TWiV 1370 Clinical Update

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Guest: Daniel Griffin

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

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VR: From MicrobeTV, this is *TWiV*, *This Week in Virology*, Episode 1370, recorded on October 29, 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. Yes, back in New York, both of us.

VR: The last *TWiV* clinical update for October.

DG: The last clinical update that will drop before the midterms.

VR: I hope when we record next week, we have good news.

DG: [chuckles] Good news for science.

VR: For science and public health.

DG: We're not partisan, right?

VR: No, good news for science and public health because things are looking bad in terms of public health.

DG: It really is, and we're going to be talking a lot about that. It is. It's been difficult times. As we approach - well, this is going to drop on Halloween. Is that right? Is Saturday Halloween?

VR: Saturday is Halloween. It is.

DG: All right. With that in mind, I thought to quote Edgar Allan Poe.

VR: Perfect for Halloween, yes.

DG: He actually has some really great one-liners, some great quotations. It's actually a little bit. I love his stories. They're perfect to read this time of the year, right?

VR: Yes, for sure.

DG: This seemed very appropriate considering the comment you just made. Edgar Allan Poe, "The believer is happy, the doubter is wise."

VR: It's uncharacteristically laconic for Edgar Allan Poe, right?

DG: Laconic. What does that big fancy word mean?

VR: He doesn't use a lot of words. [laughter] That's the opposite of loquacious. Loquacious means you talk a lot.

DG: Yes. The gift of gab. I got together with a friend of mine who's a salesman. We were talking about another mutual friend who has the gift of gab, a born extrovert, which really, if you're going to be in sales, is the thing to be born with.

VR: Of course.

DG: Yes, I would not do well in sales. Maybe I would. CDC, this is news, CDC deputy director resigns after four months in the job, on the job. Dr. Jennifer Shuford, a former state health commissioner whom President Trump appointed to a top post at the CDC to help steady the agency, is leaving after just four months in the job. "Last day is going to be November 12," the CDC said in a statement. Her departure was reported by *The Washington Post*, "Dr. Erica Schwartz, the CDC director, announced the news to staff in an email Tuesday morning."

News of Dr. Shuford's exit comes as the CDC faces criticism over its response to unrelenting measles outbreaks in the country. We'll leave in a link to it. This is a doctor with a great reputation, which she gained in part from being a data-driven epidemiologist who really understood the importance of childhood vaccines. She joined the CDC in June. She's out now. This is another loss to the CDC.

VR: Of course. This is someone who's pro-vaccine, clearly clashing with the administration and can't get anything done. So she leaves. I think it's unfortunate because we need people like this.

DG: Public health should not be a partisan issue. We do not want children sick and dying. We don't want adults sick and dying.

VR: There should be no opposition to vaccines. At the highest levels of the government, vaccines work, they're safe, they save lives. The idea that you cannot be in CDC, unless you're anti-vaccine, is just absurd and has no place in the real world. Vote, people, vote.

DG: We'll get a little deeper into why that is such an important comment that you just made there, Vincent. Bird flu, what's up with the mink? Bird flu in mink.

VR: It's funny you picked this paper. I also found it this week, and we're going to do a deep dive tomorrow.

DG: That's excellent. I'm glad. It's "Preliminary report on H5N1 highly pathogenic avian influenza in Utah mink, August 2026." Here, they're describing an outbreak of bird flu, highly pathogenic avian influenza viruses belonging to H5N1, clade 2.3.4.4b, in August 2026 that caused high mortality on a mink farm in Salt Lake County, Utah, using data generated from the USDA. Genetic sequencing of the mink viruses identified the genotype as B3.13, which currently circulates in U.S. dairy cow. Do you remember our mnemonic for this?

VR: Yes.

DG: B for bovine.

VR: B for bovine, and what was D? The other one was D, is that right?

DG: Yes, yes.

VR: Deadly? Was that deadly?

DG: Yes. D for deadly, B for bovine. OK, listen, it worked. [laughter] It worked for you. We'll find out if it worked for anyone else. This was reported on those dairies in Utah, Texas, and Idaho in 2026. Based on 10 genome sequences in Utah mink collected August 7, 2026, the mink outbreak is positioned within the 2026 cattle clade. The most closely related viruses were sampled in May 2026 in Texas cattle. Several months of unsampled transmission chains between the Texas cattle and Utah mink outbreaks leave many open questions about how the virus actually entered the mink farm.

Now, additional PB2 mammalian adaptations were not selected for in minks since the cattle-adapted B3.13 virus already had a PB2-M61L amino acid substitution. I can't believe they can. Because they get it straight in the next sentence. That amino acid substitution is associated with increased replication in mammals. All 10 Utah mink viruses that they sequenced had a PB1-K388R, so a K to R substitution at 388. This was previously observed in an H5N1 mink outbreak in Spain. Not much you see in avian hosts, wasn't seen in the cattle.

Why do we care? There's going to be a deep dive, so we're going to learn in depth why we care. Alongside pigs, infection of mink with avian influenza viruses is a particular concern. Relative to other susceptible mammals, both swine and mink express a high proportion of the alpha-2,6-linked sialic acids similar to those found in the human upper respiratory tract.

VR: Ferrets are in the same genus, they're mustelids, and ferrets are used as models for influenza virus infections. This is concerning that it's now in the mink. It's good that Spain, which had an outbreak, culled all the mink. That's a good idea. I think we should do the same, but I don't think that's happening in this administration.

DG: Yes. Not only is there this potential adaptation opportunity, but also this could be a mixing vesicle, right?

VR: That's right.

DG: Because they can get human, they can get avian, it all can mix up.

VR: Mink is not an essential commodity, right?

DG: Yes, what are we doing with mink?

VR: Mink people wear coats, mink coats, right?

DG: No, nobody does that. Do they?

VR: What else are you going to do with the mink? You can't eat it, it's tiny.

DG: Yes.

VR: Anyway, it employs people, so I don't want to say things that cost people jobs. In, what

was it, the Netherlands, when COVID got into mink, they banned mink farming in the whole country, which was the wise thing to do.

DG: This is really risky.

VR: Also, it's inhumane to kill these poor mink.

DG: Yes. I think most people at this point are not comfortable with the idea of raising mink and everything that's involved in the generation and wearing of these fur coats. All right, I'll leave that there.

More, this is in *Emerging Infectious Diseases*. We have a little bit of a theme here. The article, "Evidence of Exposure to Highly Pathogenic Avian Influenza H5 Viruses in East Greenland Polar Bears."

VR: Greenland, hey, that's the country we want to take over.

DG: I think we now own it. [laughter] That's a joke. Sorry. Here's the problem. Seasonal bird migrations to Arctic nesting grounds creates a hotspot for highly pathogenic avian influenza outbreaks, amplifying interspecies interactions and the risk for viral reassortment and dissemination across migratory flyways. You've got the birds, they're all flying over, and they end up in these Arctic nesting grounds.

Now, there have been recent detection of highly pathogenic avian influenza in wild Arctic mammals. I'm worried about the mammals. I was reading earlier today about, what was it? Seal rabies, rabid seals attacking kayakers. OK, so the poor Arctic mammals. One, we care about these animals. They also have an impact on indigenous peoples, nutritional, cultural relevance.

Now, the polar bears are Arctic apex predators that face increased challenges associated with their ecological position at the interface between marine and terrestrial ecosystems. Now, climate warming, I'm going to go ahead and say anthropogenic, our fault, climate warming, and the subsequent loss of sea ice leads to increased time spent on land and exposure to terrestrial pathogens through the exploitation of new food sources. The polar bears are starving, and they're trying to figure out what can they eat, so they spend more time on land, more exposures.

Now, cases of deceased, so dead, polar bears infected with bird flu have been reported in Alaska. That was H5N1 in 2023. In Norway, that was H5N5 in 2026. Here they go. They've got this ongoing collaboration with the indigenous hunters, and through this collaboration, heart blood was collected during subsistence harvest from polar bears that appeared healthy near the Scoresby Sound in East Greenland during the hunting season. They screened 109 plasma samples collected during 2016 through 2025 for antibodies against all the influenza A viruses.

Prior to 2024, no influenza A virus antibodies, but 2024, three bears, all male harvested in 2024, had signal-to-noise values within the positive range. Here we're going to see three of 14, so 21% of the male bears that they checked were positive. By 2025, it had increased to 43% of the bears they checked. They conducted further screening on the positive samples, basically using an avian influenza virus representative H5 and H7 subtypes in the assay. Plasma from four animals harvested in 2025 were positive with greater than 1 to 40 for

antibodies to H5N1 falling within clade 2.3.4.4b. Does that sound familiar? Suggesting that the animals had been exposed to a highly pathogenic avian influenza virus in this clade.

I like the figures they have. They've got these nice cartoons showing you how the polar bears might interact, how they might congregate. You can see them touching their noses. Then you also see eating birds and eggs, including dead birds. Polar bears will scavenge. Eating infected mammals, they'll actually hunt those. Potential transmission from mother to offspring through lactation, potential environmental contamination. Then what I really like is this figure. You've got to go to the appendix and look at the flyways, and you can see how these birds can spread stuff all around.

VR: It's not surprising that they're getting them. The birds go up there.

DG: Hopefully, people watching on YouTube can see this. You've got the North American Atlantic flyway, where basically the birds come up through the northeast into Canada. Some head west into parts of Canada. Some continue, end up in Greenland. You've also got this flyway path where they're going back and forth from Iceland, parts of Europe.

VR: Boy, Greenland is a big country. Maybe it's the curvature of the Earth.

DG: Yes. Part of it's the projection.

VR: I guess so.

DG: They do this Mercator projection where the farther north you get, the bigger you look. The closer to the equator, the smaller you look. We like to use this in the U.S. to make our country and Europe seem huge, and then Africa seem tiny. When we do our Parasites Without Borders projection, we do it from polar down, like the UN or the WHO or something.

Florida dengue cases. This is crazy, Vincent. About a month after three Florida counties declared states of emergency over what officials described as a, I like this, "wildly unusual" dengue outbreak, infections of dengue have continued to climb. Since September, the total reported cases in Florida have doubled-

VR: Wow.

DG: -from 392 to 721. Now, Ira Longini, a biostatistician and infectious disease modeler at the University of Florida, that means they create these models. They're not up there on the runway. They say they're not surprised by dengue's continued spread. "It was just a matter of time," Longini said. Longini explained that climate change, anthropomorphic climate change, our fault, is increasing mosquito populations, lengthening their active seasons, contributing to dengue's spread globally.

VR: Yes, I remember years ago when we just had a few cases and it just increased more and more and more mosquitoes, *Aedes aegypti*, and this is what's going to happen. It's going to move further and further north. Politicians don't seem to care.

DG: This is a huge problem. Now, Florida has basically endemic, autochthonous dengue cases.

VR: We have a vaccine licensed in the U.S. I don't think so, right?

DG: Right now, there's no accessible licensed dengue vaccine in the U.S. This might need to be revisited. Yes. People go to Florida all the time. We're going to start having tourists going to Disney. They're going to end up getting dengue. Little kids. There's always this idea with dengue that the worst dengue is the second case of dengue, but the worst case of dengue is dengue in little kids. Lots of comments. I enjoyed looking through the comments.

VR: Very annoyed with the way Florida public health is being managed at the moment.

DG: Yes, it really was. The comments basically were pretty much frustration and sarcasm regarding the handling of public health issues in Florida. A lot of criticisms of the current governor and Dr. Ladapo.

VR: The governor is out now. He's finished, right?

DG: I think, right? Isn't this the end? Someone new gets elected next Tuesday.

VR: The problem with Florida is they don't realize what is happening in this country, and they are not following the right trend of voting.

DG: Even think about themselves. You want to start being worried. Your grandkids come down to visit you, and now they end up in the hospital with hemorrhagic, severe dengue.

VR: There's a lot of elderly people in Florida. Daniel, who is the most susceptible to severe infectious diseases. The elderly.

DG: Yes. The youngest, the oldest. Screwworm's out of control. Look at this, Vincent.

VR: Wow.

DG: We are up to a total number of 66 cases.

VR: Also found it in a sheep, I think, or a goat? Other than a cow.

DG: Yes. If you go, you can actually go to this page, and they list all the different detections and which animals have been. They're mostly domestic cases. So far, only one wildlife case. Another 14. I mean, it was moving down, like 14 cases, four cases, three cases, and then we've already got 14, and October is not even over.

VR: A wild elk was positive. Yes. That's wildlife.

DG: That was wildlife, yes. All right. Ebola. Let's talk a bit about Ebola. We're going to start, actually, with the article. "Cross-reactive T-cell Responses against BDBV." That's easier for me to say. "Bundibugyo Virus in Humans-

VR: There you go. You got it. You got it.

DG: -after the rVSVΔG-ZEBOV-GP Vaccination." This was published, actually, as a correspondence in *The Lancet Infectious Diseases*. The recombinant stomatitis virus-Zaire Ebola virus glycoprotein vaccine, Ervebo, is a highly efficacious vaccine against the phylogenetically related Ebola virus, consisting of a recombinant VSV viral vector that encodes the glycoprotein of the Kikwit 1995 EBOV isolate.

Here, the point is this is a vaccine for Zaire Ebola, not Bundibugyo Ebola virus. Although

vaccine-induced antibodies are considered a putative correlate of protection against diseases caused by EBOV, so that's the Zaire Ebola, it remains unknown if these cross-reactive responses are actually sufficient to protect humans against disease caused by Bundibugyo.

Enter the T-cells. This is what caught my eye. Virus-specific T-cell responses are associated with virus control and protection against severe disease, and potentially, we've talked about this - you guys have talked about it quite a bit on the deep dives, can potentially provide broader cross-reactivity and greater resilience to viral escape by targeting multiple, often conserved linear peptide epitopes. However, whether this vaccination induces these Bundibugyo reactive T cells in humans was not known. To address this, this group analyzed and mapped T cell reactivity and investigated whether conserved regions within the glycoprotein are targeted. Now, they're actually pretty different, these glycoproteins. They're only about 66.3% amino acid identity. It's really quite different, right?

VR: Yes, it sure is.

DG: By multiple sequence alignment, they identified several amino acid sequences that are highly conserved, generated some peptide pools covering these regions. They then assessed the cross-reactive T cells at day 28. Right after vaccination in 20 folks. Think of this as those interferon gamma assays that we do for tuberculosis, for instance. They're basically doing that. They're looking for memory T cells using this interferon gamma ELISpot. They have a nice graphic where you can see how they lay this out. Most vaccinees with a positive response to the EBOV had Bundibugyo virus-reactive T cells.

VR: That's good.

DG: Yes.

VR: I hope it works because this is what's being rolled out now.

DG: We're hoping. It's encouraging data. What's not encouraging is the epidemic is continuing. Kenya reported the second death as Nigeria races to understand transmission of index patient. We'll leave a link into this. It's really a *CIDRAP* piece where they talk about it. As we learn more, it turns out Nigeria's index Ebola case patient was airlifted to Switzerland. Stable condition. The index patient was clinically improving, stable, conscious, able to communicate. Their lab data was moving towards baseline. This doesn't mean they're no longer infectious or anything. All the protocols are still in place. The patient was actually evacuated along with her spouse. It's a woman who we're talking about here.

The patient is a 42-year-old Ugandan woman who's married to a Swiss national who works in Nigeria. She and her husband had recently traveled to Uganda. African CDC said the index patient in both Kenya and Nigeria traveled through Uganda's Entebbe International Airport on October 3, which may have been the scene of transmission. We'll share more news as we get it. If you look at the epi curve, it is still on its way up, not starting to plateau. We are now at over 10,000 cases, almost 5,000. Actually, the update when we're recording this is already up to about 5,000 confirmed deaths for Ebola already.

VR: Yes, it's very concerning.

DG: This is very quickly on its way to becoming the worst Ebola outbreak in history. We're

not doing a lot to help, just by the way. They're making it hard for those of us who might want to help to go over there and help with this weird third-country 21-day quarantine thing that they've got going.

All right, measles. A deep dive, Vincent, for the last *TWiV*. It's where you guys discuss the article "Projected Effects of Removing School-entry Vaccination Requirements on Measles Transmission in Florida" published in *PNAS*. We're going to leave in a link. Go ahead, listen to *TWiV* 1369. Why do we care? Why is it anyone else's business whether or not you and your child get the measles vaccine, the safe, effective measles vaccine that lots of folks are spreading misinformation about?

The upshot is that, 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, children, and babies deaths numbering in the hundreds within five years. Just for all our people listening, that's what you're voting on. You're voting on whether or not you're OK with hundreds of little children dying in the next five years because that's where we're headed.

VR: It's just unbelievable that they're thinking about doing this.

DG: This is just Florida. Hundreds of little children dying in Florida because of decisions that we make.

VR: That the certain party makes, not us.

DG: Yes. All right. Vincent, I got through the text, “Observations Made During the Epidemic of Measles on the Faroe Islands in the Year 1846.”

VR: That's great. Did you get the book from the library, Daniel, or did you buy it?

DG: I bought it, but I'm going to say don't buy the book. I bought the book, but it's reproduced, and it's not a very good printing. There's actually a society that allows you to access a really higher-quality scanned PDF. That's how I read it. It was really interesting. It's long-winded. It's great like sit down. It's not one of these *Nature* papers where every single word has to be weighed and measured because you're only allowed so many per abstract, et cetera. This is 74 pages of describing the salt that cakes on the boat, the weather, the different types of food that people eat, how they cook it.

Really, the meat of it is this one observation and just the quote. Because people keep asking, if you get measles, can you get it a second time? People used to say, I don't know, maybe. The old people who had had the disease, measles, in 1781 were exempt without exception. There were, however, several houses and small villages that had not been invaded in 1781. In these, the older folk were attacked just as the others. Willan, Rosenstein, and Thuessink, in their long experience with many great epidemics, have also observed the same protective power without exception. You get measles once, and that's it.

VR: That's a great study.

DG: Yes. Really, it's fun to read, actually, I have to say. It made me miss the Outer Hebrides in Scotland where it's just - he describes the wind, these gusts come along, and you basically have to drop to the ground because otherwise you'll go crumbling away.

OK. All right. *Nature Medicine*. We have the article, "Global and Regional Burden of Measles and Vaccine Coverage among Children Under 5 years, 1990−2023: A Global Burden of Disease Study." Not good news. Using the Global Burden of Diseases, Injury, and Risk Factors Study, 2023, this group systematically assessed measles incidence, mortality, disability-adjusted life years, those are those DALYs, and vaccine coverage, either getting one shot or measles-containing vaccine, getting two shots among children under 5 years of age across 204 countries and territories from 1990 to 2023.

Between 1990 and 2019, global measles incidence and mortality declined by approximately 80% and 90%, respectively, but then it rebounds in 2020 with 15.6 million cases, 118,000 deaths in 2023. That's a 40% increase in the cases. 12% increases in the number of deaths between just 2019 and 2023. Sub-Saharan Africa, South Asia really is where we're seeing most of this.

Now, the coverage from getting a single shot in 1990 was at 67.2. We get up to 83.6 in 2019, but then it actually stalls and drops to 81% in 2023. That second shot was only 14.4% in 1990, gets up to 68.4% in 2019, got up to 71.4% by 2023, but we are basically not at that 90% in so much of the world. Expect millions of more measles cases, expect tens of thousands, 100,000 deaths per year if we don't turn this around.

VR: This increase in 2000 is probably COVID-related.

DG: Part of the 2020 was all kinds of disruptions with COVID, but going on from there, we're seeing a lot of evidence for a really, unfortunately, successful misinformation campaign.

VR: The kids will pay. That's it.

DG: Horrible.

VR: Totally unfair.

DG: All right. Now, I'll leave a link into a *CIDRAP* article where, "As Measles Soars in Pennsylvania, Some Parents are Vaccinating Their Babies Early."

Let's talk about the science here. Got an article, "Immunogenicity, Effectiveness, and Safety of Measles Vaccination in Infants Younger than 9 months: A Systematic Review and Meta-analysis" published - this is back in 2019. I wanted to go back and give some context to this decision. This was published in *The Lancet Infectious Diseases*, and they did a systematic review, meta-analysis. They searched MEDLINE, Embase, Scopus, ProQuest, Global Health, The WHO Library Database, the WHO Institutional Repository for Information Sharing database.

They consulted experts. They included randomized and quasi-randomized control trials, outbreak investigations, cohort and case-control studies. This is really robust. They did the literature search on June 2, 2015. They updated it on January 14, 2019. They assessed a number of things. The proportion of infants that seroconverted, the geometric mean antibody titer. That's the way we do a mean when we've got an exponential thing like a titer. They looked at avidity, cellular immunity, duration of immunity, vaccine efficacy, vaccine effectiveness, and safety. They ultimately identified 1,156 studies of which 1,071 were screened for eligibility; 351 were eligible for full-text screening and data from 56 studies that met all inclusion criteria we used for the analysis.

Here is what they found. We've got a nice figure here. The pooled estimate of the proportion of infants who seroconverted increased from 50% at age 4months to 67% if given at 5 months, 76% at 6 months, 72% at 7 months, 85% at 8 months. Now, that's great and all, but you can just look at the really wide confidence intervals. There's really a lot of variability here. We have the pooled geometric mean titer ratio for infants vaccinated with the first dose at age 4 to 8 months compared with infants vaccinated at age 9 months or older, 0.46.

We have this nice Figure 3. We're applying the ratio to the pooled geometric mean titer estimate of 248 for infants younger than nine at vaccination, given estimated geometric mean titer for infants age 9 or older at 539. Really, a lot of variability in the studies. Folks that are watching on YouTube can see the forest plots that we've got going here and basically looking at these different antibody titers.

Then we've got eight studies that actually assessed vaccine effectiveness of the first dose given infants younger than nine months against clinically diagnosed measles. The pooled vaccine effectiveness was, I'm going to say, only 58%, but a lot of variability.

VR: Getting the vaccine between 6 and 8 months, it's going to be variable depending on how much antibody you get from your mother, your response. That's why we see big error bars on these. You can see the graph. The bar graph is quite clear. If you get it younger, fewer infants are converted. That's interference with maternal antibody.

DG: It's a challenge when you've got measles all around these children.

VR: That's the problem. If there's measles, there should not be. There should not be measles circulating. This is the problem with the current situation. If you are living in an area with a lot of measles, like Pennsylvania, it's probably not a bad idea to get that - look, it looks like 6 to 8 months is about as good as it gets until 12 months, probably.

DG: You don't want to do it before 6. Current recommendation is 12, but WHO says you might go down to the 6-to-9-month window in basically a current outbreak situation, which is where -

VR: That's where we are.

DG: Yes, and that is where we are. If you look at the Hopkins tracker, we're up to 4,730. You can see the hot spots. There's a lot going on in Pennsylvania. Another 85 new cases just the last seven days, 1,398 total cases so far in Pennsylvania alone.

VR: I looked at a graph in *The New York Times* of why MAGA voters are turning against Trump, and the biggest issue was the price of goods. The lowest issue, 4% only of voters made it an issue, was public health. I don't understand why people are not responding to this and other outbreaks with their vote. What is your problem?

DG: Yes, it doesn't say a lot. I care more about the price of gas than babies dying.

VR: Also, down at 6% or 8% was democracy. People don't care that the democracy is being destroyed. I don't understand people.

DG: [crosstalk] cheap gas and you can have my freedom. Oh my gosh.

VR: I don't get it. I really thought we were better than this.

DG: Let's prove that we're better than this. We'll find out in a week if we are or not. We've got them here in New York as well. We've got a New York dashboard. We're up to 170 measles cases in the state of New York. This was interesting. Here's this article. You think, "Oh, we know everything." It's amazing how much we don't know. Here's the article published in *CMI,* "First Evidence of Measles Virus Detected from Exhaled Breath in Humans." Do you believe that, Vincent?

VR: It's hard to believe that this hasn't been done before.

DG: I'm a little. Maybe people scour the literature. Maybe we're missing something. Here, they studied a 23-year-old unvaccinated woman with lab-confirmed measles. From day 10, post-symptom onset, longitudinal sampling was performed for six consecutive days. Duplicate specimens, they collect them from the throat, the face, cutaneous lesions, exhaled breath.

Using these special, it's funky masks with these strips in there, these polyvinyl alcohol sampling strips. The measles virus RNA was consistently detected in exhaled breath. They've got some kinetics. They basically conclude this study provides the first empirical evidence that measles virus RNA can be captured directly from the exhaled breath of an individual with measles. I don't know. I'm just thrown that, you'd think this would have been done before.

VR: They could have used infectious virus assays before, right?

DG: Yes.

VR: It says, first evidence.

DG: Yes. All right. New York State Department of Health launched its own respiratory disease tracking dashboard. I'm going to leave in a link. It's just barely started. You can't really see much of the trends yet, but I'll keep an eye on this. I guess this is this movement. Now that the CDC is falling down, and we're not sure if we can trust them or not. I have to say right now, we're in this surge of flu.

We've got a bunch of folks in the hospital with flu right now. I'm not thinking it's a good year. If you look at the flu maps, you don't see a lot of activity on the CDC flu maps, which is a little weird considering we're mask mandates in the hospital. We got all kinds of folks coming in with flu, requiring oxygen support. Yes, it might not be quite as rosy as the charts and graphs are suggesting.

VR: The map shows low activity.

DG: Yes, it looks like everything's all good here. Nothing to see, but that's not really true.

VR: If you look at the epidemic trend from CDC, the flu line is rising.

DG: Yes, it's definitely on the way up. The flu is here. If you haven't gotten your flu shot, don't walk, run. Get that shot. You're not doing it just because, "Oh, I've had the flu. I was just fine." Remember, we've talked quite a bit about those flu vaccines might not only keep you out of the hospital, they might keep you from having a heart attack or a stroke. Another

article to hammer that home: “Effectiveness of High-dose versus Standard-dose Flu Vaccines Against Severe Respiratory and Secondary Cardiovascular Outcomes in Adults Aged 80 or Older,” was published in *CMI*.

Retrospective population cohort study conducted in Spain included 279,649 vaccinated adults based on socio-demographic characteristics, influenza vaccines, chronic diseases, clinical outcomes were looked at. They're comparing the standard dose to the high dose. Now, the high dose was associated with a lower risk of hospitalization, 34% lower. The high dose also showed improved effectiveness against lab-confirmed flu. That was a 42%. Now, hospitalization for acute MI, remember, we keep talking about get those flu shots. Here, they're saying the high dose is even better than standard dose with a relative vaccine effectiveness of 26.4%.

VR: These are in addition to the protection you get from the standard dose, I presume, right?

DG: Yes, this is extra. 26.4% RVE for having a heart attack, 32.9%, about a one-third reduction in your risk of having a stroke, pulmonary embolism, 27%. Just overall cardiovascular outcomes is effective.

VR: Get that high dose, folks.

DG: Get something, but if you can, get the high dose. What about the new mRNA flu shot? I'm all excited about mRNA flu shots.

VR: You got this, right?

DG: I wanted to get it, but -

VR: I thought you did.

DG: - I ended up getting the Flucelvax. I might go get this too. That was actually an interesting issue. We're going to talk about that in a moment, but maybe we'll get to it in our emailers. Here's the article, “Humoral Immunogenicity of mRNA-1010, an mRNA-based Seasonal Influenza Vaccine in Adults 50 and Over,” that would be me, published in *Open Forum Infectious Diseases*. Basically, one-to-one, either the mRNA or standard flu shot. They're going to look at those antibody titers. Pretty good, actually. We've got some nice data here. You can actually see a little bit better with the mRNA than the standard when you look at the different potential flus that one might get.

VR: The HAI titers are better. We'll see if that translates into clinical betterness.

DG: I think that's the issue. At this time, we just have serology data, surrogate data.

VR: We'll see at the end of this season, right?

DG: Yes. Hopefully, we'll have that data at the end of the season. RSV, still rather quiet. Just a little bit of activity starting in Florida. That's about on track. We should, as we get into November, start to see RSV. That's the typical. COVID bouncing around. We're still seeing a little bit of COVID, but bouncing around. It's very regional where the COVID activity is, right? Florida -

VR: Yes, it is.

DG: -I don't know what's going on in Florida, man.

VR: Florida's very high. So is Montana, right?

DG: Montana and Washington. Pretty high activity in California, Nevada. Tennessee's got some stuff going on, but it's very regional where we're seeing the activity. Remember, this is the same model. Let's say you've got the flu. Let's say you've got COVID. Then if you've got the flu, we have early antiviral treatment. If you've got COVID, we've got early antiviral treatment.

What about all the people that you've exposed. Let's say you live or you go and you hang out with your parents or your grandparents. In both, there's a parallel here for flu. There's post-exposure prophylaxis for those people that have been exposed. They can come in and get treatment. For COVID, there's post-exposure prophylaxis with Xocova, the X-pack, which is better than the Z-pack, which everyone seems to get whether they need it or usually not.

This is really interesting, Vincent. This makes no sense to me, so you tell me what's going on. This is this study, “Familial Factors in SARS-CoV-2 Susceptibility and COVID-19 Severity: A Nationwide Danish Study of Adult Twins and Their Spouses” published in *International Journal of Epidemiology*. You're thinking, your COVID, the severity, it probably all comes down to genetics. It probably doesn't matter who you're married to. It's not like, "Oh, I'm married to this person, so my COVID is going to be more similar to theirs."

VR: No, the spouses that control, because they're not genetically related, but the twins are.

DG: OK. Danish registry-linked study that included 83,902 twins and 37,719 spouses matched to 839,020 population controls and 379,190 spouse controls. They followed them from February 1, 2020 to 31 October, 2022, testing positive for SARS-CoV-2 infection and COVID-19 hospitalization served as proxies for SARS-CoV-2 susceptibility and disease severity. You end up in the hospital, we're thinking that's a little bit worse. They compared concordance rates and calculated heritability from biometric modeling of these traits.

VR: What does concordance rates mean, Daniel?

DG: Two things matching. They found no evidence of a genetic influence on infection susceptibility in the first two waves of the pandemic and a modest influence in the third wave. Spouses showed the highest concordance rates by a large margin in all waves. The study found no evidence of genetic predisposition to disease severity. Co-twins of hospitalized twins had no increased risk of hospitalization. By contrast, this is weird, the risk of being hospitalized with COVID-19 was higher. This is a relative risk of 3.56 with really good confidence intervals among the spouses of the hospitalized twins than among the controls.

VR: You shouldn't marry a twin. It's stressful.

DG: [laughs] That's not what it means.

VR: I'm very surprised that there's no genetic influence on disease severity.

DG: I think in this study. I'm not ready to write it out. One of the issues here, because you

think about what's going on here, is maybe the Danish population is similar enough that what you really want to compare is the Danes to, I don't know, the Spaniards.

VR: They certainly are small. It's 9 million or something like that. It may be more homogeneous than, say, the U.S. for sure.

DG: No, the population's small, not the Danes. I was like, "I'm not sure the Danes are small."

VR: No, the population not the Danes. I don't think this applies universally because we know there are genetic factors. For example, there are people who don't make interferons properly, and that's a genetic factor.

DG: There were whole families where the whole family would - all the kids would get sick. I just thought it was genetic.

VR: We should not emulate Denmark, that's all I'm saying.

DG: The reality is Denmark is quite a bit different than the world. It's quite a bit different.

VR: They own Greenland, right?

DG: It's interesting. They have a wonderful relationship with Greenland. Greenland actually has its own separate control, but they have a very nice relationship. I'm not sure it's ownership, but anyway. Not like the way we own it, Vincent.

VR: Daniel, Greenland population is 55,000 people.

DG: I think somebody was going to pay them like, "I'll give you $20,000 each if you just become the 51st."

VR: It's less than the block that I'm on here in New York City.

DG: It's amazing, right?

VR: Oh, my gosh.

DG: All right. Closing words. No one is safe until everyone is safe. We're wrapping this up. This is the last episode that's going to be part of our American Society of Tropical Medicine and Hygiene fundraiser. We may do a little bit of an overlap because I know folks at Notre Dame might be trying to do a fundraiser for Dickson. Just let us know if there's a little bit of an overlap there, because we're going to be doing that One Health lecture series in memory of Dickson. This is it, and then we're going to do Vincent's favorite fundraiser, which will be *MicrobeTV*. Go to parasiteswithoutborders.com. Click on that Donate button. All right.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Ken writes, "I would never drink raw milk, but what I'm wondering is if it is OK to eat cheese made from raw milk. When I wanted to rebuild my microbiome after antibiotics, I was advised to eat a very wide variety of fermented foods. I was told all cheeses aged at least six months were safe. Now my wife recently had antibiotics, and we were wondering about raw milk cheeses."

DG: Ken, it's interesting what you're asking. You want there to be bacteria in the cheese,

then you're asking if it's safe. In the U.S., we have this FDA rule where if the cheeses are aged more than 60 days, then they're considered safe. I put my little quotes up there. The idea is there's a certain amount of salt, there's a pH effect, but it's not the same with all cheeses. Your hard cheeses are going to be safer than some of your softer cheeses.

If you're trying to restore your microbiome, which is a separate issue, you might want to actually do stuff where there are live cultures, your probiotics, things like bifidobacterium, things like that.

VR: Yogurts, right? Yogurts.

DG: Yes. Live culture yogurts.

VR: Deirdre writes, "I love your clinical updates. As an NP in family practice, we often see many different types of infections, and I really appreciate your updates. I will share that I recently had a patient who was exposed to a bat and needed rabies vaccination. They were not bitten, and they were able to receive RIG vaccination, rabies immune globulin vaccination, between her third and fourth doses of the vaccine, they developed a rash, treated with prednisone. The question then arose, did they need a fifth dose because she received prednisone?

I tried the county rabies contact who told me they didn't know. Our practice tried consulting ID as well as other specialists, however, we weren't able to get an answer. When we sent them to the county location to get the fifth dose, they wouldn't give it to them as they were afraid the rash was an allergic reaction. I don't think it was an allergic reaction. I tried to call the CDC in Atlanta. I left a voicemail. It took over a week for a response, and the response was to contact the State Department of Health representative for rabies." Oh my God.

"We were finally able to get our fifth dose via the emergency room. Any clinical pearls would be appreciated given the nature of rabies. The wait-and-see option didn't seem wise. An additional detail, we ordered rabies titers. Those take up to a month, so no benefit there. Thank you and your team for all your knowledge and updates."

DG: Oh my gosh. What a disaster, Vincent. This is not the way -

VR: The CDC drops the ball. They can't give advice? Remember that you had a quote from a guy at CDC last week who said, "Oh, we're staffed. We can handle rabies inquiries."

DG: Apparently not. Apparently, you go to voicemail and no one calls you back, and then when they do, they're like, "I don't know." This falls into an interesting category. Why did someone give someone, in the middle of their rabies vaccination course, prednisone? Because the problem there is now you're interfering with their immune system. You're not sure how well the rabies series is going to work. You then fall into the category of, "Hey, I'm trying to do vaccination in someone who is immunocompromised, immunosuppressed." We do have recommendations for that. Your email is good because it gives me a little bit of information.

In general, if you're not sure about a person's immune system or they're immunocompromised, and there actually is a CDC link where you can find - but just have to think it through, you say, "They got prednisone. I'm going to consider this an immunocompromised person," the fifth dose is recommended, but as you point out,

checking the rabies titers also. Give that fifth dose because you're not sure if the abbreviated - It was really a few years back that we switched to the four dose instead of five in the U.S.

Give that fifth dose, but then three weeks later - and think about timing, you don't want to do it right away, three weeks after that fifth dose, check the titers, see if it's there. You may actually even end up doing more because you want to get the titers above a defined threshold.

VR: Tim writes, "I'm a 54-year-old anesthesiologist in Oregon. I developed allergic asthma with eosinophilia in 2022 shortly after receiving a Pfizer mRNA COVID booster. My asthma is now well-controlled on inhaled corticosteroids and the biologic benralizumab. I understand that association does not mean causation, but I'm also aware that in rare instances, patients can develop eosinophilia following mRNA vaccines. The mechanism appears to involve a Th2 immune skewing effect in susceptible individuals with preexisting asthma or atopy.

I have received annual Pfizer mRNA COVID vaccines subsequent to developing asthma. My question is, should I consider switching to the Novavax COVID vaccine in the setting of my eosinophilia on the off chance that continued mRNA vaccines are contributing causative or exacerbating eosinophilic asthma? I'd like to continue to protect myself with immunization. Thanks for your input and thanks for your outstanding and informative podcast."

DG: Tim, this is a great question, and just to lay it out for our listeners as well. When you're developing a vaccine, one of the things the FDA is going to require is that you show that you're getting a nice balance between a Th1 and a Th2 response. This is an old way of breaking down the immune system, but it's still actually relatively valid. The idea is the Th1 is going to be much more of a cellular response, which seems to make a lot of sense in the world of viruses. Th2 is going to be more of an antibody, also an eosinophilic response. That's going to be something we think about with parasites and bacteria. You want to have this balance.

I understand the concept of this. Putting it into practice, is it likely that it's related to the mRNA vaccine? Probably not. This isn't something that we saw with a high enough signal that it's warranted further testing. Is there some advantage to switching to Novavax over the mRNA? I don't know if we know enough here. It's a reasonable thing to consider if you're going along in a plateau and your asthma is requiring inhaled corticosteroids, biologics. You might say, "Hey, this next round I'll try Novavax and see if this plateau that I'm on - Maybe I can use less inhaled corticosteroids, et cetera." Worth considering, but it's nothing really compelling here that there's a causal link.

VR: Susan writes, "I'm a loyal *TWiV* listener. Can't thank you enough for years of providing your knowledge, common sense, humor at times, and great quotations. I have a few questions. My healthy 13-month-old granddaughter started daycare one month ago and completed the initial two-dose Spikevax series in July. Having read the AAP recommendations, it's not clear to me if she also needs to get the updated vaccine against XFG this season. Should she wait till mid-November, which is four months from her last shot, or wait a full six months to maximize the benefit?" Take that one first, please.

DG: It's interesting. The way they did the studies and the way the package insert actually is for the new COVID shots this year, the new XFG, is that you're not supposed to have gotten a COVID vaccine within the last two months. I was looking at this. It was July, so August,

mid-September. We're in end of October. You would look at this and say, "Here's a person that previously completed their series. They're now eligible, no contraindication to entering the adult world of a once-a-year COVID vaccine." The XFG, this is actually not a booster. It's an annual because that prior Spikevax was not XFG. That's the first part.

VR: Also, she completed the two-dose flu series in March. Should she get the flu shot now or wait till October, November for timing for the holidays?

DG: As we mentioned before, flu is here. It is on the way up. Get it now before you end up with the flu.

VR: Finally, "For our healthy adult children in their mid-30s and healthy adults like my husband and myself, 70, last vaccinated in late October. Can we all wait until the end of October or early November to get flu and COVID vaccinations?"

DG: The problem we have with the flu shot, as I'm pointing out, is the flu's here now. There's no point getting your flu shot after you got the flu. You want to get it before you got the flu. We've got a dozen folks in the hospital where I was at earlier today, oxygen, bad flu. Unfortunately, the flu's here early, COVID's active right now. Might as well go ahead and get them.

VR: Helen writes, "Thank you -"

DG: Actually, I want to comment about the next part here.

VR: OK. I'll read it then. "I was somewhat surprised that you have already received both. I assume that even though protection wanes, you believe you'll be protected through the winter season. I read there might be an early flu surge on the West Coast. I know there are no guarantees with all of this."

DG: Susan, I was looking through the emails earlier, and I saw this. It is an interesting issue because I remember, Vincent, it was a number of years ago when you were talking about the timing of the flu vaccine. There's two aspects to this. One is that you get your flu shot. Two to three weeks later, you get your peak of the antibodies, and then those antibodies are going to drop about 10% a month.

What's interesting too, and this came up at the IDWeek, someone asked a question about this like, "Yes, but that's antibody levels. Does that really correlate with susceptibility to the flu?" There was actually a nice Canadian study where it really showed that there was a tracking. For every 10% drop in the antibodies per month, you were also seeing a 10% decrease in your protection from the flu. It's not just antibodies that drop 10%, the protection drops 10%. Like they say, don't try to time the market, but you do want to time the flu season.

VR: Protection against what?

DG: People ending up with - it was clinically relevant, identified, going for medical attention, flu. I'm glad you asked that because I think the protection against severe disease is probably more sustained.

VR: OK. Helen writes, "Thank you for all you do to promote science education. I am a formerly vaccine-hesitant person who chose to educate herself during early COVID, and now

I'm a huge supporter of vaccines with a new hobby, studying virology and public health. *MicrobeTV* was a major player in my enlightenment." Great to hear that.

"Much to my dismay, however, I tend to have strong reactions to vaccines, especially, it seems, to mRNA COVID jabs. I have gotten all the recommended doses since 2020. I have consistently ended up in bed for two to four days with body aches, migraine, vomiting, and sometimes other symptoms, followed by a week or two of digestive trouble. You can imagine my joy in hearing that there might be a vaccine with less reactogenicity. I wasn't able to acquire Novavax in a timely fashion last year, but I was able to get Nuvaxovid at my local CVS last Friday. I waited till the weekend in case I ended up in bed. I'm happy to report that I felt crummy on Saturday and spent a portion of the day under the covers. There was neither migraine nor vomiting, and I felt fine by Sunday.

I wouldn't have known about this alternative if it hadn't been consistently mentioned during your clinical update. I had to go out of my way to request it, but I'm so glad I did. I have friends who stopped getting COVID vaccine because they don't think the reactogenicity is worth it. I'm delighted to have an alternative to suggest to them. With profound gratitude, Helen from Pittsburgh."

DG: Great, Helen. Thank you. That's excellent to hear.

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

DG: Thank you, and everyone, be safe.

[music]

[01:01:19] [END OF AUDIO]