

TWiV 1362 Clinical Update

Host: Vincent Racaniello

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 1362, recorded on October 1, 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: It is October. The year is zipping by.

DG: It is, it is, but it's interesting. Here in New York, it's suddenly switched back to summer. It's in the high 70s. It's sunny. It's beautiful.

VR: What's on your tie today, Daniel?

DG: Well, if you walk into the incubator, you might see this organism.

VR: Ebola virus?

DG: You got it. You got it.

VR: I went to see an exhibition of David Molesky's last week here in New York City.

DG: I was hearing. You didn't invite me, Vincent. Just let our listeners know. Vincent didn't invite me. I'm jealous. He should have invited me.

VR: Well, you were working, right? [chuckles]

DG: Sure. I wouldn't have been able to go. See, there could have been a free invite. You could invite me. I could say no, and you get points. [laughs]

VR: Yes, that's true. I have to think. He's into bananas lately. It's very interesting.

DG: I heard. I was thinking that that'd be really interesting. Where is his show?

VR: It was on 57th and 10th, the BMW showroom there, that famous building, but it's over now. I'll wait for him to come back. It was fun, though, to go visit him. He was very appreciative.

DG: No, that's great. I grew up, right? People may know. You may know this, Vincent. My mother was a painter and lived in an artist co-op down in SoHo. You had to exhibit your art. If it was good enough, you got invited. You could live in the art co-op. It was an old warehouse down in SoHo.

VR: Neat.

DG: Yes, it was neat. It was neat to grow up around that. And fortunately, my kids love art. It's worked out for them.

VR: Did you grow up with an appreciation for art?

DG: I did, I did. There's the story of one time. My parents then later got into collecting art. At one point, I'm vacuuming the apartment. I pull the vacuum back and damage one of their paintings.

VR: Oh, my gosh.

DG: You think about, "Oh, my gosh." My dad called up the artist, told him the story. The artist came to our house and fixed the painting, then they became friends. It had a good ending, but not a good beginning, yes. [laughs]

VR: There was a guy who came to Molesky's exhibit while I was there. Molesky said later, he has a Rubens in his house.

DG: Oh, wow.

VR: [laughs] The guy was very knowledgeable.

DG: Fantastic. All right, let's jump in. I'm going to start with a Voltaire quotation. I was looking through some of the things. There are so many choices, but this one got me with Voltaire: "Those who can make you believe absurdities can make you commit atrocities," sort of a shout-out to those people that are trying to misinform folks and succeeding, and then people end up doing stuff that they wouldn't do if they hadn't come to believe these absurdities. Speaking of that, are you ready for this first one? Oh, my gosh. This just -

VR: This is crazy stuff. Very crazy.

DG: I was doing a talk for the urgent care docs for the Optum Network just yesterday. I brought this up. It'd make everyone's job that much harder. "AI is better informed than doctors," Kennedy tells industry-backed MAHA Summit. Health Secretary Robert F. Kennedy, Jr., who has frequently advised Americans not to trust medical experts, said on Tuesday that artificial intelligence can offer patients a second opinion that is much better informed than any doctor in the country, I take offense, and has the power to free us from medical tyranny.

Mr. Kennedy made the comments during a fireside chat conversation with Vice President JD Vance at a Make America Healthy Again conference sponsored by companies that have business before his department, as well as artificial intelligence companies like Anthropic and OpenAI. This is what he says. Let's make it clear. These are some of his quotes. "If somebody tells you masks work, trust the experts. AI may tell you otherwise," Kennedy added. "If someone tells you social distancing works, trust the experts. AI may correct that.

If somebody tells you that a vaccine will prevent transmission and infection, or you need to take it to protect your grandmother, AI may say, 'It actually doesn't do that.'"

VR: Well, what if you ask AI if vaccines prevent against disease, which is the right question to ask, not with the facocta thing that he just asked them?

DG: Actually, that's good. I noticed that. I was like, "You're not asking the right questions." They remind me of the *I, Robot* movie.

VR: I have done this. I've had conversations with Claude, and it agrees that vaccines do not prevent infection or transmission. They do prevent disease. I don't think that Kennedy is right. [laughs]

DG: No, and it is. People probably saw the Isaac Asimov, Will Smith movie, *I, Robot*, and the whole big thing is it's really important that you ask the right question. If you don't ask the right question, you're not going to get an answer. You'll get an answer, but it doesn't make sense. That's the advantage of having a conversation with a human being is they can listen to your question and actually maybe talk to you a little bit about what the right question is.

We've talked about this with vaccines. The point of a vaccine, and hopefully people are getting educated, is to prevent disease. It's a question about whether or not it's going to impact transmission. Maybe there's a short-lived impact in certain situations for infection, but it's really about preventing you from getting sick, from getting paralyzed, from ending up in the hospital, from dying, et cetera.

VR: The thing that's really important here to realize is that AI makes mistakes. I know this because I talk to it about viruses. It makes mistakes all the time, and I correct it, and it apologizes profusely. I say, "Why do you make mistakes?" It says, "Honestly, I don't know. It's something about the algorithm. Nobody really understands why we make mistakes." It said many times to me, "Do not depend on me for an answer."

DG: Interesting.

VR: If Kennedy is telling people to depend on it, what the hell? It's not correct.

DG: Well, he's also undermining. It's an interesting thing. I appreciate that a lot of people are concerned about different information they get. One of the things that's true in America is that you pick who you want to have as your physician. If you don't trust that person, you get a new doctor, which we always say, like if they're not someone you trust, but you then can choose someone.

The relationship there between a patient and a physician, a provider that they trust, there's a lot of confidence there because we have selected, and we've judged, and we can change our mind. We're not assigned to a doctor. This whole idea of trying to undermine the trust between a doctor and their patient, he's in this different lawyer world. There's patients out there, they have cancer, and they can ask AI, "What's the best approach?"

There's people that have had strokes and heart attacks. There's people with severe infections. They're going to ask AI, "What is the best antibiotic?" Just as a really simple example, my daughter Daisy and I, we asked Grok. That's the Tesla AI. The, I guess, Elon Musk AI, "Hey, what's cheaper? Marine diesel or diesel that you buy at the gas station?"

"Oh, no, marine diesel is cheaper." Daisy chimes up, "That's not true." [laughs] Immediately, "You are correct." [laughs]

I'm like, "It's over \$8 a gallon for the marine diesel, and I'm seeing \$6.49 at this sign right in front of me here." All right. "WHO: Global Cholera Deaths Rise by 30% in 2025." Part of the importance of this is that we've basically said, like, all these things that are happening have consequences. People are going to die. Yes, we'll get to measles. Worldwide here, deaths from cholera rose by 30% in 2025. 7,870 people died from cholera. Cholera. Oh, my gosh. This is the highest number since 1999, since last century.

VR: Daniel, what is the reason for this? Is it increased poverty in these countries? They can't take care of so many people getting sick?

DG: There's a large number of things that go into these issues. One is that we have really pulled back all our aid to a lot of these places. Most of this is in seven particular countries: Angola, Bangladesh, the DRC, Nigeria, South Sudan, Sudan, and Yemen. These are areas, not only have we pulled back the health assistance we provided, but there also is a lot of unrest in these areas. Yemen, a bit of a disaster at the moment. DRC, yes. Now, back to problems in our own backyard. The alert, "*E. coli* outbreak linked to raw milk cheese." Oh, my gosh. Have we talked about how dangerous it is to--

VR: Yes, many times.

DG: This was actually posted by the CDC. The CDC and the FDA and public health officials in several states are investigating a multi-state outbreak of *E. coli* infections linked to Graziers Raw Milk Cheeses sold by Sierra Nevada Cheese Company. Over half of the sick people in this outbreak are children 5 years old and younger. I want to point out, not only have a number of patients been hospitalized, but there's been a number of cases of this hemolytic uremic syndrome where these little kids end up basically in kidney failure with the destruction of their red blood cells. HUS is one of the more severe outcomes of the *E. coli* infections.

VR: Why would any company want to sell this kind of milk and risk having people get very sick? Wouldn't they get sued as a consequence, or as they say on the package, you have no legal recourse if you die?

DG: It's really an interesting issue. Yes. Is it really profitable to go ahead and sell something where we're seeing here people are in the hospital, people are ending up getting renal failure? You'd think the repercussions that you sold a product that resulted in that being something that wouldn't work.

All right. Dengue, right? I was talking to the urgent care doctor yesterday, saying, "Now, when you do your travel medicine, you're going to have to say, 'Oh, Florida, that's basically like traveling to the tropics.'" It is.

We read in *The Washington Post*, "Florida counties declare emergency over 'wildly unusual' dengue outbreak." Mosquito-borne disease has infected hundreds statewide and killed one woman in Tampa." You'd think this would be all over the news, but three Florida counties have declared states of emergency as a growing outbreak of dengue has infected hundreds across the state.

Florida has reported 392 dengue cases among residents this year. Actually, I went to the CDC page, and I can't believe it's this bad. According to the CDC, and you can ogle, you can say, "Well, how many of these dengue cases are locally acquired?" I want the travel status to be locally acquired: 1,524 cases, only 484 cases from international travel. We've got over 2,000 cases so far this year in the U.S., and the majority of those are just people living in the U.S. getting bit by mosquitoes here.

VR: This is mostly in Florida, right?

DG: Yes.

VR: I assume nobody in the U.S. gets the dengue vaccine, right?

DG: Well, there are no licensed dengue vaccines available in the U.S. right now. Dengvaxia is gone. Qdenga is the one that worldwide is being used in certain areas. In the U.S. we have no licensed available dengue vaccine.

VR: Well, why do you think this is increasing? Do you think its mosquito range is increasing?

DG: I think part of it is, dare I say, climate change. I won't say anthropomorphic climate change. I'm saying climate change. The climate's changing. Global warming. [chuckles] I think it's in the anthropomorphic. That's what gets people upset when you blame us for it, even though it is our fault.

VR: It's our fault. The hell with you.

DG: [laughs]

VR: Come on, get real. It's anthropomorphic climate change. It's real. It's not fake. As the science adviser to the president recently said, "It's fake," it's just not fake at all. The numbers are real. If you can't read charts, it's your problem.

DG: Yes, the world's getting warmer. The storms are getting worse. The range of a lot of these arthropods, these mosquitoes, is changing, yes.

VR: The thing about dengue in Florida now, you get to a certain point, you have a lot of people who are infected. That's an opportunity for mosquitoes to pick up virus and transmit it. The more people infected, the more cases you're going to get. It looks like we've reached this peak now where it's always warm in Florida, so the mosquitoes are always biting. This is a real problem. Now, you're going to have exported cases to other states as people go there.

DG: That is a big issue, joking about the travel medicine business. Now, people go, and they spend some time down in Florida, right? The doctors, like, "Well, what do we tell them to do?" I'm like, "What are you going to tell them?" Like, "Oh, you need to start wearing long pants and long shirts and spring- "

VR: That's right.

DG: I'm like, "They're going to Florida." People don't go to Florida to wear long-sleeved shirts and long pants and tuck them into their socks. They go there to wear shorts and T-shirts, and they get bitten by mosquitoes. Now, it's become unsafe, and somebody dies.

VR: Florida needs to think about this because tourism is a big part of their economy, right?

DG: Yes.

VR: If people stop going to Florida - I wouldn't go to Florida. Well, I never would go anyway since they have a crazy governor and a crazy surgeon general. Now, with this on top of it, forget it. It's not like you can wear a mask. You have a big target there on your head, Daniel. You can't go there.

DG: Yes, it's true.

[laughter]

DG: The article, "Critical Role of Hepatitis B Birth Dose Vaccination in Preventing Mother-to-Child Transmission," was published in *CID* by Anna Lok from the Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor. Because we have a lot of people who seem to not appreciate the importance of this, she walks through the issues. I'm going to share a link to this. This is a good, well-written, accessible article.

Read a little bit of it. "Preventing mother-to-child transmission," it's got a four-letter acronym, MTCT, mother-to-child transmission, "is the cornerstone of global elimination of hepatitis B virus infection." Here, the issue is because the risk of progressing from acute to chronic infection is 90% when infection occurs in newborns. We also need to really protect kids under 5. Their risk is 30% to 50% for these children one to 5.

Now, effective prevention of mother-to-child transmission involves a multi-step approach. She goes through these: one, screening of pregnant women for hepatitis B surface antigen. Two, initiating antiviral prophylaxis, that's tenofovir, in the hepatitis B surface antigen-positive pregnant women with high viremia. It's cut off DNA greater than 200,000 international units per ml at 28 to 32 weeks of gestation.

Number three, birth-dose hepatitis B virus vaccine and hepatitis B immune globulin to newborns within 24 hours of birth, and completing a three-dose HBV vaccine series as part of the Expanded Program for Immunization starting at week six. In this same edition of *CID*, we have the article, "Effectiveness of Timely Hepatitis B Birth Dose Vaccination to Prevent Mother-to-Child Transmission in Ethiopia." This study, just like so many others, shows that the vaccination series starting at six weeks is insufficient to prevent mother-to-child transmission.

VR: I'm surprised they didn't mention the risk of contacting someone in the first few weeks of life that had to be shedding here in the U.S.

DG: We tried doing away, or we tried a program where we didn't have birth dose. We saw little kids developing lifelong chronic hepatitis B virus infections. This whole idea that there's these undesirable people and only those people need that, not us, not us good, clean-living people, not true. It's a fallacy. It's a fallacy that's going to lead to children dying, which we will get to.

All right, this next one's interesting. What is it doing in this section? This is, as we're learning more and more about what causes autism, not vaccines, "Congenital TORCH Infections and Neurodevelopmental Outcomes," a cohort study with sibling comparisons, was conducted

using linked data from the Swedish national health, birth, insurance, education, and death registers. This is *JAMA Network Open*.

Here, they're looking at 3,606,002 individuals born in Sweden between 1987 and 2021, including 975 who had TORCH infections. Maybe our pediatricians can rattle these off, but what are the TORCH infections? It's like asking rounds to torture people. T, toxoplasmosis, syphilis, rubella, cytomegalovirus, herpes simplex virus. Wait, that doesn't spell TORCH. Don't worry. It's OK.

Among these individuals born in Sweden, they're going to look at folks with and without TORCH infections. Congenital TORCH infections were associated with increased risk of intellectual disability, not minor, hazard ratio of 7.22. Autism, hazard ratio of 3.10, 95% confidence intervals for the autism, 2.55 to 3.76. They go through a lot of other analyses, but really pretty compelling data.

CIDRAP has some comments. Implications for the U.S., given that Sweden's demographics and newborn screening policies can differ widely from other countries, similar studies are needed to determine if the results are translatable. We hear this from Lisa Croen, PhD in epidemiology, specializing in autism and other neurodevelopmental disorders at Kaiser Permanente's division of research. Croen likewise was not involved in the study.

The population impact of TORCH infections may be even greater in the United States, Pesch (Megan Pesch, MD, MS, medical director of the Center for Autism and Developmental Disabilities at Henry Ford Health, said, noting that CMV epidemiology in the States differs from Scandinavia because of variation in public health practices. In general, (Mark Schleiss, MD, pediatric infectious disease physician at the University of Minnesota School of Medicine) Schleiss said awareness of CMV is disturbingly low, which is why he wants Congress to pass the Stop CMV Act of 2025. Basically, this would involve a screening for a congenital CMV infection in all newborns and should be the national standard of care.

VR: Daniel, CMV can cause congenital birth defects, right?

DG: Yes.

VR: For the children who are not born with congenital defects yet or infected with CMV, is that a problem, or is that why you would want to do the screening because then you would treat them with an antiviral, or what?

DG: I think the concern here, as we're seeing, is that among the TORCH infections are CMV. If you're born with CMV and it's not recognized, it's not treated, this may be what leads to intellectual disability, what leads to autism diagnosis down the road.

VR: I was at ESCV a couple of weeks ago, and there was a talk about congenital CMV screening. Many countries in Europe screen in the first trimester because that's when infection is the worst, right?

DG: Yes.

VR: Then they will treat with valacyclovir, 8 grams a day. Long-term effects not known. It's a lot of drug.

DG: Yes, that is a lot of drug.

VR: I'm just curious. What happens in the U.S. right now? Are the mothers tested, first of all, for CMV during pregnancy?

DG: Yes. As we find from this bill, two states, so Minnesota and Connecticut, currently screen for congenital CMV infection in all newborns.

VR: Newborns. What about pregnant mothers?

DG: Yes, what about pregnant ladies? Do all pregnant ladies get screened? No, not all pregnant ladies are getting screened. As you point out, first trimester, right? That's like a lot of people. Are you getting in early enough? Are you getting screened? Then if so, is there any kind of treatment that's going on?

VR: Well, that's the thing. You can get screened, but if this 7 grams a day is not really known if it's problematic or not, then what do you have? There's nothing else.

DG: Yes, no, these are all important questions that, right, oh, my gosh, you'd have to spend money to know the answer, not taking a seven-year holiday from doing the research on infectious disease. If we're really concerned about kids having intellectual disability and autism, then yes, we need to know the answer. Is that safe? Is that effective? What are the risks that we're - you know?

All right. "U.S., EU Object to UN Declaration on Future Pandemics." Imagine that, objections by the United States and a few other states appear to block a consensus agreement on the draft text at Friday's high-profile UN high-level meeting on pandemics, pushing the issue back to the General Assembly, where it could go to a vote before the close of the Assembly's annual session in December. We read here, "The United States is not in a position to support this text in full," said the U.S. representative of the debate.

Critical issues remain unresolved. "Whether it is the inclusion of divisive ideologies that lack definitional consensus or references to an unfinished negotiation on pathogen access and benefit sharing is an agreement that failed to achieve international consensus, the U.S. is not in a position to support this text." The European Union says it remains fully committed to the declaration's overarching objective, but it had reservations, saying, "The text falls short of our goals and set out explicit red lines." Any comments on this, Vincent?

VR: I don't know what the issues are here, but it seems to me, it sounds to me that this UN representative just doesn't want to sign anything about pandemic preparedness. What's the problem with it? She says it does not have a definitional consensus, which is the most ridiculous bureaucratic speak I've ever heard in my life. You mean you not agree on the definitions? Is that the problem there? Trump threw out Obama's pandemic preparedness document, and then he paid for it. I don't think the U.S. is very fond of this because of him. That's what's reflected here, in my opinion.

DG: There was certain stuff in here, which is interesting. I got people's hackles up. They talk about infodemic management, misinformation, and disinformation, and saying, "Well, we don't really have an agreed definition on what misinformation is." OK, all right. *Legionella*, we have another outbreak, right? We've been starting to discuss this. 23 people have currently tested positive for Legionnaires' disease. Most of those folks have actually ended up in the hospital. Most of them have been discharged at this point, but we have a couple of deaths.

VR: This is the South Bronx, right?

DG: Yes, this one is in the South Bronx, which is actually, last summer, we had one in the South Bronx. That's often a problem area, yes. It's that time of year, right? Hopefully, we're at the end of our *Legionella* season, right? People in the next few weeks will be turning off those air conditioners. We'll be shutting down all these. All right. Another case of screwworm. We're up to 51. That is now just marching along. What's really marching along is Ebola, right? We're still seeing that trajectory.

We are now up to 8,116 confirmed cases, 3,924 confirmed deaths, so about a 50% mortality. You can basically see it's all on this eastern border. It's right at the edge of South Sudan. It's right on the edge of Uganda. It's actually right pretty close to Rwanda and Burundi. A lot of concerns that we have that it's going to be moving into these other countries. I feel good that Rwanda will be able to keep this at bay. We saw some good performance in Uganda in the past. South Sudan has a lot of people concerned.

All right. Measles. Another person died. Five measles-related deaths. The CDC has now acknowledged two of the measles-related deaths. The little asterisk, the two on the CDC site, says, "This number is subject to change. CDC will update their reporting as additional information becomes available and relevant reviews are completed." The Pennsylvania Department of Health has confirmed a fifth measles-associated death.

We don't know much about this fifth person yet. When we look at measles, we're up to 3,782 cases in the U.S. We're up to 943 confirmed cases in Pennsylvania. The outbreak in Pennsylvania, right? More than 900 measles cases. This is the largest and fastest-growing outbreak in the nation, with 176 patients hospitalized for their infections, and now up to five deaths. Four has now become five deaths. There's 114 new cases in just the last seven days.

VR: Most under 18 years old, right?

DG: Yes.

VR: Many, not most. Many.

DG: Many. About a third are under 18 years old. A lot of people are getting hospitalized. This is close to 20% of the cases end up, it's 19%, end up in the hospital. These people are sick. It's clearly a disease of the unvaccinated. Less than 1% are fully vaccinated.

VR: Yes. Well, now that we're moving into the cooler months, do you think it's going to make an impact on the outbreak, Daniel?

DG: Part of the concerns we have are the school, right? All the kids getting together.

VR: Inside, yes.

DG: We have numbers, right? We have pretty high numbers at this point. Also, I think part of the issue is Pennsylvania right next to New Jersey and Delaware, which are low vaccine. Under the 95%, in that 90% to 95%. Also, a lot of this is eastern Pennsylvania, but you go western Pennsylvania, and we've got good old Ohio, which is less than 90% vaccine rates.

VR: It's a clear path westward for the virus.

DG: Yes. New York, we're up to 85 cases. Is that 85 cases? Put on the glasses to see. Yes, 85 cases in New York. It's spotty. You can see where it is. We had another case in New York City, so up to seven cases in New York City. Canada, we haven't talked about Canada in a while. I'm going to go do a talk in DC with a Canadian. Hopefully, they'll let him in and out of the country.

I told him to bring his own maple syrup and whiskey. Otherwise, I'll have to drink the Irish stuff and maple syrup from Vermont. A total of 5,462 measles cases as of May - Well, I think this actually seems like it's pretty old, actually, the data here, so I have to update that. Let's take a look here. Let's take a look in real-time. Let's see what the Canada data is in real time, Vincent. Let's see what we've got.

VR: 2025.

DG: Let's see.

VR: For 2026, you needed to click somewhere else. Now, we have 2026.

DG: What have we got?

VR: We have 2026, 1,120 cases in Canada so far.

DG: All right, so that's actually not as bad, right?

VR: No, it's not as bad.

DG: All right, Florida. Now, this is concerning. Florida. Measles disaster in Florida may not be far off, analysis shows. *PNAS*, "Projected Effects of Removing School-Entry Vaccination Requirements on Measles Transmission in Florida." This is an article in *PNAS*. We've heard about Florida's proposal to remove school vaccine mandates. We read, "It arrives at a moment when measles vaccination coverage in the state has fallen below the level needed to prevent sustained outbreaks."

I'll mention it's already below 90% if you look at CDC data. Here, using a mathematical model, these researchers show that repealing the mandate could trigger the largest measles epidemic in the United States in nearly half a century, with projected pediatric deaths numbering in the hundreds within five years. They report that children are disproportionately responsible for driving transmission.

Adult catch-up vaccination and non-pharmaceutical interventions, such as masking and isolation, can help, but they can't compensate for steep declines in vaccination coverage. This study, these findings, provide quantitative evidence that repealing school vaccine mandates risks making measles endemic in Florida and potentially reigniting transmission across the U.S.

VR: Florida, we got dengue. Now, we got a specter of measles. Wonderful.

DG: Yes. All right. Still minimal flu activity. We're just starting to see a little bit in a few places, but still plenty of time. Go out there, get your flu shot, and we'll keep you updated as we start to see issues there.

VR: What are you looking at for flu? This map of the U.S., all the green?

DG: Yes, so the CDC has a surveillance map where they basically - and people might remember this from the past, where it starts off with green with minimal activity, and then we go into the low and moderate, and we get to high as we get into our red, dark red.

VR: I like the graphs where they show the number of diagnosed cases, but that's not one of your links, right?

DG: Not yet. Not yet.

VR: FluView, that's what they used to call FluView?

DG: Yes. We'll start getting that once we see some rise in activity. Don't worry, Vincent. [laughs]

VR: I'm not worried.

DG: I'll keep bringing the data. All right. COVID, what happened?

VR: You have to be careful with these squiggly lines. It looks like they're going down, because if you look at the past, they do go up and down and up and down and up and down. There's a lot of noise in them. I think this peak still has some legs, frankly.

DG: Yes, we're seeing actually a little bit in the hospital. I've got a few folks in the hospital at the moment. We'll see what's happening here. Yes, I thought we were on our way down. Now, we got a little bit of an up, and we'll see over time what happens there.

VR: Wait until you see one of the letters. Oh, my gosh.

DG: [laughs]

VR: Did you know COVID is not a thing anymore?

DG: It's not a thing. We don't have to pay attention. It's all over. Why do you keep talking about it? Here's a great time for you to go out there and get your COVID vaccination. There was an article. Kathy Spindler sent me this article. It was the PICOBOO trial. P-I-C-O-B-O-O, the PICOBOO trial. "The Platform Trial in COVID-19 Priming and BOOsting." I know. It's like we should wait for Halloween for this. "The Reactogenicity of Nine Licensed COVID-19 Vaccines Delivered in Immunocompetent Adults."

This is a thing we've talked quite a bit about. People sometimes complain, and sometimes it's a barrier to people even getting a flu shot or getting a COVID shot. They're worried about, like, "I'm going to feel bad after I get this shot." That was a big issue with the mRNA shots. You get an mRNA shot. You're down for a day. Here, they do this trial. It's a randomized Bayesian adaptive trial evaluating immunogenicity and reactogenicity of licensed COVID-19 vaccines in immunocompetent individuals aged 12 years and over.

Total of 1,049 COVID-19 vaccine doses were administered to 586 adults enrolled between March 2022, September 2024. Local reactogenicity ranged from 47%, I'm going to give these common names, so that Novavax, Nuvaxovid, to 90% with Moderna. Then what about systemic reactogenicity? 69% with the Nuvaxovid, the Novavax, to 85% with the Pfizer-BioNTech shot. Severe reactogenicity events were rare. Reactogenicity events, as we see, were common but rarely severe. It looks like a little bit less with that Novavax shot as we've

talked about, compared to the mRNA vaccines.

VR: Yes, but half as many reactogenicities, right?

DG: Yes.

VR: A lot of people were talking about that on the live stream last night. Someone said that each time they get an mRNA, they're knocked out for four to five days. I said, "Well, try Novavax," right?

DG: Yes, go ahead. We've got alternatives. If you have concerns, like some people are super excited about an mRNA shot, some people would rather not, you got options.

VR: I like it a lot. I don't have any reactogenicity.

DG: Which one do you get? Do you just get whatever they give you, and you're fine?

VR: Yes, I don't even know what I got last time. How do they decide whether to give you one of the two, Modernas or the Pfizer, what they have in stock probably?

DG: You could sign up. I think I was telling the story where my wife was finding out. The day that they got the Nuvaxovid at the local stop-and-shop, she's like, "It arrived," and we go there. They're like, "Oh, we don't have it yet." She's like, "Oh, you do. It just arrived today." The woman went back. She's like, "Oh, you were right. Let me take it out of the -"

VR: Well, the Spikevax is only 65 and up, right? You have to have an underlying condition.

DG: Yes, there's rules. There's rules.

VR: I did get it. I have to check what I got. I'll let you know next time.

DG: Sounds good. All right. Before our emails, no one is safe until everyone is safe. We're in the middle of our American Society of Tropical Medicine and Hygiene fundraiser. Go to parasiteswithoutborders.com. Click on the Donate button. Thanks for all the folks that have stepped up. This is your show. This is your medical education program. This is your ability to fight back up against the misinformation pandemic. Thank you for everybody doing that.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Josh writes, "I'm writing about the antihistamine nasal spray, azelastine, also known as Astepro Allergy. A while back, five or six months, you, Daniel, had some positive, if preliminary, words to say about this nasal spray, noting that early trials seem to support the possibility of it significantly lowering the incidence among people who presumably had recently been exposed to SARS-CoV-2 of going on to develop an actual case of COVID. I haven't heard you mentioned since then, though I need to abashedly confess that I don't always rabidly listen to every second of every one of your podcasts." All right, that's it. We're not going to read the rest of this email.

DG: Yes, I'm so insulted. [laughs]

VR: "For what it's worth, when earlier today, I asked a general-purpose AI app about the possible use of this spray as a prophylactic for COVID-19, it appeared to have a generally positive opinion about it," citing a human study, I don't know the study's phase, "in which

azelastine apparently lowered the incidence of COVID in the study subjects by about 66%. I'd love to hear your thoughts and opinions on this topic."

DG: All right. Well, first off, Josh, I appreciate that even though you've already talked to AI, you're asking us, too, right? I think, according to somebody, you're supposed to do it the reverse way. You listen to what we have to say. If you don't agree, you go to AI to contradict. Yes, it's thin, right? We talked that one human study. It was interesting. We haven't heard anything since then, which is always a little concerning, right? If someone finds a thread and they pull on it, then you tend to hear if they're more consistent, supportive results. We haven't heard anything since that, so we're just left with that.

VR: Jay writes, "A letter from last week raised an interesting question. A listener asked about timing of SARS-CoV-2 vaccine following a recent infection. She had international travel coming up, so there was some urgency to getting vaccinated soon. The ACIP suggestion is to wait three months, if possible, after COVID infection before getting revaccinated. These recommendations came out in 2022. Does it still apply to our current world? Here are some of the questions it brings up for me."

"What is the immunologic rationale for waiting a minimal amount of time after infection before getting a vaccine against SARS-CoV-2? Is the rationale that time is needed for maturation of germinal centers? Are our germinal centers different now in 2026 than they were in 2020 and 2021 when the world was largely immunologically naive to SARS-CoV-2? What is the real-world evidence that supports our recommendation? Does that evidence apply to us now and beyond, or is it based on our 2021-22 world? I looked into this question a tiny bit. Barely scratching the surface, I ran across one interesting open access article from 2024. I'd like to hear your thoughts. Maybe a topic for a deeper dive."

DG: This is great, Jay. Let's walk a little bit through this. Dr. Jay Gladstein, chief medical officer out there in LA. We'll start with the labeling, right? When we moved from the prime-boost scheduled series approach to COVID vaccination to the flu model is get a shot in most people in the fall, protection through the winter, get another shot the next fall. If you look at the current packaging, it basically says, "Go ahead. Get your one-and-done shot for this season, COVID, just like your flu."

If you've had a shot within the last two months, you're not eligible until those two months have gone by; then you can get your shot. What's the story there? Why not just get a shot a month after the last shot? What's the concern there? Part of the concern is increased reactogenicity. The idea is you've had a recent shot. You get another shot. Maybe the local site reaction, which we just talked about in that study, is going to be worse because you just had one. You just saw this vaccine before.

The other, and we'll get into the immunology here, is that you've just had exposure. Yes, two to three months, you've got the germinal center maturing. Then you go ahead, and you get a vaccine. Now, you're actually going to not be interfering with the germinal center, and you're going to get a diversification, and you're going to get benefit from your vaccine. The other is this discussion, which I think is interesting.

I think about stuff like this while I'm lying on the couch. I'm not napping. I'm resting my eyes and petting the dog and thinking immune deep thoughts. The other is, you get this increase in antibodies, and is that going to affect your ability to get the benefit that you're hoping to get from the vaccine? Is it maybe more than a germinal center interference? Is it also

something about having this antibody rise, let's say, three to four weeks? There's a number of different hand-waving thoughts about why we recommend this.

Yes, the packaging is saying, "Don't get a COVID shot if you've had an infection, I guess, or other vaccination in the last two months." Our thinking, based upon our understanding in immunology, is there's a certain amount of protection you're going to get from that recent infection. Go ahead. Get a shot three months in. We even talked about a study, I think it was last week, where we looked about getting one or two shots after you've had a COVID infection. That was early days when we were doing prime-boost approach.

VR: The article that Jay sent was published in 2024, and it says that if you get vaccinated less than six months after your last infection, it impacts your immunity to getting COVID. That's a long time because then you have to balance the chance of being reinfected, right?

DG: Yes.

VR: Ellen writes, "Just a note about a conversation I had yesterday with my daughter, who is a pharmacist. She has been working at flu and COVID vaccination clinics since the COVID vaccine first became available. In late 2020, she worked clinics in long-term care facilities, and she continues to conduct clinics for institutions and businesses throughout the Greater Boston area, including Sanofi headquarters. Yesterday, she was at a large workplace clinic where most people arriving asked only for flu shots."

"Eventually, she asked one woman whether she had questions about the COVID vaccine. The woman replied that her doctor had advised her not to get it because COVID is now just the sniffles. Several employees waiting their turn then joined the conversation, saying that their doctors had also told them COVID vaccination was unnecessary. A few said they were simply done with COVID. My daughter told me it's increasingly clear to her that demand for COVID vaccination has declined each year."

"She remembers the clinics in late 2020 when she spent entire days in nursing homes wearing full PPE. When she came home, she would undress in the garage and shower before seeing her husband and children. She struggles to understand how quickly and profoundly our collective attitude toward COVID has changed." One word, RFK Jr. I'm sorry. That's my - "TWiV clinical update watchers since March 2020, My husband, retired pathologist, MGH, and I have never had COVID and still practice the mitigation strategies learned on TWiV. With gratitude and respect to you and Vincent, Ellen."

DG: Really? Thank you, Ellen. It's really tough. We keep talking. We keep sharing. I was saying last time that I have a patient in the hospital, and I can never even finish the sentence that, "Oh, so-and-so is admitted with COVID, but it's mild, right?" I'm like, "She's in the hospital. She's in the hospital on oxygen." If you consider sick enough to end up in the hospital if the tens of thousands of people who die every winter had a mild death, the little kid that my daughter's taking care of who went into DKA and is in the ICU because they got a COVID infection, these are all vaccine-preventable events.

We can reduce the risk of these issues by, what, 50% to 80%? Pretty significant reductions with just getting a vaccination. No, I think that we'll keep sharing the information, the numbers. If it's a reactogenicity issue, just switch to the protein-based Nuvaxovid. If you tolerate the mRNA shots, then you can get those as well. Most insurances, there isn't even a copay, so this is a free way to reduce your risk.

We talk about it, too. It's not just being sick with COVID, but you're going to increase your risk of new-onset diabetes after the fact. You're going to double your risk of getting diabetes because you didn't protect yourself and got COVID. You're going to increase your risk of a heart attack or a stroke. You're going to increase your risk of ending up in the hospital. You're going to increase your risk of dying. All these risks can be significantly reduced just by getting a vaccination.

VR: Keith writes, "I was listening to the recent clinical update. I believe you both mentioned recently getting flu shots. I also listened to the CIDRAP podcast, and Dr. Osterholm recommends getting COVID vaccines now, but waiting until influenza activity starts to ramp up in October-November to get your flu vaccine. He cites the waning effectiveness of the current flu vaccines as his rationale. I would love to hear your thoughts on this."

"Also, on several episodes of *TWiV*, especially 604, oral polio vaccine to prevent SARS-CoV-2 infection, I've listened to, I heard discussions about how viral vaccines might give your immune system a boost, heterologous immunity, non-specific vaccine effects. I know the evidence for this is shaky and mostly for live attenuated vaccine, but could spacing the flu and COVID vaccines out give your immune system a leg up?"

DG: Keith, these are great questions. The timing of our vaccines. We're doing a timing of our vaccines based upon flu, for instance, that it's going to be a seasonal thing. We're usually going to see rises in November and December. Sometimes that actually doesn't happen until the spring break March surge. By then, you're like, "Oh, I got my shot in the end of August, beginning of September."

You're like, "September, October, November, December, January, February, March." We do see this 10% decline in protection over time. It's like trying to time the market, right? It's hard to do. We're expecting. We're hearing predictions of an early flu season. If that pans out, then getting flu shots now. If not, then you have to ask the question. If you start to get a surge in March, you get your flu shot in September; maybe you got it a little bit early.

VR: What he points out about the attenuated vaccines, remember, they're doing early COVID. Before vaccines, people were touting you could get MMR or polio vaccines, the infectious versions, and they give you a little boost for a couple of months. This has been shown in studies carried out in the Soviet Union many years ago. It's just that these vaccines are not infectious, the flu and the COVID vaccines that we're talking about. It's not an issue.

DG: It's interesting, right? What's the best vaccine to prevent COVID? It's a COVID vaccine.

VR: It's the one you get.

DG: Actually, yes. The other, I think, interesting. I remember the early days of COVID. This is March 2020. There was one of the chiefs of medicine. He was like, "Oh, can we do this test? Can we do this test?" I was like, "You know what the best test is to know whether or not a person has COVID? It's to get the COVID test," but yes. [laughs]

VR: Yes. All right. Amy writes, "I typically aim to get COVID vaccinated in mid-November. My family's upcoming fall-break travel plans in mid-October to Florida's Disney World. I'm wondering if my family should try to get our COVID vaccines in late September to provide protection to my husband with comorbidities, my children, 5 and 8, and myself, an outpatient internal medicine physician."

"I'm proud to say that both my children participated in the Pfizer vaccine trial when conducted in our hometown of Nashville. We were all vaccinated last year against COVID in mid-November, given Christmas travel and time spent with elderly loved ones. I really appreciate the podcast and have listened for several years now. It's a great source of support and information as I try to figure out what's best for my family and my patients. I do also have a supportive pediatrician. Of course, I will ask his opinion."

"I was thinking about skipping the COVID shot for my kids this year, but a recent horrible case of adenovirus at back-to-school time, no COVID diagnosed at this point, requiring ER visit with IV fluids, along with our travel plans to Florida, has me thinking I will get my children COVID vaccinated to lower any risk of another ER visit. I don't think we will take the flu shots until we get back from the fall break. Of course, I will keep an eye on the CDC flu maps, which I hope are still decently reliable. Thoughts on that?"

DG: Yes. Amy, this is great. Just walk through this for everyone what we're thinking. Part of what you're thinking is you want to get the protection before you're at risk of exposure, right? If you've got upcoming fall-break travel plans, mid-October, if you're going to go to Disney World, we've already talked about how frightening Florida can be this time of - but anyway, yes, you can start thinking about what's the flu activity, what's the COVID activity, and timing that because as we've talked about, you get the most protection, we'll say three to four weeks after the shot.

We've talked about the numbers that we see with flu, where you get decreased - The protection against severe disease, that has a decent durability. Sorry that you had this painful wake-up call, but kids can get sick. That's why we have children's hospitals. Kids can get really sick from viral infections. They can end up in the hospital. What is it, a quarter of the kids with COVID that end up in the hospital end up in an ICU? They need IV fluids. They need oxygen support. On board, it sounds like you are going to do both the flu and the COVID shot. Maybe try to keep track of those flu maps. By mid-October, which is coming right up, we may be starting to see flu activity down there in crowded Florida's Disney World.

VR: Remember, leave your shorts and short-sleeved shirts at home. Bring long-sleeved pants and shirts.

DG: Got to worry about dengue now.

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

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

[music]

[00:53:34] [END OF AUDIO]