TWiV 1282 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.

[music]

VR: From *MicrobeTV*, this is *TWiV*, *This Week in Virology*, Episode 1282, recorded on December 24, 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: You have a red bow tie, a little festive touch there, Daniel.

DG: It is being perceived as like in the holiday cheer, but if you look closely, it is in the holiday cheer. It's every year, from the rooftop comes the influenza virus. Is that the way it goes?

VR: In the window, influenza through the window.

DG: Yes. Instead of the chimney, she cracked the window and influenza.

VR: I don't think that's very much holiday cheer, is it?

DG: No. The red nose, right? I think that's why Santa's nose is red.

[laughter]

VR: What's the medical term for red nose?

DG: Oh, actually, red nose. You're not thinking about the rhinorrhea or the rhinitis, but the actual outside redness. That's a good one. I'm not sure.

VR: What's coryza? Remind me what that is.

DG: Coryza is the redness inside the nose, right?

VR: There's no word for a red nose. Oh, well.

DG: There probably is. Probably lacking in that. You Google that for me, Vincent. How do you say red nose in Latin? Because I'm thinking about people have rosacea. Say it.

VR: There is a term. It's rhinophyma.

DG: Rhinophyma.

VR: R-H-I-N-O-P-H-Y-M-A.

DG: The rhinophyma of the holiday season.

VR: The phima. I don't know how you say it. Rhinophyma. Next time you have a patient, tell them that and see what they say.

DG: Oh, my gosh. Look at that. Rhinophyma. Let's jump in. We got a lot to cover today. It's a busy time of season, as I mentioned, seeing a lot of flu activities. I've got my coffee here because it's been the middle of a long week. I want to be very positive this time. At least I'm going to try. I'm going into it, like out of the gates with that as my goal. Nothing in life is to be feared. It is only to be understood. Now is the time to understand more so that we may fear less.

VR: I agree. I think that a lot of the misunderstanding comes from fear.

DG: I think it's true. It's interesting. I'll admit, I sometimes look through the comments after we post a show. It's always interesting because some of the people, "Oh, you were spreading fear." I'm like, "We're not actually. We're spreading knowledge. We're sharing tools and ways to stay healthy and live longer, and ways for your children to be healthier and live longer and have better lives. It's not fear that we're spreading here. We're actually spreading knowledge and power and the tools for a better future."

VR: Truth is not fear. No.

DG: It's like, "Oh, don't put your hand in that hot water." It's like, "Well, why did you tell me it was hot? Now I'm going to burn myself." It's like, "No, no, I told you it was hot," so you wouldn't. I'm pointing out what's going on. I will start off by pointing out bird flu, talking about bird flu. From the USDA, we hear just a few days ago that the first detection of highly pathogenic avian influenza in a dairy herd in Wisconsin, and this is a problem because the cheeseheads out there, they love their dairy products.

On December 17, they completed whole genome sequencing and confirmed that the virus is H5N1. Then they tell us it's clade 2.3.4.4b genotype D1.1. The analysis indicates that this detection is a new spillover event from wildlife into dairy cattle, separate from previous events.

VR: That's very interesting because so far all of the cattle viruses have been from the same origin, right?

DG: That was the spillover in the Texas, Oklahoma area, and it was genotype B for bovine. We talked about that. Now, D for dairy. I don't know. I'm going to get all confused here. It's interesting that we're paying attention. We're seeing now another spillover event, so wild birds into the dairy cattle. We'll keep an eye on that. The poor cows, right? They get the bird flu. We discussed on IDPodcast rabies from a skunk. It was a skunk that attacked a bunch of steers. It made them all rabid, reminded me of Old Yeller.

OK, so Marburg, Ethiopia. Ethiopia's Ministry of Health has reported 14 laboratory-confirmed illnesses, including nine deaths. We'll keep track of what's going on there. Not good news. Not spreading fear, but just want to point out to people, I was worried about

this number. I don't know if there was round numbers. As human beings, we sort of see as milestones. As of December 23, 2025, a total of over 2,000, so 2,012 confirmed measles cases reported in the United States. We're a few weeks away. I think it'll be next month officially announced that measles is no longer eliminated in the United States.

VR: There was a time when there were no cases in the U.S. Zero. All of these are vaccine-preventable. What's the problem, folks? Why do you have this happening?

DG: It's really tough. Stay positive here. I was reading an article recently that was sent to me by someone who used to work at the FDA. [laughs] It was about this family. It was even a provider, I think, was quoted in there saying, "Oh, we were all really worried. We heard about all these measles cases, but we gave all the kids the vitamin A and some other stuff." Ivermectin, maybe, was mentioned. Oh, fortunately, it's much better now. Only a couple children died. I read this stuff, and I'm just like, "What world? Children should not be dying. All these children should not be ending up in the hospital."

About 10%, 20% of these kids end up in the hospital. We're talking about hundreds of kids ending up in the hospital for something that you could just get your vaccines and not have to worry about. Then all the post-acute measles increased infections because of the immune amnesia. Just what a disaster.

VR: This is going back to the quote, one death is a tragedy. A thousand is a statistic. One death, it's someone's child. It's a tragedy to them. If you look at the numbers, there's no tragedy involved. You can't look at it that way.

DG: Each child - I think there was a family - I know there was a family where their child was under 6 months. We talked about this, where their child got pertussis because someone else chose not to vaccinate. Their child was too young to vaccinate. They did all the right things, and their child ends up in the hospital. Not the only child, seeing a lot of these. It's really tough because this is not what we're hearing about in the news. We're hearing about the Epstein files, we're hearing about all kinds of other craziness.

Some huge ballroom that's going to be four times the size of the White House. We've got children getting sick. We've got children dying. Maybe as a physician, I have this weird bias towards wanting people to be healthy. Up in Canada, week 50, 24 new measles cases, total up to 5,353. We've got measles in Canada. We've got measles in the U.S. We've got measles in Mexico. Welcome to the good old days. I guess this is great again. A lot of flu.

It's interesting. I was talking to the ICU doc today, and she said, "Hey, I'm hearing something about some new mystery virus going on." I'm like, "Oh, yes, it's on Twitter." I was like, "Yes, it's called influenza A, but you didn't test." Who knows what it is? We are seeing a lot of - Influenza A is at high levels. If you look at the map, we are about as bad as it gets. New York City, New York State, Long Island, we are in the very high. Lots and lots of flu. We're seeing lots of folks come in the hospital.

I had a gentleman earlier this week, really horrible. A man in his 40s, he got flu. He ended up having a stroke. Really horrible. We've talked about this connection with you get the flu and then this increased risk of cardiovascular, so strokes, heart attacks. To be taken seriously. If we look at the epidemic trend, it's increasing. Flu is increasing all across the country. Everyone's going to get together for the holiday. The holiday, the holiday weekends, the holidays. Then we're going to see even more spread. The hotspots, pretty soon, the whole

country will be the hotspots.

The predominant, that 90% of it, is this H3N2. Then speaking about children dying, we talked about 288 pediatric deaths occurred last season. We're already up to three flu-related pediatric deaths this year. CDC still telling us some things, 4,600,000 flu illnesses, 49,000 hospitalization, 1,900 deaths from flu so far this season. Now this might bring people back. The only thing worse than COVID is comparing it to the flu. I don't know if people remember headlines along those. Here we have the article, “Increased 30-day Mortality Risk in Coronavirus Disease 2019 Compared to Seasonal Influenza,” published in the *International Journal of Infectious Diseases*.

From Korea, we have this nationwide population-based cohort study that utilized the National Health Insurance Claims Database, including individuals newly diagnosed with COVID-19 or influenza. The primary outcome was 30-day all-cause mortality. These are big numbers, 12,802,169 patients with COVID, 2,888,777 patients with flu were analyzed. COVID-19 was associated with significantly higher 30-day all-cause mortality compared with flu. Almost twice. The all-cause mortality adjusted odds ratio, 1.76. This risk remained consistent when they looked across all the different subgroups, and, I should say, particularly higher risk were observed among adults aged 18 to 64. That was almost a threefold risk all-cause mortality.

The hospitalized patients, adjusted odds ratio, 2.55. Those with a myocardial infarction, 2.24. It's really interesting. I've had people criticize like, "Oh, you shouldn't be looking at all-cause mortality." I think that's the message we're trying to make here. It's that if you get the flu, if you get COVID, if you get RSV, it's not just that first week. When you follow these folks out 30 days, 90 days, here, 30-day all-cause mortality, they may not die in that first week, but they may have a heart attack. They may have a stroke, and they may end up succumbing as a trigger being this infection.

VR: I don't see the value of doing this because I teach my virology class. If you're studying virus infections in, say, lab animals, you would never compare poliovirus with Ebola virus. You can't. The animals are different. The inoculation is different. The virus is different. All you can do is compare different polioviruses or different Ebola viruses. This, who knows what the inoculum was? Who knows how the hosts differ? They don't even control for vaccination. Maybe more people are vaccinated against influenza virus. I think this is not a useful study because I think it's fraught with complications that could change the outcomes.

DG: Those are interesting comments. I think where they go with this is basically like COVID is still very serious because a lot of people say, right, it's this offhand, "Oh, COVID, it's now just like a bad cold." I don't know. It's a bad cold with lots of people still dying.

VR: Hey, people are dying. It's a problem, right?

DG: Exactly.

VR: You don't need to compare it to anything. Just get vaccinated.

DG: Yes. Get vaccinated. We have those broad recommendations. Basically, 6 months of age and on up, get vaccinated. That's really the best thing you can do.

VR: Daniel, people, they don't compare heart attacks with cancers and diabetes and stroke.

You don't compare these diseases. They're impossible to compare. There's no point. Each one has its own issue. Just get vaccinated. We have vaccines. Get them. There's no reason not to.

DG: Vincent, this is for you. What happens if you've got your vaccine, now you end up, you're sick. Do we have any treatments for the flu?

VR: We do have treatments for flu. We have two.

DG: We do. We've got oseltamivir, the well-marketed Tamiflu, and we have the potentially more effective but the poorly marketed baloxavir, Xofluza, single pill, one and done. That's not going to work because you know what? You're still going to be feeling sick two or three days later. With the Tamiflu, you're still on the medicine. The Xofluza, you're done.

VR: Daniel, you've left out Relenza, the other neuraminidase inhibitor. Nobody prescribes that? It's an inhalation thing, I think.

DG: It would be interesting to look at market share, but we really don't use it very much.

Vincent: It's weird because it's inhaled, and if you have flu, you're going to cough when you inhale something, right?

DG: It's in that disc, and it's like a powder, and some people end up with bronchospasm. The big pharma's listening, and they're like, "Oh my gosh, why are you saying negative things about Relenza?" [laughs] I will look into it. I'm going to put a question here for next week. What is the market share, and just where are we with that?

VR: I think also someone told me that you prescribed them Tamiflu, and I said, "Why didn't you have him prescribe baloxavir?" He said, "It's too expensive."

DG: Yes, and this might be a market issue too. Are they actually making sure that it's available in the different pharmacies?

VR: It's a shame when cost determines health treatments, right?

DG: Yes, it is. We've got that. Relenza or zanamivir, we'll talk about next week, and what's going on with that. RSV. RSV, as we've talked about, has this trend. It usually starts in the South. It starts down there in Florida and moves up, and we're seeing that it has moved up. It's actually declining in Florida, but the rest of the country, it's growing. We're seeing this tripledemic here in New York, where we're starting to see lots of cases of RSV as well.

RSV is on the way up, and there are vaccines for this. We've got vaccines for adults. We've got vaccine that the ladies can take during that 32 to 36 weeks. We've got the monoclonals, but here's a question that we're going to talk about. Vaccinating mom, giving the kids monoclonals, what's better? Can we compare that? Is that OK, Vincent? Can we compare these two?

VR: Yes, you can compare treatments. Of course, that's how clinical trials work, right?

DG: It's the same virus. I'm like secret option C where I get both, but here in the U.S., it's an either-or. We have the article, “Nirsevimab versus RSVpreF Vaccine for Respiratory Syncytial Virus-related Hospitalizations in Newborns,” published in *JAMA.* Population-based cohort

study using data from the French National Health Data System. Maternal vaccination with the RSVpreF vaccine during the 32 to 36 weeks was compared to the passive immunization with the monoclonal nirsevimab. Infants were matched one-to-one, and then they're going to follow them and basically see how they did.

What do you guys think? Is it going to be the vaccine and mom during that window, or is it going to be the monoclonal antibodies? Which is going to win? Which is better? Which is more effective? In this study, we've got a total of 42,560 infants. We ended up with 21,280 per group. Half get the vaccination, and the mom, and the half are the kids who get the monoclonals. Of the 481 hospitalizations for RSV-associated lower respiratory tract infection, 44% occurred in the monoclonal group, 55.9% in the vaccine group. Negative 11.8% difference.

Basically, lower risk of hospitalization for RSV-associated lower respiratory tract infection. Adjusted hazard ratio of 0.74. It's about 26% lower with the monoclonal versus the vaccine. Lower risk of severe outcomes, including ending up in the pediatric ICU, the PICU, where my daughter works. Adjusted hazard ratio of 0.58. They're about 42% reduction there. Reduction requiring ventilator support. Hazard ratio of 0.57. It's about 43% reduction in ending up on a ventilator. Also, about a 44% reduction and requiring oxygen support. Head-to-head, it looks like the monoclonals came out ahead.

VR: Probably, the antibody titer is higher because you're giving it directly to the babies, whereas you're depending on placental transfer from the mother, right?

DG: I think that - Even the timing, you think about, because maybe mom gets the shot in September, and so when is the baby born? The kids are getting it, boom, right at birth, before they leave the hospital. You've got really good timing on this delivery as well.

All right, the COVID update. This is a mixed picture here. If we look at our multicolored curves, and I zoomed in a little bit, we saw it starting to come up, and then I think we're going to have to see what happens here with this wobble.

We're getting up to moderate in one area - a couple areas, actually, the Midwest and the Northeast here. The interesting thing is we're seeing this, but if you look at the epidemic trends, most of the country looks like it's growing. We'll have to see if we get a wobble, and then it keeps going.

VR: The curve is two weeks late, right?

DG: That's a problem, too. The curve is two weeks late. I would let you know, come on, it'd be great if we had more real-time data on our fancy multicolored curves that we like to track over time. In general, we're seeing COVID, numbers are rising, so keep that in mind when you're making decisions about what to do. Again, vaccine, another illness that we can reduce severity and the impact with vaccination.

Is that true? This I like. It took a little while coming. People had ideas, and we're going to have to tease out the data we have here a little bit because part of the conclusion is going to be we don't have as much data as we would like to make the conclusions we would like to make. We've got the article, “Association Between COVID-19 Vaccine Immunogenicity and Protection Against Infection and Severe Disease in,” and I highlight this, “Clinically Vulnerable Patient Populations: A Systematic Review and Meta-analysis of Observational

Studies." published in *CMI*.

The goal, the aim of this study, is to investigate the association between vaccine immunogenicity, right? What kind of an antibody level do we get? What kind of a T-cell response do we get? Compare that to the vaccine effectiveness. Then, in this particularly, this is clinically vulnerable populations, so not just a broad population study. They use this random effects meta-analysis model to pool the relative risks of COVID-19 post-vaccination infection. They call it something else. Something involves breaking and through, but I'm going to change that.

Post-vaccination infection, hospitalization, death. They identify 3,305 articles. Of which, 45 observational studies are included in the review. Now, negative antibody responses after getting that COVID-19 vaccination was associated with higher risk of post-vaccination infection. It's really interesting. The relative risk is only 1.82. Nobody thought it would be more dramatic. You get a shot, you don't see any antibody response, and you see this go up.

Now, COVID-19-related hospitalization, that's where you see it, 5.88. Almost a six-fold relative risk. Death, 3.66. Three- to four-fold increased risk of death, you get the shot, and then you don't see any antibodies. Now, this is where we have to tease out. Lack of T-cell response was associated with a higher risk of post-vaccination infection. That's a relative risk, 2.08. Even a little bit higher than not getting antibodies. Here's the thing that you're probably waiting for. "Dr. Griffin, what about disease severity? That's what the T-cells are going to protect us for?"

I want to make a couple comments. They point out that the evidence for a correlation between T-cell responses and protection against infection outcomes in vulnerable populations is even weaker than for antibody assessment. I'm going to agree with that. They suggest this largely relates to additional logistic and cost implication required for research studies. They're just not looking is part of the issue. If you don't look, if you don't have the data, it's hard to draw that connection.

I think we're discussing a vulnerable patient population here, so there may be differences in their immune system. I will say, in healthy controls, T-cell responses have been reported to protect against infection and are informative regarding ongoing protection when the antibodies wane.

VR: I have a few comments here, Daniel. Just a few. First of all, as Mark Crislip would say, these meta-analyses lump the good with the bad.

DG: I think what he would say is that you take the cow piles and you pile them so high that they magically become gold.

VR: Not every study is done the same way with the same rigor. You really can't lump them all together. It's not fair. You should go and look at them individually. Secondly, OK, antibodies and T-cells are also non-neutralizing antibodies that are important for COVID. We're not looking at these here. Finally, in the original clinical trial of COVID vaccines, antibodies correlated with protection. Neutralizing antibodies, that's what they looked at. To a certain extent, T-cells as well.

We already know this. In a trial of 40,000 people, which was double-blinded and placebo-controlled and enrolled populations, not an observational study. That's the standard there,

not this.

DG: Yes. COVID, moving into, now you got COVID. You got your vaccine. You did everything you were supposed to, or you didn't. The article, "The Effect of Remdesivir and Nirmatrelvir/Ritonavir on Mortality in Patients Hospitalized for COVID-19 During the Omicron Era: An Emulated Target Trial," published in *CMI.* Here we've got the results from a retrospective population-based cohort study. Patients were included from six acute-care hospitals in Stockholm, Sweden, during the Omicron Era. Among 4,060 included patients, only 19% received antiviral treatment. Overall mortality was 9.1% at 30 days, 13.8% at 90 days.

I want people to think about those numbers. The adjusted risk ratio of antiviral treatment was 0.80. About a 20% reduction for 30-day mortality, about a 22% reduction for 90-day mortality. That's another thing to think about. We've been talking about this for a while, clapping everyone out the door. People keep dying once you've clapped them out the door. If you actually look at the really nice figure, most of the folks, they're not dying in the first 10 days. You actually really start to see the separation at 30 days, and then it keeps separating more out as you get to 90 days.

VR: No, but Daniel, we're going to wait and see if it goes in your lungs before we give you Paxlovid, OK?

DG: In other words, wait and see if you die.

[laughter]

VR: We are laughing. Don't get offended. We're not laughing -

DG: We are laughing because it's a little bit frustrating, because we still see this to this day. Here we have more evidence. I'd say, a lot of hospitals are really restricting access to antivirals because they are ridiculously priced. I'm going to say that out loud. The data is there that it can make a difference. These exorbitant prices, that becomes a little bit of a different discussion. These are not diseases where you wait and see. Because the window closes.

We talked about flu. You've got 48 hours really, to see a benefit with COVID. Really, it's the first five to seven days that you get the most bang for your buck. If you wait till the second week, diminishing returns. Second week, we might do steroids, we might do anticoagulation, pulmonary support, but really, a diminishing impact when it comes to antiviral therapy.

VR: Daniel, let's say you have a hospitalized patient with COVID, and the doctor says, "We're going to wait and see before we give you Paxlovid." Can the patient demand to have Paxlovid?

DG: Interesting. The patient could. The patient could demand. The patient could say, that's not consistent with the guidance, that's not consistent with the science, what are you doing here? They make a little bit of a stink, yes.

VR: I think our listeners would probably do that. Remember, you have the right to say, "I want Paxlovid."

DG: You have the right to say, I would like an infectious disease doctor to consult. That's a challenge. As we've talked about, only 10% of the counties in our country are adequately staffed with folks like me; 80%, don't even have a single infectious disease specialist, which is really tough. That's going to wrap us up. I'm trying to keep it not only positive, but not so long-winded because this is the holiday season. Just a few reminders to people. One, no one is safe until everyone is safe.

What are the best ways to keep people safe? The safe, effective vaccination. Science supports universally recommending those flu vaccines from 6 months of age all the way up. We've got recommendations for RSV vaccination, both the active and passive. COVID vaccination. We've talked about this repeatedly. The science, the evidence supports really 6 months of age all the way up, whether it's protecting you from long COVID, from being sick, from duration of sickness, from ending up in the hospital, dying, or having sequelae afterwards.

I want everyone to pause the recording right here. I want to thank everyone who's done this so far, who've gone to parasiteswithoutborders.com and clicked that Donate button. Your funds - We had a meeting, a *MicrobeTV* meeting last night. We were talking about, do we introduce ads? We do not want to introduce ads. We want this to be your show. You keep it your show by coming and supporting us. I say us because we are in the middle of our *MicrobeTV* fundraiser doubling your donations up to a maximum donation to *MicrobeTV* of $20,000.

VR: It's time for your questions for Daniel. You can send yours to Daniel@microbe.tv. Josh writes, "I'm a GP, family physician from Victoria, Australia. I'm a big fan of the show. I have a question regarding rabies vaccination and Australian bat lyssavirus, ABLV. Every year, my partner, well, 30-year-old female, stays in a holiday cabin for one week in rural Victoria, and every year, a bat sleeps in the same room from the rafters. This has been happening for years, and the bat has never harmed her, but it does concern me that she could get bitten or scratched, especially if unaware while she is asleep.

It's very rare, but there have been four deaths from ABLV in Australia since it was first detected in 1996. My understanding is that the disease is almost identical in presentation and outcome as classical rabies. I have raised with her the idea of rabies vaccine as pre-exposure prophylaxis, which I believe local guidelines would support. I wonder what your thoughts would be if you would recommend vaccination in this setting."

DG: It's really an interesting question. Here in the U.S., we see most of our transmission from bats. We have this guideline for if you realize you're sleeping in a room with a bat, you should go ahead and get your rabies vaccine. Part of the idea is that the bite from a bat, these really tiny, sharp teeth, can be something that you do not even know happened. It can actually be painless. It can occur while you're asleep. That's this idea that there might be this issue.

You're making it even more complicated because I don't know about any data, whether we look at the protection of the standard rabies vaccine against the bat lyssavirus. Maybe in a second, I'm going to ask you to chime in, Vincent. No, I think she's going here. There's been a bat every year. I don't really see the harm other than the financial of getting a rabies vaccination series. I would sleep better knowing I had gotten such a vaccine series. Vincent, any thoughts? I guess we're speculating.

VR: I did look it up. The rabies vaccine does confer protection against ABLV. In fact, it's recommended for people at risk for bat encounters.

DG: OK, there we go. I will say, go ahead. It seems like a reasonable thing.

VR: I just want to know how you know there's a bat sleeping with you if you're sleeping.

DG: It's interesting. I've been in places like this where, oh, yes, there's a cute little bat sleeping up in the rafters. I remember - oh, this is really a great story. In Accra, Ghana, or Accra, depending on how you pronounce it. There's a military hospital. When you drive down the road during the day, there are millions of bats just sleeping in the trees.

VR: Cool. Have you ever seen the bats fly out from the bridge in Austin?

DG: I have not. I have not.

VR: Austin, Texas, there's a famous bridge, and the bats roost under it. Then at sunset, they all fly out at once. Many, many, hundreds of thousands of bats. It's quite a spectacle.

DG: Oh, it's amazing to watch. The same thing you get in these places. Wherever there's a large concentration, right at sunset, the sky darkens because it's so many bats.

VR: We went to see it one year when we did *TWiV* 500. We went to see it. Now I guess I could check that out. I was in Australia one year, and Linfa Wang, the Batman, took me to a golf course right next to the lab. There's a roosting place for gray-shouldered bats. We could see them all hanging there. We were just before sunset. As the sun went down, they all flew off. It was really amazing.

DG: Oh, that's amazing. That's great.

VR: He said, "Just watch. One bat will lead the way." In fact, one bat, they start moving their arms because they're all bundled up hanging up. They start moving their arms, and then one flies off, and they all follow.

DG: That's great.

VR: What if that one is wrong?

DG: Where's he going? You went the wrong way, buddy.

VR: We have a postscript from Josh. "It would be great to see an episode on your show, if you have not done so, on Buruli ulcer, an interesting non-healing ulcer caused by *Mycobacterium ulcerans*. There has been a rapid increase in case numbers over recent years in Melbourne, which is interesting given it seems to be usually a disease of tropical regions. It is not yet fully understood, but there seems to be an interesting transmission mechanism involving mosquito bites and possum feces." Oh, that's interesting.

DG: Yes. This is really - I had the privilege during the end of the pandemic years of going to the Buruli Center of Excellence in Western Africa. What a horrible disease. You have these ulcers, but the edges, it's undermined. You can stick a Q-tip under there, and it's just - What a horrible disease.

VR: Will writes, "I recently heard that hand-washing with soap rinses the virus away rather than destroying it." OK, I know where Will heard this.

DG: [laughs] Yes, I do too.

VR: You're misrepresenting what I said, Will. I said, for norovirus, soap is not going to destroy the virus particle. Neither does alcohol. You have to wash your hands vigorously to remove the bulk of the virus particles. Envelope viruses, yes, it's going to inactivate it, but not norovirus. Anyway, Will went out to ChatGPT and said viruses with lipid envelopes get inactivated, and you need to do it 20 seconds to disrupt the virus and dislodge them from creases, nails, et cetera. He wants to know what's correct. I have heard for some viruses that alcohol cleansers do not destroy the virus.

DG: Yes, I think that's a helpful breakdown is we've got our enveloped viruses. As you mentioned, an alcohol should work well on the enveloped viruses. It should work well on a lot of our bacteria. Even interesting, even like *C. diff*, where they do special precautions, you must use soap and water, unless you're visibly soiled. Studies would say that the alcohol is effective. Then you get into things like norovirus. No lipid, it's this protein shell, and then you're really trying to get the stuff off your hands with the soap and water.

VR: These viruses, poliovirus, norovirus, rotavirus, they pass through your intestinal tract. That's very harsh. In fact, when I used to purify poliovirus in the lab, I used soap to disrupt the cells, and the virus was totally fine. Here you go. Amy writes, This is not our friend Amy. Maybe she's our friend, but she's not Amy Rosenfeld. “I'm confused as to whether my healthy 22-year-old son should receive a COVID booster. He received the original three-dose mRNA series. My impression based on hearing your and Vincent's podcast was that the original three doses are sufficiently protective due to T-cells such that most people do not need booster shots.

However, with all the talk about the recent attempts to restrict access to vaccines, which is, of course, terrible, I find myself wanting to take advantage of vaccines whenever they're available. My question is, is there any reason why for a healthy 22-year-old to receive yearly COVID boosters if they have received the original three-dose series?"

DG: Perfect example. I have a 20-year-old son, I have a 23-year-old daughter, and they each get their yearly COVID boosters. Why do they do that? There's a couple of benefits. One is there is about a 50% reduction in the risk of getting symptomatic COVID. That's nice, reduce the risk of symptomatic COVID. The other, in this age group, they're really not at high risk of ending up in the hospital, ending up dying, but they are at risk of getting Long COVID. We just keep seeing more and more data that getting the extra doses or each dose you get each year is going to be associated with a reduced risk of that post-acute sequelae of COVID.

Those would be the reasons. It's different thinking than in your elder, where the person might end up in the hospital, where they might not survive, and where we're talking about decreased hospitalization risk, we're talking about decreased risk of death.

VR: Sue writes, "I've been a huge fan of your show since the dawn of COVID." Wow, it's poetic, right? "Thank you so much for offering your expertise to those of us who need it. I am soon to turn 80-year-old female who yesterday finished a robust reaction to topical fluorourcil on my face for AK. I am in need of a COVID booster, and I'm wondering if my immune system will be too busy healing my face to build an optimum immune response to

the Pfizer vaccine. Also, CVS only offers Pfizer or Novavax. Any advice on which is more effective for my age? I've chosen Moderna in the past."

DG: Yes, treatment with fluorourcil for the actinic keratoses. These are those potentially precancerous lesions on the skin. We've talked a little bit about Pfizer and Moderna, the mRNA vaccines versus Novavax, protein-based. Really, nothing out there that's like, "Oh my gosh, slam dunk, this is a better vaccine." Some people are moving towards Novavax because less reactogenicity. If you're getting over this topical treatment for your AK, that might be something to consider. Think about how you've responded in the past. If you were down and out with Moderna for a day or so, maybe the Novavax will be milder. I really think the best vaccine is the one that you actually get.

VR: Shudder some writes, "Thanks for covering the study on pemivibart/Pemgarda, on your last podcast. I've been very curious about the similar VYD2311 product designed to be given as intramuscular shot. Clinical trials begin year-end 2025, and top-line data are anticipated mid-2026. If the study is successful, could this become available to people who are immunocompetent but high risk for other reasons, or available to anyone who might desire extra protection? Do you have any thoughts about whether monoclonal antibodies could and should be used in addition to vaccination to further reduce infection and Long COVID?"

DG: It'll be exciting to see the data here. I've been a little disappointed with the lack of update. There are certain populations, particularly, we think of immunocompromised people who have organ transplants, people who maybe got anti-B cell therapy, who really don't make the antibodies when they get the vaccine. We talked about doubling your risk of ending up in the hospital or mortality if you don't make those antibodies. Why don't we just give those to you? It's exciting that we're going to have another trial looking at this. Once we get the trial data, I'm optimistic. Once it's out there, we'll have to see if there's any movement and people doing a little bit better job of protecting these vulnerable populations.

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

DG: Thank you, everyone. Be safe and enjoy the holidays.

[music]

[00:43:31] [END OF AUDIO]