This Week in Virology

TWiV 1224 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. From *MicrobeTV*, this is *This Week in Virology*, Episode 1224, recorded on June 5, 2025. I'm Vincent Racaniello, and you're listening to the podcast all about viruses. Joining me today from New York, Daniel Griffin.

Daniel Griffin: Hello, everyone.

VR: You're shaking your head. You're not in New York. You look like you are.

DG: No, just my son Barnaby was sneaking into the recording studio. I don't think he realized the important business that was about to go on.

VR: I don't need to ask you what's on your tie. It's the logo for Parasites Without Borders.

DG: It is, and it's a reminder - hello, everyone. I am in New York, and it's a reminder that, yes, we can only do this great work with your support. Yes, we'll ask at the end as well. Yes, Parasites Without Borders needs your support if we're going to keep doing all the great work we do. We're just about to release, probably next month, this free online tropical medicine training course. We're supporting the work down in Panama of our ongoing fundraiser for FIMRC. Yes, go to ParasitesWithoutBorders.com, and send us some cash.

VR: The P is a worm, right?

DG: The P is an Ascaris, and I have to say, oh my gosh, Dickson and I went back and forth, I don't know how many hours went into making sure this was appropriately Ascaris-shaped, the pointy end.

VR: The end has to be pointy, right?

DG: You remember some discoveries.

VR: I do.

DG: Oh my gosh.

VR: By the way, today is Dickson's birth anniversary, June 5th. I don't know how old he would have been, but we do miss Dickson.

DG: Yes, today would have been his birthday if he was still with us. That came up as one of

my calendar things. Yes, miss Dickson. All right, let's jump in. I've got this quotation to start with, "Pardon my sanity in a world insane." Seemed very appropriate. With that in mind, I'm going to start with attack on science, a striking headline, and this has been covered on the last Friday deep dive, but for our clinical update listeners, “White House Health Report Included Fake Citations.” The Trump administration released a report last week that it billed as a clear, evidence-based foundation for action on a range of children's health issues.

But, as we read, they cited studies that didn't even exist. You get these fictitious studies. There's 522 references, and now they've got this - well, they say it's a corrected report, but how many of the issues have they actually fixed? It appeared that when you went through this original report that they basically said, "This is what we want to be true," and then they made up a number of citations. At least seven of the studies were never even published. They made stuff up. They made up fake articles to support what they decided they wanted to be true.

What's really odd is someone actually asked like, "Well, who wrote this report?" No one signed their name, so we don't even know the author or the authors. Can you imagine that? They even asked. They asked Karoline Leavitt like, "Hey, who wrote this? Was it written by AI?" She said, "I can't speak to that." We've got this report.

VR: AI often makes up references. I wouldn't be surprised if it were AI-generated.

DG: That's interesting, right? Not only does AI make up references, but we saw through the period of COVID, like for instance, the ivermectin crowd, people who would tell me that sometimes, "Daniel, you just know things are true." How? You're clairvoyant? You have to do a study. You have to look. You have to go see.

What they would do is they would actually go beyond this. They would make up studies and they would say, "Oh, yes. We did this study in Brazil. We had 1,000 got ivermectin and 1,100 didn't." I'm like, "But you didn't actually do this study." "Yes, but we made believe we did and we published an article." You go to the hospital in Brazil and you're like, "So they say they did this study?" They're like, "No. It didn't happen." At least MAHA didn't go and make believe they made studies. We'll see what happens next.

VR: It's really embarrassing, frankly. Read your last part because that's really the key.

DG: Yes. I think this is a glaring example of finding confirmation bias. Now investigation should precede ideology. The first draft of this paper would end up with an investigation of ethics if handed in for a high school assignment, much less the highest health agency in the United States. Just imagine this like if your son, your daughter, it's going to be your son, right? Just get my bias there. Handed something in and they say, "I don't seem to be able to find this article." "Oh, I just made it up."

VR: This is what the worst scientists do, right? The very worst who never discover anything and never get anywhere. This is what they do and they're just trying to get away with lies and misinformation as usual.

DG: Yes.

VR: Everything they release is just horrible.

DG: This is just striking and it was interesting because, "Oh, there was some formatting errors." This is not a formatting error. When you make up citations that don't exist, you put in authors, you put in titles, journals, just sort of mix-mash.

VR: When Leavitt says, "I can't speak to that," does that mean it was generated by AI and she can't admit it?

DG: It was, "I can neither confirm nor deny," right? It was like people are curious like who wrote this thing and like, "Yes, I'm not going to tell you."

VR: Apparently, many of the presidential - what are they called? I forgot the word. The things that he writes to do things, the presidential proclamations. It's not the right word. Apparently, they're written by AI also.

DG: I guess executive order.

VR: Executive orders. Thank you.

DG: Yes. There's several articles out there trying to make sense of all this, right, because we're getting this MAHA report and now we're getting all this stuff on what's going on with the CDC guidelines and we talked about this last week. Suddenly, we had this tweet, the social media tweet, where RFK, Jr. is basically saying, "We're no longer going to recommend vaccines in certain groups."

Several articles came out trying to make sense of this, and one of the headlines which caught my eye, which I will leave a link into, was, "CDC Contradicts Kennedy and Keeps Advice that Children May Get COVID Shots." We heard about this. We discussed this. Now, days after Health Secretary Robert F. Kennedy Jr. announced that COVID shots would be removed from the federal immunization schedule for children, the Centers for Disease Control and Prevention issued updated advice that largely countered Mr. Kennedy's new policy.

We're going to hit on this a couple times today, but the agency kept COVID shots on schedule for healthy children 6 months to 17 years old, but they did add a new condition. They said children and their caregivers will be able to get the vaccines in consultation with a doctor or provider, which the agency calls shared decision-making. The shots will also remain available under these terms to about 38 million low-income children who rely on the Vaccines for Children program, according to an email update from the CDC on Friday.

VR: Daniel, this shared decision-making, is that really any different from what's done already?

DG: I'm hoping that they can actually - because we keep having this. We talked about this with the RSV vaccine, right, when it first came out, and this is actually what we hope is going on, that people aren't just reading the news or watching the news or listening or going through social media and then deciding what to do for their children.

The ideal is your child has a relationship, you as an adult have a relationship with a healthcare provider, so the child is in a relationship with a pediatrician, go and see the pediatrician, and you ask. You say, "Hey, I hear about this new shot, and what do you

recommend and why?" That's what it's supposed to be. It's not supposed to be this paternal, and it isn't. This isn't necessarily the doctor saying you have to do this. This is the pediatricians out there educating parents about the pros and the cons and as we keep talking about, the incredible benefits of vaccination.

What I think is hopefully going to happen, hopefully, I'm going to sort of nudge, nudge for this, is that these conversations used to be pretty quick. It used to be, "Hey, here you are. This is what we recommend. The nurse will be in a moment to give you those vaccines." We're now seeing these conversations are expanding.

Parents have a lot more questions. Pediatricians are spending more time in the room discussing this. We probably just need to update it so that there's an incentive so that the pediatricians start making more time in their schedule for having these discussions, because this is going to add time. There's going to be effort. Pediatricians are going to have to, I think, know a little more and understand a little bit more about how to have these conversations in a constructive manner, because as we're seeing, the other side of the aisle is spending millions misinforming people so that they come in with a lot of misinformation.

All right, so what do I have here next from Reuters? The recent behavior by people at our public health agencies triggered the resignation of pediatric infectious disease expert, Dr. Lakshmi Panagiotakopoulos. How do you pronounce that, Vincent?

VR: Panagiotakopoulos.

DG: OK. I think that's Greek, right?

VR: It is. The last name is Greek. Lakshmi is not.

DG: Yes.

VR: I think it's Pakistani, but not Greek.

DG: Yes, so I think we have a sort of mixed background on the names. We get an email from this infectious disease expert to the work group colleagues saying that her decision to step down was based on the belief that she is no longer able to help the most vulnerable members of the U.S. population.

Now, she was involved with the Advisory Committee on Immunization Practices. I'm sort of putting the name together, thinking this Pakistani woman may have married a Greek guy, right? I think that might be what happened here. The ACIP meeting is still scheduled to meet on June 25 through June 27. I'm really curious. We'll follow and see what comes out of that meeting. The final chapter is yet to be written here.

While we're talking about this in this front part, I wanted to point out that the mess we are in did not spring into being this past January. As we read in the article, “Trends in County-level MMR Vaccination Coverage in Children in the United States,” published in *JAMA*, there has been a U.S. national-level decline in the childhood measles, mumps, rubella vaccination, the MMR vaccination rate. We really see this between 2019 and 2024. You can see it's going along and yearly number of reported measles cases.

Then we've got on the right side, we've got an MMR rate sort of seeing these percentages. The MMR rate, for those of us that are maybe watching on YouTube and seeing this, we can see the U.S. mean MMR rate, the U.S. median MMR rate, and we're seeing we're doing pretty well, right? We're above 94% all the way up until 2020. Then we see this, I'm going to say precipitous decline. It probably has to do with the scale of this. You see it really dropping down below that critical level.

At the same time, you're starting to see these yearly reported measles cases. 2019, we see a bunch, got a little bit of an uptick in the MMR. Then we see a few cases. Then 2025, it's been a banner year so far, over 1,000 cases. We're really with this trend of dropping MMR coverage. It even gets worse when you look at county-level MMR vaccination, and you can see, over this period of time, so pre-pandemic MMR vaccination rates, look at Texas, right?

Texas was like solid dark blue, greater than 95%. Things were looking pretty decent down in Florida and Alabama and Tennessee, great job there. Then you go post-pandemic and you can see really huge drops throughout Texas. We're sort of seeing what happened with that. Huge drops, Florida, Alabama not looking quite as good anymore. Then they break it down.

This is my favorite one, Vincent, because I'm recording over here in New York. You're at New York at the moment, so you can take some. Who's doing the best? County-level pre-pandemic and post-pandemic MMR vaccination rates. Who's the best? What's the best state in the whole country?

VR: New York.

DG: New York, right? We got to move quite a way down before we see Jersey. It's in the middle there. Oh my gosh, we get out to Colorado and Arizona, and yes, not so great.

VR: Hawaii and Wisconsin, they're terrible.

DG: Yes, Wisconsin is really terrible.

VR: Wow.

DG: Yes, so not looking good. We'll circle back to measles again. I did want to mention bird flu. Apparently, we do not have to worry about bird flu because the U.S. has cancelled its contract with Moderna to develop the bird flu vaccine. The Trump administration cancelled a nearly $600 million contract with Moderna to develop a shot for human bird flu.

The decision also forfeited the U.S. government's right to purchase doses ahead of a pandemic and cancelled an agreement set up in January to prepare the nation for potential bird flu pandemic. This was built on a prior investment of $175 million last year. Andrew Nixon, HHS service spokesman, we hear a bunch from Andrew: “After rigorous review, we concluded that continued investment in Moderna's H5N1 mRNA vaccine was not scientifically or ethically justifiable.”

VR: What is this ethically stuff? What the heck is that about? Nixon's an idiot. He doesn't know what he's talking about. Now, maybe it didn't work so well. That's one thing. I don't know the data. Ethically, there's nothing wrong with mRNA vaccines, is there, Daniel?

DG: There isn't. It's a target, as we're going to see. It's interesting. It's a target of certain groups in our country. Instead, though, our plan is to import infected birds into the country. The story, "Canada Wants to Kill 400 ostriches. Kennedy and Dr. Oz Want to Save Them." There's this outbreak, right, of avian flu in the ostriches up in Canada. Canada's outbreak of the H5N1 has been most prevalent in British Columbia, where the avian virus has killed 8.7 million birds since 2020. That's more than half of the national total, right? Half of the birds, they're gone.

Now, in December, a young ostrich at Universal Ostrich Farms fell ill with symptoms that looked like pneumonia. Testing revealed it was the H5N1 virus. Just over a month later, 69 of the 468 ostriches on the farm had died. Now, Dr. Oz, who oversees Medicare and Medicaid for the Trump administration, offered to relocate the infected birds to his 900-acre ranch in Florida and said, “the Canadians should stop putting their heads in the sand.” I like that. He suggested that the ostrich farm presented an opportunity for researchers to study herd immunity of the birds by keeping them alive.

VR: Right. Dr. Oz is a surgeon, right, Daniel?

DG: So I hear.

VR: Not an infectious disease specialist, right?

DG: Not a vaccine expert, no specific training in immunology. No.

VR: Sure. I'm sure Florida is very thrilled to have these ostriches in their state. It's ridiculous.

DG: Yes, I don't think it's going to happen. I don't think the Canadians are going to.

VR: He doesn't even know what herd immunity is, I'm sure.

DG: He's read about it on his smartphone. All right. The U.S. Department of Agriculture, USDA, Animal and Plant Health Inspection Services confirmed a third H5N1 avian flu outbreak at a large layer farm in Arizona affecting nearly 1.4 million birds. Now, since the middle of May, the virus has hit three of the state's large layer farms. I was thinking of like layers, but I think they're like layers, like layers of eggs. All in Maricopa County, leading to a loss of more than 5 million birds. The outbreak wiped out about 95% of the birds at Hickman Family Farms facilities and has shuttered all of the company's West Valley farms.

Now, this is just a little background here. Hickman's vaccinates chickens already. We are already vaccinating chickens for other disease that we're vaccinating for. You ready for this? Chickenpox. I thought that was cute. Adding another vaccination wouldn't actually change procedures, according to Hickman. Animal rights organization Animal Outbreak said the most commonly used method of depopulation of chickens is called ventilation shutdown plus, right? You find out your birds are infected, you're going to go ahead and you say, "OK, we got to depopulate, basically kill all the chickens." How do they do it?

This ventilation shutdown plus involves sealing a barn's ventilation. Just think here we are, right? We're down in the Southwest, right? Maricopa County. You're down here in the Southwest, you seal the barn's ventilation and you turn on the heat and then basically you cook these birds to death. This takes a few hours. Now, there's actually a humane

alternative. You could actually just put in carbon dioxide instead of the ventilation shutdown. It's faster. It's more humane. The chickens become unconscious very quickly, but it's more expensive.

Now, the USDA has a Livestock Indemnity Program that compensates farmers for livestock deaths in excess of normal mortality. According to the department, for an egg-laying hen, you're going to kill all these hens, and people can do the math on this. The payment rate is $12.17 per bird. If all six million birds qualify for that compensation, a payout of $73 million to Hickman's.

VR: This method, this ventilation shutdown plus is horrible. It's inhumane. It shouldn't be allowed.

DG: It's hard. Considering that we, the taxpayers, are going to dole out $73 million in compensation, let's spend a little bit of that on carbon dioxide. If we're going to do this, let's do it humanely. I think one of the things I want to point out too is this whole concept of studying herd immunity. These chickens, these ostriches, these are relatively inbred animals. 100%, they all die, and they all die a horrible, painful death.

This whole watching herd immunity, they don't understand genetics. They need to listen to *TWiEVO* or something. If they listen to *TWiEVO,* you're going to get in trouble, Vincent. They're going to deport you because you're getting a little political over there. You and Nels Elde send you back to what? Italy? Italy. Is that where you're from?

VR: I was born in the U.S.. Listen, Daniel, *MicrobeTV i*s getting attacks and the site keeps getting brought down periodically. Someone is trying to shut us down.

DG: Oh my gosh.

VR: The denial of service attacks.

DG: Yes. I wonder where that could be coming from. All right. Measles. United States. Total cases in the U.S. We are up to a total of 1,088 confirmed measles cases reported by 33 jurisdictions, right? That's up another 42 from the week before. We've added a couple jurisdictions from the week before. I'm going to start keeping track of that. Now there is going to be a wastewater way of monitoring measles, which I think is great. There's going to be data on wastewaterscan.org.

I have to say, at this point, I was playing around with a little, it's a little cumbersome. I'm hoping it gets refined, but I'll leave in a link, and that'll get refined, but also we have, I don't know how many people are following this story, but Colorado, the Colorado Department of Public Health and Environment and the Denver Department of Public Health and Environment have confirmed a Denver County resident tested positive for measles. The vaccinated adult was a passenger on Turkish Airlines flight 202 arrived at DIA, Denver International Airport, Tuesday, May 13. The individual is recovering at home.

Now, this latest case patient is a vaccinated adult Denver resident who's on this flight. Now, to date, seven Colorado cases are associated with this out-of-state traveler who flew while infectious. Apparently, an out-of-state traveler acquired this overseas, confirmed case of measles, traveled through Denver International Airport, stayed at the Quality Inn and Suites

Denver International Airport while infectious. The individual arrived at the international terminal on a Tuesday, May 13, then went to a hotel for the evening. On Wednesday, May 14, the individual returned and boarded a domestic flight.

I think what we've got here, and I think this is something important to point out is, when you have an infectious disease, it's not just your problem. Now we've got all these other people, infected, having issues as well. This is why we care about vaccination, not just for vulnerable people, but for all the people, because your freedom to not vaccinate ends at basically the tip of your neighbor's nose. Any comments there, Vincent?

VR: Yes. This is what happens when you're not vaccinated, because people are always bringing in measles into the country, and this is precisely the way it happens.

DG: Canada, not so great up there. We're up to 2,755. Another 244 new cases. Moving there. I'm going to leave in links, as I do, to information about vaccine safety, things about measles, mumps, rubella, the facts and myths about measles and the vaccines. Just hot off the press, I just added this to our show notes, the, "Government Accountability Organization to HHS: Fix Persistent Deficiencies in Infectious Disease Testing Before Next Pandemic." What? We're going to have another pandemic? "National Testing Strategy Needed."

The panel formulated four recommendations for HHS Secretary RFK, Jr. I'm going to run through these. One, develop a national testing strategy that sets clear roles and responsibilities, improves collaboration, and features a coordinating group. That was an issue last time, right? I think we all remember just the delays in getting tests out there, and that was needless. That need not happen again. That really need not have happened in the past. That could have really had a major impact.

Two, periodically update the national diagnostic testing strategy to incorporate lessons learned from infectious disease threats with pandemic potential. Number three, either establish a national diagnostic testing forum for infectious disease with pandemic potential or expand an existing group. Number four, ensure that the national testing forum meets regularly. That makes a lot of sense. Then they give specific actions, encourage diagnostic test research and development. Oh my gosh, that's going to require funding. Expand the number of organizations able to perform diagnostic testing, broaden communication of testing guidance, and increase standardization of diagnostic test data collection.

OK. All right. Just running through our big respiratory pathogens. We're, for the moment, outside the flu season. Levels are low. RSV also, things are nice and low, staying low across the country. Now, COVID, I'm a little worried here, Vincent. I want to point out that the data here is always a little old. You look at the wastewater, it's looking really pretty good, right? I did walk into an ER this morning with a bunch of COVID patients. I'm a little worried that this nice downward trend may be about to take -

VR: Are we going to have our summer spike again, Daniel?

DG: Yes, I think we're going to have our summer spike. This is difficult. I did sort of vent a little bit here. A lot of people realize that the COVID vaccines give us about six months of protection. This whole treating COVID like the flu and the idea that you get a booster in the

fall for the winter season, and we basically saw this last year, the summer season was worse than the fall.

A lot of people would like to go get a shot now so that they've got that boost going into summer. Maybe they're healthcare workers, maybe they're traveling, maybe last time they had COVID, it was really severe. Maybe they have certain medical comorbidities, maybe they have Long COVID. It's a challenge now because of all this communication and tweeting and I'll say miscommunication about access.

I had a patient the other day go to get their COVID vaccine, and they were refused at the pharmacy. The pharmacy said, "I'm sorry, you don't check the box. Are you severely immunocompromised? Otherwise, no, you can't get a vaccine." They had to go to another pharmacy where they finally realized like, "Oh, my doctor recommended it, I'm traveling." They were able to get access to the vaccine. Really crazy, right? That a person has an immunization recommended by a doctor and the pharmacy won't give them the medication.

VR: They have a prescription, I presume, right?

DG: It's a vaccine, right? You should be able to go and get your vaccine if it's recommended. Isn't that what they talked about, shared decision-making? You went to the doctor and you said, "Hey, this summer surge is coming up. I'm going to be traveling. I'm going to be working around children. I got really sick last time," whatever the reason might be that shared decision. No, now, RFK, Jr., he's going to - even though you're not supposed to listen to him for medical advice, he's going to prevent you from taking the medical advice of your provider.

All right. Moving on to COVID active vaccination, oh my gosh, we never really left this subject. This had a lot of folks upset and some people not upset. On Friday, May 30, 2025, the FDA approved a new mRNA COVID vaccine, a brand new COVID vaccine from Moderna. It is brand new. Let me read the letter from the FDA to Moderna. “We have approved your BLA,” biological license application,” for COVID-19 vaccine, mRNA, mNEXSPIKE, effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce COVID-19 vaccine mRNA mNEXSPIKE under your existing Department of Health and Human Services, U.S. License No. 2256.

COVID-19 vaccine mRNA mNEXSPIKE is indicated for active immunization to prevent COVID-19 caused by severe SARS-CoV-2. mNEXSPIKE is approved for use in individuals who have been previously vaccinated with any COVID-19 vaccine and are 65 years of age or older or 12 through 65 years of age with at least one, and they say, risk factor. Interesting. What do you think about it? In line with the approval that we saw for Novavax.

VR: This is what, a variant-specific vaccine? It's a booster basically?

DG: Let's go to the Moderna webpage, get a little more, because I was curious, what is mNEXSPIKE? Is this better? Should I get this? Should I just get Spikevax? There was a randomized observer-blind active-controlled phase III clinical trial, I'll leave in the clinical trials identifier there, where they enrolled approximately 11,400 participants aged 12 years and older, that's where we get the age here.

The primary efficacy objective of this study was to demonstrate the non-inferior vaccine efficacy against COVID-19 starting 14 days after mNEXSPIKE compared to Spikevax, Moderna's original. Participants received either a 10-microgram dose of the new vaccine, or 50 micrograms of the old vaccine, so less mRNA here. Now the mRNA 1283, that's the mSpikevax, the lower mRNA, showed a 9.3% higher relative vaccine efficacy compared to mRNA 1273 in individuals aged 12 and older. In a descriptive subgroup analysis, 13.5% higher in adults aged 65 and older.

VR: These are the same recommendations as we heard recently, 65 and up or 12 through 64 if you have a risk factor.

DG: Yes. It's sort of interesting, it seems like that's where we're moving in this space.

VR: I got the impression that they were not going to approve any booster, any variant vaccines without a clinical trial, but here, apparently, 11,400 participants, this is a substantial clinical trial.

DG: Where's that saline placebo-controlled? Yes, I don't know what's going on there. All right. Yes, you had a bunch of folks quite upset.

VR: Daniel, you can't do a placebo here, you have to use the other vaccine. You can't withhold, as you know, standard of care. The comparator was mRNA 1273.

DG: What they'll argue, and I think this is real, and say, OK, so last year maybe 20% of people or 15% of people got boosted. You got all these people who are not getting boosted. What if you offer them, you say, "You know what, would you be in our control group? Would you be in our saline group? We'll pay you some money, you're not planning on getting vaccinated anyway." I guess the problem you run into is it's not really blinded, like you sort of know.

VR: That's right.

DG: Want to get the vaccine. Is their behavior different? Are they different? I guess it comes down to they're demanding placebo-controlled trials, but are they - how blinded does it need to be? Exactly. Now what's going on, actually, as we talked about the CDC and what RFK, Jr. said? I'm going to leave in a bunch of links here.

If you go to the CDC COVID-19 vaccine recommendations, you see this box. It's a little ominous. COVID-19 vaccine recommendations. It's got a little triangle with an exclamation. “COVID-19 vaccine recommendations have recently been updated for some populations. This page will be updated to align with the updated immunization schedule. Learn more.”

Then if we go ahead and we actually follow these, and, Vincent, I'm going to open these so you and I can go through these together. We're going to look at these-- what are the current vaccine recommendations, right? I do want people to - particularly you pharmacists that are refusing to give people a vaccine. We go to the page, COVID-19 vaccine, routine vaccination. You can click and open it. It says age 18 and older who are not moderately or severely immunocompromised and previously vaccinated. They are recommending yearly shots for most folks, and they're actually recommending that you go ahead, and if you're 65 or immunocompromised, you get two shots a year.

Now, if you look at the CDC page for the minimum age 6 months to 12, up to 18 routine vaccinations recommended, they do actually add to this section, this whole shared decision-making, which is great, which is actually what I think we should be encouraging, right? I think it's great for the CDC to make recommendations and provide guidance, but ultimately, you do want to have a conversation so you as a parent, you as an individual feel comfortable. You're part of this shared decision-making.

Shared clinical decision-making vaccinations are individually based and informed by a decision process between the healthcare provider and the patient or parent guardian where the parent presents with a desire for their child to be vaccinated. Children 6 months and older may receive COVID-19 vaccination informed by the clinical judgment of a healthcare provider and personal preferences and circumstances.

Then, there's the adult section where, as I mentioned, one dose of the boosters and 65 and above, two doses per year. As I've talked about, there may be certain circumstances where we say, "This isn't really quite influenza." There are these two seasons. We want to be thinking about how that impacts it. If you and your doctor have this shared decision, interesting.

VR: This does not jive with the RFK recommendations, right?

DG: It's really the RFK tweet, right? It's a tweet. It was not very clear what exactly he was saying. You go to the actual site. This is what it's saying. He says, "Oh, this is exactly what I was saying." I don't know. You're not a great communicator in that, RFK, Jr.

VR: 18 and up, you can get vaccinated even if you don't have a comorbidity. What RFK, Jr. said, below 65, you need a comorbidity. That's not what the CDC website says.

DG: Yes. I'm going to say he's not a clear communicator because a lot of people took away a very different message. Obviously, this person who tried to get vaccinated, that pharmacist took away a very different message from the tweet. We're seeing very clearly the current CDC. You go to the webpage. This is what they're saying.

VR: They don't have 12 years. They have 18 years and older routine vaccination. They don't have the 12 years, although they do say 12 years for the Novavax is the minimum age. In the routine vaccination, they don't have below 18 years of age. I don't understand where those come in.

DG: Let's go, child immunization notes. You can go to this table by age, and then they take you to a section where you click on notes. We'll go to the section where they do, yes, interesting, shared, clinical shared. Shared clinical decision-making, if people follow the link and want to follow this along, ages 6 months to 17 who are not moderately severely immunocompromised. They break this down 6 months to 4. If you're unvaccinated, you're going to get either two doses of Moderna or the three doses of the Pfizer, right, incomplete initial vaccine. Then they're going to recommend one dose of Moderna, one dose of the Pfizer. Completed your initial vaccination.

Then you're going to go ahead, and you're just going to get these one doses aged 5 to 11, unvaccinated or previously vaccinated. You're going to get one dose of either the Pfizer or the Moderna, age 12 to 17. If you're unvaccinated, you're going to get one dose of Moderna

or Pfizer, or you're going to get the Novavax two doses, zero, and then three to eight weeks. If you're previously vaccinated, this is right off the CDC page, one or more doses of Pfizer or Moderna, one dose of Novavax or two or more doses of Novavax.

VR: OK. Basically, you have to look under shared decision-making to see the whole story.

DG: Yes, you really do.

VR: OK.

DG: Yes, it makes it more challenging to navigate, but, yes, not really actually seeing that much has changed here in the recommendations.

VR: Yes, apparently not. OK.

DG: All right. I don't know what's going on. Anyway, OK, Pemgarda, remember, passive vaccination. We have a little bit of updated science here. We've got a new article, "Safety and Efficacy of Pemivibart, a Long-acting Monoclonal Antibody for Prevention of Symptomatic COVID-19: Interim Results from a Phase 3 Randomized Clinical Trial (CANOPY)," published in *CID.*

It's a little difficult to sort of navigate this, but I'm going to walk us through it. This is interim analysis of safety and efficacy of Pemivibart in individuals with significant immunocompromise. That's going to be cohort A. Then we're going to get cohort B. These are people without significant immune compromise.

We're going to end up with these different groups. We're going to end up with this group A, and these are participants with significant immunocompromise, and they're going to get Pemivibart. Then you're not going to have, basically, a significant immunocompromised group that doesn't get it. Your control group is actually going to be people without significant immune compromise who did not get the Pemivibart. That's where your placebo is going to be, right?

This sort of the whole idea is that we're anticipating more cases, more deaths, worse outcomes in immunocompromised people than people who are not immunocompromised. You don't really need an immunocompromised placebo. You're going to use your immunocompetent. They'll be your placebo. If you can do better than them with Pemivibart, we're going to consider that a win. We're also going to have the group of people who are normal, not immunocompromised, who are going to get Pemivibart.

We're going to get the three groups: 306 folks with significant immunocompromised are going to get Pemivibart. Then we're going to have 317 people without significant immunocompromise, they're going to get Pemivibart. Then we're going to have sort of a placebo group for both,162 patients without significant immunocompromise, they're going to get placebo. You're going to see some drug-related adverse events related to the infusion, right? There'll be some infusion reactions.

About half a percent actually had anaphylactic reactions, right? One in 200. You're monitoring this, and if they have an anaphylactic reaction, you're going to stop, you're going to treat them. This is done in a medical center, it's not something you just pick up, do

yourself. In cohort A, participants with significant immunocompromise that received Pemivibart, the composite COVID-19 incidents through month six, we're going to get out to month 12 eventually, but through month six, 3.7%. We're going to compare that to the immunocompetent who got placebo, they were at 11.9%. That's a really nice reduction.

Now, then you can look at the without significant immunocompromise, those that got the Pemivibart, and we can compare those to the ones that are in the control placebo group. Basically, across the board, we're seeing this 84% standardized relative risk reduction. Really, really effective. This is real world, this isn't just, do I get certain levels? Pemivibart was originally approved in immunocompromised folks based upon immunobridging data.

Here, we're actually seeing in the people without significant immunocompromise, we're seeing people that got Pemivibart, only 1.9% got infected where the placebo. 11.9. That's tenfold reduction. Maybe this is not just for immunocompromised. Maybe people that don't want to get a vaccine want to look at a passive monoclonal treatment. We saw a lot of that in the early days. People didn't want to get vaccinated, they didn't want to get remdesivir or whatever, but they did want to get monoclonal antibodies. Good to have options.

All right, COVID early viral phase, no big changes there. COVID early inflammatory phase, and we sort of saw a mix of both patients today in the ER. Folks coming in already hypoxic, folks coming in, in that first week, just not doing well at home. What about late phase? I have to say, this is a pretty exciting study that's going to close this out today. This is an article, “Genome-wide Association Study of Long COVID,” published in *Nature Genetics*.

Here, these researchers performed a genome-wide association study for Long COVID, including up to 6,450Llong COVID cases and 1,093,995 population controls from 24 studies across 16 countries. Now, they discovered association of FOXP4 with Long COVID. This is independent of this associated with severe COVID-19. This is just FOXP4 associated with Long COVID. The signal was replicated in 9,500 Long COVID cases and 798,835 population controls.

Let's go through this a little bit. They have a nice Figure 1, where you get this geographical overview of studies contributing to the Long COVID genome-wide study. You can see there's a number of sites in the U.S., Europe. You've got a site there in the Middle East. You've got a couple of sites there, it looks like over in Japan. Then, I love these Manhattan plots. I spent a little time in a genome-wide association study research lab. You do all these Bonferroni corrections for the different statistical analysis and really shoots out here on chromosome 6. We've got something going on.

This is where we're seeing the connection with FOXP4. To understand whether higher FOXP4 expression was seen in Long COVID, they move on from this GWAS study. They collect blood from participants with or without active SARS-CoV-2 infection. They actually find that higher FOXP4 levels in non-acute COVID-19 samples was associated with this increased risk or increased association of Long COVID, odds ratio 2.3, but acute COVID didn't really sort this out. If anything, it was the other, right? We had a p-value of 0.62. Not really seeing much acute. It's more after the fact. I'd love to see pre the fact.

A little bit about FOXP4 because maybe our listeners are, "What is FOXP4?" It belongs to the subfamily P of the forkhead box transcription factor family genes expressed in various

tissues, including the lungs and the gut. Just background, FOXP4 has been implicated in airway fibrosis, the promotion of lung cancer growth and invasion. FOXP4 expression of both alveolar and immune cells in the lung and the associated severe COVID-19 and pulmonary disease such as cancer really sort of lends credence, lends weight to the idea that FOXP4 may participate in local immune responses in the lung.

VR: Of course, FOXP4 has normal functions as well. You can't just antagonize it to take care of this disease, right?

DG: Yes, it looks like there's certain variants that they saw. It may be certain variants, it may be certain levels of expression and activity that are playing a role here. Yes, there may be some way to, I think, modulate, right? You don't want to knock this out because this is really sort of a critical transcription factor.

VR: The GWAS points out polymorphisms, do you know if they're coding or non-coding?

DG: I believe they're all coding. Yes, these are coding, yes. It has to do with sort of different FOXP4 activity.

VR: Interesting, very interesting.

DG: Yes, it's actually, I would say, I had to spend a lot of time because it's a very - there's a lot here when you start looking at a *Nature Genetics* article. All right, I'll leave a link into if you're worried about science and us continuing to fund great work like this, which is really going to be interesting going forward. I've got a link in to reach out to your representatives.

As we've been saying for five plus years, no one is safe until everyone is safe. We don't make America great again by only worrying about what occurs within our borders. We do have to worry about that, by the way. We have to worry about the entire world. We're one global community. For us to do the work we do, for us to continue to communicate, for us somehow to fight off what are these denial of service attacks we're now getting and all the other threats, please go to parasiteswithoutborders.com, click on the Donate button. Even a small amount helps.

May, June, and July, we're in June now getting into our second month of our Foundation International Medical Relief of Children fundraiser. We're doubling your donations, trying to get up to that maximum donation of $20,000. I think I mentioned last time, I got some exciting stuff going on in Uganda. We're trying to get the places back open and functioning in Peru and other places. We need your support. Thank you.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Lisa writes, "Thanks as always for your light in this darkness. Two things. Since the start of the COVID pandemic, I've started summing up crackpot health theories advice this way. Pseudo-science, it's perfect for the pseudo-smart." Very good.

DG: It's catchy.

VR: "What is it going to take for people to realize what a gift immunizations are? Reopening or rebuilding schools for the deaf and schools for the blind that were in every major city and most states and were shut down because of the admirable success of our nation's

vaccination program. Life was very different for children before IZs and it is nonsensical that people who proclaim that life is so precious show disregard for children's lives and the quality of children's lives. I'm just venting to sympathetic ears. Lisa."

DG: Yes, Lisa, vent away. The crazy thing is this anti-science, anti-vaccine movement. It's not new. It was going on back when there were all these horrible tragedies right in front of you. I remember reading something about like you go back to just soap and water and they're like, "Oh my gosh, more people have died catching a cold from a bath or a shower than -" It's just like even hygiene, even washing hands was something that people fought against.

VR: Shikha writes, "Thanks for all your excellent reporting and scientific discussions the last few years. As an immunologist living in New York, you've really gotten me through tough times. I've been experiencing post-viral pericarditis the last few months since January, and I'm given high levels, high IgG levels of Coxsackie B strains. Doctors have determined this is the likely cause.

While symptoms have been gradually decreasing over the past few months, whenever I'm exposed to a new virus, doesn't matter what, they trigger again. Chest pain, eye twitching, swollen lymph nodes, extreme tiredness. I only had COVID for the first time in December '23, early '24, and feel that some part of how I respond to new viruses has changed. What do you think about this? I know Coxsackie is quite rare in adults, but I was traveling to India at the end of last year. Have you seen this before in modulated immunity based on COVID infection?"

DG: Yes, I think two comments. Yes, unfortunately I've actually seen cases where people develop a post-viral pericarditis from Coxsackie B. This is usually the way we make the diagnosis. It leaves me a little unsettled, right? We do the serology, it comes back greater than 600 across all the different serotypes. That never made as much sense to me as I would have liked if we saw one. I would love if there was some sort of molecular confirmation.

What exactly is going on here? Is there some nonspecific activation? The teaching is that, yes, this is Coxsackie and you developed a Coxsackie B post-viral pericarditis. Then the other thing you bring up, which is interesting, is the impact of COVID on inflammation. We certainly see people, they've had COVID before when they have ongoing elevated CRP and other markers of inflammation and then other clinically less easy to measure. Yes, there does seem to be a well-established post-COVID impact on the immune system.

VR: Lisa writes, "A few weeks ago, a coworker who had brought her son to work because he had a doctor appointment for respiratory issues told me he had a COVID infection when he was 1 and that his lung development fell behind at the time. He's been catching up, but it's been a long process. Has COVID infection in the very young been found to slow lung development, or is it more likely to be coincidence that her son had infection and had lung development slow at the same time?"

DG: Yes, so we certainly see people get COVID and then they have ongoing pulmonary issues afterward. We see that in all ages. I'm not sure so much lung development, maybe it's fibrosis, inflammation, ongoing impacts on the lungs. Certainly well-described that a lot of people, they get COVID. It's not just one or two weeks. There can be ongoing issues that go on for months and months, in some cases, more than a year.

VR: "PS, regarding your comment, wondering what would happen when younger people try to get vaccinations at pharmacies if the guidelines about at what age a vaccine is recommended change," which we don't know if it has yet. It doesn't seem to be. "From my recent experience, I would expect the pharmacy website wouldn't let people under the new recommended age schedule an appointment online for a vaccine.

Since the pharmacy chain recently pointed out to me that pneumonia vaccine was now recommended for people over 50, I tried to schedule, but their website wouldn't let me. It must not have been updated. I scheduled it online with their main competitor instead and got vaccinated over the weekend. That seemed easier and more efficient than testing whether the first pharmacy chain would have vaccinated me if I showed up without an appointment."

DG: Yes, that's a challenge. A lot of this is people putting programming in, click this box, click that box. I think a big thing, and maybe we have some folks involved with the big pharmacy chains listening, but ideal would be you put in your age and then you get a list. Do you have any of these features? Click the box.

I think for most people, they're not going to know what counts as a risk factor. According to Vinay Prasad, a third of all folks under the age of 65 are going to have a box that they could check. That was what he was sort of touting, but you got to go make it easy to click the box. Otherwise, we're going to have people who are eligible, who should be able to go ahead, who are somehow not going to be able to.

VR: Rita writes, "Our son Daniel will be at large meetings in Boston in June. These will be unmasked events. He would like to come see us over the weekend. He's up to date with vaccines. We would love to see him. His family is now in Florida, have not seen them for two years. We are in our 80s, had chemo in 2023. We are up to date on vaccines and Novavax, flu, RSV and pneumonia vaccines. We're trying to figure out the best approach so he can visit us. Testing, when, what kind? He will be staying with us. Masking all the time with meals and all would be difficult. Any chance of advice would be appreciated."

DG: Yes, so a number of features that really stand out here. We are in our 80s, right? We talk about, forget about risk factors. Age is the biggest one. Then we get this mention of chemotherapy. Maybe there are some other health issues going on as well. Yes, count yourselves as higher risk or high risk individuals for bad outcomes. Yes, watching for symptoms, testing.

A lot of the stuff that we learned over time about testing first thing in the morning, because we can still see some asymptomatic spread. There's definitely ways to mitigate or reduce the risk. It's really critical. During your 80s, you want to see family. I do think that there's a way to do this and to mitigate the risk. If you get sick, then remember, early antivirals really are indicated, recommended, and evidence-based.

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

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

[music]

[00:56:03] [END OF AUDIO]