TWiV 1316 Clinical Update

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Guest: Daniel Griffin

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

[music]

VR: From *MicrobeTV,* this is *TWiV*, *This Week in Virology*, Episode 1316, recorded on April 23, 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: You have a very dark bow tie on there, Daniel.

DG: It's hard to tell. Apparently, this is supposed to be a hepatitis bow tie, little virions on there. Maybe people can see if they zoom in. It's an artist's rendition. It's very hard to--

VR: Are the Dane particles on there? Is that it?

DG: I don't think so. I think they're just these circular virions, supposedly. Yes, it's not as classic as that nice scarf that I stole from the incubator last time I was there.

VR Yes, nice Dane. They have the Dane particles. They have the long particles and the regular. Hep B, it's always a mix of particles.

DG: I think that's like all things in life. It's always a mix. The whole idea that there's one gene, one specific viral sequence. It's always a quasi-species. I think, who coined that.

VR: Even humans, every cell in our body has a different sequence from the next one.

DG: Yes. I don’t think people realize. It's small. The fidelity of our DNA polymerase. Yes, it's not 100%. There's some sort of selection that goes on there. Interesting facts.

VR: What is it that you said? Everything is what?

DG: Everything is a quasi-species.

VR: Before that, you said something even more -

DG: Even more profound?

VR: Even more profound. It's going to be Daniel Griffin's quote. All right, well, I'll go back and listen.

DG: [laughs] You can listen.

VR: One day, someone will quote you.

DG: All right. People probably can hear that your voice there is a little raspy because you're not 100%, but you start at 110, so you're just a little bit--

VR: 120-.

DG: "In health, there is freedom. Health is the first of all liberties." That's by Henri-Frédéric Amiel. He's not an American, so I'm not sure how that's actually pronounced. He's a philosopher. I thought that was very appropriate because there's all this discussion about health freedom. Here's this idea that, actually, the first and foremost freedom that everything else stands on is health.

VR: Basically, RFK Jr. is trying to take away our liberty because he wants to take our health away.

DG: Yes. He is willing for his own personal gain to compromise our health and the health of our children, the health of our country. It's this classic, like, "Oh, I'll call it the Clean Water Act, which means the water doesn't have to be so clean," or Make America Healthy Again, which is like, "Well, not really," as the pesticides are allowed to increase under his watch, and he attacks vaccines and all the rest.

VR: Daniel, we're not going to let it happen.

DG: We are not going to let it happen. Let me jump in. We've got a few things to talk about here. “Kennedy Will Not Back CDC Director Nominee’s Pro-Vaccine Status: RFK Jr. Won’t Commit to CDC Nominee’s Vaccine Decisions.” We've got a link here to a *New York Times* article. I'll read some quotations here. "'If Dr. Schwartz is confirmed, will you commit on the record today to implement whatever vaccine guidance she uses without interference?' Representative Raul Ruiz, Democrat of California, asked Mr. Kennedy during a tense hearing on Capitol Hill, the secretary's fourth congressional hearing since last Thursday.

'I'm not going to make that kind of commitment,' Mr. Kennedy replied. In response to other questions from Dr. Ruiz, a physician, Mr. Kennedy said that he approved of Dr. Schwartz's nomination and had spoken to her multiple times, but had not spoken directly to Mr. Trump about her selection."

VR: OK, Daniel, let me get this straight. He asks Susan Monarez if she will implement whatever vaccine guidance he issues, and she says no, and he fires her. By this, he should be fired.

DG: [chuckles] The problem with Kennedy, the situation he's gotten himself into, it's very clear that this anti-vaccine stance is not popular among most of the electorate. It's people who are educated, people who are not drinking some weird Kool-Aid are well aware that this is one of the most effective, safe ways of keeping our children and our community safe, is vaccines. There is this fringe, this small group of followers that have made Mr. Kennedy rich. He's been catering to those, but he's been told, and you saw a bit of this in these, I think about seven different hearings, there's a lot going on here, where he actually went ahead, and he said, "We recommend the MMR for all children in America. That's what we

do."

That just came out of his mouth. He just said, "I have never been anti-vaccine."

VR: Oh, this is just lying right in front of Congress. Can you believe it?

DG: It doesn't seem to bother him, and I think that should bother us. People who can lie without any shame, that's worrisome.

VR: When did his department advise this? Throughout the outbreak, he's never said anything. He's never done anything to vaccinate kids.

DG: No, and one-on-one, he's like, "Hey, you made the right decision not vaccinating. It's a personal decision." I think right now, he's under a lot of pressure because Trump's cleaning house. If you're going to hurt his party's chances in the midterms, your position is in jeopardy.

VR: I would love to see him fired.

DG: Next, *New York Times,* "Trump Administration Live Updates: Kennedy Says His Department Advises Every Child to Receive Measles Vaccine." As we just mentioned. Robert F. Kennedy Jr., the health secretary and longtime vaccine skeptic, told the Senate committee on Wednesday that his department has advised that every child to get the measles, mumps, and rubella vaccine, a stark contrast with past remarks. Mr. Kennedy has previously called the vaccine a personal choice and said it was not up to him to provide medical advice, urging parents to do their own research."

VR: OK, it's not up to him. Historically, the ACIP has recommended vaccines to the states, and now they're not doing that anymore, right?

DG: Well, part of the issue, and we've covered this, is that since Kennedy came in, there has not actually been, since this revamp, an actual, valid ACIP. The ACIP is supposed to be an expert group, a group of experts. I know that we did the charter, but the charter does not create a group of experts. It's a flawed charter. Yes, we've got a rotavirus outbreak. We've got a lot of rotavirus, but we've also got a lot of norovirus. If you're out there, vomiting, diarrhea, not feeling well, it could be both rotavirus or norovirus.

VR: Exactly how I feel right now, Daniel.

DG: [laughs] I was thinking that.

VR: I think it's more likely that I have noro rather than rota, no? Given my age?

DG: Yes, I think norovirus is more prevalent. It's particularly the vomiting. Rotavirus is more of a diarrhea-predominant. Really getting a lot of the vomiting makes us think norovirus. Yes, we've got a couple of links here that people can follow. A staggering number of people believe unproven claims about raw milk and vaccines. I'm going to be doing an appearance on this dairy podcast talking about some of the issues. We've seen issues with raw milk for years. The classic that I've seen in several cases is *Brucella*.

Not only do people drink raw milk here in the country, but we have a pretty significant Greek community. They get the raw milk and the raw milk-based cheeses smuggled in. It is

smuggling, basically. They're sneaking it in when they come home from visiting Greece. Then people get *Brucella*. That's that disease, I think. We talked about the Maasai. They keep getting repeated *Brucella* infections. When I talked to them, everything was good until I mentioned vaccines. They're not very happy.

VR: Why? Don't people understand they're good?

DG: Vaccines or pasteurizing milk? Both.

VR: Both.

DG: [laughs] All right, and measles. Let's jump in. Measles, that was really bothering. "Why does everyone want to talk about measles? It's not my fault," says RFK Jr.

VR: Excuse me. Of course, it's his fault. He's not vaccinating people.

DG: It is his fault. It's not just his fault. Now, he's been working on this for years. He's been feeding this misinformation engine. He's been profiting off it. He's been doing talks. Now, he's lying in front of Congress. "Oh, I've never been anti-the measles vaccine." We have years and years. It's funny. It was one of the episodes where he's being grilled. The person says, "So you said this." He's like, "I never said that." They said, "Well, I have the tape. Should I play the tape?" "All right, OK. Maybe I did say that, but I don't remember saying that. I don't agree with you."

VR: He needs to be put under oath, and then we would get to the truth. Otherwise, he lies, and he goes to jail.

DG: Yes. There needs to be a consequence for lying. There is a consequence, but it's not for him. It's all these children. Hopkins has us up to 1,851 confirmed U.S. measles cases so far this year, and we're only in April. The United States, if you look at the CDC numbers as of April 16, they have us at 1,748. Another 34 cases just in the last week, by their count. We just keep getting more and more.

This is an article I think worth reading. This is, dangers of “individual choice” public health policy, is the detailed death of a 10-year-old in Manchester, England, by her mother. I read through this. Very upsetting. The story is this little girl, Rae, five months old. The little girl was exposed. She's younger than six months. She gets exposed, infected with measles. This is not her fault. This is not the mom's fault. This is the fault of someone who's unvaccinated, who gets measles, who exposes Rae.

Rae gets sick, ends up hospital visit. She recovers. We're thinking everything is great, but then our listeners may be familiar with what potentially happens next, what happens here. Seven years later, Ray has seizures at school. She's taken to the hospital. She develops muscle weakness. They realize that she's got subacute sclerosing panencephalitis. Basically, she dies.

VR: It's horrible.

DG: It is horrible.

VR: This is not a mild disease, as RFK says.

DG: No, it's not. This little seven-year-old is now dead.

VR: If everyone had been vaccinated or over 95% of the population, it would be very little circulating measles virus, and she wouldn't have gotten infected.

DG: Yes. This is completely vaccine-preventable. This little girl's death. This is what happens when some individual exercises what they feel is their medical freedom to take away all the freedoms from this seven-year-old little girl.

VR: It's just nonsense.

DG: It is nonsense.

VR: This whole idea of medical freedom is nonsense, as I've said many times before.

DG: Yes, medical freedom is freedom from disease. That's what medical freedom should refer to, not your freedom to get sick and make other people sick.

VR: If your doctor says your child should get this vaccine, you do it because that's what the doctor is trained for. You don't know any better than your doctor.

DG: Yes. Don't ask a trial lawyer for advice on medical care. Next thing, people will be asking their doctors to help them write their contracts, represent them in a court of law. It's silliness.

VR: Daniel, I remember getting all the vaccines as a kid because they used to hold me down in the doctor's office. My parents never questioned whether I should be vaccinated. That's the way it should be.

DG: It's very straightforward. All right. Flu, finally. We're pretty much out of the flu season. I think this'll be the last time that we look at these, basically, bright green influenza season maps until probably next fall when we see it come back. That's the great thing about flu, is we pretty much have a winter surge, and then it comes right on down. Then we get a really nice break, and then it returns the next fall.

VR: It behaves like a winter respiratory disease, not like SARS-CoV-2.

DG: Yes, unfortunately, which has that summer as we've been seeing for quite a while. All right. Well, one of the things I've got here in flu is the article, “Prevalence of Influenza and Other Respiratory Viral Infections in Deceased Persons: A Population-based Observational Study Over Four Influenza Seasons,: published in the journal *Clinical Microbiology and Infection*. I'm going to go through this, but then, Vincent, you and I are going to have to talk a little bit about what this actually means, what we really make of this, because it's easy to run with the headline.

Excess mortality during periods of respiratory virus circulation is very high compared with the number of reported deaths because of these infections. Here's the idea. Maybe we're missing some cases of flu. People are dying, and we're not attributing it to the flu. Here, this investigation, deceased persons, regardless of the cause, were swabbed post-mortem and tested by PCR for respiratory viruses in the 2016-2017 to the 2019-2020 seasons in Navarre, Spain.

This is right before COVID. Post-mortem results were compared with the diagnoses from clinical PCR testing. Of 857 deceased persons with a valid test, 36.4% were positive for respiratory viruses. Then they break that down. 11.4% had rhinovirus, 11% influenza, 7% common human coronavirus. This is pre-SARS-CoV-2. Fifty-nine folks, so 6.9% with RSV, 1.6% para-influenza, and just under 1% had an adenovirus, and just 0.7% with metapneumovirus. We also see bocavirus. We see one enterovirus. This is, remember, right at the beginning. They had one patient with SARS-CoV-2. Just going into that.

Now, the prevalence of any respiratory virus remained high throughout the seasons, and they break down. Among people who tested positive for influenza post-mortem, the minority, so only 41%, had been hospitalized, and 17% had a positive test result for flu within 30 days before the death. The prevalence of influenza post-mortem, 11%, contrasted with the prevalence of the pre-mortem diagnosis, which was only 2.7%. Most of these folks, they end up dying, and no one knew they had the flu until they got tested. Only 1.4% of deaths recorded with influenza as the cause of death.

VR: 1.4%. What did they die of?

DG: That's the interesting thing here. Did they die with flu? Was it incidental? Because what they're trying to suggest here, and I think this is why we have to be a little careful with this, is like, oh my gosh, all these people die in the winter. It's all these deaths due to flu, but no one thought it was flu. No one went to think of flu. Now, there is a certain mortality that flu causes acutely from the acute respiratory flu syndrome. There's also a certain amount of death that occurs in the post-flu period from MIs and strokes and other things.

They're trying to suggest here that, oh, only 1.4% of the deaths recorded flu as the cause of death, but the actual, what is that, 90-fold higher actually. I'm not sure that I really buy the math on that.

VR: It's possible, I guess, if it's on the death certificate in MI, that maybe it's exacerbated by influenza, right?

DG: Yes, some of them might be. I do think they're saying, "Boy, we see this real significant increase in deaths, much more than are getting tagged as due to whatever viral thing." It's interesting, but I'm not sure that we have all the pieces here.

VR: This is an interesting study, but it would be interesting to repeat it somewhere else. The anti-vaxxers would say this is vaccine-induced death. That's their playbook.

DG: That would be their playbook. I think the way you do this study is you look at a population, and then you've got to somehow divide them out. You almost have to test everyone, and if someone tests positive for a respiratory virus, what's their likelihood of dying relative to someone who gets maybe once-a-week swab, and they never test positive, just to really make sure this isn't just incidental.

VR: Daniel, if someone comes in the hospital and has just had an MI or some other heart problem, do they test them for any infections?

DG: They're usually not going to test for a respiratory infection. Because it's that infectious disease history, I will ask them. If they come in with chest pain and somehow I'm involved in the case for whatever reason, I'll ask. I'll say, have you had the flu or RSV or some upper

respiratory infection in the past? Three to four weeks is what I'll ask about. As we know, yes, a lot of people have, but it's also winter, respiratory season. A lot of people have who are not showing up with MI. It's hard to tease all that out.

VR: There's always people who are at risk.

DG: Yes, it's true.

VR: Interesting.

DG: All right, RSV. I put in, based upon our discussions last week, the all-viral activity peaks. You get these really nice curves. We're really on the way down, so the viral activity is really going in the right direction. Then also our RSV, and you can see RSV is really still moving on the way down, so getting out of that RSV season as well. Remember, think about your different regions, because there's still a few areas. This is really impressive data.

Here's an article, “Maternal RSV Vaccination and Reduced Risk of Hospitalization for Babies in England 2024-2025.” This is a report from the UK Health Security Agency. I don't know, maybe in the Griffin household, we talk about different topics, but my daughter, Daisy, she's a pediatric ICU nurse, and she did one of these things where she worked a whole stretch in a row, maybe this sounds familiar to people that work with me, and then gave her a chance to have five days off.

One of the things she was doing is there was a little girl who had been in the pediatric ICU with RSV, but was actually getting better. Little kid, sick enough to end up in the pediatric ICU from RSV, previously healthy child. The bright side to the story is she was telling this girl, "Hey, I have five days off. You will probably not be here. I bet you'll be home with your family." Yes, my daughter went back to work yesterday, and that little girl is home with her family.

That is preventable as we're going to see here. Here, bivalent pre-F maternal vaccination against respiratory syncytial virus, RSV, was introduced in England on the 1st of September 2024 for pregnant women from 28 weeks gestation. Here, they used linkage of routine databases to build a retrospective cohort and study the association of vaccination with rates of RSV-associated lower respiratory tract infection, hospitalization in infants between September 2024 and March 2025. Are you ready for this?

Vaccine effectiveness. This is vaccinating mom, was estimated at 81.3% in the fully vaccinated group. In cases with 10 to 13 days between vaccination and birth, as expected, lower vaccine effectiveness was only 50%, but it reaches 84.9% if received at least 28 days before birth. They have a really nice figure where you can actually see this impact.

VR: It's really amazing that you vaccinate the mother, and it has such a good effect on the child.

DG: Isn't that fantastic?

VR: Yes.

DG: That is just great numbers. If you're able to do it 28 days before birth, 85% reduction. Amazing stuff. All right, more RSV. I thought of you. I always think of you when they do experimental human challenge studies. You have strong opinions on this, just strong

opinions in general, but on human challenge. “Viral Dynamics of the Respiratory Syncytial Virus During Experimental Human Challenge: Insights for Transmission and Protection,” published in *JID, Journal of Infectious Disease*. Here, they analyzed high-resolution viral immunological and clinical data from 225 adults experimentally infected by RSV with mathematical models developed to characterize RSV host-pathogen interaction.

Infectious virus, this ISA. I love the information, I appreciate the ethical issue, but infection virus was detected three days post-exposure and cleared by eight, defining a median window of detectable infectious virus shedding. Infectious virus, they're going to do some PCR, but they're also going to do virus shedding here. Approximately five days. In contrast, the viral RNA persisted longer with a median clearance time of 12 days.

Finally, the analysis of clinical evolution showed a significant association between the occurrence of symptoms and viral dynamics. While pauci-symptomatic, so people with not a lot of symptoms, these pauci-symptomatic individuals represented 35% of this population, they accounted for only about 5% of the infectious virus shedding. The sicker folks are the ones that are shedding more infectious virus. Really nice figure here where you can see the infectious virus, you could see the RNA detection a little bit earlier.

VR: It's very interesting because that's totally different from SARS-CoV-2, where if you don't have a lot of symptoms or you're asymptomatic, you can still be shedding a lot of virus. This is just transmitted from the sick people. If you're sick with RSV, you should stay home. This study was done outside of the U.S. It's either France or Germany. I was just looking at it. It would not be allowed to be done here because what happens if these adults get runaway RSV? What are you going to do? Is there an antiviral you could treat them with? No.

DG: Yes, no, we don't. Yes, we don't have any effective treatment. Really nice figures, though. It's really nice to look at this. Also, to make a point of, I'm not sure that five days is really enough if you look at the time of clearance. You probably need to say a week. I know we've gotten our carpal unit quarantine, but it really should be a Constantine unit quarantine, the seven days, thanks to Emperor Constantine.

VR: What's interesting here is that the viral RNA persists longer than infectious virus. This is very common in RNA virus infections. Just because you're PCR positive does not mean you're infectious. We had this discussion all the time with SARS-CoV-2.

DG: It's amazing. I'm not sure everyone's gotten the memo, but yes, just the fact that you pick up the RNA or the antigen does not mean you have infectious virus there. You need to do a different test to find out.

VR: Which we don't do.

DG: No.

VR: A study like this will give you a guideline. It's your window.

DG: At least you get a sense. Yes, you get a sense here. They've got infectious virus. They do this time since exposure. They've basically, you're about six days out, is when you start to see infectious virus. It goes out to just a little past 11, so maybe the five is OK with that. Then the PCR is staying positive right out to day 15, so that's going to stay positive.

VR: Remember that you can have infectious virus, but may not be enough to transmit to someone. That's the key.

DG: It's not a binary. It has to be a certain amount. All right, COVID. We've got our updated, multicolored curves, and it looks really good. Actually, I'll tell people, go to the link, go to this, and I'll leave the link into it because you've got this slider thing where you can adjust where you want to look, and by adjusting where you want to look, you can zoom in. You can really see that we're down. We're actually probably as low as we've been since the early days, since before the pandemic. We are really at a super low level of SARS-CoV-2 in our WVAL.

VR: Daniel, why don't I see the July 2025 spike here?

DG: Yes, I don't know. It's actually strange when I zoomed in. I was like, "Where is that, and why is it -"

VR: Because you see a really big spike about a year ago, last December. It's much higher than it was this past year, which is interesting.

DG: Yes, it is strange.

VR: You should see that because in other charts that we look at, we do see the summer outbreak, but not here.

DG: I like the old chart, actually, by the way, [laughs] when they start changing how we get to see our data. You get used to it. You have a certain expectation. Well, what about vaccination for COVID? Is it worth it? Are we done with that? Well, the article, "Clinical and Economic Benefits of Seasonal COVID-19 Vaccination in Germany: Results from the ROUTINE-COV19 Study, September 2022 to March 2024," published in *Eurosurveillance.* These are results of a retrospective, real-world study based on German claims data provided by a regional SHI fund, which covers more than 3.4 million individuals in two German states, accounting for about 50% of the population in these states, so really huge.

The dataset contained comprehensive information on outpatient, inpatient services, pharmaceutical treatments, diagnostic codes, procedures, vaccination records, rehab, work absences, demographic characteristics, age, sex, so a ton of data. Now, 73,066 vaccinated individuals were successfully matched to 73,067 unvaccinated individuals. After matching, the two groups really highly comparable, mean age about the same, same breakdown sex-wise. The rate of documented SARS-CoV-2 infection was 1.04 per 100 patient years in the vaccinated group versus 1.21 in the unvaccinated group, so relative risk of 0.86, but overlapping confidence intervals.

Then we look at, and this is really the issue here. For incident Long COVID diagnoses, we're seeing a relative risk of 0.43, so more than a 50%, so basically a 57% reduction in folks that get Long COVID, and really nice figure here. We can see a reduction in overall respiratory illnesses. You could say a trend. I want to point out a non-statistically significant trend towards less SARS-CoV-2 infection, but a really dramatic reduction in folks that end up getting Long COVID.

If you look at more severe stuff, this is what we care about, right, Vincent? We don't just care about a positive test. COVID-19-related hospitalizations, relative risk, 0.41. It's about a

60% reduction in ending up in the hospital due to COVID. Actually, if you look at respiratory infection-related hospitalization, that was also reduced.

VR: Yes. When you look at disease, you get a really big impact because infection is not supposed to be stopped by vaccination. That's why it's not statistically significant. Long COVID, hospitalizations, it's great. It's really good.

DG: I think that's the point. I think sometimes people miss that. Even all-cause mortality, there's a third where you see that. You see a really statistically significant reduction in not only all-cause mortality, but even more dramatic with COVID-19-related in-hospital mortality. Really impressive. Yes, they conclude, and just putting it all together, COVID-19 vaccination under routine care conditions in these two areas was associated with reductions in morbidity, mortality, healthcare utilization, and, actually, indirect costs. It saves money to get folks vaccinated versus ending up having to pay for all this.

VR: If you're scared of Long COVID, there's one solution: get vaccinated.

DG: Imagine that. What is it? The answer is never violence. It's always get vaccinated.

[laughter]

VR: They're trying to say people are scared of getting vaccinated, and this should not be.

DG: Yes, they've been lied to. People are lying to them. They're scaring people. That's just wrong. The open-access article, I like to point out, when people are open access in their articles, "Effectiveness and Safety of Molnupiravir among Patients with Mild to Moderate COVID-19: A Prospective, Observational, Cohort Study," published in *Scientific Reports.* Cut to the chase. Yes, not really doing much. These are the results of a multi-center prospective observational study that included all mild adult COVID-19 cases for whom molnupiravir was recommended at healthcare institutions in two cities in Turkey.

These included six primary care centers, six tertiary care hospitals in Istanbul, one primary care center, two tertiary care hospitals in Ankara. This is from March 29, 2022, to September 29, 2023. During the early and late phase of the study, Omicron BA275 and XBB1 were the circulating variants. The primary outcome was hospitalization, death, or new oxygen need due to COVID-19 within 28 days of follow-up. They look at the effects of molnupiravir on viral clearance, biochemical tests, antibody levels.

Total of 844 patients, 402 molnupiravir, 442 no molnupiravir. Mean age was 66. 75% were vaccinated. Primary outcome occurs in eight patients with no significant difference between the groups. molnupiravir showed no effect on clinical improvement. Viral clearance was higher in the molnupiravir group on day three, but higher in the untreated group by day 10. Serum SARS-CoV-2 antibodies on day 28 were lower in the molnupiravir group. The effectiveness of molnupiravir in reducing hospitalization and death may be insufficient in previously immune COVID-19 patients.

VR: Is this the case where they get molnupiravir in hospital or before they go to the hospital?

DG: This is all across the board. You've got primary care. You've got hospitals. Basically, the whole gamut of people being recommended molnupiravir, really not seeing much of a

difference.

VR: Because remember, in the original studies, there was about a 30% reduction to hospitalization. I don't know why there's a difference. You don't think the strain matters, the variant matters?

DG: I don't think it's the strain or the variant. Now that we're seeing 75% of folks vaccinated. That 30% is just really not enough in this group to show a significant impact. It was a disappointment, unfortunately, with molnupiravir. It's never really gotten what we were hoping from the early preliminary data.

VR: It would have been nice because it's an oral medication.

DG: It's oral, no drug-drug interactions. It's just a very easy lift, except it doesn't really work. All right. We have a couple here in our Long COVID section. By a couple, I mean two. The open-access article, "Divergent Inflammatory and Neurology-Related Protein Levels in Long COVID Following Primary and Post-vaccination SARS-CoV-2 Infection." They say breakthrough, they use that word. Published in *Communications Medicine*.

The title could use some work on several levels. For background, they start off with, "while persistent inflammation has emerged as an important feature of this condition, it is unclear if immune responses from COVID-19 vaccination or SARS-CoV-2 reinfection exacerbate or mirror the initial inflammatory responses."

I'm not sure about this title. Let's talk about what do they actually do. They're going to quantify 182 inflammatory and neurology-related proteins in plasma using multiplexed proteomics. Plasma samples from the COVID profile cohort conducted in Victoria, Australia, were collected six to nine months after first infection, but before COVID-19 vaccination from individuals who had recovered from COVID-19. We've got 21.

From individuals with Long COVID, we've got 12. This is to establish baseline plasma profiles. Protein levels were benchmarked against unvaccinated SARS-CoV-2 naive individuals. We've got N of 24. They also performed longitudinal analysis in a subset of individuals, 34 folks, where paired samples collected two to three weeks after a third COVID-19 vaccination and after SARS-CoV-2 post-vaccination infection that were available to assess inflammatory and neurology protein plasma levels after antigen exposure in these contexts.

After employing some interesting methodology to analyze the data, they find that the immune signature is different between what we see with vaccination and what we see with infection after vaccination. I'll leave in a link.

VR: What does that mean?

DG: It's only interesting in my mind. You say, yes, the way we respond to a vaccine is different than the way we respond to an infection. I think we knew that, but there it is. There it is. This is something I was actually talking with my wife earlier today. It is amazing. A little girl that I'm continuing to help guide through the Long COVID process, and I may have mentioned this young girl in prior *TWiVs*. I'm still helping the mom and her navigate things. She's now 14, so she's younger. I've always tried to help her primary providers take care of her.

She was a little girl that her parents wheeled her into the office in a wheelchair. This is a little girl who danced and played and was a normal child, after COVID, ends up in a wheelchair. Now she's had some issues. She got another repeat infection, ended up in the children's hospital. Just this amazing thing, we've talked about this. There are multiple clinics out there with hundreds of kids in these clinics, thousands of kids when you add them up, who are still suffering from Long COVID.

Here, this article, “School Difficulties and Long COVID in Children and Adolescents,” was published in *Academic Pediatrics*. In this study, cross-sectional data from the NIH-funded Research in COVID to Enhance Recovery, pediatric observational cohort was analyzed to assess associations in school-age children, 6 to 11, adolescents 12 to 17, between Long COVID and caregiver-supported school-related functional outcomes. Here, the LC, the Long COVID, was defined using the RECOVER age group-specific symptom-based LC research indices.

Primary outcome was worsening of child grades. Secondary outcomes included difficulty paying attention, limited fun with friends, and having or requiring an individualized education program, so an IEP. The cohort included 1,976 children, 406 school-age, 1,570 adolescent. 18% of the school-age children, and 29% of adolescents with Long COVID had reported worsening grades compared to 7% and 11% without Long COVID. This is a relative risk of 2.18, more than twice. Adolescent, relative risk 2.39, so even more. In both age groups, children with Long COVID were more likely to have difficulty paying attention, limited fun with friends, and required individualized education programs.

VR: Long COVID is a chronic illness. RFK Jr. says he wants to deal with chronic illnesses. Let's get on it, RFK Jr.

DG: The only bright side here is when this new group came in, they initially wanted to cut all funding for Long COVID research. Remember that quote? “We have better things to spend our time and money on.” Oh, my gosh. All these, and here we have little kids suffering, issues paying attention, issues participating in school, issue playing with their friends. These are little kids, come on. These are things where we really need to work so that we have treatments that we have hope for these little kids.

No one is safe until everyone is safe. We're just wrapping up our Floating Doctors fundraiser, hoping to double your donations. This last week, actually, we had some pretty good donations. Thank you, all the people that are stepping up. There's not much time left for us to get to our target and give our maximum donation of $10,000 to Floating Doctors.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Mark writes, "When my daughter was pregnant, she received the ABRYSVO RSV vaccine during her third trimester. Shortly after the baby arrived, RSV swept through the house. The toddler brought home a mild cold from preschool, and the visiting sister became quite sick and tested positive for RSV. The father also became ill. Remarkably, the mother and the newborn stayed healthy.

While Abrysovo is officially licensed to protect the infant, and Beyfortus may be slightly better at protecting the baby than Abrysvo, this anecdote suggests it may provide a bonus layer of protection for the mother, too, which was very helpful in a busy household with a newborn and a two-year-old."

DG: I like that, Mark. Unfortunately, it's the anecdotes that drive people, great data, and N of this and relative risk, but you tell a story about here's this mom, and oh my gosh, you've got the little baby, you're exhausted, the last thing you need is to have a bad case of RSV. Here's the like, "Hey, you get this vaccine, not only going to protect your baby, but it's actually going to protect you because you might end up getting RSV because the other little kids in the house, et cetera." Great story.

VR: Eric writes, "Are you aware of any evidence that Xofluza does not work well against the A strain of flu? Last week, during a visit to my son's doctor while waiting for the results of his rapid flu test to come back, his pediatrician suggested he may prescribe him Tamiflu if the test came back positive. As a dutiful listener of your weekly updates, I of course said, 'But what about Xofluza? Isn't it more effective than Tamiflu according to the research?' He replied that Xofluza didn't work well against the A strain of flu and that those were the cases that he'd been seeing lately in the Bay Area where we live.

Fortunately or unfortunately, the test came back positive for flu B, so we agreed to prescribe Xofluza for my son who subsequently experienced a quick recovery. Thank you for insights and always evidence-based guidance.'

DG: Oh, Eric. Oh, Eric. I feel so bad. This is one of those things. Hopefully, it was just an honest mistake by a busy clinician, and maybe they'll listen to this episode and get it straightened out. As you point out, the research suggests it might be a little bit better than Tamiflu.

VR: Ellen writes, "For those of us in our low 80s who had the most recent vaccination last fall, should we get another vaccination now, six months later, although COVID is not widespread at the moment and the current vaccine seems to be less effective against the new variant? Getting it now would give us the six-month window until the fall, when we should get vaccinated for the coming expected winter season, and hopefully, a newer, more effective vaccine will be available. Any thoughts would be, as usual, most appreciated."

DG: Yes. We've talked about the fact that the timing of the coverage, the effectiveness of the vaccine, and the 12 months of the year, they don't always know exactly. It needs to stagger the surges every six months. That would be very convenient if the virus was staying on our calendar. What you really want to think about is usually we start to have a climb in July, August into September. June is a great time to get a vaccine. Then we get a little bit of a pause. Then November, we tend to move into the next one. Thanksgiving, Christmas, November, December, January, February, we get into that. That's why early November or late October is the other time.

Those are not exactly six months apart, but that's fine. This whole idea that, oh, I have to wait six months and a day to stay on this cadence, what really is important is the timing of the vaccine before that next surge, because we really see about a six-month protection.

VR: Jordan writes, "I have a patient who contracted dengue virus infection this winter in Costa Rica. He's planning on living there six months out of the year going forward. Two questions. Would it be beneficial for him to get a dengue vaccine, and how would I get one for him in Colorado? He's in his mid-50s and healthy. I wrote to the CDC, and they essentially reiterated what's available on the website, that there are three vaccines, only one, Dengvaxia, in the U.S., and it is not recommended for adults. I feel their reply is directed at U.S. travelers in general and not this specific situation. Been watching *TWiV* and

its community for five years now. Thanks for all you do."

DG: Yes, there's some interesting features here. One of the issues with dengue is you get one infection from dengue, you survive it, and then the concern is you get a second infection with a different serotype. Maybe you get dengue 3, and then next time you get dengue 2. Maybe you get dengue 2, next time you get dengue 1. Particularly as time goes by, you get this antibody-dependent enhancement. People get worse. What is sort of an issue is people who get sick in Costa Rica, now they're going to go live in some area where there's a different serotype of dengue circulating.

In a sense, there's sort of an advantage. Like, OK, if you got sick in Costa Rica and you're going to go live in Costa Rica, maybe that's going to be less risky than going somewhere else. What I would say, and I think now that we have vaccines here, is this is a perfect person to go have a discussion with a travel medicine doc and then sort of look at the risk/benefits of protection going ahead and potentially getting the Dengvaxia.

VR: Jeffrey writes, "I listened, as always, to *TWiV c*linical update 1314 today. As a cardiologist, I take umbrage that cardiologists are unaware of the importance of inflammation in the precipitation of myocardial infarctions and other acute ischemic events. This topic has been on the front burner of research in the genesis of plaque activation for over 30 years. I refer to, most notably, the work of Dr. Paul Richter at Harvard. Also, the recent reviews on the importance of adipokines by Dr. Milton Packer at Baylor." Milton Packer used to be at Columbia. Remember him?

DG: Yes.

VR: "Practicing cardiologists have been well aware of acute MI following severe respiratory infections for years. It is, however, very encouraging to see data on vaccines, and it reinforces the routine use of vaccines. Thanks for letting me rant."

DG: No, Jeff, I appreciate this. When I went to medical school at NYU, and that was last century already, that was the teaching, this whole idea of unstable plaques. It wasn't just, oh, the plaque gets narrower and narrower, and then you have your MI. The idea was you have this unstable plaque, and maybe some of the things the statins do are helping to stabilize those plaques. This is one of those tricky things.

Yes, we keep trying to push this message that your risk of an MI goes up after some of these viral infections. Yes, to be honest, the educated cardiologists, a lot of those that I work with, they're aware. We're really preaching to the audience, preaching to the folks, like, hey, another good reason to get a flu vaccine or an RSV vaccine or a COVID vaccine is think of it as protecting your heart type vaccine. We love to give cardiologists a hard time.

VR: It's mainly because the pundit cardiologists who like to talk all the time and don't know what they're talking about, not the practicing ones.

DG: Yes. Unfortunately, there's a new book out, *Comma*. Unfortunately, the author of that book was on some kind of a web thing with that particular cardiologist who will remain unmentioned. What his first question was, "Oh, have you looked at much about the single-cell sequencing data?" I'm like, "Did you read the book, buddy?" A little annoyed with that particular cardiologist at the moment. I'm like, "Come on. If you can take the time to be on the show and self-promote, take the time and read the book.

VR: Right, of course. Finally, Kafi writes, Kafi doesn't have a record of polio vaccine. "I am contemplating taking the polio vaccine, hearing about the spread of polio through excrement following vaccination. I wonder whether there's a way to kill the virus before the toilet is flushed. Disinfectant, Clorox, other, if feasible. Any suggestions for a technique regarding length of time to allow disinfectant to be effective before flushing? How many days should such a treatment continue in order to be effective? Certainly would prefer preventing spread to others."

DG: All right, Kafi. We got a lot to talk about. I'll go first, but Vincent, I'm sure, is not going to leave this without comment. The first is we really should be just using inactivated polio vaccine. We should not be using oral polio vaccine.

VR: Globally, yes.

DG: Just globally. Here in the U.S., very clearly, we don't. Why do we not use oral polio vaccine in the U.S.? Because we do not agree with vaccinating kids and then paralyzing a certain number of them, because that's what happens. There was all this. Actually, in that book that I was mentioning, there was a whole discussion about the new, the novel oral polio vaccine. It's going to be so great. It's paralyzing kids. It's not great.

What is great is using a vaccine technology that does not result in paralyzed children. If you go ahead and you get the injected inactivated polio vaccine, you don't have to worry about this. You don't have to worry about shedding this maybe reassorted or recombined or changed, now virulent polio virus. As I think we've talked about, Vincent, you can comment on this as well. There was this original idea that, oh, but if you take the oral, then that's going to give you this long-lasting gut immunity. The injected polio vaccine gives you really similar if you look many, many months out. Thoughts?

VR: The way polio is spread is not from your toilet, but from you. You go to the toilet, and then you don't wash your hands, and then you have polio virus on your hands, and you give it to someone else. If you're shedding polio virus, first of all, you don't know it. Many people in this country probably are. You should just get vaccinated. It's not going to stop you shedding, but at least you're not going to get polio if you haven't been vaccinated. You and everybody in your house should get vaccinated, and that's the solution. You could throw bleach in your toilet, but that's not really a long-term solution because you could shed for a long period of time.

DG: I think that's a misconception, Vincent, that people have. They have this idea that we look in wastewater, and they think, "Oh, well, the wastewater is how it's getting." That was even in this book, that somehow it gets from the wastewater to other people, but that's not what happens. It's you've got polio. You've got the virus. You're shedding it. You go to the bathroom. The stuff that goes in the toilet gets flushed. That's all good, but the stuff that's on your hands because you didn't do a really good job of washing your hands. Then you go back out to that barbecue, which is what happened in New York. You go back to that barbecue, and you're shaking hands. You're touching stuff.

You're getting infectious virus on stuff. You are directly transmitting it to other people. It's not going from the wastewater to other people.

VR: Yes. Polio is a virus transmitted in waste, fecal material, but it doesn't go from wastewater to people, as you say. Neither does flu or RSV or COVID that we look for in

wastewater. It's a sentinel to tell us how many people are infected, basically. Get vaccinated. That's *TWiV, w*eekly clinical update. With Dr. Daniel Griffin. Thank you, Daniel.

Daniel: Thank you, and everyone, be safe.

[music]

[pause 00:53:17]

[00:53:33] [END OF AUDIO]