This Week in Virology

TWiV 1168 Clinical Update

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Guest: Daniel Griffin

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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 1168, recorded on November 21, 2024. 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've got this black and white bow tie with icosahedra on it.

DG: Can the Rotary Club symbol anywhere there?

VR: Must be polio then, right?

DG: Maybe, if it's really true that polio is caused by a virus. Maybe we'll talk about it today.

VR You mean I spent 40 years of my career working on what I thought was a virus, but really isn't? It's like Tony Fauci said, "I spent 40 years working on infectious diseases, and my goal was to convince rednecks to wear a mask." That's what my career goal was, right? Yes.

DG: All right. I was just over in London visiting my son, Barnaby, who's studying over there. I haven't seen him since August. We visited the Churchill War Bunker.

VR: Very interesting place. I enjoyed that very much.

DG: It's worth a visit. Then we watched the *Doctor Who* episode, something with the Daleks, where you actually see some scenes that are mocked up. I don't know if they were shot in the War Bunker. I was looking for a Churchill quotation. What I realized is a lot of times things are

attributed to someone. They never actually said it. It was really someone else. Misattributed. It turns out that this quotation that I'm going to use for our episode today is actually from Victor Hugo, the author of *Les Mis, Les Misérables*. Also wrote *The Hunchback of Notre Dame*. Actually, my wife, Jessica, and Barnaby saw that play in London the night that I was flying the red eye to get there. Here we go. "You have enemies? Good. That means you've stood up for something sometime in your life." We'll see where that fits in.

VR: I know some politicians who have a lot of enemies, and I'm not sure it's from standing up to someone.

DG: Unfortunately, now as we're learning, scientists and physicians have somehow gotten a collection of enemies. Just a public service announcement. We are in the middle of that McDonald's E. coli outbreak. Since the CDC launched an investigation just back in October, October 22, the Shiga toxin-producing E. coli outbreak has sickened over 100 people, over 30 people hospitalized, four cases of folks with that life-threatening kidney disease called hemolytic uremic syndrome, the death of a man in Colorado. Apparently, this is all coming from contaminated onions.

VR: Always hold the onions at McDonald's.

DG: Yes, maybe that's just the thing for now. Just if you're going to go to McDonald's, hold the onions.

VR: I don't really visit, but someone told me if you ask for something without onions, they have to make it fresh so they don't use one that's sitting around for hours.

DG: Oh, so it's a way to get fresh food.

VR: Now there's even a better reason because it makes you sick.

DG: You might die. You might end up with kidney failure. You might end up in the hospital. I think you do that fundraiser at the beginning of each one, but I'm going to talk about the anti-science and anti-vaccine movement briefly and just say that we need your support, listeners, we need your support now more than ever. I appreciate all the emails expressing appreciation for what we did during the pandemic. Right now we need your dollars to continue our work. Now, right now I think many people are concerned about where they can get reliable information.

I've gotten a number of questions about some new people that might be involved in some of our institutions in the next administration, really specifically RFK Jr., but some others. I really want to stick to sharing science and medical knowledge, so I want to spend very little time on this. More than anything, I'm going to give people some links to where they can go to get more. I will briefly make some comments. First off, qualifier, I have never actually met RFK Jr. myself, unlike President-elect Donald Trump, who I have actually met, but that's a story for another day.

Initially, some of what RFK Jr. says sounds positive at first glance. I recently listened to a one-hour talk that he gave. He's a good speaker. He started out as an attorney working to clean up our rivers and force big corporations to be compliant with the Clean Water Act. Dickson

and I are happy, clean up those rivers so we can go fly fishing with our kids, grandkids. He suggests that we exercise and eat a better diet. He suggests we reduce all the processed food we eat, but then throws me a little and wants us to stop using canola oils and instead deep fry our foods in lard.

Apparently, he will eat at McDonald's when they start deep frying their fries in lard. OK [laughs]. He also talks about how important science education is. He wants people to have access to the information they need to make educated decisions about their health and the health of their children. Maybe, if he has a role in our next administration, he's going to leave a link into *This Week in Virology* right where they can come, but maybe not. RFK Jr. has come to some interesting, concerning conclusions when he reads the scientific literature, such as advancing the idea that HIV AIDS is caused by lifestyle choices and not due to an infection.

That's concerning and wrong. He suggested that polio is due to toxins in the environment and not due to a viral infection and has recommended against vaccination. I'll leave in some links here so our listeners have a chance to read more and understand why so many people are concerned. One place people can go to is factcheck.org. Leave a link in there. They start by writing RFK Jr. or Robert F. Kennedy Jr. is no stranger to factcheck.org. One of Kennedy's most common and pernicious false claims is that vaccines are not tested for safety in clinical trials.

"Vaccines are the only medical product that is not safety tested prior to licensure," Kennedy said in a July 15 *Fox & Friends* interview. "We should have the same testing, placebo-controlled trials, that we have for every other medication," he also said to *Fox News*. "Vaccines are exempt from pre-licensed placebo-controlled trials. None of the vaccines are ever subjected to true placebo-controlled trials," Kennedy said in an episode of *The Joe Rogan Experience*. "It's the only medical product that is exempt from that prior to licensure." Kennedy's been saying this for years.

Our listeners, they know otherwise, right? We've shared studies on the COVID vaccines. All vaccines undergo, I guess, pre-safety testing prior to authorization or approval and continue to be monitored afterwards. To claim the vaccines are not tested for safety, it's just false. It's lying. The first polio vaccine was famously tested. I was actually reviewing this. You can get a PDF of the original articles from the 1950s. The massive placebo-controlled trial with more than 600,000 children, and I'll leave in a link to that. The COVID vaccines and the newly approved RSV vaccines for older adults are recent examples of shots that were tested in placebo-controlled trials.

In December, Kennedy falsely claimed the COVID-19 vaccine was the deadliest vaccine ever made, citing deaths reported to the vaccine adverse event reporting system. We've talked about it. I'm going to leave in links. We talked about when the Pfizer-BioNTech vaccine trial was published in *The New England Journal.* Participants in the trial were randomly assigned in a one-to-one ratio to get either the vaccine or saline placebo. That's what RFK Jr. says he wants. Moderna, efficacy and safety of mRNA-1273 SARS-CoV-2 vaccine. This was, again, the mRNA-1273 vaccine provided as a sterile liquid, was administered by injection, injections were given 28 days apart, or saline placebo.

Very clearly, here he is saying things that are not true. We'll leave in a link to a - I watched this, Vincent, this five-minute video summarizing a lot of the false information propagated by

RFK Jr. I just want to not fail to mention the fact that, yes, this can lead to bad outcomes. I want to just talk about the Samoa incident because this is a very recent, this is just right before this pandemic. Samoa incident in 2018, two infants in American Samoa died when nurses accidentally prepared the vaccine, the measles/mumps/rubella, with expired muscle relaxant rather than water.

Instead of putting in the diluent, the water, they add an expired muscle relaxant, paralyze the two children, and they die. It's not the vaccine. It's the fact that they just injected two children with a muscle relaxant. Now the Samoan government temporarily suspended the vaccination program. Anti-vaccine advocates flood in, including Kennedy and his nonprofit. They flood the area with misinformation. The vaccination rate dropped to a dangerously low level. The next year, a traveler shows up with measles, spreads through the population. We end up with more than 5,700 people sickened, end up with over 80 deaths, mostly in little children.

The Samoan government's like, "We have nothing to do with you. No thank you. We just have 80 dead children." That's a problem. This is not innocuous. You have to be honest. I still don't get how you can get away with lying and people still listen to you. I'm leaving a couple more links. I also want to make it clear that this should not be a partisan issue. We have people who are Democrats. We have people who are Republicans. We have people who support the Green Party, the Working Families Party, the DSA. This didn't just start in 2016 when a Republican administration came in.

I'm going to leave a link into a *Wall Street Journal* article that was recently shared with me. I actually read it, but then it was shared. I'll put it in there. It's, “How Science Lost America's Trust and Surrendered Health Policy to Skeptics.” I want to take a certain responsibility, and Vince and I can discuss this. They suggest, I'm not going to agree with everything they say, they suggest that lingering resentment over pandemic restrictions helped Kennedy and his Make America Healthy Again campaign draw people from the left and the right.

First of all, I'm not sure how true this is. As these lockdowns that people are upset mostly happened under Trump during 2020, year one of the pandemic. There's a disconnect there. Then we have, and this I'll agree with, doctors, scientists, and public health officials are asking themselves how they can win this trust back among their post-election revelations. Don't underestimate or talk down to those without a medical degree. I thought this would be a good chance for you and I to have a few -

VR: What's interesting is that since he's been nominated for head of HHS, and this is why you can never believe a word he says, he says, "Oh, I don't want to take away your vaccines. I just want you to have the safety information that you need." As you know, the safety information is all out there already. It's on websites. All the pre-licensure and licensure information is there. Most people choose not to read it. What is he going to do? I just don't understand. There was a good op-ed in *The New York* Times by Michael Osterholm where he said, "It's not clear what data RFK Jr. wants because it's all out there already. He wants parents to make a decision about vaccinating their kids, which is just a disaster in the making."

DG: Yes. There's a couple of points. What is the story? Polio is not actually due to an infection, Vincent?

VR: This is crazy. This is just crazy. It spreads with all the characteristics of an infection. We made a vaccine against the virus and that stops paralysis. Even we made a vaccine that causes some paralysis. The virus is causing it. There's just no question. As I said earlier, I spent 40 years of my life working on poliovirus. I can guarantee that it is a virus.

DG: Yes. That's number one. It is too. I think we all know that. I think most of us actually believe in germ theory. HIV due to lifestyle, that's just, how outdated and offensive to suggest that, people are sick because "they deserve to, they made lifestyle choices." Mercury. Interesting, right? I understand the history. Get the heavy metals out of our rivers, and there was a whole discussion. We've talked about, mercury, which has now been out of the vaccines like 20 years now. The only vaccine that a child might get would be these multi-dose flu vaccines, which you can choose to get the single dose.

Right now, mercury is out of the childhood vaccines. I don't think autism has suddenly dropped. That becomes sort of an issue because that was their argument. The reason we're seeing autism is you got mercury. We got to get that out of the vaccines. It's out of the vaccines, it's kind of the issue. Maybe we need a diet specialist. Should I really be deep frying my food in lard? It sounds great because I want everyone to eat healthy and by that deep frying your food in lard. OK. I actually go to McDonald's every so often, Vincent, not very often, but yes. I do the Big Mac and I usually get it with the onions on there.

VR: Yes, you could get a fresh one, just hold the onions.

DG: The other, I guess, is this issue, is it worth debating someone who's disingenuous? I've watched the discussions. If you're really not actually wanting to learn and listen, which is what we want to do in science, if your goal is just to win the argument and sway people over, that's not productive. I think that's an issue. As I started off and I'll circle right back to, this is not a partisan issue. I think there is a communication issue. When we got these vaccines, a ton of money was spent getting people access to those COVID-19 vaccines.

How much of our federal budget went to communication? Zero. I think that's a mistake. I think it's reasonable. If you sit down, you say, "I want to make an appointment to discuss a vaccine with my doctor." Our current system doesn't - what code do I put for that? They want to spend maybe half an hour. I'm happy to have that conversation, but our system doesn't really do that. Then, Vincent, what's this Project 2025, what's up with that?

VR: The project, the 2025 is a 900-page document, which is the blueprint for how the conservative right feels that the government should look like in 2025. It includes taking away all power from CDC to make any kinds of recommendations, taking away a lot of the power of the NIH and also of the FDA. I don't know if you've heard, Daniel, but RFK Jr. has said he's going to have an eight-year pause on infectious disease research. What do you think about that?

DG: I actually, I listened to that, to that presentation. Why eight years? I was like, "Why eight years?" Then it occurred to me, this is when he was still running for president. He thought he was going to beat Trump and he was going to win and the eight years were his two terms. He was going to somehow, basically, we're going to stop doing research on infectious disease. Maybe we'll circle back to this, but does that mean like, "Hey, if you've got Long Covid too

bad, that was your fault. You should have been healthier and getting more of a suntan and eating more deep-fried foods."

VR: No Long Covid research, that would be gone.

DG: Which is a disaster. Eight years of no more training people so after that eight years, then yes.

VR: Also, if we have an H5N1 pandemic, can't do any research.

DG: No. No. I don't see how this jibes with the Trump administration. Trump was the one who was the head of the ship, so to speak, when we had operation warp speed using my Star Trek analogies there. Billions of dollars were spent on getting us a vaccine that really turned things around. How is RFK - I know Trump would like to take credit for that. I don't know how this will go forward.

VR: No reasonable person would agree to suspending infectious disease research for eight years. It makes zero sense. It is the idea of someone who knows nothing about infectious diseases. I'm sure RFK Jr. has all his vaccines, by the way, Daniel.

DG: He did, but apparently it's because his wife told him he had to.

VR: I see.

DG: Apparently, yes. Apparently people wanted to come over to a party at his house. They had to test themselves before they came. I don't know what they're testing themselves for if viruses don't cause COVID. It's not funny. It's very troubling. To point out that this did not all just start, we're going to jump into measles with the article, “Measles: What Goes Around, Comes Around,” published in *JID*. Did you have any last words before I jump forward to the actual science?

VR: Yes, I want you to go to this website, which is safecommunitiescoalition.org/RFK. It will have a place where you can write a short letter to your senator and hit a button and they will email it to your senator. Everybody needs to do this. Write a letter saying, "Do not confirm RFK Jr. for head of HHS because he has anti-science views that are not -" HHS is in charge of American's health and he is not going to do that by suspending ID research for eight years. Safecommunitiescoalition.org/RFK, it's really great. They even have a little draft letter for you there that you just need to fill in who you are and where you live.

DG: OK. Published in JID. This is not going well with measles. So far this year, and then we have data up to November 7, almost 300 measles case reported in the United States. This is the most since 2019. Most since pre COVID-19 pandemic, and I'll leave in a link to the most current CDC data on that, which hopefully we'll still be allowed to keep getting. Back in 2019, that year we saw over a thousand measles cases and we hadn't seen a number that high since 1992. A couple of things to say, measles is a big deal compared to how well the vaccine is tolerated.

Forty percent of the measles cases so far this year ended up in folks being hospitalized. This isn't just, "Oh, I got a rash." Of the folks that got measles, unvaccinated or we just don't know

the status, that was 89%, only had one dose, 7%. We're talking about 96% of folks where they're unvaccinated or not fully, only 4% of folks that actually had two MMR doses. I'm going to leave a link into a really nice figure. It goes back to the 1960s and you can see this back when we're having smaller population back then, we're having about half a million reported measles cases per year in the United States.

Then in the 1960s, we get the vaccine is licensed, 1963. By the end of the 1960s, we are down to a few thousand cases a year. You see a few little blips. Then someone comes along and says, "Maybe we should be giving a second dose. Maybe one's not enough. Give the second dose, gets introduced in the end of the '80s, 1989." Then we really see this really low level. Actually, in 2000, elimination is declared because now we're just seeing a few hundred cases a year down from half a million. Just want to point that out.

VR: Now it's back.

DG: Now it's back. Yes. Now it's back. Just to go like, what is going on? Part of the issue is that we've been losing ground on vaccinations for a while. I want to point that out. This didn't just happen in the last four or five years. This is not that, "Oh, when we introduced COVID-19 vaccines and mandated, that's when things went south." I actually put in, and maybe David, will put these up for the YouTube folks to watch. If you look in 2023-2024, where we have data, there's a nice map of the U.S. Where are the places where we have that goal of greater than 95% coverage? It's only a few states. It's California. It's New Mexico. It's Mississippi. I now can get that right because I know where the river is. What is that right above there? Is that Tennessee?

VR: Yes. Tennessee, it looks like a trapezoid almost. Then the one above it, which doesn't look at all like a trapezoid is Kentucky.

DG: Yes. Kentucky, not so good. Ohio. Ohio, less than 90%. Minnesota, Iowa, Wisconsin, less than 90%. Florida, Georgia, less than 90%. Really a lot of these areas. Go back to 2009, 2010. It's almost like the map changed a little. Back then, Texas, New Mexico, Oklahoma, Louisiana, Mississippi, Arkansas, all doing great over 90%. California was actually not doing so great back then. Worldwide, we're not doing well. There was an estimated more than 10 million cases of measles in 2023, which is a 20% increase over 2022. We are well into issues with vaccinations.

All right. Flu. We're starting to see a trickle. We're starting to see some flu cases, I'll say. We have the article, “Underutilization of Influenza Antiviral Treatment Among Children and Adolescents at Higher Risk for Influenza-Associated Complications — United States, 2023–2024.” This was in the *MMWR*. You can see from 2017-2018, folks were doing a pretty good job. Eighty-six percent of high-risk children were actually getting antiviral medication. These are hospitalized kids. Here we have it dropping down to 59%.

VR: Daniel, if you go to the hospital with flu, is it too late to be getting an antiviral?

DG: It isn't, actually. It's part of this idea that the people who end up sick enough to end up in the hospital may have a prolonged period of viral replication, because in general, we know in the outpatient studies, you really got to get your antiviral in the first 48 hours. This is that interesting. If you end up sick enough that you end up in the hospital, there still is a benefit.

These are children, teens hospitalized with suspected or confirmed flu. They're not even treating them.

Mpox, just give everyone an update there. Danish Biotech Bavarian Nordic said on Friday, and that was last Friday, "Lots of orders." Orders for delivery of its vaccine for mpox and smallpox in 2025 currently totals around 2.4 billion krones. That's $340 million U.S. People knew what a krone was, but it's the Danish dollar or something, the Danish currency.

I think the big thing here is that we missed a lot. We have the article, “Serological Evidence of Mpox Virus Infection During Peak Mpox Transmission in New York City, July to August 2022,” published in *JID.* A really simple concept here was to draw some blood and ask whether we had missed a lot of those mpox infections. Are people going to test positive for having a prior infection? Maybe we just missed that. They found that approximately one in 15, and these are vaccine-naive people, a little over 6% in this study, had antibodies to mpox during the height of the New York City outbreak, indicating that, yes, we missed a bunch.

Overall seroprevalence was 6.4%. Then they break it down, about 4% among cis women, so women still identifying as women, born as women, 7% among cis men. There really was a little bit of variation, but not a lot of variation based upon race or ethnicity or age group or HIV status or even number of recent sex partners. I think the big takeaway is we missed a bunch.

RSV, starting to see a little bit of activity. I was enjoying explaining this to an unfortunate woman who ended up in the hospital with RSV, was consulted on earlier today. I think there's a growing awareness.

We're starting to see moderate activity in Wisconsin, in Ohio, in Maryland, in Connecticut. Little interesting, usually, we see that pattern where it comes up from Florida and Georgia. We're seeing this spottiness, and I don't know what's going on with Maryland. We'll circle right back to that with COVID. That seems to be the only area with that 2% to 4% activity, provisional deaths due to COVID-19 in the past week. Everyone else is in that less than 2% across the country. The wastewater, it's still down, Vincent.

VR: Looking good. Very good.

DG: If your bets are in, except for-- what is that, the Midwest is maybe starting to come up a little bit there, if you look closely?

VR: Yes, maybe. We're at the end of November, and last year, it went up at the beginning of November. It's not a big difference in timing, but I'm hoping for the best.

Daniel: Yes. We'll see. Last year, it really started to go up end of November. We saw our peak end of December, January. We'll see. I would love, if you were correct, Vincent, if we actually got so much immunity in this last summer surge that we had a quiet winter. I think we could use a break.

VR: I have a question for you, Daniel. We try and match the COVID vaccine with circulating variants, right? Which is infectious disease research. We're not going to do that anymore under RFK Jr.?

DG: No, not for a while. No, don't got to do that anymore. All right. Let's move into ventilation and transmission. The article, "N95 Filtering Facepiece Respirator Reuse, Extended Use, and Filtration Efficiency," was published in *JAMA Network Open*. This is this whole issue. Can I just keep wearing that N95? The N95 masks or respirators are designed to filter 95% or more of, they say viral, but really particles and to hopefully prevent the person wearing them more than anything from getting the infection. In normal situations, you wear the N95, one patient contact, you toss it out. During the COVID-19 pandemic, and I have to say in a lot of places throughout the world, there was extended use, there was reuse. The question I look at here is, is that OK? Is that safe? Are you still getting protection when you use the N95? The headline got me a little worried, but let's go through it. Here are the investigators conducted. They're not going to do any more of this stuff either, Vincent, I guess, right?

VR: No.

DG: This would fall. We won't know the answer to whether or not this is safe. Anyway, multicenter, prospective cohort study at six United States emergency departments to assess N95 reuse. They're looking at physicians, nurse practitioners, nurses, and looking April 2021 to July 2022. You've got different respirator models they're looking at, but really the primary outcome was, are you going to get below that 95% threshold? The exposure of interest was reuse. They're going to look at the number of shifts. You wear it for one shift, two, three, four, five. We're really not even looking at just the one use and toss it out.

They reported the mean and the median filtration efficiency by shifts worn, stratified by the different types of N95s. They end up enrolling 365 folks wearing the N95 for an increasing number of shifts. They find out that there is reduced mean filtration efficiency with the more shifts that they do, which is really interesting. Some people had this idea that they were going to dirty and then even filter better when you wore them. The proportion of respirators that dropped below 95% was 1.8% after one shift, 10% after two shifts, 28.8% after three shifts.

It sounds horrible until you actually look really closely at the data. It's really this magical line of 95%. You can see the total filtration efficiency. They've got a nice figure where you look at the number of shifts. It's really, I think the table is the most helpful. If you look at the table and you look at the number of shifts and you look at the filtration efficiency, the mean goes from 99.5 to 99.2 to 97.8 to 96 to 95 to 94.2 after five shifts, which is actually 94.2, it's still pretty close to 95. The median was 96% after five shifts. Using that threshold sounds really scary. Oh my gosh. 30% of the masks are below this threshold. If you look at the actual raw data, you're still mostly up in the mid-90s. Really not so bad.

VR: You could use them five shifts. It would be OK, right?

DG: It really looks like it. It looks like 94.2%, oh, it's below 9 - your N95 becomes an N94. We also have the article, "Lower Levels of Household Transmission of SARS-CoV-2 VOC Omicron Compared to Wild-type: An Interplay Between Transmissibility and Immune Status," was published in *JID*. I am hoping as time goes by, we can combat the many convenient myths with the truth. One myth has been that Omicron is much more transmissible because of some change in the virus and not due to our change in behaviors. Some idea that this is more of an upper respiratory virus, not due to vaccines and prior immunity, but due to some intrinsic change in the virus. That's the myth.

One great way to address this question, as we discussed on *TWiV 1160*, is by looking at secondary attacked rates in different settings, as was done in the article, “The Risk of SARS-CoV-2 Transmission in Community Indoor Settings: A Systematic Review and Meta-analysis,” published in *JID.* That study showed that there was no intrinsic difference in the secondary attack rate that could be attributed to the viral variant. Now here we have an article looking at household secondary attack rates, March-April 2022, during the Omicron BA.2 wave in the Netherlands, 67 households were included consisting of 241 individuals, median age of 33.

They found that pediatric index cases were more likely to transmit. Shock. (chuckles) The walking biohazards in our homes. You know what? Transmission was negatively affected by household members' immunity. They found that the Omicron variant was very transmissible within households. However, the transmission rate was lower compared to prior studies highlighting the effect of immunity. They have a really nice Table III. In terms of immunity, prior infection and previous vaccination combined resulted in about a 50% reduction in secondary attack rate in the exposed and in terms of the index case.

Let's walk through this because this is, I think - who knows who's still listening. No, people are still listening, Vincent. If you look at people who they've never been infected, they've never been vaccinated, that's going to be our reference. This is going to be the index case. This is the person gets sick. They get sick, they've never been infected before, they've never been vaccinated. They're going to be our baseline. The person got infected before, they get infected again, that prior infection is going to reduce their risk of spreading to others about 50%.

What if you got vaccinated and now you get COVID? You're going to reduce your risk of spreading it to those you love by about 90%. What if you got vaccinated or infected before, you're going to reduce that by a little bit more, so about 92%. That's actually interesting. The thing you're going to find out here is this whole ethical, this public health discussion. "Why should I get vaccinated? I don't really want to get vaccinated. I was infected before, I'm already reducing my chance of spreading it to others, spreading it to those vulnerable patients in the workplace, already reduced that by 50%. You want me to reduce it to 90%. I'm not OK with that." OK. Washing your hands in the workplace.

The other, and this is really interesting, is they actually looked at this sort of a dose-response curve relative to antibody titers. You get the antibodies day one before you've really had a chance to get any kind of a boost from this current acute infection. They use basically people who have an antibody titer of 0, less than 10. That's our reference. Just a low level. Just being greater than 10, that's about a 50% reduction. You really don't see much more until you get greater than 1,000. It goes from 50% to a 60% reduction. You get to greater than 10,000, that's when you really see that 85% reduction. Prior vaccination, hybrid immunity, and having really high antibodies.

VR: We've tried to convince people that there's nothing intrinsically different about the virus. It's all about immunity. The paper you did before on the SAR study, and now this shows, it's really about immunity in the population. I would guess that disease severity is also going to reflect that.

DG: Yes. It's really troubling. Here's our chance to highlight just how incredibly powerful our immune system is. Here you're comparing infection to vaccination and hybrid. That's really

what's changed our world is immunity, not the virus. The virus has not really changed. Here are all these physicians, scientists, people in healthcare. Here's your chance to really say, "It's what we've done that's made a difference," as opposed to, "Oh, we just got lucky and the virus got mild." We made things the way they are today.

All right. Speaking of vaccination. This I like, this is a great study. This is a study, the article, “Enhanced Placental Antibody Transfer Efficiency with Longer Interval between Maternal RSV Vaccination and Birth,” published in the *American Journal of Obstetrics & Gynecology.* This really this question of, so you get that RSV vaccine during the pregnancy, we say last trimester, but should you do it early in the last trimester, give time for those antibodies to develop, give time for those antibodies to transfer? They conduct this prospective cohort study in two academic centers. They enroll over a hundred individuals who get the RSV vaccine during pregnancy.

Basically, that's what they say, is that if you do it earlier on, so you get it about 30 weeks prior to the 30 weeks versus later on, that 32-to-36-week window, you're going to get higher placental transfer of the maternal antibodies and much, much better than infection. Well, for several reasons, much, much better, but much better transfer of those antibodies. Really suggest to get it at the beginning of that third trimester. This is a log better than an infection is going to give you as far as protecting the child.

VR: This is a little earlier than approved, right?

DG: It's a little bit earlier, yes. Not advising you to do any earlier than the recommended, but do it right at the beginning of the recommended window.

VR: Don't do it later because they say doing it five weeks before delivery is not good.

DG: Yes. All right. We will move into the early viral phase. We have our guidance and what is our guidance? The number one is get these folks in antiviral therapy, particularly Paxlovid. What's going on? We've got this article, “Perceptions and Barriers to Outpatient Antiviral Therapy for COVID-19 and Influenza as Observed by Infectious Disease Specialists.”

This is not just all providers. This is, we're asking the ID docs. This is, “Infectious Disease Specialists in North America: Results of an Emerging Infections Network (EIN) Survey, February 2024,” published in *Open Forum Infectious Diseases*. We've discussed a number of times that antiviral therapy is underutilized for outpatients at increased risk for severe COVID-19 or influenza.

Here they conduct a survey, hoping to offer insights into treatment barriers from the infectious disease specialist perspective. We all can come up with our ideas, but here we're actually going to look. These investigators emailed an online survey three times to almost 2,000 of the members of the Emerging Infections Network who are practicing clinicians.

We have a nice table where you can go through and say, "What were the issues?" The first is, "Who are you thinking about prescribing this for?" Factors typical providers consider when prescribing, right?

VR: Yes.

DG: Number one is, do they have some sort of immune compromise? Immunosuppressive condition or medications. Number two, underlying medical conditions, age. We're still up at about 90%. Then falling below, the patient asks about it, patient requests it. Consideration of immunization, prior infection. Then the next two, these are going to be what I think are really interesting. What are patients' perceived patient barriers? They're saying, when you talk to your patients, what makes them hesitant? The number one concern was side effects. Safety. Is this safe? Are there any side effects?

You know what they were most concerned about, Vincent? Getting a bad taste in their mouth. [chuckles] Have I mentioned that if you tell them to take a Reese's Peanut Butter Cup with the chocolate and the peanut butter, that actually prevents them from getting a bad taste? OK, so you can get rid of that and say, have your Reese's Peanut Butter Cups. The other, and it's about half people, is people don't appreciate, or they don't think that they're at risk for severe disease. That might be a discussion that, "I've been vaccinated, I might be in my 70s, I might have heart failure," so there might be an issue there.

The other, and this is really important, "I just don't feel that sick." It's sort of, "I don't feel that sick. Why do I need treatment? I know I tested positive." Then patients were the ones, about half the time, that wanted to ask about rebound. Then about a third of the time it was, "How much is this going to cost? Is that going to be an issue?" Now, interesting, when you go to the providers, the providers are not concerned about rebound. If you're a doc out there, still asking about rebound, come on, get on with it. Get on the bus, is that the expression?

VR: [laughs]

DG: Get on the ship? I don't know, so I'm sorry, get on with - The big thing for the doctors was they were concerned that they might make a mistake when it comes to drug-drug interactions. After that, they're concerned like, "Am I going to be able to get treatment there within that treatment window?" The approval is the first five days. We've talked about the fact that Day 6, Day 7, you still may get some benefit.

They're a little less concerned about adverse effects of treatment. There's some question about who's eligible, but really, it was a minority. It was only about a quarter of the docs that actually had questions about whether or not treatment was effective. Again, that's the thing. If you're an ID doc and you're not keeping up with the literature and you're not aware that this stuff makes a difference, you're actually in the minority. Most ID docs are well aware that these antivirals make a difference.

I will leave in a link to - is this fear of drug-drug interactions real? There was a nice article, “Pharmacovigilance of Drug–Drug Interactions with Nirmatrelvir/Ritonavir.” In this article, this was looking at, in the U.S. alone, about 15 million courses of treatment with Paxlovid have been given so far. There've only been 594 potential drug-drug interactions. Mainly, that was tacrolimus and simvastatin.

VR: It's very interesting, these free text responses, where 48% of them were skeptical about the benefits of antiviral treatment. Now tell us the numbers again. What percent reduction in progression to hospitalization?

DG: A 90% reduction.

VR: How can that be skepticism? [chuckles]

DG: It's amazing. I know there's questions about number needed to treat. I was having a discussion last night with some other clinicians about Long Covid. If you use the umbrella, you say PASC, post-acute sequelae of COVID, it is compelling that early antivirals reduce your risk of developing an autoimmune disease, reduce your risk of a cardiovascular complication, reduce your risk of a heart attack or a stroke.

It's not just keeping people out of the hospital. It's keeping more and more folks with Long Covid from having that develop and all the other issues. If you can't do Paxlovid, we've got remdesivir, molnupiravir, convalescent plasma in certain contexts. Not much changing in that early inflammatory phase. That's when folks have that second or bad week when they feel rotten, they get the hypoxemia that drives hospitalization deaths. Steroids, right patient, right dose, anticoagulation, pulmonary support, maybe remdesivir if we still are in that window, immune modulation.

Actually a lot this time, Vincent, I'm glad you jumped on early because we have a lot on late phase PASC/Long Covid. There was a *Science Translational Medicine* special, Volume 16, Issue 773, published this month. The whole article focuses on Long Covid. There's really a lot in here. There's a really nice editorial where they talk, *"*Initiating Long Covid RECOVERy", a little 'y'. RECOVER has five major components which they talk about. They talk about the five symptom-based clinical trial platforms to launch multiple interventions.

There's a nice viewpoint, "Consequences Beyond Acute SARS-CoV-2 Infection in Children," pointing out that this is an issue in children. "Infection-associated Chronic Conditions: Why Long Covid is Our Best Chance to Untangle Osler's Web." I suspect that the title is a nod to the book, *Osler's Web: Inside the Labyrinth of the Chronic Fatigue Syndrome Epidemic* by Hillary Johnson. I'll leave a link in case people want to read that.

They do have the section where the authors write that, "William Osler, the father of modern medicine, emphasized the importance of listening to patients to discern important features of their condition. However, contemporary medical practice relies heavily on diagnostic tests, which are currently inadequate to confirm the presence of an IACC." Just really some interesting discussions, "Sex Differences in Post-acute Infection Syndrome."

They throw in, "Symptoms after Lyme Disease: What's Past is Prologue." I got an interesting figure there for people that are looking for parallels there. Then the review section, "Animal Models of Long Covid: A Hit-and-run Disease*."* They review the current state of Long Covid animal models. I like it just because they got pictures, little cartoons of the wild-type mouse, the genetically modified, the hamster, the ferret, the non-human primate. The ferrets are really cute. Does it make you want to get a ferret as a pet there, Vincent?

VR: I have one right on my shelf behind me.

DG: [laughs]

VR: A little fuzzy guy. Where is he? Right there. [chuckles]

DG: I see him. Yes, I see him. OK. “Translating Insights into Therapies for Long Covid.” They also have the research article, “Sex Differences and Immune Correlates of Long Covid Development, Symptom Persistence, and Resolution.” Really, there's a lot in here. This is a great issue, so I will leave in a lot of links, too.

I'm a little worried, Vincent. Are we allowed to keep doing infectious disease research on Long Covid or this will be eight years, sorry? I'm worried about this whole concept that like, "Listen, it's your own fault. Your food's deep-fried in lard. You weren't staying thin enough. You weren't visiting the tanning salon. You weren't getting your testosterone supplement." There are people who have diabetes. There are people who don't get the recommended amount of exercise. There are people who actually have diabetes and heart disease and other things.

I don't think it's OK to say, "Well, oh, that's why you need to worry." Anyway, maybe this leads right into my quotation, "No one is safe until everyone is safe." This refers to everyone in the world. This refers to people over the age of 65. This refers to people who might have a medical condition. This refers to people who might have extra weight or have some medical condition that they're fighting with.

Help us continue to make these recordings to share the actual science, so I want everyone to go to parasiteswithoutborders.com, click that "Donate" button. We're doing our *MicrobeTV* fundraiser where for November, December, and January, we're going to double the donations up to a potential maximum of $20,000 for *MicrobeTV.*

VR: We need your help now, folks. Please help us out. It's time for your questions for Daniel. You can send yours to Daniel@ microbe.tv. Don writes, "I'm 64 with several underlying conditions and receive recommendations from my medical provider network I should get a pneumococcal vaccine. I noticed there are several of them, so which one should I get?"

DG: I'm going to make it easy, Don. The PCV20, so this is the conjugate versus the polysaccharide. It's really, say, latest and greatest. There is a PCV21 and there's a little sort of combat back and forth. Most docs are still using the PCV20 as conjugate vaccine. It's a one and you're done as far as we know. We've been doing this for a while with the PCV, the conjugate vaccine, so that's what I'll recommend.

VR: Susan writes, "I'm planning an extended stay in Ecuador, three to six months. Although no vaccines are required for U.S. citizens to travel there, some are recommended by CDC. The chikungunya vaccine is recommended for adults over 65, especially those with chronic health conditions who will be engaging in outdoor activities at elevations below 7,500 feet. I've always been a mosquito magnet. I have no chronic conditions. Do you think this vaccination is necessary for me personally?"

DG: Well, Susan, I always like to give general recommendations. What's the story here? There's this IXCHIQ, I-X-C-H-I-Q vaccine. It's a chikungunya vaccine. It's actually made by this small boutique Austrian - in Vienna, I think they're located. What are the recommendations? Currently, this vaccine is recommended for adults traveling to a country or territory where there's a chikungunya outbreak, so that's recommended.

Then they say “considered” if you're traveling to a place where there's been an outbreak maybe within the last five years, where there might be risk. Recommended versus considered.

This is one of the interesting things. I was talking to one of my partners earlier today, Dr. Lee, and she was talking about how her neighbor was asking her about, "Hey, I'm going to South Africa. Should I take any vaccine? Should I do malaria prophylaxis?"

She was saying, "You're going to spend this time in South Africa. It is recommended to do malaria prophylaxis." Her response was, "I talked to my travel agent and they said people have more side effects than benefits," so she said, "You did what? You talked to your travel agent, so you're going to take their advice over mine." I'm going to say if you're going to spend three to six months in Ecuador. There's going to be a certain amount of money you're going to spend traveling to and from, I would say schedule a visit with a travel medicine specialist.

You'd be amazed the helpful advice. Then they're going to really be able to tailor for you where are you going to go, and there are other things. Should you be thinking about typhoid? Should you be thinking about what sort of water you brush your teeth with? Things like that.

VR: Janet writes, "I'm a grandmother, have a 2½- and almost 6-year-old. My children got their routine vaccinations, but they were born before chickenpox came around. At the time, I didn't understand how vaccinations worked. For my third child born in '84, I waited on DPT because that's when supposed links to autism were in the news. I thought it was being a responsible parent keeping my baby free from the pertussis vaccine.

He did end up getting it because my doctor explained how serious the illness would be for him. My grandkids have received two COVID vaccinations in this past early July. They both had COVID. My son got them flu shots yesterday. He told me he decided they'd either have a flu vaccine or a COVID, but not both because it was too traumatic all around. If you're going to choose one, which would you choose, or would you provide an argument for pushing both?"

DG: There's a lot, Janet, there's a lot in your email here. The first is, let's just talk about the autism issue. An unscrupulous, I'm going to say unscrupulous, individual basically published a fraudulent article. They got in their head they were suing somebody and they thought it would be helpful for them to put money in their pocket by basically falsifying stuff. They published an article, which was later retracted, where it was suggested that there was an increased risk of autism associated with vaccines.

That's a scientific question, which can be answered. You say, "Is this true? Is there an increased risk of autism associated with vaccinations?" The answer is a clear no. There was even this whole idea that, "Oh, it's because there's mercury in the vaccines." Again, this has been looked at, multiple studies, actually, and some of the links will be put in earlier and the RFK discussion, over 15 studies now, where this been looked at. This was taken seriously. If that's true, that's really a problem.

I understand, you fell victim, and I think a lot of people fell victim to these snake oil salesmen who really just - they take advantage of individuals. They lie. They spread misinformation. They publish stuff that's not true. Then, fortunately, that gets taken down, but it doesn't matter, unfortunately, too late. Just to make sure we hammer that in, vaccines do not cause autism. Unfortunately, we now realize you could probably recognize autism, the lack of a child making eye contact with mom, even before they start going for the vaccines.

We're also realizing things with other conditions. That's number one. Number two, yes, Secret Option C, get both. They're not too traumatic all around. We recommend flu shots. We recommend COVID vaccines. I'm going to recommend Secret Option C, just get both.

VR: Suzanne writes, "Thank you for your weekly podcast. I look forward to listening to them and feel you only tell what science proves. I'm a little disheartened since listening to a podcast interview with former CDC Director Dr. Robert Redfield. He mentioned a couple of things that has rocked my COVID world. The one that bothers me the most is relating both the mRNA vaccine and COVID infection to Long Covid.

He mentioned the spike in either one is what causes Long Covid. Was floored by this since I've had eight mRNA and recently Novavaxxed. I do have more pains in my body the past couple years. Is Dr. Redfield legit? Is this true about the vaccines? I hope my mind can be of ease. I don't think I will go back to mRNA and I will only rely on Novavax, even though I have to cross the border to the States from Canada and pay $199 USD out of pocket."

DG: A couple things here. A little, well, more than a little disappointed in Robert Redfield. I'm going to leave a link into the *FRONTLINE* PBS special, "The Virus: What Went Wrong?" Actually a lot of quotations in there and Robert Redfield's behavior in the early days of the pandemic. I don't know if you ever watched this, Vincent, but over 2 million people have watched the YouTube link in addition to it, was aired *FRONTLINE* PBS.

I'm in there. I had a little cameo and I look exhausted, which I probably was at the time. Robert Redfield, he's director of the CDC. He's on vacation with the family. Hears that there's this problem in China, but he's on vacation, so he basically is like, "Well, listen, I'm on vacation. I'll deal with it in 10 days when I get back." Isn't that what you would do as the head of the CDC? Like, "Don't bother me. I'm on vacation."

VR: No, not at all.

[laughter]

DG: Then, of course, he's like, "Well, it really wasn't my fault because it was a bioweapon that the Chinese engineered and unleashed." He just basically is willing to support conspiracy theories, say stuff that's not true. Let's just start off with the source. Now, what is the science here? The majority, the vast majority, almost all the folks that we see with Long Covid, they got infected. They developed Long Covid, so post-acute sequelae of COVID-19. We really don't fully understand.

It's amazing that this guy has figured out the biology when the rest of us are spending tons of time trying to understand what's really driving Long Covid. It probably isn't the same thing in everyone. Now, are there individuals who develop a Long Covid-like syndrome after vaccine, a vaccine adverse event? Yes, there are. There are thousands of individuals. We're not talking about over a million that died from COVID. We're not talking about the hundreds of thousands of people that died because they did not get vaccinated.

We're not talking about the 70,000, 80,000 people that died this last year alone from COVID, but we are. There are a few thousand people I've taken care of and continue to take care of some of these individuals that developed a Long Covid-like syndrome after vaccination. Most

of them have gotten better with appropriate treatment. No, he's not legit, but just that's what the data is, and yes, your risk of Long Covid is significantly reduced by vaccination. Also, we've discussed it's actually reduced by getting boosters.

It's been suggested, it just saying vaccines are safe and effective. We start saying the risk-benefit ratio clearly favors vaccination, clearly favors getting boosters. If you're worried about Long Covid, the best way to reduce that risk is to get vaccinated. That's going to significantly reduce your risk compared to any rare, rare side effect of a vaccine.

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

DG: Thank you, and everyone, be safe out there.

[music]

[01:02:47] [END OF AUDIO]