TWiV 1322 Clinical Update

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Guest: Daniel Griffin

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

[music]

VR: From *MicrobeTV*, this is *TWiV*. *This Week in Virology*, Episode 1322, recorded on May 14, 2026. I'm Vincent Racaniello, and you're listening to the podcast *All About Viruses*. Joining me today from New York, Daniel Griffin.

Daniel Griffin: Hello, everyone.

VR: I can cheat because I already did a podcast with you, and I know what's on your tie. It's not an STI because today is Thursday, and so it is influenza virus.

DG: The interesting issue is tomorrow, my middle daughter, so we're recording this Thursday. Friday, my middle daughter, Eloise, is graduating with her master's in elementary ed. I'm going to the graduation, but it's a Friday, so I'm going to wear my gonorrhea bow tie.

VR: I don't know if that's kosher.

DG: [chuckles] I have no choice. They had to schedule it on a -

VR: Because it's Friday--[crosstalk]

DG: -Friday. Yes, because it's Friday.

VR: What school is she graduating from?

DG: William and Mary.

VR: Oh, down in Virginia.

DG: Down in Virginia, yes. My wife, her two sisters, all my kids, apparently, we're all Virginians now.

VR: All right. Enjoy.

DG: Yes. No, she's actually got herself a job. Imagine that. She's going to be a fourth-grade teacher at Magruder Elementary School in Virginia. She's excited.

VR: Nice.

DG: All right. Let's jump in. We've got a lot to talk about. I'm going to start with an E.O.

Wilson quotation. "The real problem of humanity is the following: We have Paleolithic emotions, medieval institutions, and godlike technology. It is terrifically dangerous, and it is now approaching a point of crisis overall." What did he know? Oh my gosh. [chuckles]

VR: I've been trying to unpack this for a while now. I'm sitting here looking at it for the last hour. The emotions are old, right?

DG: Human beings are human beings. We lose our tempers. We get angry. We get spiteful. Human beings are human beings.

VR: I don't know about this point of crisis, though.

DG: I don't know if that's true. I love these quotations. I actually love the ones that I don't quite agree with completely, because it allows you to unpack them, and discuss them.

VR: I think that, ecologically, we're approaching a crisis, right, for sure. We have the capacity to do almost everything. I mean, science and engineering advance all the time, right? That's incredible. Maybe we can save ourselves, but we have to have the will, and that's the problem now.

DG: Yes. E.O. Wilson really was talking about the environment pretty much always, I think, right?

VR: Yes.

DG: Yes. All right. Well, I figured we would talk a bit about hantavirus. I think people are excited to talk about Hantavirus, to learn about hantavirus. This is an evolving story, so there'll be things we keep talking about. The first, and I want to do this in an educational entertainment, what do we call it? Edutainment approach, where we try not to get too doom and gloom. We try to educate, but at the same time, keep people engaged.

Yes, the world is not ending like that quotation sounded. May 10th from the CDC, we have interim guidance for public health assessment and management of people with potential exposure to Andes virus. I like the fact that they're calling it Andes virus, because it's not like every hantavirus is the same. I think a lot of times I hear doctors say something about hantavirus. I'm like, "No, you're talking about Sin Nombre. We're talking about Andes virus."

First off from the CDC, we have case definitions. They discuss the definition of contact, and then they define what is considered an exposure. Exposure, number one, being aboard the MV Hondius at any time from April 6th, date of symptom onset for the index case through the date of this embarkation of the exposed passenger cohort. Two, being within approximately six feet of a symptomatic case patient in an enclosed space for a cumulative duration of equal to or more than 15 minutes. It's interesting that they come up with those six feet, 15 minutes, a déjà vu here. Having direct physical contact with a symptomatic case patient, or having contact with respiratory secretions, or other bodily fluids from a symptomatic case patient.

VR: I don't know how they can say six feet in 15 minutes. There just is not enough data to tell that.

DG: I'm glad that you bring that up. Yes, let's talk about that a little bit right here. We're going to circle back to this, of course. It sounds to me they're assuming a certain type of

transmission.

VR: I don't buy this at all. The KLH flight attendant in Johannesburg, she talked to the sick Dutch woman, and she did not get infected. If you want to board a plane, you go up to the little desk. You're a few feet away. Maybe she was there for five minutes arguing to get on the plane, and then she said, "No, you can't get on it," and she didn't get infected. I don't know what other data they have.

They can't have any other data. I'm sure they have not talked to everyone, and followed everything that they did. My interpretation is that you can be in the same room with someone. If you sleep in a cabin on the boat, that's close contact. You bump into each other all the time. If you danced with someone on the boat, I don't think walking by someone is going to do it.

DG: We'll get into some of the what do we know about transmission. It almost seems here like they're making certain assumptions already about this particular, Andes viral - We'll call it variant strain, whatever. We don't quite know yet. They also talk about incubation period. The CDC has four to 42 days with a median of 18 days. We'll talk about what we actually know from prior outbreaks.

Then, this is interesting. This is going to come up. They actually talk about a high-risk contact. They say that if you are a high-risk contact, and this is, I have to say, I wasn't sure if this was out of *The Onion,* or the CDC, but we're going to read this anyway. Maybe you need to think about who is on the MV Hondius. What is it like for a couple to go on the 21-day trip? You'd spend $50,000 for those 21 days, right?

Because you'll notice some of the recommendations, you're like, "Who are they talking about?" High-risk contacts have the option for home-based management. If you basically want to just go hang out at home, that's fine. If you want to go hang out at the National Quarantine Unit in Nebraska, that's an option, or you could find some place with your health department. Basically, do whatever you want. We're pretty flexible here.

If you're going to go home, basically, if the home-based management is preferred, then the health department should coordinate with these high-risk folks. The individual should have a suitable home environment with access to a designated space in the home to isolate away from others immediately if symptoms develop. Apparently, until you actually really are symptomatic, we're going to talk about that. Ideally, you should have your own private bathroom, but again, only once you start to get symptoms for the duration of monitoring period. Again, we're assuming here that you're only contagious once you actually have symptoms. We're going to -

VR: I don't know where the data is for that. I mean, for COVID, obviously, you shed in the presymptomatic period. How do they know? [chuckles]

DG: This is interesting. We're going to talk about that, because maybe they don't know. Now, health department should identify a hospital with capacity.

VR: Wait, before you go on, this location. Someone asked me last night on the live stream, wouldn't it be better for people to stay home than put people in the hospital at risk? Are there hospitals that can handle this, or some that cannot isolate a patient?

DG: Yes, there's two aspects. One is that really long incubation period. You're hanging out in the hospital at $2,000, $3,000 a night for, what? Eight weeks? It's a long time. The other is, if you do end up getting sick, and I think we've talked before, I've managed patients with Sin Nombre here in the U.S. Not Andes, so slightly different, but these people, they get sick really quickly. They need critical care, the ones that get particularly sick. There's a spectrum of illness here.

They may need extracorporeal membrane oxidation. This is ECMO where you put in a catheter. You're running their blood through basically an external lung device that's taking the role of the lungs for them. You're going to need a proper critical care-enabled facility to take care of these folks. Then, this is where I think they asked someone from *The Onion* to write this section on their travel advice. Health departments should advise high-risk contacts not to travel during the monitoring period.

However, if they do intend to travel, travelers should be by chartered flight. They say should. There's no shall here. Basically, they say here, "We don't want you to travel, but if you are going to travel, try to travel in your private jet."

VR: That doesn't sound like the old CDC to me. This sounds like some shared decision crap.

DG: Yes. By the way, if you are going to take a vehicle, try to stay in your own private vehicle. Don't get on a bus or a train or something. Then, ideally, we don't really want you to travel, but OK, if you want to travel, that's OK. Ideally, if you're going to travel, try to stay in the U.S., but if you're going to travel internationally, apparently, that's OK. Just let us know, because we'll work with the destination authorities, give them a heads-up.

VR: We have the opportunity to just stop this outbreak, right? By all the people who are known to be infected, to stay and put for two months or whatever it is, and that's the end of it. Then, nobody goes to the landfill down, or the dump site down in Argentina, and that's it. They're letting people move around.

DG: Maybe we have a reverse zoonosis here. Maybe these people then, it gets into our rodent population instead of Sin Nombre, we now have this Andes virus that once it gets into people, it can go -[crosstalk]

VR: The Andes virus has a very specific rodent, the pygmy rice rat.

DG: Are we sure it's restricted to the pygmy?

VR: Well, that virus has never been seen anywhere else, right? That's the only thing you can do, but I'm sure it's not restricted, right?

DG: Let's talk about that. What do we actually know? That was the CDC just saying stuff. I'm going to leave in a link to a number of articles. I'm even going to leave a link into your hantavirus on board with Professor Vincent Racaniello, which is getting a lot of views, a lot of listens and views, so that's great. As I've already pointed out, and we want to be careful to point out that we're not discussing the North American Four Corners Sin Nombre hantavirus, but instead we're talking about the Andes hantavirus.

Now, the hantaviruses are zoonotic viruses with nearly global distribution all around the world, but we break it down into two severe disease types in humans. There's the

hemorrhagic fever with renal syndrome, so that's your hemorrhagic fever, people bleeding, people going into kidney failure. That's the type of disease we're seeing in Europe and Asia. There's also the hantavirus cardiopulmonary syndrome. That's what we see here, the New World, the Americas hantavirus presentations.

There also are some novel hantavirus species in Africa, so more to come. There's a nice table in one of the papers where you can actually see a number of the different hantaviruses in the Americas, a number of the different ones in Europe and Asia. They have case fatality rates which range in Europe and Asia, it's actually a lower case fatality rate than the New World ones that we see here.

VR: By the way, just this week, a case of hantavirus pulmonary syndrome was reported in Illinois, in a Winnebago County resident who had contact with mouse droppings while cleaning his home. This is Sin Nombre virus, right?

DG: Yes.

VR: It just illustrates routine endemic domestic exposure, which is ongoing. This is a rare disease in the U.S. There have only been 800-some, or maybe 500-some cases. Let me look at the number.

DG: 800, yes. It's under a 1,000. [crosstalk]

VR: 864. It's very rare, but it happens. Keep away from that mouse poop.

DG: [chuckles] That's actually - Then, let's bring us to the reservoir. There are a number of reservoir hosts. Most of these natural hosts actually carry the virus, carry it for their lifetime, a lot of them. To the best of our knowledge, they don't appear to get sick. They appear to have a relationship here, probably been there for quite a while. Rodents are the main natural hosts of the hantaviruses.

The hantaviruses have also been detected in bats. That should get people thinking, moles, shrews, reptiles, and fish. We have certain ideas that there's only certain hantaviruses in certain hosts, but just to give that range. Now, next question people probably want to ask, is how long do the hantaviruses remain viable in the environment? We have some data for particular hantaviruses.

The Puumala virus, and people can look up in our chart, and see that's a Europe, Asia, Finland, Sweden, Belgium, Germany, France, Russia, Northeast Europe. We have some data on the Puumala virus. It remains infectious for up to 15 days in the voles bedding. It can remain viable at room temperature after five days in a wet environment, 24 hours if you dry it. Now, the Hantaan virus survived in wet conditions for eight days at 20C, nine days at 37C. The Hantaan virus also a Europe, Asia.

Now, here's I think the thing about the Andes virus. Person-to-person transmission of the Andes virus has been documented in Argentina and Chile. I'm going to leave in like half a dozen different reports of this. There's a really nice article that was in *The Lancet*. For person-to-person transmission, estimates of incubation periods range from nine days and 40 days with a median of 23 days.

It could be out to eight weeks. I've got the reference where they actually suggest that it

could be as much as eight weeks. CDC says 42 days, so that might be an issue. There's also, in some of these articles, a really nice-- How do we see the presentation? There's an exposure. There's an incubation period. We can discuss, is it really 42? Is it really longer? Is it really going to go out to eight weeks or 56 days?

VR: They're holding these people for eight weeks, right? They're assuming that's the maximum.

DG: Holding, meaning by the way, please don't fly your private jet internationally. If you are going to do that, let us know. I don't know if there's a lot of holding going on. This is going to come up because we're going to talk about when people transmit. There's the incubation period before you get symptoms. Then, there's this interesting period, the prodrome. What is a prodrome? This is going to come up again. This is when you're like you don't feel 100%, but you may not necessarily have a fever yet. You're not really sure. You just, "Oh, I don't feel so great." Then, there's when you actually move into the disease period, right?

VR: It's actually when you get symptoms, but they're not characteristic of the disease. They're non-specific. Like measles, you might have a fever, or coryza, but then you get the rash, and that's clearly measles. That's out of the prodrome.

DG: Perfect. Now, we're going to get into - Let's look at one of these. There's a really nice paper where they go through, and this is the 2018-2019 person-to-person event. This was published in *The New England Journal of Medicine*. You can really look through. I love when they have these figures. You can see the index patient, and who they spread it to, and who they spread it to, and who they spread it to. In this outbreak, they actually traced this first person-to-person transmission event to a birthday party with approximately 100 guests. This -

VR: Wow, 100 people at your birthday party. That's nice.

DG: [chuckles] I don't think, yes.

VR: No, it's not nice.

DG: I'm an introvert. That would overwhelm me. I'd be like back out the back door. The index patient attends the event for 90 minutes, and was, they say reportedly symptomatic. They had fever and malaise. They had fever. They didn't feel well. Think of how many times you're like, "I don't feel so great. I feel like I got a fever, but I really got to go to this birthday party." You go anyway. Not me, but other people apparently do that.

They show up. Now, five persons. They're going to name them. It's nice in the figure. You got five persons that were seated close to patient one. Then, they reported symptoms consistent. Patient two and patient six. They're going to spread it to two other people at the birthday party. They're going to feel sick 14 and 24 days after the party. Now, patient two was the likely source for six infections in other persons during the, are you ready for this? Early prodromal phase, because of his active social life.

Here he is just not feeling a hundred percent, but not necessarily having any symptoms that make you think, "Oh my gosh, this guy has hantavirus." I do want to point that out because this sort of -

VR: He's going around and hanging out with people.

DG: Hanging out with people. Not feeling 100%, but not necessarily sick, right?

VR: Not enough to keep him home, obviously.

DG: Exactly. Apparently going out. He's going to go out enough to give it to six other people.

VR: So far, he's been symptomatic when he's infecting other people. There's no evidence so far of asymptomatic.

DG: Not asymptomatic, but prodromal. I think, yes, that's important. Because remember, early on in the COVID, we had this German woman and she traveled. She goes, "Well, I wasn't 100%, but I just felt a little bit rundown. Maybe I had a little bit of a fever." I guess we're seeing. You could be just a little bit rundown, and a fever and doing this. Patient two, the social guy, he dies 16 days after symptom onset.

His spouse, this is like, it's déjà vu. His spouse, this is patient nine, was febrile while attending his wake. Now, this is great. Now you've got a sick person with fever who's at a wake, a bunch of people at the wake, an additional 10 persons who attended the wake and were in close contact with patient nine became ill between 14 and 40 days after the wake from patient two. Someone didn't get sick for 40 days. The remaining 12 patients were in contact with at least one previously symptomatic patient. Four patients may have been infected by more than one person.

VR: You think about a wake, people are shaking hands, they're hugging each other, so they get pretty close, right?

DG: An Irish wake. I remember people kissing my grandma on the lips. She's in the coffin there. There's a lot of -

VR: It's a bit much for me.

DG: Yes, I think so too, but yes, that's my tradition. [chuckles]

VR: Oh my gosh.

DG: On the basis of evidence from five reconstructed person-to-person transmission events, here's what they say. The root of infection in secondary cases was possibly through inhalation of droplets or aerosolized virions. Of the 17 of 33, 52% secondary transmission events, transmission from an infected person to a contact who later became infected could be accurately established as a day of onset of fever in the primary case, so half the time.

Half the time, we can really say it was that first day. Half the time, yes, we're not sure. OK. Where do we stand on Andes hantavirus? I'm going to leave in a link to the transcript and recording of the CDC update on their hantavirus response from May 13. We're recording this on the 14th, the day after. There's some misspellings in the transcript.

For instance, they met the plain, P-L-.A-I-N, not the P-L-A-N-E. They met the plane. I'm not sure how that works. I think they mean P-L-A-N-E, for instance. We're getting used to this lower level here in the U.S., guys. If you listen -

VR: They're using AI to write this and-

DG: Probably.

VR: -not checking it.

DG: Yes, just review it. Come on. This is like people are going to read this stuff. They stated, "This particular virus has a long incubation period, so the monitoring period is 42 days." They're not saying eight weeks here. They're just saying, "We're going to do six." In the six weeks, 42 days started with departure of the ship. May 11t was the day one. It's not really departure of the ship. It was departure from the ship.

Again. OK sorry. There was a question about the passenger who was considered a mildly positive case if he had been retested back here in the U.S. They responded that they were in the process of testing currently, and we hope to have those results back in a day or so. [chuckles] As far as the lack of any strict quarantine, they report, "We're taking a conservative approach on this. We really are encouraging people to stay at their homes, and work very closely with the state and local health departments to ensure that they are appropriately monitored in that space."

We've got a *Wall Street Journal* article, "CDC is Walking a Tightrope with its Response to Hantavirus." Here they point out that several leaders now running the country's top health agencies, including Acting CDC Director Jay Bhattacharya, have publicly criticized COVID-era restrictions, and are now working to explain the level of threat posed by hantavirus. I'll leave a link into that. This is a nice article.

They've got this article already in *The Atlantic* by Katherine Wu, “What Happened on the Hantavirus Cruise, According to a Doctor on Board.” It's a nice firsthand account. This was a doctor who was on board as a passenger. He's actually this world-renowned birder. Then, the ship's doctor gets too sick to take care of anyone, so now he's taking care of the ship's doctor and all the folks on board.

VR: He got sick, too?

DG: Yes. He got sick, too, is what I hear.

VR: Should have worn a mask.

DG: He was. He actually - They had some N95s on board. Vincent, keep this. This guy was, as he said, he was using COVID-era precautions. He had the N95. He was putting on an apron. He had gloves. He still got sick, Vincent.

VR: Wow, that's interesting. There was a breach somewhere.

DG: There's some kind of a breach.

VR: De-gowning is a certain procedure, as you know.

DG: It's true. It's true. No, there's a whole process. [crosstalk]

VR: You're going to contaminate yourself.

DG: Then, this is hot off the press. I'll leave this in. Mainly, I'm leaving this in because they have just like a wonderful - It was these graphical abstracts. It's hot off the press, "Andes Hantavirus Outbreak on a Cruise Ship - An ESCMID Emerging Infections Subcommittee (EIS) Rapid Assessment," published in *CMI*. Really nice. There are some issues. I like the first panel in this. Hopefully, this will be up for folks on YouTube.

You see the MV Hondius, and it leaves the southern tip of South America. Then, it heads off. It's heading a little bit east and north. We're going to ultimately head towards the Canary Islands off the west coast of Africa. Then below that, they have St. Helena and all these people flying all over the place. I feel like St. Helena is maybe in a slightly different area on the map maybe, but that's OK.

Then, they show each of the cases. You can see case number one, unfortunately, confirmed and died. Case number two, confirmed and died. Case number three, confirmed and died. Case number four, confirmed, critically ill. Confirmed, and suspected.

VR: Let me update the numbers, because I just did this yesterday for the stream. As of May 13, 11 total cases, nine confirmed and two probable, three deaths. A fourth is possible. The lady in France is on ECMO now. They think she's on her last leg. Forty-two days quarantine. That's the number, at least for the Nebraska passengers. They're in the University of Nebraska Medical Center. Then, there are two unrelated cases, one in Illinois and one in Italy that you're looking at.

DG: What do you think, Vincent?

VR: The real question, this is going to stop. This is stoppable with infection control. We saw that in the Argentine outbreak. The real question is whether this is a zoonotic infection, or has it become a human virus. I think it's a zoonotic infection. It's like Ebola. It's like MERS, coronavirus. You get short chains of human infections via close contact that are stoppable with proper isolation procedures.

The next outbreak is going to be another spillover. This is going to be gone from humans. It's not a human virus. I'm interested to see the sequence. If any changes are there, say compared to what's in this landfill, if they find it there. That would suggest human adaptation. I think it's not. I think it's not an HIV that becomes a human virus. I think it's Ebola, MERS, coronavirus, Nipah. You all need a West Nile virus. Every human infection is a spillover. That's what I think. I think that's the key question here. It is not a human virus.

DG: This was a cruise ship. This was a particularly unique exposure scenario.

VR: It is unique, yes. People don't realize that animals are full of viruses, especially rodents, which are 40% of mammals. Now, you often don't see rodents, but you see their excrement. Be careful. The place where the two were thought to have gotten infected is a garbage dump in Ushuaia, I think, or somewhere down south there. They say it's just littered with rodents and rodent poop. It's easy that there's an aerosol of virus to anyone that goes in there. I'm sure they're going to try and isolate virus there. We'll see what's going on.

DG: That'll be interesting to look at. Look at the sequences there. Look at the sequences that they'll be getting. I don't think the sky is falling. It's interesting how interested people are in this, and how much of a news item it is. Think about it. There are probably hundreds of cases of Andes virus that have happened. People could get sick and get on an airplane.

This is interesting and all. I don't think the sky is falling here. I do think a little bit of humility is warranted. We don't exactly know how this transmits in different situations.

VR: I think that I always say don't take a cruise, but now I'm also going to say don't go birdwatching, because there's probably mouse poop all around you.

DG: I have to say, though, these cruises, if they offered me a free trip, they look like amazing experiences.

VR: No, I'd never go on a cruise. You're close to too many people. That's really close contact. Look at norovirus outbreaks on cruise ships. The same reason, right? You can't avoid being contaminated. You can't get away from people. Why do I want to be in a tin can with 5,000 people? This was smaller, but really.

DG: [chuckles] All right. Let's jump into measles. The numbers are still going up. Measles cases per the Hopkins tracker up to 1,967 from 1,923. That's another 44 cases just over the week period. CDC has us at 1,842. We're quickly approaching that 2,000. We're already heading pretty close to what we had last year. Fortunately, we have gotten out of the flu season, so we'll revisit that when it rears its head in the fall, but we're up to a total pediatric death so far, 158 deaths this season, so pretty upsetting there.

What can we do about the flu? Well, we have this article. Oh my gosh, an mRNA vaccine for flu, Vincent. The article, "Efficacy and Safety of an mRNA Seasonal Influenza Vaccine in Adults," was published in *The New England Journal of Medicine.* They start with a statement, "Seasonal influenza causes substantial illness and death in adults 50 years of age or older, even with current vaccines." We continue to cover this as well as the issues in children who die of flu, or get seriously ill. Here we have the results of a phase 3 double-blind active control trial.

They randomly assigned adults 50 years of age or older to receive the trivalent mRNA-1010 vaccine, or a licensed standard dose comparator. The primary efficacy endpoint was relative vaccine efficacy against RT-PCR-confirmed influenza-like illness. Basically, getting symptomatic flu A or B. A total of 40,703 - [crosstalk]

VR: Wow, that's big.

DG: Huge, right? 40,703 participants received the mRNA or the standard dose. We had over 20,000 in each group. Followed them out for 180 days. When you look at the results, we saw that 2% in the mRNA, 2.8% relative vaccine efficacy. Remember, these are comparing one vaccine to another. Is this vaccine better than the other, not just better than not getting vaccinated?

It was 26.6% better than the standard vaccine, so met criteria for non-inferiority, superiority, and higher-level superiority. As far as adverse reactions, a little more, right? Reactogenicity with the mRNA vaccine. You've got some injection site pain, fatigue, headache, and these were all above the standard ones. Now, mostly reactions were mild to moderate and transient.

Serious adverse events were reported in 2.2% of the recipients of the mRNA, 1.9% in the recipients of the standard dose. Then, they have this really nice Figure 1, where you can look at all participants, folks that have one or more high-risk conditions, folks that are 65 or

older. Then, they even look at different frailty scores, body mass indexes, so all across the board, we're seeing good efficacy if you're fit or fat. The Edmonton Frail Scale is a widely used clinical tool to measure frailty in older adults, and they use this to look at the frailty scores.

VR: This is Moderna, of course. What was the - Over 50 years of age, OK.

DG: I'm going to have to be over 50, but then they even do a subgroup analysis, where you look at folks greater than 65, and that's great, but then you even break down. Actually, the people who did the best were the people who were the healthiest. Interesting.

VR: This should go to the FDA for licensure, right?

DG: Well, this is the one that they didn't want to look at. I want to see what happens on that. I mean, I would like this as an option. I'm over 50.

VR: I would get this because I think the flu vaccine we're using is just old-school technology, and it's not so great.

DG: It's like the latest iPhone. We got running around with our flip phones. I feel like I'm in an old 1960s *Trek* episode. All right. RSV, we have the article, "Maternal RSV Vaccination, Infant Nirsevimab or Both: Interim Analysis of a Randomized Trial," published in *Pediatrics*. That's really a question. These are the results of this prospective, randomized open-label phase 4 study at eight U.S. sites of mother-infant pairs, and they get randomized one-to-one-to-one-to-one. You get all these different options.

You get, mom gets the vaccine alone, mom gets the vaccine, infant gets nirsevimab, mom gets the vaccine, and the infant gets nirsevimab at three months, or the infant just gets nirsevimab. They follow these mother-infant pairs for 12 months, and then we end up with the report of the interim data here. In total, 181 mothers were enrolled. Both products alone, or in combination were safe. No related serious adverse events were observed in mothers, or infants. Nirsevimab well-tolerated.

The RSV pre-F vaccination boosted maternal RSV antibody titers 17.35-fold at the time of delivery, and titers were durable for three months post-delivery. The geometric mean transfer rate of the antibodies was higher than 1.3, similar across groups. Basically, maternal vaccination, infant nirsevimab, whether you get them separate, or in combination were safe, and we got these really nice high titers of antibodies.

All right. COVID is your favorite part, right, Vincent? The multicolored lines, and look how low they are.

VR: It's the lowest they've been in a long time, right?

DG: Maybe SARS-CoV-2 is going away.

VR: No, it's not going away, but there is a lot of -

DG: [chuckles] Vincent, but it's on the way. If I just follow those lines out, it's going to hit zero.

VR: That's an asymptote. It never gets to zero. A lot of people are now immune, so inter-

outbreak is going to be low, I think.

DG: I hope so. I hope we're going in this -

VR: Not zero. I mean, you still see cases, right?

DG: Yes, unfortunately, we still see cases. We may be in this spring break, and then what is it? July, August.

VR: In July, we're going to see. Someone asked me last night, "Why do I need to get one in the summer? It's not circulating." I said, "Well, it is. There are outbreaks in the summer and the winter, so that's the reason."

DG: No, for the over 65, now is about when you start thinking about time to get that shot for the summer, the summer surge.

All right. We have the article. I like this article because it addresses this misconception. Let's talk about it. The article, “Life Lost Due to COVID-19 Pandemic: A Model-Based Cohort Analysis of Mortality Displacement in the Registered Population of England,” published in *PLOS One*. As mentioned, I like this study because it addresses this idea that people have out there, like, "Oh, people who died from COVID, they're probably just about to die anyway."

There's a bit of blame on the patient here with this idea that these people that died from COVID, either they ate too much, they didn't take care of themselves, they're so old, they’re going to die anyway. Here, these investigators conduct a study where they used retrospective linked data from March 2020 to September 2022 for the cohort of all individuals in England alive at outset.

They simulated the survival of every individual in the population with a positive COVID-19 test, with or without the assumption that COVID-19 affected their survival, taking account of their personal vulnerability. They used the difference between these simulated survival times to estimate mortality displacement. How long those who died would have lived had they not gotten COVID-19?

They found a median mortality displacement of 4.8 for females, and 4.4 for males at ages 65 and over. Basically, what they're going to conclude here looking at this, was the life expectancy of those who died of COVID-19 was substantial. Most of those who died at ages 65 and over were unlikely to have been close to death. Basically, these people had about four and a half to five years left to go, and then COVID knocks them off early.

VR: People always make stuff up. I’m really happy that they actually tested it, and showed that they're wrong.

DG: I like this because they say all the time, "They were probably going to die pretty soon anyway. They were going to die of something." Well, not like, we're all going to die of something, but I want that period of time to be distant.

All right, the article, “Ensitrelvir for COVID-19 Post-Exposure Prophylaxis in Household Contacts,” was published in *The England Journal of Medicine*. This is this question, right?

Someone gets COVID and you're exposed to them, you're living in the same household, maybe you're in that nursing home. Is there anything you can do to protect yourself? Failure

with Paxlovid. Paxlovid didn't actually achieve what we're going to see here. Here with ensitrelvir, we've got a double blind randomized placebo-controlled trial, randomly assigned persons who were SARS-CoV-2 negative on local diagnostic testing, but were household contacts of a patient with COVID-19, so it was an index patient.

They either got ensitrelvir, and it's 375 on day one, 125 milligrams daily on days two through five. They'll need to make an ensitrelvir pack that they can have these in, or you got placebo. This is within 75 hours after symptom on index, and the symptom on the index patient. Primary endpoint was COVID-19. Basically, you had to have symptoms, you had to have a positive PCR.

All the patients undergo randomization. The modified intent to treat population included over 1,000, so 1,030 participants in the ensitrelvir group, over 1,000, so 1,011 in the placebo group. Mean age, 42.4, 71.1% had undergone randomization within 48 hours after symptom onset in the index patient; 37% had at least one risk factor for severe COVID-19, but majority didn't. The incidence of COVID-19 was lower in the ensitrelvir group, 2.9% versus 9%. Almost a 70% reduction, and really no issues with side effects, adverse events.

VR: How do people get this? If someone tests positive, can they ask their doctor to give this for the family members?

DG: This is going to be something that they're going to need FDA approval. Right now, it's something that I think it's Shionogi makes ensitrelvir. I think this is something that's available outside the U.S. The idea would be with data here, you would go to the FDA, and they've probably already talked to the FDA, but who knows what goes on these days. You say, "Here's compelling data. This would be a useful." Particularly, I think of as great role in like a nursing home when you have outbreaks.

All right. I'm going to wrap us up there with no one is safe until everyone is safe. I'm going to leave a link to reach out to your representatives if you feel like you want to ask them to be doing something for you. I do want everyone to pause the recording right here and go to parasiteswithoutborders.com. Click the “Donate” button, because right now, May through June, we're doing our FIMRC fundraiser, so Foundation International Medical Relief of Children fundraiser, doubling your donations up to that maximum donation of $10,000.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Scott writes, "I saw this *Cell Host & Microbe* paper about developing monoclonal antibodies against measles for those who can't be vaccinated. It's sad that we as a society cannot vaccinate to a level to protect babies and vulnerable people while protecting ourselves against this miserable disease, and must rely on expensive prophylactics instead. This paper suggests we could employ a strategy like nirsevimab and RSV to protect babies from measles until they are old enough to get vaccinated. I was wondering about your thoughts of the feasibility and practicality of a monoclonal for measles, especially for such a young population since there is a benefit for a monoclonal and RSV in babies. Would the same hold true for measles?"

DG: I like this idea. I think this is a great thing.

VR: OK. Ann writes, "Is there an actual definition of close contact?" We discussed this a little, but let me read the question. "When I've heard descriptions that are publicized to allay public fears, they sound like close contact means spending significant time in the same

room, or sharing tableware, et cetera, implying that someone outside of the household is really not at risk, but some of the victims on the cruise ship do not seem to fall into that category. Their connection was much more casual."

Who knows? Who knows what they did? Really, people don't tell you what they did. Yes, I went to the other guy's wife's room while he was gone. No, they're not going to say that, right? That happens. I think that happens.

DG: Yes, that's the problem. We always say history is the most important, but least reliable. Yes, so some of the stuff we're hearing is like, "I was in the dining room with those people. I never really even sat at the same table." We don't know. That's the really tough thing is trying to get that history, trying to pin down.

VR: They didn't have to sleep with them. What if they had a drink and they get a little tipsy, and the husband goes away, and they have a little kissing over there at the bar. Come on, folks.

DG: That doesn't go on in my world there, Vincent. I don't know about - [laughs]

VR: The world out there is pretty crazy. Anyway, in one study of Andes, I saw some screenshots. They seem to be finding transmission in as little as a five-minute conversation, but I could have been misreading that. The follow-up to that question would impact what kind of quarantine is appropriate for the potentially exposed cruisers. If they are simply being told to quarantine if they feel sick, does anyone really think that they will stay home any day they have the sniffles, in case it's day one of symptoms?

DG: Yes, so this is interesting. How they're doing this, should it be done differently? We're all Monday night quarterbacks. We'll definitely go back, and if they fumble the ball here, we'll have a lot to say. If it goes really well, whatever. It just won't say anything. For instance, people who listen to this clinical update often may remember the time I was in Uganda during the Ebola outbreak.

I'm not sure if you remember this, Vincent. We recorded while I was there. I'm trying to avoid the Ebola cases. I go directly to Jinja, which is the source of the Nile. I stay at Sergio's. He's this Indian guy who owns a guesthouse there. I get there and I'm thinking, "I have circumnavigated anywhere where there's going to be Ebola." I'm like, "What are all these Doctors Without Borders doing hanging out at Sergio's guesthouse?" It was because a couple young lads had snuck into the back of a truck. Then, they end up having Ebola, and they're there in Jinja.

When I get back to the U.S., the CDC folks, they meet me at the airport. They don't know because I actually connect through somewhere else. When they realize that I just come back from Uganda during the midst of this Ebola outbreak. I hang out in some special room, waiting. They come. We have a big interview. They basically said, "Hey, go home. We're going to check on you. If you at any point have any symptoms, then here's what you're supposed to do." It really was this casual.

Because we have this all the time. People travel. They're in areas where something could come back. I was in the town of Jinja and there was Ebola there. They waited until I finally let them know, "Hey, I feel fine. No symptoms. It's been three weeks." Then they said, "OK, we're going to shut down the Ebola. We'll say this is all good." It's this issue about we don't

really know exactly how close.

We don't really know how we need to do the quarantine. What was it? Craig Spencer was off bowling when he was - He's the guy who had Ebola ultimately ends up in his eyeball. He's bowling with his buddies when he starts to feel bad. Then, he takes the subway to get home.

VR: Efi writes, "Thankful to you and Vincent for all the good science you are sharing with us all these years. We hear about cases of hantavirus and want to ask for your insight on whether you think it can be of any concern to food safety based on what we know. The fecal oral transmission concerns animals, correct? Do you believe that transmission via saliva, or airborne droplets can even remotely make this virus of concern to food, or its production/processing environment?"

DG: This is a great question because two things come to mind. One, I think you're concerned could this be a fecal-oral type of transmission? Could somehow you get this orally? The one thing we've seen to date, and I'm not going to predict the future, but we sort of - What is this? Like when you buy stocks, past performance does not predict future performance? It does to some extent.

This has always been a respiratory, an inhaled, the entry is through the lungs, not through the gastric lining or intestines. That's a good thing. The other thing we've talked about is, how one of the ways people get sick is that the rodent feces, the viruses in the feces gets aerosolized. What about these folks on the cruise ship? You're sick. You have your number two in a toilet. You flush it.

We all know what happens when you flush a toilet, right? It creates this plume, right? You're in this ship with these wonderful ventilation systems. Did you know, Vincent, 30% of the fuel used on a cruise ship is for the ventilation systems?

VR: Oh, wow.

DG: It's amazing. Which is good and bad, because when I flush the toilet and create this plume, and I've got hantavirus, and maybe there's viable infectious hantavirus in my poo, I don't necessarily want this really efficient ventilation system sucking that. I want it straight out to sea. Now, supposedly, the way the ventilation system is, all the fresh air now gets pulled in, I think, from the starboard side. It's supposed to be fresh air.

VR: It really depends. It can be mainly respiratory transmission, but there can be incidents. For example, in SARS-1, there was an outbreak at an apartment complex, where a guy had a lot of diarrhea, and he flushed it and it spread to neighboring apartments via the plumbing. There can be exceptions to the general transmission rule, I think.

DG: It is tough because if you are the exception, now you're the one who's sick and with a 30%, 40% mortality, it's disaster.

VR: Someone asked me last night, "If there was rodent poop in food, would that get you?" I said, "Well, first of all, if you see a big bunch of rodent poop in your food, you shouldn't eat it."

DG: Don't eat it. [laughs]

VR: If there's just one pellet, which you don't see, I doubt that would be enough. Daniel, if you ate some hantavirus, would it aerosolize in your mouth, and you inhaled it?

DG: Probably not. These are good questions. These are why you do science. What a great high school science project.

VR: Marcus writes, "Episode 1320, you were discussing pediatric ear infections following RSV. You discussed the diagnosis of ear infection following viral illness. I'm a pediatric nursing professor. Differentiating viral versus bacterial ear infections has long been a struggle. Like you mentioned, many pediatric viral ear infections still get treated with antibiotics. This should not be the case, though, because since 2004, the AAP has had recommendations for watchful waiting when an ear infection is identified. If children are older, their symptoms are mild, they recommend waiting to see if symptoms progress, or self-resolve in order to avoid antibiotic overuse in a viral infection.

Only the very young, or severe cases are given antibiotics due to the concern for not treating a bacterial case. However, many parents still ask for antibiotics, and many providers still prescribe them. It continues to be something the AAP pushes for to improve antibiotic stewardship, but it's difficult to gain acceptance.

Thank you and the whole *TWiV* team for your work. I'm a recent listener within the past few months after a colleague recommended your show, it's been a great way to stay on top of the many changes occurring in vaccines that are impacting my population of focus in pediatrics. We are still out here trying to teach the next generations of healthcare workers the truth about the importance of vaccines. I've unfortunately had to remove all CDC vaccine sites from my lectures, which was not something I ever thought I'd have to do, but look forward to the day I can welcome them back when experts are back in charge." Oh my gosh.

DG: No, Marcus, I am right on with this. This is great. Yes, way too many antibiotics being used for viral illnesses, despite guideline recommendations that are, what, 22 years old?

VR: Eli writes, "I heard that four unvaccinated U.S. children developed tetanus, and at least one was treated with immune globulin. Was this standard immune globulin pooled from many people, or that from volunteers who have been repeatedly vaccinated to boost the titer of anti-tetanus toxin antibodies?"

DG: Eli, you got to watch our *Puscast,* because we cover that on the *Puscast*. We go through and discuss all that, so plug for the *Puscast*.

VR: OK. Lisa writes, "Thank you again for your updates. I thought hiking was a low-risk activity for respiratory diseases, except if hiking in a cave-like partially enclosed space, or if you were camping. Do the people who got infected with hantavirus, and then boarded the ships just hike without camping in a normal open-air environment? How would a person get infected in an environment of fresh air and good air circulation?"

DG: Yes, Elisa, I think the concern was there was so much feces just kicking as you walked, that there was actually aerosolation of the virus.

VR: Supposedly, they got infected at this Ushuaia landfill.

DG: Yes, people have decided that's true. I don't know if it's true. Yes, that was -[crosstalk]

VR: It's apparently a very dirty, rodent-infested [crosstalk] landfill, and it's got the rice rat in it, and is probably a lot of, if you're walking around, you're disturbing. It's not just a pristine, nice hike in the woods.

DG: Yes. It had the right host, reservoir Andes virus, you're in the right place. Yes. Not really your typical trail hike.

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

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

[music]

[00:53:27] [END OF AUDIO]