TWiV 1338 Clinical Update

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Vincent Racaniello: *This Week in Virology*, the podcast about viruses, the kind that make you sick. From *MicrobeTV*, this is *TWiV*. *This Week in Virology*, Episode 1338, recorded on July 9, 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. [chuckles] I'm actually on dry land this time, Vincent.

VR: Yes, no life jacket.

DG: Yes.

VR: I see you have a bow tie, so we can say what's on your bow tie.

DG: I don't know. Are you able to zoom in? Can you get a good look at that?

VR: I can't zoom in, no.

DG: Okay. All right. Well, maybe David will zoom in. Our YouTube watchers can see the little - it's *Giardia*.

VR: Yes, I just see dots.

DG: [laughs] Well, let's start off. We got a few things to talk about today. That's not going to be too bad an episode, but lots of stuff is going on. There's always stuff to talk about. I'm going to start off with a Mia Hamm quotation. Do you know who Mia Hamm is there, Vincent?

VR: Yes, soccer player, of course.

DG: I'm a bit obsessed with the football, the beautiful game. She has been always a role model for a lot of folks. She became a mom, and she has all kinds of great comments about things. Not only a fantastic football player. Also, I guess it was - what was it? Pert shampoo commercials or something may have made her more famous. [laughter] "Failure happens all the time. It happens every day in practice. What makes you better is how you react to it."

VR: I like that very much because, at least in science, you fail a lot. Do you fail a lot in medicine, Daniel? I think probably you do because it's not your fault either.

DG: Hopefully, I'm learning. Hopefully, I get 30 years plus from the time I got my MD, and hopefully now I'm still learning, still learning.

VR: If you lose a patient, it's not failure, really, is it?

DG: Usually not. Yes, usually it's not. Unfortunately, we do as much as we can. Maybe we don't do as great a job as we look back on and would like to have done. We're not God. There's only so much we can do-

VR: That's right.

DG: -and we're battling against the disease. All right. Well, we've got a bunch to talk about. The first time is how long did this take. News. This is a little shocking. We're going to go through this slowly and really point out what happened here. Air Force trainee in San Antonio, Texas, died from flu. Young, healthy Air Force trainee died last month at Lackland Air Force Base in San Antonio from the flu. This individual was 25, and they died on June 16th.

Now, influenza swept the Air Force Base in June. It only took one month after Defense Secretary Pete Hegseth made the flu shots voluntary rather than mandatory for American troops. Nearly 300 troops ended up sickened by influenza. It didn't take that long. It took a month for this change to result in the death of an American soldier.

VR: This is, of course, what happens in boot camp. You put a lot of people together. You introduce a virus, and this happens. That's why we immunize. This just underscores why this decision by the secretary was just boneheaded. It was dumb. It was ignorant, and it should not have happened. I don't know why he has the power to do that and why he thought that this was all about medical freedom. Rather, it's about staying alive.

DG: My understanding is they've basically reversed this. A month later, we already have one person dead. The reason this has been mandatory is that, sure, this is a young, healthy individual, but these people are going through training. Maybe they're not getting as much sleep. They're basically in a situation that puts them at risk for bad outcomes. This was an ignorant decision. Fortunately, it's very quickly been overturned.

VR: Has he apologized? No.

DG: That's crazy. Where's the shame?

VR: Nothing. Nothing at all. This whole administration -

DG: You made a decision, and someone's dead. You should call up and basically say to that family, "I screwed up."

VR: Of course. Publicly say this was the wrong decision, but they will not because this is their thing, medical freedom. Yet this kid, 25 years old, a whole life ahead of him, dying for a useless reason. He has many other reasons to die. He could fly a plane and crash, or he could be in combat. No, he has to die of a vaccine preventable disease. This is absurd.

DG: Yes. All right. Now, this right in response, or contrary, or I'll say contrary to that, the FDA committee unanimously recommends its first vaccine since 2023. Oh, my gosh. The FDA's top vaccine advisory committee voted unanimously to recommend Moderna's mRNA influenza vaccine. It's called mFlusiva for adults 50 and over. This was its first time reviewing a new vaccine application since 2023. The vote by the-- this is VRBPAC. This is the Vaccines and Related Biological Products Advisory Committee. It's a step towards what may be the

first vaccine filed and approved under the second Trump administration. In February, the FDA, remember this? They declined to review Moderna's application for the mRNA flu vaccine, but then reversed its decision two weeks later after criticism. Here we have this.

VR: No, it's good.

DG: Yes. Now, what's the science? That's why we're here. This decision was based on science. It was based on the results of a Phase 3 double-blind active control trial published in May in *The New England Journal of Medicine* in the article, "Efficacy and Safety of an mRNA Seasonal Influenza Vaccine in Adults. "We're going to talk a little bit about this, and then I'm going to sort of like the straw man, like what's the criticism? What are they going to say?

In this robust study, 40,703 participants - we end up basically with half and half. 20,350 get the mRNA vaccine. You've got 20,353, they get the standard comparator. They don't get saline. Basically, this is the deal. There's a flu shot that works. The question here is, is this one better? Median follow-up is 161 days. RT-PCR-confirmed protocol-defined influenza-like illness was observed in 2% of the folks that got the vaccine and 2.8% of the folks that got the standard dose. This is a relative vaccine efficacy of 26.6%. It is non-inferior. It's superior. There's actually a higher level of superiority here. It's 27% better than the standard.

Now, what about safety? Everyone says, "Oh my gosh, safety. You never look at safety." We always look at safety. Solicited adverse reactions were more frequent with mRNA vaccine, the 1010, than with the standard dose. A lot of folks, most folks actually got injection site pain. Pain where they were injected. They got that reactogenicity, that fatigue about 45% versus 20%. We saw headaches, 38% versus 18%. We saw that myalgia, 35% versus 11%. Most of the reactions, they were mild, they were moderate, they were transient. Now, there were about 2% of these serious adverse events in both the mRNA group and in the standard comparator group.

There were three events in the mRNA felt to be actually vaccine-related, two in the standard one. Then, if you actually go into the appendix, because I just want to point out, we spend a lot of time - I spend a lot of time looking at adverse events. You go to the appendix, you see these AESI, so adverse events of special interest assessed by the investigators related to study vaccination. We saw one case in the mRNA of platelets going down and myopericarditis. In the standard comparator group, we saw one case of the pericarditis and one event of Bell's palsy.

Now, according to the education by the Cardiac Event Education Committee, no cases of acute myocarditis, myopericarditis, or pericarditis were identified in the mRNA 1010 group within the conservative 42-day risk window following vaccination. Put all that together.

VR: Well, I think it's good that we have another option. The thing is that it's not much better than the standard vaccine. We've always criticized the standard vaccine. It's just an inactivated virus preparation, right?

DG: Yes.

VR: It's very old. It's many years old. It was developed in the 1930s. This isn't much better. We have to fundamentally change the flu vaccine if we're going to really get substantially better.

DG: I think there's two aspects. One is yes. It's not as much better. We want it to be much better, 27% better, 2% versus 2.8%, absolute about 1% difference. Not that impressive. There is one good thing is that this technology allows you to more closely match what's circulating. This is when you get a good match, 27% better. When you don't get a good match with the standard because you had to decide six months ahead of time, the mRNA vaccine is going to work, the other is not going to do very much. That's the other side, I guess.

VR: The other aspect is that this is easier to make. You don't need to grow virus in eggs and extract it and purify it and all that. This one, maybe it's not easier, but it's better. It's cleaner preparation. It's not old technology. As you said, you could change the vaccine more quickly as well.

DG: Yes. You have quicker response. All right. Now, this is another. I think this is really important. We just talked about this healthy individual in their 20s dying of the flu. I just want to point out that people do die of the flu. Here, we have this published in the journal *Pediatrics*, and so it's the article, "Influenza Vaccine Effectiveness Against Pediatric Death in the United States: 2016-2025." These investigators conduct a case-cohort analysis comparing current-season influenza vaccination status among reported influenza-associated pediatric deaths, kids that died from flu, with survey estimates of influenza vaccination coverage in pediatric age groups, underlying medical conditions, current seasonal influenza vaccination.

All this status was obtained from surveillance case reports. They estimated the vaccination odds ratio and the 95% confidence intervals comparing influenza vaccination among children who died with vaccination coverage in comparison cohorts. We're really asking about the ability of the influenza vaccine to prevent pediatric deaths. Here's what I want people to just take this number. From August 2016 through July 2025, you ready for this? Over 1,000, 1,234 laboratory-confirmed influenza-associated pediatric deaths. These are kids 6 months to 17 years of age. Over 1,000 little kids died.

We've talked before about the fact that these deaths are often in kids that before this seemed completely healthy. Now, of the 1,086 reported deaths with influenza vaccination information, where we knew what was going, only a quarter, 23% of 530 children with underlying medical conditions, and 13% of 556 children without known conditions, were fully vaccinated against influenza. Majority of these kids who died, not fully protected. Influenza vaccination coverage in survey cohorts was 49%. They're going to give us a vaccine efficacy of 80% overall, 77% among children with underlying medical conditions, 87% among children without known conditions. This is efficacy for preventing death from the flu in children.

VR: This is important. It means that most of the kids who die would have benefited from vaccination. Not all of them, but most of them.

DG: We can't prevent all these deaths, but we could prevent a lot of these deaths. It seems crazy to me. No parent is going to drive around without putting their child in a child seat. We're not talking about over 1,000 children dying from not being in a child seat. No parent's going to drive around drunk with their kid in the car. There's all kinds of things we do to keep our children safe. This seems like one of the things that should clearly be in that list.

VR: I wonder why these kids who were vaccinated died anyway. That would be very

interesting to try and understand, right?

DG: Yes. There were, as we saw, there was 23% of the folks with underlying medical conditions, 13% of the kids who were otherwise healthy. You saw basically hundreds of kids, even vaccinated, still dying.

VR: What would be interesting to know if that's different from an older group, if the percentage is higher because they are young children, or is it similar? I don't know the answer to that. Then what's the mechanism? Are they not responding? Are they responding incorrectly? I think it would be important to know because that way you could possibly fix it with maybe changing the vaccine.

DG: Well, also responding. We've talked a lot about how a lot of times children don't get the antivirals, or maybe they don't get them as promptly, and that needs to change. I think part of it you got to appreciate. These kids, they can get sick really quick, so they can go from being fine to, 48 hours later, not being alive. All right. Vaccination, early treatment, make smart decisions. All right. I called this next section not a virus. We got that email. They're like, "Screwworm, Dr. Griffin, is that a virus?" Every so often, full disclosure, we're going to discuss stuff that's not viruses.

VR: This is clinical update. It doesn't say virus.

DG: It's clinical update.

VR: Although it says *TWiV*, but it's clinical update.

DG: Yes, so you get a few things. One, screwworm, we saw another four cases this last week, so we're up to a total of 33 cases. Why do we care? What's the issue here? Now we're up to 33 total animal cases. It's across the border. It's in New Mexico and Texas. It's a huge problem in Mexico, which we care about as well. We care here in the U.S. One is this is horrible. It's horrible for the animals that get infected. We've gone through sheep and goats and dogs and cattle. The biggest issue, the biggest economic threat, is to the beef market. This used to be over $1 billion in costs annually from the devastation of having this in our country. This is a threat to the beef market. It's also a threat to sheep, and dogs, and people, actually.

VR: Although at the numbers we have so far, it's not. If it can be contained, what are the efforts to contain this in the U.S.? Do you know?

DG: The biggest thing they're doing now is the irradiated flies. The female, the lady, the screwworm ladies, they only have sex once, and then they get basically a plug. If that sex is with an irradiated, sterile male, that's the end of it. Takes that lady screwworm out of the population. She's not going to produce offspring. That's been incredibly effective. That was incredibly effective. That pushed it all the way down to the Darién gap. We had a wall of irradiated mosquitoes. That's probably the most effective way of countering this. That's what they're starting to do now. A couple other not viruses, Legionnaire's disease. I don't know, Vincent, have people been asking you about this?

VR: Yes. It's really unusual. It's on the Upper East Side here in Manhattan.

DG: Right. Usually, what is it, in Harlem. Usually, it's in the Bronx.

VR: Yes, it's either in Harlem or the Bronx. It's in not well-to-do neighborhoods. I don't know why. Maybe the water towers are better kept on the Upper East Side, but now it's there. Yes, it's very interesting.

DG: I'll leave in an article to Jessica Nix's, "Upper East Side Legionnaires' Outbreak Source Remains Unknown." It's behind a paywall. I'll give you a little summary here. That was a great start, Vincent, because we're going to talk about how people get this and how people cannot get this. The New York City officials have not identified the source yet, but we'll talk about what we think it is. Upper East Side, we've already had 28 people infected, 21 are hospitalized. That's probably an undercount. Many more people are probably infected, not hospitalized, not aware.

The smoking gun are these rooftop cooling towers. The New York City Department of Health already has gotten samples from 87% of roughly 150 of these rooftop cooling towers. They're doing PCRs. They're basically racing to do the testing to figure out which ones need to be cleaned, which ones might be the source. Then they warn people, basically, if you feel like you've got the flu, you feel sick, contact a healthcare provider and let them guide you through this. Not everyone needs a test. There can be some judgment about who needs testing. The testing is mainly a urine antigen test in the case.

That's the situation here is people breathe in water vapor. The water vapor has the *Legionella* bacteria in it, so you don't get Legionnaire's disease from someone else. You get it from breathing in that vapor. A lot of times, these cooling towers can be the source of that. It gets warm. It's been warm. That warmth allows the bacteria to multiply, so perfect, ideal conditions for more and more bacterial growth. Also, it's hot, so more people are inside breathing the contaminated moist air, and then they end up breathing it in. The incubation is pretty quick. It could be two days, it could be up to seven days. It's pretty quick from exposure to getting sick.

VR: The bacteria, by the way, grow inside of an amoeba, which grows in the water.

DG: Yes, amoeba and paramecium. It's not just swimming around. It's in those, yes.

VR: Now, are the towers always full of *Legionella,* or are there times of the year when it's higher than others? Do we do surveys of water towers in New York to know?

DG: It's higher during certain times. We usually see *Legionella* with a summer cycle. We'll often see it early spring, summer, and then into the fall. You don't see a lot of *Legionella* in the middle of the winter, particularly in the Northeast or some other areas of the country where you might see a few cases here and there. For instance, Las Vegas, every couple months, you're seeing them because of the different climate and the different way things work there.

Recently, there were some issues in the tropics because in the tropics, you got that warm temperature. That really is conducive for *Legionella* to grow. Then they have air conditioning. A couple of reports of stuff down there. Now, they're doing PCR. You want to have no *Legionella* bacteria in these cooling towers. If your molecular test is positive, you got to bleach it, you got to dry it, you got to clean it all out.

VR: Now, if a patient has *Legionella*, how do you treat them?

DG: You treat them with certain antibiotics. It is important, certain antibiotics. One, you want to identify. We talk about the urine antigen test, but you can also send off sputum and sputum studies because the urine antigen test, as we've talked about, I think, on *Puscast*, you're only detecting about 30% of the cases. It's not highly sensitive. You treat with the macrolides. You could treat with azithromycin. You could treat with doxycycline. You could treat with a fluoroquinolone like Levaquin or Cipro.

All right. Cyclospora, we got a parasite in the news. We always have a parasite. Not a virus.

VR: Not a virus.

DG: Not a virus. [laughs] I'm not going to talk about the fact that we often have a parasite in the news, but this is a parasite in the news. Cyclospora outbreak. Outbreak of diarrhea-causing parasite grows to more than 1,000 cases. Cyclosporiasis outbreak in Michigan exceeds 1,000 cases. As of today, Thursday, July 9, when we're recording this, 1,251 cases out there in Michigan. It really is exploding. I like this. Explosion of the explosive diarrhea.

This is a parasite. Historically, we've had outbreaks from contaminated raspberries, basil, leafy greens. Some of the fast food restaurants, preemptively, and I really applaud them for this, have said, "OK, we're not going to be putting cilantro on things until we figure out if that's the source. We're not going to be putting lettuce on things." I think they're also not putting guacamole, but come on, you can put the guacamole. Charge extra.

VR: This is mainly from contaminated food then?

DG: That's usually, yes. That's really how you get it. The problem here is that this parasite is chlorine resistant. The idea of using bleach and some of the other things, you've really got to wash it off, so soap and water.

VR: What's the ultimate source of the contamination of the food?

DG: It's people. This is only people. Some people have this, and then it's a fecal-oral. Maybe they're involved in the collection of the food. Maybe they're somehow involved in the food chain. They've got it. They're not washing their hands. They're contaminating. Maybe we're using, what is it, night soil.

VR: How do you treat it? Will it just go away on its own?

DG: Not necessarily. Some people, a young, healthy person, this might go away. It might seven to nine weeks. Now, sometimes it can actually last quite a while, I have to say, jokingly seven to nine weeks. Immunocompromised people, they can get quite sick. You really should not die of this. It's something where you can rehydrate. The history is interesting. This was first really identified as an issue in Nepal, and they treated it with Bactrim, with TMP sulfa. That's very effective. That's really the number one treatment. There are some other options if that isn't working for you.

All right, Ebola, things are not going well. The Ebola outbreak in the DRC has reached another grim milestone, as greater than 500 people have now died. Only July 5 healthcare workers in Ituri, or on July 5, healthcare workers in Ituri issued a 24-hour notice of an impending strike, saying that working conditions were too poor to continue. To follow that along, yes, now they have actually gone on strike.

Some of the healthcare workers in Congo's Ebola outbreak have basically said now, as we're getting up to almost 600 deaths, they're not getting paid. They feel like it's not safe. They're not getting the appropriate gear that can help them stay safe. They don't feel like they're treated fairly by authorities. This is not great. If you look at numbers, so the CDC, I just went there, this is as of July 6 in the DRC, 1,708 confirmed cases, 580 confirmed deaths, 20 cases in Uganda, staying steady there with only one death. There's a confirmed case in France.

VR: Well, tomorrow on *TWiV*, we will have another Ebola expert, Tom Ksiazek from UTMB. You'll want to hear that this weekend.

DG: Oh, that's fantastic. Listen to us on Saturday and listen to that on Sunday. All right. The measles cases keep going up. We're up to 2,184 on the Hopkins tracker and per the CDC, 2,170. Basically, I think August, we're going to pass last year's total. We're now living in a country that has measles where we see thousands of measles cases every year. Not great.

Let's jump into COVID, Vincent. What do you think? We're looking at our multicolored lines. I had to follow this new link.

VR: Yes, it's looking good. It's really flat. That one line is still dropping.

DG: Yes, look at that.

VR: Still more time to go.

DG: The Northeast, it's never been that low in the Northeast, like ever.

VR: No. It's very interesting. We still have time before it would go up if it's going to go up. The graph that we have here, it looks like, I don't know, the second week in July, maybe it starts to go up.

DG: Yes, we still have a little time.

VR: Can't tell, but it is low.

DG: Going back historically, yes, this is not -

VR: It's good that it's low, right?

DG: Yes. We'll keep an eye. We'll let folks know. Now that it isn't anything to worry about, do we need to worry about treatment? Well, the article," Nirmatrelvir/Ritonavir for the Treatment of COVID-19 in Children Aged 6 Years and Older," was published in *Pediatrics*. This is an ongoing Phase 2/3 interventional open-label study evaluating nirmatrelvir/ritonavir, so Paxlovid, in pediatric participants with mild to moderate COVID-19 at risk for severe disease. This is that first week. These are folks that are at high risk twice daily, Paxlovid for five days.

These are folks who are at least 6 years of age and at least 40 kilograms or 20 to less than 40 kilograms. They've got a second cohort they're looking at here. They're going to end up with different doses based upon their weight. What do they find? They find that Paxlovid was safe. It was well-tolerated. As far as adverse events, they saw some loose stools. They saw some headaches. No discontinuations for treatment-related issues. No treatment-related serious adverse events were reported. No hospitalizations. They did see robust reductions in

the SARS-CoV-2 RNA from baseline to the end of treatment.

All right, COVID late phase. We've got a couple articles here to talk about. This first article, the article, “Efficacy and Safety of Rivaroxaban, Colchicine, and Famotidine–loratadine with Specialist Supportive Clinical Care for Fatigue in Patients with Post-COVID-19 Condition in the UK: A Multisite, Open-label, Randomized Controlled Trial,” published in *The Lancet Infectious Diseases*.

VR: Can you tell us what these drugs are, Daniel?

DG: Yes. Let's tell you this right away. The first one, rivaroxaban. These basically are direct oral anticoagulants.

VR: Nice.

DG: Think of it as modern rat poisoner, the modern warfarin. Colchicine, that's the gout medicine. Famotidine, loratadine, these are basically antihistamines. The famotidine is the GI, the loratadine is more of an allergy antihistamine. These are medications that people have thought would hold promise. They go ahead, and they're going to do this one-to-one-to-one-to-one. You're going to get either one of these drugs, or you're going to get no drugs. You're going to do this for 12 weeks, and then they're going to do this fatigue assessment scale, and they're going to see how well you do.

I'm just going to cut to the chase. They find a statistically significant, but unclear if it's clinically significant, basically 1.5-point change with colchicine and the antihistamines, not with the direct oral anticoagulant. Then when they stop, things go away, so they don't really see much beyond that. I'm not overwhelmed. This isn't like, "Oh, gosh, this is great." Yes.

VR: This is not going to solve the Long COVID problem?

DG: It's really not. There were tiny, tiny reductions. It didn't last once they stopped them. It was not necessarily clinically significant, but a statistician said, "Yes, it is a little bit different." A little disappointing. All right, the article - and I think this goes more to support the idea that there are post-acute sequelae. There are long tails to some of these infectious diseases. This whole idea that, oh, you get sick and now you should be fine, stop complaining.

Well, the article, “Long-term Sequelae Associated with Severe West Nile Virus Disease in Maricopa County, Arizona, 2021,” was published in *Open Forum Infectious Diseases*. Here we've got 159 patients with West Nile virus disease, and 75 patients who mostly had COVID-19 and cocci. They're going to compare some other diseases here, and they're going to do these standardized assessment tools. They're going to do them 17 to 24 months after hospitalization.

Now, what happens here? Among patients with West Nile virus, 40% end up getting transferred to long-term care facilities, 83% experienced ongoing symptoms, including fatigue, myalgia, arthralgia, pain, problems with sleep, memory, and concentration. Overall, 33% reported disabilities, 55% reported worse health than before the illness. It turns out that long-term sequelae in patients hospitalized with West Nile virus were common up to two years after hospitalization.

They go on to say that it looks like there are similar common inflammatory or physiological pathways leading to the post-infectious sequelae and outcomes related to hospitalization. Basically, an awareness saying providers caring for patients with West Nile virus should make them aware that there could be a prolonged and possible incomplete recovery process.

VR: That's a lot. 40% in long-term care facilities.

DG: It really is a lot.

VR: Wow.

DG: West Nile virus can be really bad stuff.

VR: You got to protect yourself from mosquitoes, folks.

DG: Not great.

VR: Wow.

DG: All right. Well, no one is safe until everyone is safe, particularly while there are mosquitoes in the world. I want everyone to pause the recording right here. Keep getting updates from Foundation International Medical Relief of Children in Uganda. Uganda has been doing a really good job so far with the Ebola outbreak, but that's because of the support that the people have there that they need. We are in the middle of our May to July fundraiser, hoping to send a maximum donation of $10,000 to FIMRC, particularly to help support the Bududa, Uganda site. Go to parasiteswithoutborders.com, click on the Donate button. Even a small amount helps.

VR: It's time for your questions for Daniel. You can send yours to Daniel@microbe.tv. Mark writes, “Regarding the doctor who said she is unable to give shingles vaccines in her office due to it being a Part D service." It's Medicare Part D. "I am an internist. We give Shingrix in our office. Medicare pays for it. There's a program called TransactRx. They are a private vendor. Patients get the same coverage in my office that they would get in the pharmacy. Some insurance plans do not participate, so we check every patient beforehand and let them know what their copay will be as the website tells us in real time. It's very easy to use. We sign up for it, and it allows us to give our patients vaccines. This is not a new program. The writer needs to have a talk with her office manager."

DG: Mark, this is great. Hopefully, our listeners, TransactRx, this is really a great option. Hopefully, more people hear about this, more people will be aware of this, and then more people will then have access to the wonderful dementia prevention vaccine.

VR: Spread the word, folks. We know you can do that. Susan writes, "My then-teenaged son was temporarily put on a steroid that apparently tamped his immune system enough to cause him to get shingles. He was around 17 at the time. He's now 32. Should he request to get this shingles vaccine early or just wait until the recommended age of 50-plus? Thanks for all that you both do to keep us well-informed and educated during this dark time for public health."

DG: This is a slightly complicated question you asked, Susan. If you had said, Oh, my son is immunocompromised, he had shingles, what should we do? He's not 50 yet." The vaccine is

indicated for folks 50 and older. It's also indicated for folks 18 and older who are at increased risk because of immunodeficiency or immunosuppression. It would really come down to the question, is he going to be on steroids again? Is his immune system going to be tamped down because of something like that? If this was a one-time deal and that's behind you, you don't necessarily go ahead and get the vaccination. If there's going to be immune issues again, the second indication is for the folks under 50 who are potentially at risk because of an issue with the immune system.

VR: He got shingles, so he has latent virus in ganglia. He could, after 50, get it again. That's the idea, right?

DG: Yes. His risk would go up when he hits 50. Hit 50, go ahead and get your two vaccine doses as recommended. Unless he's going to be steroids again, if this was one and done, he's back to a normal immune system, the recommendation would wait until you're 50.

VR: Jeff writes, "Long-time listener to the podcast. Reaching out because I am curious. I know there are a variety of viruses which cause viral hemorrhagic fever disease. Are there analogous pathogenic eukaryotic species which cause hemorrhagic fevers? If so, like what? If not, why do these symptoms present in viral infections?" Is there anything other than viruses that cause hemorrhagic fevers?

DG: Yes, I was thinking about this. Eukaryotic infections would be like our helminths, our worms, our fungi. I can't think of any kind of a hemorrhagic fungal infection or hemorrhagic parasitic infection. I'm thinking it's certain viruses.

VR: According to AI, some bacteria like *Rickettsia* and *Leptospira* can cause. Malaria can be associated with hemorrhagic fever. Did you know that?

DG: Actually, yes, that's interesting. That would be your eukaryotic. I like that, actually, as a thing.

VR: Then some worms can cause hemorrhagic fever.

DG: Which worms? I'm curious about that.

VR: Let's see. This is actually a paper. Oh, interesting. This article is viruses, so I don't know which worms would be involved because it sent me to this article, but it's not worms.

DG: I know it's not popular, but I like AI. It's helpful for questions like this.

VR: Well, if you can go to the literature and confirm it, that's always good.

DG: That's key. You got to do that next step so that you can ask these questions like, hey, and then you bring up, you're like, yes, actually, oh, Lepto, yes, I didn't think about that. *Rickettsia*, yes, that's great. Not eukaryotic, but not viral.

VR: Well, then if they don't give you a reference, what they did here, you can ask them what's the reference for that, and then you go look at it.

DG: Yes, and that's key. Otherwise, they can hallucinate or just tell you what-

VR: Of course.

DG: -they think you want to hear, which I like that too, but [chuckles] I wanted to--

VR: Brooklyn writes, "Thank you for all you do. Why have we not seen more deaths with this year's measles outbreak?"

DG: Brooklyn, it's about one in 1,000 acute deaths. We're 2,000, so one or two deaths is all we'd expect, so we're doing OK there. Unfortunately, and this is the problem, is the risk of death is going to go up. It's going to be threefold higher for all these individuals for the next two to three years. That's going to be very interesting to try to connect those deaths. Hopefully, people are following these individuals that had measles over the next few years. There's also several years later, there's the neurological issue that can occur. It may not have been enough time. Hopefully, these kids are getting good care. I really do not want to see kids dying of measles in the United States.

VR: We have not had any deaths in 2026, but we have over 2,000. It's just probably too close, right, statistically?

DG: Yes. Yes.

VR: Mary writes, "Thank you in advance for taking my questions. As a board-certified emergency physician, I am anticipating my use of Xocova. As the FDA has approved Xocova for post-exposure prophylaxis for COVID, will testing for COVID be required prior to starting the medication to ensure the patient is not already infected? Also, what is to be done once the patient has started Xocova and then becomes sick with COVID symptoms? Does one stop the medication and switch to Paxlovid? I understand that Xocova is used in Japan to treat COVID. What is the effectiveness of Paxlovid versus Xocova for treatment of COVID? Thanks for all that you do at *TWiV* for your dedication to the science."

DG: All right. Mary, this is great because this brings us back to the science. What was the FDA approval based upon? It was this study where you have the index patients, these are the folks that have COVID, and then you've got the household contacts. What they do is they do the point-of-care, they do the rapid test, they go ahead, they start people on Xocova, but they also go ahead and they do PCR. What ends up happening is some of the folks, actually a fair number, like double-digit percent of the folks that get started on Xocova, end up having positive PCRs.

You're actually starting it on some of the people. It's more effective at preventing COVID and people that don't have it. If you actually remove those people in the analysis, so intended to treat versus people who confirmed PCR, you don't have it, does it prevent it? 80% prevention, that's great. Yes, certain people had it, and then Xocova doesn't have the indication for treatment. If you're using it for prevention, great, go ahead, take the ensitrelvir, the Xocova. If the patient actually gets diagnosed with COVID, then the recommendation is to treat with Paxlovid.

Comparing effectiveness, Paxlovid versus Xocova for treatment, here in the U.S., we have the compelling data that we've talked about repeatedly, randomized controlled trial, and then the post-analysis where Paxlovid is effective for treatment. The Xocova doesn't have basically FDA-level data to get approval for that here in the U.S.

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

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

[00:42:52] [END OF AUDIO]