

TWiV 1360 Clinical Update

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Guest: Daniel Griffin

Aired 25 September 2026

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

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From *MicrobeTV*, this is *TWiV. This Week in Virology*, Episode 1360, recorded on September 24, 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: On this date in 2008, I released *TWiV* No. 1.

DG: Wow, 2008, so that's 18 years. Am I doing this right?

VR: 2008 to 2018 would be 10, to 2028 would be 20, so it's 18 years, yes.

DG: Wow, wow. Two years from now, we'll have to have some big 20-year celebration, 20 years of *MicrobeTV*, 20 years of *TWiV*.

VR: Yes, 20 years. I was walking down the street in Manhattan today, and a guy shouted, "Hey, Professor."

DG: That's awesome. That's funny.

VR: "Nice to see you in the real." "OK."

DG: Now, that's nice. Unfortunately, Vincent, it's starting to feel like fall, starting to feel like the summer.

VR: Summer's gone. It is cool here. I had to wear a wool coat today.

DG: Yes, and I was disappointed. I had big plans. I was going to go sailing this weekend with my parents, but we got a nor'easter blowing in. I had on schedule to fill the boat up with diesel so she'll be all ready and everything. We did do that today. Are you ready for this? \$8 a gallon. What's going on? I thought I heard that everything had become more affordable. \$8 a gallon for boat diesel. Wow. OK, well, let's jump in on that note. This is a Sylvia Plath quotation from *The Bell Jar*. I don't know if you're a big Sylvia Plath fan.

VR: I did read *The Bell Jar*, yes.

DG: It's great. "If you expect nothing from somebody, you are never disappointed."

VR: It's still true, but it's hard not to expect things from people, right?

DG: Well, our listeners could probably guess maybe there's particular individuals where I just remember this quotation. Oh, wow. OK. Let's start off with our news.

Kennedy questions vaccine safety at Children's Health Defense event. HHS Secretary Robert F. Kennedy Jr. This was September 17. This is last Thursday. While we're actually busy recording science communication, this individual was addressing a conference organized by the anti-vaccine group Children's Health Defense. Playing up the safety risks of vaccines and telling the audience they have a strong and steadfast friend in the White House.

Kennedy said that while vaccine injuries are likely rare, there's no way for us to know this because the system for reporting vaccine injuries is broken. Kennedy spoke to the group amid a nationwide measles outbreak that has reached 3- well, when they write this CIDRAP article, 3,471 confirmed cases, four measles-associated deaths reported in Pennsylvania. His only mention of the outbreak was in reference to vaccine injuries.

VR: This is not true that the vaccine injury system is broken. It actually works very well. Didn't we pick up myocarditis and blood clots during COVID vaccination?

DG: The system, actually, if you understand how it works, and that's a problem if you're a lawyer as opposed to someone trained in science and medicine, it really, it's amazing, its ability to, after the vaccines are out there, pick up these incredibly rare, one in 100,000, one in a million, these rare vaccine injuries. Vaccine-associated issues that you don't necessarily see in these trials where you may have tens of thousands of people in your trial, but you start picking up things that are much less common when you have your vaccine adverse event reporting system. This is just feeding into this anti-vaccine rhetoric.

VR: No, it's totally incorrect to say that the vaccine injury system is broken. It works. If you don't see that in what's happening, then you're just blind to it.

DG: Yes. It conflicts with the agenda here. I think, just point this out, here's an individual who was actually asked by certain individuals in the White House, one in particular, to stop with this anti-vaccine messaging because it does not play well with most of us. Most of us we want our children protected, we want our communities protected. We're going to see a little bit as we go forward about how some of this rhetoric has actually resulted in incredibly expensive and damaging results.

Next, Trump says some routine immunizations will be split into five separate shots. Vaccine experts say it won't work. This is like those \$2,000 tariff checks. What did you spend yours on, Vincent, your \$2,000 tariff check? Did you ever get that? Anyway.

VR: I did get it. I sent it to you.

DG: OK, I joke. President Donald Trump said Friday, this is last Friday, right, that his administration is planning to recommend that certain childhood immunizations be broken up into five separate shots, each with a small amount of the vaccine. These 20% doses would each be given six months apart, he said, instead of a child going in and having a tremendous amount of different vaccines pumped into a big proportion of the body. I think he is under the impression it's like a soda can amount, which is not true.

We're going to recommend that they do five doses marked, you ready for this? One, two, three, four, five. I don't know how he came up with those numbering system, but that they should be given in six-month intervals so that a small amount of the vaccine gets pumped into the body, Trump said. Such a plan would render vaccines ineffective, and wouldn't make them safer, said Dr. Paul Offit, director of the Vaccine Education Center at CHOP, Children's Hospital of Philadelphia.

Trump's idea to split up the shots is buffoonery, said Offit, a vaccine inventor. He noted that vaccines are studied extensively, so their dosing schedule is optimized for efficacy and safety. He said that reducing the amount administered and giving more shots would make it so the vaccines don't work while doing nothing to increase safety. Offit also pointed out that vaccines don't overwhelm babies' immune systems, as they expose us to much less than we encounter every day naturally.

"You make a billion new B and T cells every day to handle the onslaught of viruses and bacteria from your environment," Offit said. "Vaccines are literally a drop in the ocean of what you encounter and manage every day. The notion that vaccines in any way are overwhelming your immune system, causing chronic disease, is just fanciful." Additionally, many vaccines, including TPT, MMR, are not manufacturers' individual vaccines today. Separating vaccines would require changes in manufacturing that would be difficult to implement and confusing. Maybe we'll talk a little bit more. Vincent?

VR: This is buffoonery. What a great word. This is total buffoonery from a guy who knows no science, and there's no science behind this decision. He wants to give kids less vaccines. His big thing is they get too many, but now we're going to break it up into multiple shots. This doesn't make any sense. As Paul said, They're not going to work anymore. You need to give a certain amount of antigen. This is terrible that the president is getting involved in something he knows nothing about.

DG: It's a huge problem. One is this idea that we're going to give smaller doses. This homeopathy dose. If you don't give the proper dose, you don't get the immune response that you're hoping to elicit. You don't get the protection you're hoping to achieve. Buffoonery. Then it gets even worse. The whole idea, how is this going to happen? Somehow, some magical capitalist, independent pharmaceutical company is going to develop these individual five separate shots, going to somehow get through an FDA approval process.

Somehow, think of the number of people that would have to be enrolled in these trials to see enough mumps, to see enough rubella, to see enough measles, and all the other issues. How many years and hundreds of millions, billions of dollars you're talking about. You're going to see we're already spending billions of dollars because of the buffoonery that's been going on.

VR: No, you can't even test these. There aren't enough cases of any of these diseases to test them.

DG: Yes, that's the big thing. How could you do these trials? You would need to actually have lots and lots of cases. You could do trials as we did in the early days of COVID when you had lots of COVID.

VR: No, first of all, we shouldn't even talk about testing them because it's not indicated. The

vaccines are fine the way they are. There's nothing broken. Nothing needs to be fixed about them. This is just political maneuvering.

DG: That's what so much of this is. Yes, they're safe. They're effective. All right. Another. I feel like this is just like the calamity. It hasn't even been two years. "Multistate Hepatitis A Outbreak Potentially Linked to Frozen Clams." You can't even eat without worrying that you're going to get sick. You can't even eat your clams.

As of September 17, 2026, 37 illnesses have been identified as being associated with the outbreak from four states. Illness onset dates range from July 30, 2025 to June 23, 2026. Among identified case patients, aged range from 6 to 40 years old. About half of them are male. Of 37 people with information available, 81% ended up in the hospital from eating those frozen clams.

All right. Typhus in Los Angeles. What is going on? I feel like I'm making this stuff up, but it's true. The Los Angeles County Department of Public Health is investigating a localized outbreak of flea-borne typhus in the Wilshire Center neighborhood of the city of Los Angeles as cases continue to rise across the county. What is this? Are we in the trenches of World War II? Seven symptomatic cases linked to this outbreak have been identified. Six of the seven people were hospitalized. This is the second outbreak for flea-borne typhus reported by Public Health this year. Flea-borne typhus can affect anyone. People are often exposed around their homes by infected fleas carried by pets or wildlife.

In LA County, infected fleas are commonly found on rats, free-roaming cats, and opossums. Be careful when you're playing with those free-roaming cats, those feral cats. Although this and the other cluster center in one neighborhood, the risk of flea-borne typhus is countywide. Cases occur across the county and among people with a range of housing and socioeconomic circumstances. Are you ready for this? So far this year, over 100 cases have been reported in LA.

VR: What are the symptoms of typhus, and why would you have to be hospitalized?

DG: You can get super sick. High fever, sepsis, dropping blood pressure. All right.

VR: I don't know why this is happening. You can't blame it. There's no vaccine, right, so you can't blame that.

DG: We have really disassembled our public health system. We've cut people. We've cut funding. The normal surveillance that might be in place. A lot of the services for some of the people that are at risk for this. There's a number of things that we're seeing. All right. We're doing it because there's this absurd idea that we have this epidemic of autism caused by the vaccines. I don't know if you've caught that.

VR: Heard of that.

DG: That's why people don't give their dogs rabies vaccines anymore.

VR: What? Wait a minute. Wait a minute.

DG: You haven't heard of dog canine autism from the rabies vaccines? Vincent, it's not a thing.

VR: They're afraid of autism? Are you serious? Would you even know if your dog had autism?

DG: Well, they fail to make eye contact.

VR: Oh, come on.

DG: Your cats no longer will text you back.

VR: Somebody asked me the other day, why would you not vaccinate your dog? I don't understand at all. You need to protect your dog because they're going to have contact with wildlife.

DG: They do. I was up since 4:00 AM this morning because the foxes have figured out this is their game now. They come into the yard, and then they go to the back door and harass my lab. Then when she goes out, they run, but they basically run through, and now they sit outside the fence. I've gone out with them. The foxes like to sit there. Yes, you see, dogs will interact with foxes. They'll interact with raccoons. They'll even maybe in a stream. We have leptospirosis in the local stream. Yes, you've got to protect your dogs, your cats. We have a lot of vaccines that protect our animals. Then not only are you protecting them, but what happens if there's some sort of an issue where now your neighbor gets exposed?

All right. Here we have another article. I just want to point out that this is a literature that is growing. We have lots and lots of studies here. We're going to talk about this publication now. It's not like, oh, please look at this one cherry-picked study that supports my agenda. This is another robust article, "Cumulative Incidence and Prevalence of Autism Spectrum Disorder," published in *JAMA Pediatrics*. These are the results of a prospective population-based screening and diagnostic assessment. Conducted in 12 consecutive birth cohorts in South Korea among children born from January 1998 to December 2010 and ascertains at age 7 years between January 2005 and December 2017.

All children age 7 years entering elementary schools constituted the target population. Among more than 62,000 children, 2,077 screened positive and were invited for detailed evaluation, and 881 completed comprehensive diagnostic assessments. Data were analyzed from January 2024 to July 2026.

Population-wide standardized screening used the autism spectrum screening questionnaire, diagnostic assessments, including the autism diagnostic observational schedule, autism diagnostic interview revised, cognitive testing, and record review. These were all administered to screen positive children. Clinical consensus best estimate diagnosis were determining according to the DSM. This is the *Diagnostic and Statistical Manual of Mental Disorders 5th Edition*.

Across consecutive birth cohorts, both seven-year cumulative incidents and prevalence estimates of ASD, so autism spectrum disorder at age 7, remained stable. Ranging from 1.9 for incidence, from 2.0 for prevalence, with no statistically significant increase or decrease. They go on basically to say the findings from this cohort study suggest that detection-related factors may contribute substantially to reported increases in ASD occurrence estimates.

I'm going to leave in a link to the *CIDRAP* article where we read that the prevalence of ASD,

autism spectrum disorder, remained stable across consecutive birth cohorts. The pattern suggests improved detection rather than increased autism spectrum disorder occurrence and does not support this concept of an autism epidemic. The findings of this cohort study indicate seven-year cumulative incidents and age-7 prevalence of ASD remained stable. Any comments on this? I thought we'd at least give this a little bit of a discussion. Here we are on *This Week in Virology*. Why are we discussing autism?

VR: Well, because some people who erroneously claim that vaccines, specifically MMR, cause autism, right?

DG: Yes.

VR: Many studies have discounted that. Here is one showing the incidence hasn't increased in the past. This is a seven-year cumulative study. If vaccines were causing autism, you would see the rates increasing as additional babies are being vaccinated every year. That's not the case. It's another nail in the coffin for this idea.

DG: I think it's really important. I think as clinicians, we have these discussions. A lot of times people say, "Oh, I want to delay the vaccine, or I'm worried about vaccine because of the neurodevelopmental impacts." Really, really clear and another incredibly well-done, robust study, that is not true.

VR: No, no.

DG: The vaccines basically prevent disease. They do not cause neurodevelopmental disorders. One of the things we're seeing is different types of autism. There's, as I pointed out here, a spectrum. There's one, two, and three. Three is the non-verbal, really high needs. Then the level one, which we're seeing many more diagnoses, these are people with minimal supportive needs. As we see here, when you really look closely and you follow, you're going to get the same numbers. If you do a better job of awareness, you're going to diagnose more of those level ones.

Level three is you're going to basically pick those people up without really needing to do a lot of effort. It's great that we're hearing a lot about autism. It's great that there's a lot of excitement to understand the causes. What is not great is this erroneous concept that vaccines are causing them. I was just listening to the recent *TWiV* at ASV. Why do people interested in virology care about vaccines? What was the answer to that question? If you wanted to tell someone one thing about viruses, what would you tell them?

VR: Get vaccinated.

DG: Get vaccinated. All right. Another as the world is falling apart. We read in the *AP*, Florida is experiencing one of the worst surges of dengue fever in decades. We're talking here about autochthonous. These are people hanging out in Florida, getting dengue in Florida, not traveling somewhere cool. The Florida Department of Health confirmed a death on Friday, an individual died from dengue. We have seen more than 130 locally acquired dengue cases. Much more than -

VR: There is a dengue vaccine. Is it used in the U.S. at all?

DG: Not really, but I think we're going to have to start rethinking that. It's normally

considered a travel vaccine.

VR: This local transmission means that mosquitoes have dengue virus in them and they're bringing it from person to person.

DG: Yes, actually, and that's the whole idea. Someone's got dengue, and they're viremic, and they get bitten by the female mosquito. Then the female mosquito is then going to go bite a second person, and you're going to end up - the mosquito is going to be the vector. Now, I guess when you do your travel clinic, you're going to have to go and say, "I'm thinking of traveling to Florida, and so I have to worry about dengue, I have to worry about measles." It's becoming a foreign country down there.

Let's also make sure we bash on New York City because we have our second major *Legionella* outbreak going on at the moment. We're up to 22 people. We already had a couple deaths from this outbreak. This is in the South Bronx.

VR: This is in the South Bronx.

DG: Another case of screwworm this last week. Screwworm is now full-fledged across the border, so New Mexico and Texas.

VR: I've been watching this map over the past months, and it's getting bigger and bigger.

DG: Yes, and it's getting a little farther in, right?

VR: Yes.

DG: It's not just right at the edge there. It's all the way into Central Texas and moving up New Mexico. The last two cases, another case in New Mexico, another case in Texas. The one that we talked about last week was a horse.

All right, Ebola. A little bit excitement news. I read this, and I was like, "Am I really reading this?" Just now, just Saturday, 9/19/2026, they began vaccinating healthcare staff against Ebola in the DRC. I'm going to put my glasses on for this, in Bunia. This is the epicenter of the fastest-growing outbreak of Ebola in history. The provincial governor is telling us that, particularly, they're worried about healthcare workers because they have high exposure rate, they're very involved in the response, so they began vaccinating the healthcare staff.

Healthcare workers and other frontline workers were prioritized to receive the Ervebo vaccine that was effective past Ebola outbreaks. Clinical trials are ongoing to find a licensed vaccine for the current outbreak. This is the Bundibugyo virus. We've got that as an update. You can see the CDC now, they're following out the first six months. You can see that here we are still with a pretty significant trajectory up to confirmed cases, 7,672, confirmed deaths, 3,699, and still a solid chunk. I'm going to say 10% to 20% of folks are not actually being followed who are diagnosed with Ebola, lost to follow-up. We have ongoing transmission there.

VR: I hope this vaccine does something because, as you know, it's against Zaire and it's not Bundibugyo.

DG: It's tough. It really is tough. I know that we, the U.S. government, is giving some funding to help with this outbreak, but we don't have the same boots-on-the-ground assistance that

we provided with the big West African outbreak. It's tough. If you went there to help, you would have to then spend 21 days in some third place before you'd be allowed to come back to the U.S. They're really making it difficult for those of us who might want to go and help.

All right, but we've got a lot of problems here at home, Vincent. Pennsylvania asked CDC for emergency assistance amid RFK Jr. clash over measles. Pennsylvania's health department has started the process of requesting emergency assistance from the CDC to help control this deadly and rapidly spreading measles outbreak. The request for that assistance, known as Epi-Aid, comes on the condition that the CDC publicly recognize the four people who died from measles, which the agency has so far refused to do.

In the letter, Pennsylvania Health Secretary Debra Bogen said it was important for state and federal officials to have a trusting relationship built on respectful, transparent, and factual communication. "The CDC's choice not to publicly recognize the deaths undermines our response," Bogen wrote. "For this reason, if CDC is unable to transparently and accurately communicate information about those measles-associated deaths, the department will respectfully rescind our request for a CDC Epi-Aid."

Now, much of the conflict seems to be around how upset RFK Jr. is that people actually do die from measles. The article. "U.S. CDC Works on Standard Definition for Measles Death as Cases Rise," was published in *Reuters*. The U.S. CDC is working with the Council of State and Territorial Epidemiologists to develop a standardized case definition for measles deaths, the agency said.

Here are the details. We're going to get one, two, three, four, five, six points. The CDC reported 3,471 confirmed measles cases in the United States as of September 17, up from 3,294 a week earlier, with no deaths recorded for 2026 in its national tally. I think since then they've added, they've actually recognized one.

The Pennsylvania Department of Health reported two more deaths, both in unvaccinated individuals, bringing the state's total to four.

The CDC, however, has not included the deaths. They're moved away from its previous reliance on state health departments.

The Pennsylvania Health Department, as we just discussed, sought emergency support, but they want the agency to recognize these four deaths.

The CDC said it would update its reporting as more information becomes available and relevant reviews are completed.

Now, on Wednesday, this is, I think, something, the U.S. Senate Health Committee's Republican chairman blamed the Trump administration's approach to vaccines for recent measles deaths in Pennsylvania.

VR: Now, you know who that is, right? Cassidy.

DG: Yes. I'm torn about Cassidy. He could have prevented this from happening.

VR: He could have.

DG: He basically asked someone who lies to your face, "Will you promise me that you'll stop lying?"

VR: This whole thing that the CDC is not putting these deaths up is just childish behavior. The CDC has always taken the data directly from the states and put it up. They don't need to do their own investigation or anyone else's investigation. This is playing games, and it's just unbecoming of the CDC. Unbelievable.

DG: It's horrible. We've talked a little bit, and we'll talk about this more. Not only have we already had people die from measles, but we're going to potentially have people with delayed effects. This is not cheap. This is not cheap in terms of human life and suffering and all the hundreds of individuals that have ended up in the hospital, mostly children, but also lots and lots of, shall we say, millions of dollars.

Let's talk about, this is a *JAMA* article, "Cost of a Measles Outbreak in an Urban Shelter." Measles outbreaks, as we've been discussing, are costly and challenging to control. A measles outbreak associated with a Chicago shelter, say Chicago, Illinois, shelter, which primarily affects shelter residents, resulted in substantial public health response costs, direct medical costs, and productivity losses.

What did they find? The economic evaluation of 57 cases of measles and 3,569 contacts, here they estimated the cost was \$8.7 million. This was made up, direct, \$153,000 per measles case, \$3.6 million in response costs, \$4.4 million in direct medical costs, \$684,000 in productivity losses, and affected children missed 17,113 school days. This is an incredibly -

VR: Wow.

DG: - costly thing when this happens. Then we have, this is a Fox News thing. You ready for this? Fox News, we hear that measles at the Philadelphia airport, two possible measles exposures within a week, the latest at Philadelphia International Airport. They give us a little bit about those potential exposures. Not great.

VR: I heard there was an exposure at CHOP also.

DG: Yes, there was. Children's Hospital -

VR: Oh, boy.

DG: - of Philadelphia. It's Paul Offit's hospital. He's not going to be happy about that.

VR: No. What's going on there? Yes, I continue to follow the Hopkins U.S. Measles Tracker. We're up to 3,568 measles cases. You can see where the big epicenters are. Maybe this is a time for us to recommend people listen to the latest Deep Dive ASV-TWiV where SSPE is discussed. What's really tragic there is this is an incurable manifestation, a delayed manifestation of measles infection. You look at, say, OK, over 3,000 people have been infected. For every 600 kids who get infected prior than 1, we're going to see a case of SSPE where, five to 10 years after the fact- so five to 10 years from now - this process has already been set in motion. These children over a year will basically progress from a normal, healthy child to a vegetative state, where the only way to keep them alive is to have them non-verbal, with a feeding tube, on a ventilator. That's happening. We are letting that happen. I just want to point that out.

VR: There's no way that the U.S. is going to maintain its measles elimination status. They're meeting in November. 3,500 cases, just no way.

DG: The only way you maintain it is by lying, by just making believe.

VR: The numbers are there even though they've been trying to suppress them, right?

DG: Yes. You can go on the CDC site, and you can actually look at the yearly measles cases, and you can see how they cluster across the country. For those watching on YouTube, you can see the first map of the U.S., and basically you can see there really are a number of Pennsylvania, Utah, South Carolina, where we're seeing 500-plus cases in those states, and then the next 100 to 500, Texas, Florida, Ohio, Virginia. Wisconsin, Arizona. It's terrible, but you can see how this maps relative to MMR vaccine coverage for kindergartners, and it's horrible.

There's the category of less than 90%, which is just waiting for the other shoe to drop, and it's Oregon, Idaho, Utah, Arizona, Alaska, Hawaii, Colorado, Oklahoma, the Dakotas, Minnesota, Wisconsin, Iowa, Missouri, Georgia, Florida, Ohio, New Hampshire. What is going on up there in New Hampshire, guys? Come on.

VR: Now school has begun, and this is going to get worse. Unbelievable.

DG: Yes. Last year, for the full year, we had 2,242, and we were bemoaning that, but we're already now approaching 4,000. Probably get there by the end of the year, unfortunately. We now have our New York State measles dashboard. You can see clusters in particular areas, but we're up to 62 in the state, and half a dozen confirmed cases right here in New York City. All right. What can you do? We're heading into flu season. As we mentioned, you can get vaccinated. Oh my gosh. Vaccines work, but even if you want to get in the weeds, which particular vaccine should you get?

Here we have the article. We're talking about flu shots. "Immunogenicity and Safety of an MF59-adjuvanted Cell-derived Higher-dose Quadrivalent Influenza Vaccine in Adults Aged 50 Years or Older: A Phase 3 Randomized Controlled Trial," published in *The Lancet Infectious Diseases*. They're going to look at immunogenicity and safety of. We'll look at three different vaccines and how are we going to keep these apart. We've got our MF59-adjuvanted cell-derived, higher dose. This is the aQIV with a little C; the little C for cell. The MF59-adjuvanted egg-derived, so that's the aQIV without the C.

I want to put a little E at the end for egg, but I don't know. They didn't do that. I wanted to do it. Then QIVr, so that's the recombinant with the little R. We're looking at adults 50 and older. That would be the people like me. These are the results of a Phase 3 randomized observer-blind, parallel group, multi-center study where folks were randomly assigned 3:2:2. Three, they're going to end up in the cell, and we're going to end up with relative to two in the egg and relative to two in recombinant. Then they're going to do age stratifications.

They're going to look at people 50 to 64, but then we're going to separately look at people 65 or older. They give a breakdown, how much of hemagglutinin and how much of the squalene is in each of the different preparations. The participants received one vaccine dose. This is a one-shot. This is not part of a series or a scheduled approach. This is just, you get your one flu shot, and then we see how people did. Primary immunogenicity objectives

were lot-to-lot consistency of three batches of the cellular. They're going to look at the GMT ratios.

They're going to look at non-inferiority. What do we find out? The cellular was non-inferior and actually superior to the egg at Day 29. GMT ratio of 1.53. They're going to break this down for the difference. That's for Flu A, H1N1, 1.2 for Flu A, H3N2, 1.73 for Flu B, Victoria - that's all there is now - and 1.71 for B, Yamagata. Corresponding seroconversion rate differences were 16.8%, and then they're going to break it down for the different - Basically, it was non-inferior, so that the cell was not only non-inferior, but actually superior to the egg-based for all the different components.

Compared with the recombinant, the non-inferiority criteria is met for three, but not for the Flu A, H3N2. The cellular was well-tolerated, except there were some slightly higher rates of local and systemic, really reactogenicity, but these were always mild, moderate, transient, self-resolved. Really serious adverse events were low across all vaccine groups. They pull it all together. Basically, here's the takeaway. For folks 50 and older, the high-dose cellular was non-inferior and actually superior to the high-dose egg for all four flu strains. Then we basically see that one issue for the Flu A, H1N1 relative to recombinant, but no new safety concerns or any issues here. Let's get to our favorite part of the show, the multicolored blue-washed lines. We may have peaked, actually.

VR: It's very interesting. It could be a little peak this year, lower than last year, this first peak, and that would not be so surprising, I think.

DG: Yes. It might have this little narrow bump. It's hard to know. I wish they hadn't blue-washed it and changed things around. Was this really a smaller peak? I think it was a smaller peak.

VR: If you look all the way to the left to last year, 2024, well, actually, we could look to 2025 because the whole thing is on here. We have a July to September peak, which is much higher than what we are having now. Then you have one in December. I suspect this is going down because it's the end of September now. That should be it until December.

DG: I hope so. It's very regional, too, when you look at the map. The folks that had a COVID-19 peak this fall, it was Florida, it was Texas, it was California, it was Washington. Much of the Midwest, the Northeast, not much happened. All right. This is interesting. This is a question I think that came up a lot. Different folks would get those mRNA COVID shots. Then some people would be down for the day, maybe even down for a couple of days. Really would have a lot of reactogenicity. We just were like, "Oh, that's great. That means your body is doing a great job."

Then what do you say to the person who's like, "Yes, I got the shot, but I feel just fine."? "Oh, your body's not doing a great-" We just never went there.

VR: No.

DG: Commended the people who were knocked down. To be full on it, I never really felt that bad, but I surely milked it. I was like, "Oh, Jessica," my wife, "I can't really do anything for Saturday. I'm just going to lay in low. I'll be here on the couch listening to Noah Kahan." Anyway, we have the article, "Baseline Interferon Signaling in Monocytes and Antibody-mediated Innate Activation are Associated with Reactogenicity to mRNA Vaccines,"

published in *Science Translational Medicine*. There really is a great editor's summary. I like when they do these.

I'm just going to read you the editor's summary, but I'm also going to a little bit from the authors as well. "One of the barriers to vaccine uptake is reactogenicity, where vaccination induces transient pain and systemic symptoms; a problem that became particularly evident during COVID-19 vaccination campaigns despite affecting only a fraction of the population. Here, Madelon et al. aimed to tease apart the drivers of this reactogenicity using samples from COVID-19 vaccine recipients and animal models, finding that monocytes and vaccine-induced antibodies at the injection site, as well as early interferon gamma production by T cells drove early inflammatory responses associated with reactogenicity.

"Moreover, individuals with a higher baseline interferon response signature in monocytes were more likely to have systemic symptoms after vaccination. These data point to both mechanistic drivers and potential baseline biomarkers of reactogenicity, providing a framework to potentially reduce vaccine side effects and predict who might be most likely to develop them."

Then, from the authors, really focusing on, "Systemic adverse events were associated with stronger interferon and pro-inflammatory responses after the second dose of a COVID-19 mRNA vaccine, which were also correlated with magnitude of the antigen-specific adaptive responses. This heightened inflammation occurred within 24 hours of vaccination, originated primarily from the injection site, and was characterized by enhanced recruitment and activation of myeloid cells, particularly monocytes. Two mechanisms contributed to this response: Early interferon production by muscle T cells generated after the first dose and Fcγ receptor-dependent cytokine induction by vaccine-antigen-specific antibodies. Consistently, serum antibody levels before vaccination correlated positively with reactogenicity."

VR: I don't know how you would use this to determine who's going to have a bad reaction. You can't screen everyone before, right?

DG: Yes, you're not. Then what would you tell them? "Hey, your antibodies levels are really high. You're going to have more reactogenicity." I guess you could maybe counsel them like, "Hey, you're probably going to have a lot of reactogenicity," but you're going to spend \$80 all the time to check people's antibodies or check any of the basal interferon. I think if anything, the takeaway is we understand the mechanism. If you're having a lot of reactogenicity and it's making you hesitant to get a COVID shot, then maybe you get the Nuvaxovid Sanofi product. Right?

VR: Yes. No, I think you just get the Nuvaxovid. If you're worried you had a bad reaction, get Nuvaxovid. It's nice to know the mechanism.

DG: Yes, if you do fine with mRNA.

VR: It's nice to do the mechanism. That's great. Maybe future vaccines could build that into them in some way to prevent it, but I don't think immediately this has much use.

DG: Yes. People definitely had a lot of questions. Sometimes we just want to know, and now we do. I'm hoping by the time we record next time this will be resolved, but CDC inaction delays COVID shots for low-income children. We talked a little bit this last time, but

although hospitalizations due to COVID-19, in the middle of this fall surge, the CDC has not yet announced when COVID shots for the most vulnerable children in the country, those eligible for the Vaccines for Children program, will be available.

This is significant. The VFC, so the Vaccines for Children program, offers free immunizations to more than half of U.S. children. I'll say that again. This is affecting more than half of U.S. children, including those who are uninsured, underinsured, eligible for Medicaid, or American Indians or Alaska Natives.

VR: This is even worse than the CDC not putting the measles deaths on the website, because this is affecting a lot of kids. There's no reason not to get this program going. This is unconscionable. This is just ridiculous, folks.

DG: It's really terrible. We're going to wind it up with this. This is another doomsday article here, Vincent. I don't know. Sometimes the truth is upsetting, but the truth is the truth. Here we have this article, "Loss of Vesicular Monoamine Transporter 2 in Striatum of Long COVID and Relationship to Neuropsychiatric Symptoms," was published in *EBioMedicine*. This is basically, COVID is causing Parkinson's disease. This is a case control study, and it was done August 2022 through April 2025 in Toronto, Canada. It included 24 adults with Long COVID and 24 age-matched healthy controls.

The healthy control sample was extended to 43 for exploratory analysis. A little bit of background here. Several neuropathologies have been proposed in Long COVID, including basically how does this happen, what's going on in the brain, what's causing the pathology. A couple ideas. One, loss of synapses, ongoing infection, mitochondrial dysfunction, overexpression of AMPA receptors, sequelae of gut microbiome imbalance, and persistent immune response with gliosis. While some think there may be some identifiable neuropathology, authors point out that identifying neuropathology in Long COVID in humans is difficult because this requires either post-mortem brain tissue or brain imaging investigations of specific pathologies.

Getting a brain biopsy of someone who's alive, that's really difficult. Brain imaging, we can do that. There's some concern that perhaps Long COVID can represent some impact on the dopamine system in the brain of sufferers. There are several reasons why dopamine terminals in striatum could be vulnerable to injury. Let's go through the risk issues. First, individuals with Long COVID show elevated markers of microglial and astroglial activation in the striatum, with some investigations reporting more widespread elevations. Gliosis from excessive synaptic pruning and/or greater generation of reactive oxygen species may damage dopamine-releasing neurons.

Second, direct infection of dopamine-releasing neurons innervating the ventral striatum, dorsal putamen, and caudate is possible since their cell bodies in the ventral tegmental area and substantia nigra express a relatively high density of angiotensin converting enzyme 2 receptors. You're shaking your head there, Vincent.

VR: Just because a cell has a receptor doesn't mean it's going to be infected.

DG: Even if it doesn't have a receptor, you can get in through fusion.

VR: It's how measles virus does it. There's very little good evidence that SARS-CoV-2 is actively reproducing in the brain. This really bothers me, this idea of direct infection.

DG: It's good that you point out these are just theories. These are ideas. These are why we think that we should look here. The third was a preliminary post-mortem study of eight controls and 13 individuals died of pneumonia from acute COVID-19, albeit some with pathology of early dementia and one with Parkinson's disease, as most were elderly, reported detectable SARS-CoV-2 transcripts and lower dopamine neuronal density in the substantia nigra.

OK, so that's fine. They got these ideas, but let's actually go ahead and do what they do. They're going to do this study where they're going to use PET imaging to look at dopaminergic nerve terminal integrity in the ventral striatum, dorsal putamen, and dorsal caudate. Primary outcome was comparison of this, basically, this is a type of PET. I'll give you the alphabet soup once. Positive superscript 11C, DTBZ - (+)[¹¹C]DTBZ - binding potential, (BP_{ND}), and PET measure of VMAT2 binding. Basically, they're going to be looking at these ways of doing PET imaging to look at dopaminergic activity.

The first, this is going to be our DTBZ, was significantly lower in 24 individuals with COVID versus 24 age-matched healthy controls. Apathy, motor slowing, and memory decline correlated with lower levels in the ventral striatum, dorsal putamen, and caudate, respectively. Maybe for the people watching on YouTube, I'm going to actually put up the data here so you can actually see there's a lot of scatter here. Of course, if you look at Figure D, they're going to cherry-pick a really nice figure. That is pretty compelling, right, that nice figure they have?

VR: Yes.

DG: They've got the voxels per stratum. Basically, this is on a color chart where a normal healthy individual is going to have bright red areas looking at dopaminergic activity. Then the folks with Long COVID, they're going to have not much red going on there. Then if you actually look at basically, the dot plots - they're using triangles here - there's really a lot of overlap, right?

VR: Totally. The differences are not great. This huge scatter, yes, it's hard to know.

DG: You get your stats. The medians are different, but there's really a lot of overlap here. What does all this mean? Approximately 95% of VMAT2 binding in striatum is contained within dopamine-releasing neurons. A reduction in this DTBZ BP is inferred to represent a loss of dopamine-releasing neurons. This interpretation, consistently applied as VMAT2 PET imaging, is a well-established method to detect pattern and progression of loss of dopamine nerve terminals in neurodegenerative illnesses and prodromal states like Parkinson's disease.

Loss of dopamine nerve terminals may be contributing to symptom correlates of apathy, motor slowing, and memory decline, suggesting improved function of dopaminergic responses or synapses as a new therapeutic direction to treat Long COVID. It's interesting.

VR: What kind of treatments could you do for that?

DG: I thought about this. They talk about a bunch of stuff. The thing that came to me was things you might try in folks with Parkinson's. Things like Sinemet; basically giving them dopamine. It'd be interesting. Pretty quick on and off with those. You can even do a very short Sinemet trial to see, hey, if you do Sinemet, is that going to help with apathy and

motor slowing and memory decline? It seems like a low-hanging fruit after this study to potentially try.

No one is safe until everyone is safe. We are in our ASTM and H fundraiser. Call this the Dickson Despommier fundraiser, actually, because we're going to be headed to Washington, DC in November.

We're going to be starting this five-year One Health Dickson Despommier Memorial Lecture Series. This is a big one. We're hoping to get up to a maximum donation of \$100,000. Your donations will be doubled. Hopefully, we're going to get an anonymous donor that will help us do that. Go to parasiteswithoutborders.com. Click on the Donate button. I have to say, thanks, everybody. Really, people have really stepped up. This could be something that you feel like you were part of.

VR: It's time for your questions for Daniel. You can send yours to Daniel@microbe.tv. Chris writes, "Weekly listener since January 2020. My wife and I are expecting our first in November. We plan to keep them out of daycare and avoiding communicable settings as much as possible until they start chipping away at vaccines. I had been planning a strategic day trip to Canada at age 6 months in order to qualify for an early MMR dose with international travel with two doses later on the normal schedule. I just want to make sure I understand what you said last week.

The balance of the clinical evidence shows that this early shot weakens protection against measles even after all three pediatric shots. That's distressing if true, but important to know since I don't want to make things worse by trying to make things better. I know many, many expecting parents in my area who are also doing strategic international day trips for this reason."

DG: This is a good question. Vincent, please feel free to jump in on this. We've talked about the studies on this, and the sweet spot really may be nine months. We do it at a year because we really were not under the gun, but now they're seeing thousands and thousands of cases. There is a suggestion that it might make sense to try to move that earlier. When you move earlier to six months, we actually were seeing that that early six-month or earlier shot may impact the robustness of our later responses.

VR: Yes, six months is the problem. I don't know that nine has been studied as well. Right?

DG: Yes. I think we talked about the two ideas. One was that - and maybe this changes - there might be enough maternal antibodies that if you're doing the six months, it's almost like you're not getting as good a dose, but then why would the future doses not get you up to where you want to get?

VR: No, that's [unintelligible 00:53:22] No. We did the study on *TWIV* a long time ago where they showed 12 months is really the best time, but it is risky because then you're exposed in those months to measles. In a current situation where there's ongoing measles, this is a problem. There is a clear inhibition of antibody response by the second two doses when you start early. Right?

DG: Yes. Six months, unfortunately, I really think it's too early. I'm not sure the strategic dose at six months, but now that we're seeing thousands and thousands, it's like, oh my gosh, you're having a child, and it's no longer safe in the U.S.

VR: If you can keep the child away from things until nine months, that would probably be the best thing. What do you think, Daniel?

DG: It is tough. You actually have to be a, I don't know, bit of a jerk, I guess. I had an issue, probably. Full disclosure. My oldest brother was anti-vax. I don't know if you knew this, Vincent.

VR: I didn't.

DG: He's coming to visit with his unvaccinated kids. He was living in California. There was an outbreak of measles going on. This is a number of years ago, so people probably can know the date. My mom is all excited, like, "Oh, we're going to get all the cousins together." I'm like, "No, we're not. I am not going to expose my little kids to unvaccinated -"

VR: Yes, that's the right decision. You cannot come. No.

DG: It's just, it's tough. So, he did. He vaccinated his kids. Oh my gosh, that was so hard.

VR: That's good.

DG: Yes, it was excellent.

VR: All right. Patricia writes, "My cousin is very immunocompromised. Is there a COVID vaccine she can have? She also has reactions to many additives and chemicals. Is there a COVID vaccine in trials that she could have once approved?"

DG: Oh, Vincent, you know the answer to this. Our listeners, everyone, one, two, three.

VR: Yes.

DG: Nuvaxovid.

VR: That has an adjuvant also, the mRNA vaccine.

DG: A lot less, yes. A lot less as far as reactogenicity. You could actually get them all, to be honest. If you are someone who reacts to a lot of things, maybe doing the protein-based Nuvaxovid, Sanofi approach. I guess the other is just this question, have they had any of the vaccines? How have they done with those?

VR: Immunocompromised, you cannot have infectious attenuated vaccines. These subunit vaccines should not be a problem, right?

DG: Yes, and the mRNA ones are fine. Actually, this is someone who, depending upon the level, they might still qualify for the Pempgarda. That is the passive antibody treatment.

VR: Janet writes, "If you've had a documented case of flu B, should you wait three months before getting the annual flu vaccine, like you've recommended for getting a COVID vaccine after a documented COVID case?"

DG: This is a little more of a challenge, Janet. Let's think it through. We'll work it through together. You've got the one circulating flu B. If you've got a case of flu B, you probably are going to be in pretty good shape for the next three months, but you're not protected against the different flu As that are going to circulate. Usually, we don't recommend people wait.

We say when you get better, go ahead, get that shot because it's really going to be flu A that are going to dominate in the epidemic flu season.

VR: Connie writes, "I'm 77, pretty sure I had measles as a kid. Do I assume I have immunity, or does it wear off substantially in people my age? I'm traveling to eastern Pennsylvania and wonder if a booster would be a good idea."

DG: Connie, it sounds like you're going to be able to get a booster for free. No. [laughs] We do think that measles infection confers lifelong protection. It is interesting. The recommendation historically hasn't been, but then it was, oh, but if you're going to head to some area in the world, whatever. No, we normally wouldn't recommend another vaccine.

VR: Carol writes, "Thank you for the great information in the videos. I have to watch the video to check out the fun bow ties Dr. Daniel wears." I didn't ask you what you have on today.

DG: It's *Yersinia pestis*.

VR: Wow.

DG: It's a plague.

VR: Plague. "Many years ago, I thought of getting a measles vaccination because I have no memory of getting the disease. Instead, my doctor ordered a titer and said my immunity was present, so no vaccine was necessary. Many years have elapsed, and now, with measles circulating and also no memory of having mumps, though I know I had rubella, I decided to get an MMR vaccine. It was free, so why not? The pharmacist had the nerve to say it can't hurt to get boosted, while standing there ready to plunge the syringe into my arm, which I thought was hilarious.

My question is, the general recommendation is to get two shots. I've only gotten one. I'm 71. I don't think I ever got MMR, certainly not as a child since it wasn't available then. Will this vaccination provide me with protection by itself, or should I get another?"

DG: Oh, this is good. Let's walk through this. Originally, the MMR was one shot, and then a number of years later, there was a second shot. That second shot recommendation was based on the measles component and the fact that you're getting a higher effect with that second shot, not necessarily based upon the mumps component. As I guess I'm reading here, you had some evidence. I don't know your age, which would be helpful.

VR: 71.

DG: 71. If you're 71, then you probably actually had measles, right?

VR: For sure, yes.

DG: Yes, you're probably set at this point.

Vincent: Michelle and Andrew write, "My husband has acquired alpha-gal syndrome about 15 years ago when we lived in North Carolina amongst the ticks. He has heard that the new flu shot might have a change to a formulation that would cause problems with folks with alpha-gal. I've been listening to *TWiV* since the pandemic started, and so you were the first

that I thought to ask. Can you help with this question?"

DG: Yes. This is great. This is like trivia night, but actually trivia that makes a difference. There is actually one flu shot - it's not really a shot - the one flu vaccine that you need to avoid. It's a spray. Why is that? Because they actually use gelatin in the spray. If you have this alpha-gal, you actually can potentially have an anaphylactic reaction to FluMist. Go ahead, whatever flu shot you want, just don't do the flu spray.

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

DG: Oh, thank you, and everyone, be safe.

[music]

[01:00:40] [END OF AUDIO]