is the ChAdOx.

VR: Bundibugyo, soft g.

DG: Bugy, like bourgeoisie, Bundibugyo. I'm going to work - You know what you've got to do? You've got to give me a little phonetic thing in there so I can stop embarrassing myself. The vaccine was developed by the University of Oxford's Oxford Vaccine Group and Pandemic Sciences Institute using the same technology that you use for the Oxford-AstraZeneca COVID-19 vaccine, as they say, which is estimated to have saved around 6 million lives during its first year of use. That's pretty impressive.

The speed of the program has been enabled through a truly collaborative and global approach and is built on decades of vaccine manufacturing capabilities at the university's clinical biomanufacturing facility. I think I'd just leave the speed of the program, just the efficient rollout; the ability to roll it out is because of these manufacturing capabilities that are because of the university's facility and also the famous Serum Institute of India.

VR: They have 600,000 doses already.

DG: Yes, 620,000 doses of this vaccine.

VR: Amazing.

DG: Yes, it's like there's enough doses to not only do a proper trial, but then when we have the evidence to really roll it out. It'll be interesting. You've talked about it in the deep dive, and we've talked about it. How important is vaccine versus just good contact tracing and preventing the spread?

VR: Well, Tom Ksiazek seemed to think that contact tracing was the most important. This is a problem in this area where there's not a good contact tracing network established yet. That's why it's probably still spiraling out of control.

DG: Yes, I think this may also help with - I won't go into too much detail here, but a lot of healthcare workers are basically going on strike, refusing to work because they don't feel like they're getting adequate protection. They don't have the proper personal protective equipment. They're not being paid. They're working in harm's way with, what, a pathogen with a 40% mortality. That's, I think, a vaccination for healthcare workers that was shown to be effective would be quite something.

We've got also the article, the correspondence, actually, “Cross-reactive-” Do you want to just say that word every time we come across it? You can pronounce it differently.

VR: Yes, Bundibugyo.

DG: “Antibody Responses after Receipt of Licensed Ebola Vaccines,” published in *The New England Journal of Medicine*. This group evaluated cross-reactive antibody responses against multiple filoviruses using serum samples obtained from West African adults and children who were enrolled in the PREVAC randomized clinical trial. The analyzed samples obtained at 28 days and at three months after vaccination with several of these different vaccines.

We've got the Ervebo, and that was a single dose or prime boost. They had the Zabdeno, the Mvabea, and basically what they found, and they've got some nice figures here, cross-reactive antibody responses against this particular virus that we're seeing in the DRC was detected across all vaccine formulations and at both time points.

VR: Yes, so these are people vaccinated with the Zaire Ebolavirus vaccine, and so yes, there is some cross-reactive antibodies to Bundibugyo, but we don't know the clinical impact of these antibodies yet. Whether or not they're going to impact disease.

DG: I think that's the big thing, yes. Yes, these are just antibody levels. Antibody titers is what we've got here. Yes, what about efficacy? Measles, more measles cases in the U.S. We're up to 2,321 per the Hopkins tracker. Actually, CDC is pretty close. 2,318. The last week, 68 new cases have been added to the count per the CDC. We've already gone quite a

bit past the total number of confirmed cases last year. We haven't seen this many measles cases in decades.

I have a lot of ideas on why. I do blame our government and the misinformation. Historically, when there was starting to be a measles outbreak, the CDC would go in, and there'd be education and awareness and vaccination opportunities. What we had instead was people going down there and saying, "Good on you for not vaccinating your child. Oh, they did die, but your son's still alive." It just, yes, this is horrible.

Now, still moving. We're not really in the respiratory season, but we keep getting a little more data on some of our interventions here for RSV. The impact of nirsevimab, so that's the monoclonal antibody; it's a prophylactic. Impact of nirsevimab in its second season on RSV and non-RSV admissions in children under 5. Here we have - where was this article published? Want to look that up for me there, Vincent, while I go through the data?

VR: Yes.

DG: These are results of a retrospective study that was conducted at a tertiary center in Tarragona, Spain. They included children under five hospitalized with acute lower respiratory tract infections, wonderful acronym ALRTI, during the RSV seasons. Between 2018 and 2025, they excluded the 2020-2021 because of the COVID impact. Demographic data, length of stay, PICU stay, need for ventilatory support. Among 1,384 of these acute lower respiratory tract infection hospitalizations, 661 more RSV-confirmed, 375 required PICU admissions, a lot.

After nirsevimab rollout, hospital admissions due to RSV decreased from 5.04 to 2.5, so about half, more than half. Hospitalizations due to non-RSV also decreased from 5.1 to 3.54. PICU admissions also declined by more than half. No differences were observed between first and second post-implementation seasons in hospitalization, need for respiratory support, PICU, or length of stay.

VR: I wonder why this other non-RSV decreased as well.

DG: I think what can happen is, we see this with flu as well. Maybe you get flu, maybe you get RSV, and then you're vulnerable that next week to get these post-viral bacterial infections. I'm assuming that that's the impact they're seeing. They get admitted, they say, "Oh, it's not RSV, but it might be post-RSV."

VR: This was published in *Pediatric Infectious Diseases*.

DG: COVID. Actually, a patient today, I got to check on the repeat test, but they had a positive COVID test, Vincent.

VR: Well, I see a little uptick there.

DG: See that little uptick?

VR: Very tiny. I think that's the West.

DG: It is. The West has this tiny, it's still in the very low, but it's like a little uptick in the very low. The Northeast, which is really very low, a little bit uptick out there. Yes, I'm going to have to see if the test on the patient that I'm consulting on comes back positive. If you look

at a map, actually, there are moderate wastewater levels in Alaska. We're starting to see from very low to low in Washington, California, Nevada, Texas, a few other places. We'll keep following this.

A couple of interesting other articles. I'm going to, a little bit about COVID and Long COVID. One was the article, “Remdesivir and All-cause Graft Loss Among Kidney Transplant Recipients With Symptomatic COVID-19,” published in *JAMA Network Open*. Here was this sort of thing about, "Hey, remdesivir, it's really expensive. Let's try to limit people getting remdesivir. We're spending all this money. Is it really making a difference?" It's actually important to have the data where you ask this question. Here is, if you get COVID, you're at increased risk of losing that kidney, which is precious kidney transplant. A lot of these facilities really pride themselves on their outcomes with their kidney transplants.

Here you look at data from a retrospective cohort study, as mentioned, published in *JAMA Network Open*, where they emulated a target trial using observational data from five hospitals within the Johns Hopkins Health System. Adult kidney transplant recipients with a functioning allograft and symptomatic COVID-19 from March 2020 through January 2024 were eligible. Patients who received anti-SARS-CoV-2 monoclonal antibodies, Paxlovid, or molnupiravir were excluded. We're looking at remdesivir here. Follow-up continued for up to one year. I guess I could look at those others; it would be a separate publication.

Among 432 kidney transplant recipients with symptomatic COVID-19, median age 54, a little bit more than half were male, 41% initiated early remdesivir, 59% no remdesivir. Over one year of follow-up, early remdesivir initiation versus no remdesivir was associated with a lower risk of this ACGL, so that's acute graft issue, losing your graft basically or having a rejection; hazard ratio of 0.53, so about a 50% lower risk. Now the association between early initiation of remdesivir and lower risk of all-cause mortality did not reach statistical significance, but the hazard ratio is 0.51; the confidence interval overlap, 0.24 to 1.06. Similar overlap with Long COVID, hazard ratio 0.65, confidence interval 0.21 to 2.05.

VR: That's very good. Good result.

DG: Yes. Basically, if you've got a kidney transplant and you get early remdesivir, you're at risk of acute kidney transplant rejection, about, yes, so pretty big. A couple interesting articles in the Long COVID section. The first one we'll talk about is, Skeletal Muscle Properties in Long COVID and ME/CFS Differ from Those Induced by Bed Rest,” published in *Nature Communications,* because here's this whole idea, well, people with long COVID, they're just laying around, they're not doing anything, so it's all about deconditioning. There's nothing really going on here, nothing to see.

Well, this is an interesting study because they get a whole bunch of people and they're like, "Hey, you're going to be the controls, and you're going to like 60 days of bed rest." Wild, right? I don't know. Maybe a certain type is willing to do that. They're going to compare whole body exercise responses and skeletal muscle adaptations after a strict 60-day bed rest in healthy people with those in Long COVID and ME/CFS patients and healthy age and sex match control.

VR: This means they're in bed 24 hours a day for 60 days?

DG: You're getting up, you're going to the bathroom, but pretty much, yes, you're pretty much on bed rest. It's like, you think about if you had a pregnancy complication, they're like,

"Bed rest," you stay in bed. Yes, so I have the figures because each figure basically is a point that they convey, and there's some interesting things here. The first figure they have is basically bed rest results in alterations in respiratory and cardiovascular responses to maximum exercise, but they're not seeing this in Long COVID and ME/CFS. The physiological, the VO2 max and those measures, those actually are different. It's not just deconditioning, at least on this.

Then, and I think this is where I get more interested, bedrest, this Figure 2, bed rest - and this is open access, by the way, bed rest induces muscle atrophy with no change in fiber composition, but patients with Long COVID and ME/CFS actually have a change in the fiber type composition. Interesting. This is actually an objectively measurable difference in what's going on.

Then there's actually Figure 3, and they say bed rest decreases both SDH activity and oxidative phosphorylation capacity, which relate to maximal oxygen uptake. You get this lower SDH activity and oxidative phosphorylation capacity in patients with Long COVID and ME/CFS, but they don't relate to maximum oxygen uptake. It's interesting, but then this is, again, I guess I have my favorites: Figure 2 and Figure 4. Figure 4, capillary-to-fiber ratio following bed rest is proportional to muscle fiber size, while both patients with Long COVID and ME/CFS have reduced capillary-to-fiber ratio for a given fiber size.

VR: Although I can't see that from the graph, Daniel.

DG: Yes, it's statisticians. Statisticians are saying it looks a little bit different. Yes, this isn't quite as impressive as I'll say. Yes.

VR: Basically, something's going on with muscles in the Long COVID and ME/CFS patients. We have to figure out what it is.

DG: Yes. I feel like the biggest separation you're seeing is some of the Figure No. 1, where you actually look at the VO2 max data. You really see there's separation. The other stuff is, OK, yes, there's something going on here. Definitely a difference, but yes, there's a lot of overlap in what we're seeing.

Now, the next one, this one has me worried. I don't like this next study. It's like, if you don't like the truth, but this is the truth. This is this article. It's the article, “Loss of Vesicular Monoamine Transporter 2 in Striatum of Long COVID and Relationship to Neuropsychiatric Symptoms.” This is in *The Lancet*, one of *The Lancet* journals. This is a case-controlled study. It's from up in Canada. We've got 24 adults with Long COVID, 24 age-to-match healthy controls. Then the healthy control sample was extended to 43 for exploratory analysis. There is a little bit that we need to know. I'm going to try to walk us through this in an understandable way.

I'm thinking of this as if we know about Parkinson's disease and the importance of these dopaminergic neurons and dopaminergic junctions. This study is going to use a certain type of PET scan in Long COVID. This particular type of PET scan is going to give an index of vesicular monoamine transporter 2, which is actually a well-established marker of dopaminergic nerve terminal integrity in particular parts of the brain, ventral striatum, dorsal putamen, and dorsal caudate. There was this idea that certain reductions in these dopaminergic nerve terminal would occur in some of these areas in Long COVID.

They based that on the fact when you look at some animal models where you see some of the apathy, anhedonia, motor retardation, there seems to be this. They're going to go ahead, and they're going to look at these areas. What's really threw me back is this figure that I've put in, Vincent. There's two aspects that bother me about it. One is they actually find, basically, I'm going to say, really dramatically reduced dopaminergic terminal integrity in folks that have Long COVID.

VR: Yes.

DG: You know what? The healthy folks that had COVID in the past, there's actually a drop in signal as well.

VR: Yes. It's not as much as the Long COVID.

DG: I mean, Long COVID, it's dramatic. You're actually seeing some loss, too, in particularly the superior part in some of the folks with, "I had COVID, but I'm otherwise healthy." I don't know where they find these "I never had COVID" folks.

VR: Yes. Something's happening to this enzyme. Again, we don't know the cause, whether it's viral replication, whether it's cytokines, inflammation, maybe it's antibodies as well, autoimmune antibodies. Who knows?

DG: Yes. We're definitely left without a mechanism. I'm not excited about the idea that getting COVID is somehow correlated with the loss of some of my dopaminergic activity in my brain. I'll even link to this, yes, so people can take a look at this. Before we get to our emails, no one is safe until everyone is safe. I feel like that's more true every day, unfortunately. We are getting here to - well, we're right at the end of July. This is going to be the end of our Foundation for International Medical Relief of Children fundraiser because that just goes right to the end of July. Then we're going to be moving it to ASTMH, and I'm very excited about that. I should mention that as we move into that, because I think by the time a lot of people listen to this, we'll be in the August through October, we're actually going to be doing a memorial lecture series for Dickson Despommier. We're going to actually be pushing for a higher drive because we want to fund basically a five-year lecture series in memory of Dickson Despommier, a tribute to Dickson. Go to parasiteswithoutborders.com, click on the Donate button, and we'll be doubling those donations so we can get to our goals.

VR: It's time for your questions for Daniel. You can send yours to Daniel at microbe.tv. Cathy writes, "Hello and thank you for your informative clinical updates. I am a 60-year-old woman living in England who recently decided to purchase two times Shingrix privately, given that I'm not eligible for free vaccination against shingles on the NHS until I am 65. For what it's worth, two vaccines cost me £500."

DG: It's a lot of money.

VR: It is. "I have a couple of questions regarding Shingrix. One, does it have any cross-reactivity with herpes simplex type 1? The reason I ask this is because I had been constantly plagued with HSV-1 around my mouth for the past four years. Topical and oral acyclovir provided only a very temporary clearance. One of the reasons why I decided to pay for Shingrix is that I figured that maybe my immune system is not that robust and that VZV would be the next dormant virus to reactivate. Interestingly, since my second Shingrix shot

three months ago, I have not had any reactivation of HSV-1.

Is it possible that Shingrix offered some cross-reactivity against HSV-1 or, alternatively, that the activation of my immune system by the Shingrix vaccine helped to clear HSV-1? I certainly had a reaction to both Shingrix shots and felt quite unwell for three to four days after each one." Let's take that one first, Daniel.

DG: Yes, we'll start there. We don't think that there's a cross-reactivity with HSV-1 from the Shingrix vaccine. You do raise an interesting thing. Is there some sort of immune activation that was triggered? It's great to hear that you haven't had an HSV-1 reactivation since then. I don't think it actually cleared the HSV-1, but it might be doing something to help suppress that. Maybe it's a placebo effect. I'm hesitant even to mention that because then it'll go away. No, if you're not having HSV-1 activations, that's great. We do think that the immune response is different enough that a VZV protection is not going to be HSV-1 protection.

VR: Two, "Will I need a booster Shingrix in the future? How long does Shingrix vaccine effectiveness last?"

DG: We don't really know, actually. We've been saying, "Oh, it's great, you're good. We measure some antibodies." Now that we're getting this data on dementia, protecting you from dementia, that's the next thing. How often do you want a boost to continue to have that protection? We're particularly seeing it in the ladies. That seems like a study that I would love to find the results from. Maybe it's not going to protect me from getting dementia, but there's a lot of people I care about who might actually benefit from this.

VR: Finally, "I submitted a question a few months ago about having had measles at age 11, I was unvaccinated, and whether I should have the vaccines I had been given as a small child again. At age 60, owing to possible immune amnesia. Just to let you know that my doctor was willing to give me the polio vaccine as you recommended."

DG: Oh, Cathy, this is actually a great question, right? Because initially you're thinking, oh, you had measles, you don't have to worry about measles, but you had measles at age 11. That was probably after you got a lot of those basic standard childhood vaccines. Did getting measles and that immune amnesia actually impact your response to those vaccines that you got before?

In a case like this, a lot of times we actually will repeat those vaccines. Polio vaccine, great. That seems like it's worth doing. You're probably getting your tetanus, diphtheria, acellular pertussis every 10 years. Go ahead and do that. No, excellent question. I would go through with your doctor what vaccines had you been given before this age and consider redoing them.

VR: Owen writes, "We have shingles, the sequelae many years later of chickenpox. We have the years-later sequelae to polio. We have long-line disease and Long COVID. I saw a recent case in the UK of sequelae to measles. The patient died. I was discussing this with an endocrinologist. She said she had a case of sequelae to measles when she was an intern. She did identify it in the medical record as such before the attendings figured it out." It sounds like SSPE, Daniel, doesn't it?

DG: Yes, that's what it sounds like.

VR: "I wonder with the jump in measles cases what cases of sequelae to measles we have coming down the road, so to speak, in 20 years or so. This could be interesting. I have not seen any discussion of this. I've been a regular listener to TWiV for some time now. Original academic background was physics and electrical engineering. Reading virology is most interesting. Viruses are fascinating both -" actually, Owen writes, "Viri are fascinating both as a reader and as a victim. OK, do excuse the Latin plural."

DG: We ended up actually going down that road today discussing how the fact that if you're under a year, one in 600 children six years later will develop a terminal neurological inflammatory condition, SSPE. We saw a case of that here actually in the hospital where I was rounding this morning. You're a little older; the numbers are going to be lower. Now that we're seeing thousands of cases every year and now that measles is back, we're going to see not only all the acute issues, but we're going to see the sequelae, which is horrible.

VR: Raze writes, "I'm 60 years old, had chickenpox, but maybe not measles as a kid. Mom doesn't recall. I'm taking care of elderly patients, 85 each, going to a wedding in South Carolina where they got lots of measles. I'm thinking time for a booster, one dose or recommended two? Thanks for all you do." He provides his measles IgG titer. It's less than 13.

DG: Interesting, 60 years old. You're born, what, 1966. You would have thought you would have been one of these people that was targeted for vaccination. If you weren't vaccinated, I'd go ahead, go ahead and get your shot, get your second shot. Go ahead and do the series because looking from your titers, hearing from your history, it sounds like maybe somehow you were left out.

VR: Jill writes, "Infection preventionist from Kansas and dedicated TWiV listener. We are seeing an increase in *Candidozyma auris* in Kansas. Any consideration to adding this emerging pathogen to your weekly update rotation? This organism is an infection preventionist nightmare in preventing exposures, and I would love to hear more visibility about this pesky pathogen. Thanks for all you do. Stay the course. Had to throw in a sailing reference with your amazing updates."

DG: All right, Jill. Jill, maybe this is like a cross-fertilization. You've got to start listening to the *Infectious Disease Puscast*. I always cover articles on *Candida auris* or the now-renamed *Candidozyma auris*. There's a particular hospital in New York City which is actually quite a hotbed for *C. auris*. Actually, I think there are more cases there in that one facility than any other hospital in the country. This is one of those nightmare pathogens. *C. auris* is actually developing resistance to a number of our antifungal agents. There's also this whole issue that it's becoming more thermotolerant.

Really, this whole fear about the gap, like why are human beings warm? It's so that we don't all die of the fungi, but the fungi is getting used with global warming and other things to warmer temperatures. This is all inspiration for wonderful shows like *The Last of Us*. Yes, I will periodically mention *C. auris*, but really where you're going to hear a lot is go to the *Infectious Disease Puscast*.

VR: Jen writes, "Clinical updates have been the heartbeat of my week for seven years now. Your evidence-based perspectives have kept me calm when I was anxious, and on the flip side, helped me stay alert when I might have been complacent. Thank you. I felt bewildered by your reporting on COVID this year. For months, you've characterized current transmission

as basically nonexistent in a very merry tone. While I join you in celebrating lower summer levels, I'm surprised that you aren't discussing the fact that baseline transmission for COVID is so persistent and high that even what CDC calls very low levels carry a substantial disease burden.

We know that wastewater categories like very low don't work on absolute scale. Rather, they compare a site's current levels to its lowest point within the last two years, and the lowest points of the last two years have not been all that low. Nationwide, very low can still mean hundreds of thousands of infections per week. As you have emphasized so often on this program, perhaps one in 10 infections results in long-term health conditions. It doesn't take much math to determine that very low transmission is disabling staggering numbers of Americans this summer, a number that would make your head spin if we were talking about a disease like measles.

I respect the weight you assign to every life. Over and over, you've said that one person dead or disabled is too many. With love, why the cavalier attitude toward a number of new deaths and disabilities that would make you outraged if you were reporting on polio, Legionnaires', or cyclosporiasis? Can you imagine celebrating only thousands of new daily or weekly infections of one of those pathogens as low enough to laugh about on air? It's very difficult to take basic COVID precautions to protect myself and my family when experts write COVID off as nothing to worry about.

I know that is not the perspective of this show's hosts, and I would applaud more alignment between your reporting on COVID prevalence and the burden it places on all of us human beings out there, especially the chronically ill and disabled people who have been pleading with us to take this more seriously, and children who cannot meaningfully consent to the risks their caregivers expose them to believing that COVID is not transmitting at all right now. Thank you, and thank you for all you do."

DG: No, Jen, this is actually a good sobering email that you sent us because it's tough. I was just sharing this article where it looks like maybe people who got mild COVID who didn't end up feeling that they had symptomatic Long COVID might actually have some damage to the dopaminergic neurons and neuron transmission sites in the brain. No, this is devastating because it's not just deaths. It's not just hospitalization. It's also people that get sick and end up with Long COVID. We've got all this. It's interesting. I think it's relative. We were at a point when we had 2,000 deaths a day, and so now we celebrate the fact that we're at this "very low level." It's a relative.

When we went for decades without seeing many measles cases, and now we're in the thousands, it's a comparative thing. No, I actually think that hopefully you don't perceive it as a cavalier attitude when Vincent and I joke about when the next peak is going to be because that's basically what we're trying to point out is that there's a pattern here. It goes down, but it comes up. The opposite of everything goes up has to come down. Well, unfortunately, what we're seeing with flu, we see with RSV, and now we've been seeing for several years, COVID rates may go down. That still means thousands of new infections each week, but then they go up to hundreds of thousands, millions of infections each week.

VR: The problem is, of course, that weekly counts are no longer tracked for COVID because the testing is a lot of home testing. It doesn't get reported. If you go to the CDC site, they say the week of August 1, there were 1,600 new laboratory-confirmed COVID hospital admissions. That's what they use as a metric, hospital admissions. I don't know if there are

hundreds of thousands a week, Daniel. Do you think that's correct?

DG: I don't think hundreds of thousands, but there are. If you think about that many admissions and what percent admissions, you're talking about thousands or tens of thousands, but yes, I don't think we're in the hundreds of thousands.

VR: I don't think we laugh at it or joke about it. I think we are just trying to look at this wastewater graph and make a prediction, but we're certainly serious about all this. That's *TWiV* weekly clinical update with Dr. Daniel Griffin. Thank you, Daniel.

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

[music]

[00:49:10] [END OF AUDIO]