This Week in Virology

TWiV 1170 Clinical Update

Host: Vincent Racaniello

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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VR: From *MicrobeTV*, this is *TWiV, This Week in Virology*, Episode 1170, recorded on November 27, 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: We're recording on the eve of Thanksgiving, but when this drops, the holiday will be over.

DG: Here in the U.S. for our international listeners, Thursday is Thanksgiving Day. I think it was the first time that natives of our great country gave free food to illegal immigrants.

Vincent: What did they get in return? They got kicked out. Oh, my gosh.

Daniel: Then, what, Friday is Black Friday when we basically buy things. People don't know Americans. We're at heart capitalists, if nothing else. That is one thing that we were always true to.

VR: Oh, Daniel, but just wait. Now we're going to have tariffs that are going to raise prices. No more Black Fridays.

DG: I don't know what's going to happen there.

VR: Now, Daniel, your tie is very dark. I have no idea what's on it.

DG: I thought it was very Thanksgiving-esque. It's got this brown colors and these red flagellated beaver fever organisms. It's Giardia. I thought that was appropriate. When this will

drop, it'll be Saturday. Vincent, I don't know if you know this. This is when our *TWIV* aficionados rope in the uncle from Boston, everyone else. You've got to listen to this great science-based podcast.

VR: You should. You should do that. Also, at the Thanksgiving table, don't forget to mention to go to parasiteswithoutborders.com and donate to *MicrobeTV*, and your donations will be matched.

DG: Exactly. All right, let's jump in. I'm going to start with a Dostoevsky quotation, "Nothing in this world is harder than speaking the truth. Nothing easier than flattery." Maybe that's very appropriate, and that's all I will say on that topic. OK, [laughter] moving into influenza. What was it? Someone recently said the holiday season is the season of respiratory viruses, and that's really the case. Think of us last year at about this time. We were just starting to see some activity, District of Columbia, Georgia, Louisiana, starting to get into the low-moderate flu activity. In general, we're still minimal, but this is when everyone gets together, and then usually December, January, things rise.

I'm going to leave in a couple links. There's an epidemic trend map, and you can see all the areas where flu activity is growing. The entire West, you can see Washington all the way down to Texas. Just think of that swath. Here in the Northeast, New York, Connecticut, Massachusetts, we will see in coming weeks. RSV, respiratory syncytial viruses. Yes, this is *TWIV* listeners educate family and friends about RSV, not the RBP virus, but the respiratory syncytial virus. We now have ways of protecting the youngest among us and the oldest among us. Bird flu. Lots of questions here. Vincent, are you up for a short discussion about bird flu?

VR: Of course.

DG: All right, I'm going to leave in a link to the *News Explainer*. This is in *Nature*. It's a *Nature News Explainer* article. “Why a Teenager's Bird Flu Infection is Ringing Alarm Bells for Scientists.” Then I'm also going to leave in a link to the *MedCram* video, “H5N1 Mutations Detected in Canadian Case Favor Human Transmission.” We previously discussed the child up in Vancouver, Canada, a teenager who ended up in critical condition after being infected with an avian influenza virus.

What has gotten people talking, what Vincent and I are going to chat a little bit about, is the viral genome sequences released last week suggested that the teenager is infected with an H5N1. This is that avian influenza virus, the bird flu. As they say, bearing mutations that might improve its ability to infect the human airway. I watched the *MedCram*. It's actually quite good. It's very sophisticated. I was impressed. Vincent, what's going on?

VR: If this were going to be a pandemic, it would already be here. You remember 2009, H1N1, they saw a few cases, and then all of a sudden, boom, they were all over the place. It's not like, oh, we see this case and we wait a couple of weeks. No, it would be starting already. Now, I'm not saying this is not why we should not worry about it. We should be reasonably prepared. What's going on? The Canadian case, there's no cow involved because no cow is infected in Canada with H5N1. It's an avian source.

Yes, it has changes in the genome that are needed for transmission. As we learned in 2015 from the Fouchier and Kawaoka experiments on transmission in ferrets, you need more than

just a few changes in the HA and the polymerase. You need other changes as well. These don't have them yet. They're needed. I wouldn't say favor transmission. They're needed for transmission. They're not sufficient. Who knows? It's not ready to prime time, this virus in Canada. That's it.

DG: I have to say, I am not as they say, alarmed. I don't hear the alarm bells ringing. It's interesting. That ferret experiment gave us really, I think, helpful information for us to put this into context. I think that was what people got a little upset about, the concept of that as gain of function, because it was gaining function to transmit in the ferrets or something. I'll leave in these links. People can look into this. The is, sky is not falling. The end is not in sight. I will also mention the CDC confirms H5N1 bird flu infection in a child in California. This may be a little bit different.

The CDC confirmed that this child in California, is the first child in the United States ever to be infected with an H5N1, is my understanding. Now, this is actually along the lines of some of the other cases we've been seeing here in the States where I'm going to say we see two types. Vincent, you tell me your thoughts. We tend to see, I'm going to call it, the cow-adapted H5N1. They tend to be mild because of sialic acid receptors, often eye involvement, mild symptoms. When it jumps directly from the bird to human, that is often when we see the sicker individuals, like the described case up in Canada. In this case here, the child, mild symptoms, got some flu antivirals, actually is reportedly doing quite well.

VR: I want to make a comment, Daniel, and you cannot say a word. I will understand, OK? If we have a pandemic of H5N1 in the next year, we can't have any infectious disease research. All of the science establishments are going to be broken by the next administration. Folks, worry about it in that sense. I'm not so worried about the virus, but I'm worried about our response should it become a pandemic.

DG: Maybe along those lines, we also hear, are you ready for this, Vincent, bird flu detected in raw milk sold in California. I'll leave a link into that.

VR: Listen, bird flu is a disease. They did not detect the disease in the milk. They detected avian H5N1 influenza virus, OK?

DG: Probably just the genetic material. Probably not doing plaque assays or anything.

VR: No.

DG: All right, just to put that in context for all the raw milk drinkers among our listenership, maybe just among our listenership, this one episode. COVID update. Still a couple areas, Minnesota and Mississippi. I think I'm getting that right. In the 2% to 4%, the rest of the country were in the less than 2% of deaths are due to COVID. Crazy. I'm reassured. Less than 2%, less than one in 50 people who died this last week died from COVID. It's here to stay. The wastewater is reassuring. Last year about this time, we were already seeing a rise. If you look at the wastewater across the country, everywhere, it's minimal. That's, I think, encouraging. This doesn't rely on us making the diagnosis. It doesn't rely on people getting sick. All this is, is basically people are using the toilets. This is encouraging.

VR: We may enter December without a rise, Daniel.

DG: We're almost there. Yes, actually, when this drops, it'll be December. Yes, going to see what happens. We should have a bet for what's going on January 1st. I'm hoping that Vincent is right. We just had so much immunity from this fall surge that we're going to get a little bit of a break. We are starting to see the epidemic trend. We're starting to see some areas where actually things are growing in the wrong direction. It's really minimal level, little bit of a trend in the New York area, a little bit of a trend in the Midwest, a little bit of a trend out West and Texas area. We'll leave in some more links for people to look into that.

All right, the article, "Association Between Use of a Voluntary Isolation Center and Reduced Household SARS-CoV-2 Transmission: A Matched Cohort Study from Toronto, Canada," published in *CID*.

I'm going to start by reading the background. Throughout the COVID-19 pandemic, many jurisdictions, this is in Canada, established isolation centers to help reduce household transmission. However, few real-world studies support their effectiveness. Here, what they did is they compared the risk of transmission among households where first case used the Toronto Voluntary Isolation Center, opposed to some of those mandatory isolation centers in other parts of the world. They compared folks that took advantage of this voluntary isolation, compared to households that just did the routine self-isolation. This is data from prior to vaccine availability. We got to go put that in context.

The first thing I did was to stop to see, where were the authors from, because I think this matters. As I mentioned, this is Toronto, Canada. We really did not do this isolation center thing here in the U.S. As I mentioned, some areas in the world where it was mandatory. If you got a positive diagnosis, you were in a mandatory isolation center. The median duration from the first case symptoms, this matters, to checking into the isolation center was three days. There was a certain amount of height of transmission prior to check-in. The median check-out date was 11 days.

The attack rate among households was 5.2%, in the folks that use these isolation centers, compared to 8.4%, where people just did it on their own. I think people can guess the quicker you went and isolated, the more significant reduction in transmission. Also, larger, more crowded households, getting out of that context made a big difference. In general, we saw about a 50% reduction in the household SARS-CoV-2 attack rate prior to the availability of vaccines, if you actually left the house and took advantage of one of these.

VR: What is this isolation center? They take a family from a house and put it in another house? Is that how it works?

DG: No, it's really individuals. These are individuals, and they basically, hey, I got COVID, and then they go, and you get your room. I guess some of the places, like in China, for instance, I saw some of the photos, it was a big hall. Everyone in there was COVID. It was the idea that it was a particular variant, everyone else had the same variant, fingers crossed. In other areas, I have to say, like in Germany, where people were ending up getting a particular infection, they were trying to cohort them by variants. You didn't end up with one variant, now you've got a second variant. Because we saw that, where you can get, and you might even get mix and match.

VR: You have to stay in your room, is that the idea?

DG: That's the idea, yes.

VR: What do you do for food? People bring you food?

DG: Yes.

VR: OK, so, this is not sustainable on a large scale, okay? The U.S. would never do it. In the U.S., the family is the nucleus. You take a member out of the family and put them away for whatever, 10 days, it's not going to work.

DG: Yes, so, what we did here is, hey, you stay in your own room, wear a mask when you come out.

VR: I don't even know why we bothered to look at this thing. Maybe there are some countries where they enforce it and they think it's useful.

DG: I sort of applaud them. People went ahead and they did stuff that they thought made sense. It's important for the next pandemic to ask, did this work? Actually, you say, 50% reduction. That sounds great on the surface, but then you're like, OK, so wait a second. You went from 8.4 to 5.2. That's about a 3% reduction. An absolute 3%. How many people do you need to isolate to protect one person from getting it? That's where it's adding up. It's a lot of money. It's a big investment.

VR: Also, the psychological impact of disrupting a family, putting someone away for two weeks or whatever. That's not good. They can't work. I think there are all kinds of problems. We should have learned that the lockdowns and isolations were really disruptive measures that messed up far more than infectious diseases. I would not do this.

DG: This is probably a good time to mention this and probably the right audience to mention this. We got a lot wrong. There were a lot of missteps.

VR: Yes, for sure.

DG: We got it wrong. There wasn't some group of people that got it all wrong and then there was the bunch of us now who are angry because we knew. A lot of this was, people had good intentions, but it's important to do the science like this so that we could say, you know what, that was a bad idea. That did not work.

All right, vaccinations. Ooh, this is a hot topic, I guess. I'm well aware that not too many people have gotten or are planning on getting the updated COVID shots.

We're going to discuss the percentages on that a bit later, but first we have this article, “Risks of SARS-CoV-2 JN.1 Infection and COVID-19 Associated Emergency Department Visits Hospitalization Following Updated Boosters and Prior Infection: A Population-based Cohort Study,” published in *CID*. It always takes time to get the data. Here we're getting the data from a booster during this past period. Let's just put this in context. Fall 2021 is when Omicron

was declared a new variant of concern, starts to spread. Here we're looking at 26 November 2023 to 13 January 2024. This is last year, just to put this in context.

They conducted a retrospective population-based cohort study looking at Singaporeans aged 18 and over. We're going to look at the impact of boosters, prior infection, basically what happened last year. We're always going to be one year behind. This is another one of those real-world studies where we see what is happening at a population level. Here's the total of, you ready for this, over 3 million, 3,086,562 boosted adult Singaporeans looked in the study. Then they throw us even this big number, 146-million-person-days of observation. During this period of time, 28,160 infections were recorded, 2,926 hospitalizations, 3,747 ED visits.

They compared to individuals that had been last boosted greater than a year ago to those that had just gotten the XBB booster eight to 120 days earlier. They found that getting an updated booster eight to 120 days earlier was associated with a lower risk of getting the JN.1 infection, about 41% reduction. Hazard ratio 0.59. What about, your chance of ending up in the ED. We saw almost 4,000 ED visits. Folks that got boosted had about a 50% reduction in those ED visits, and hospitalization about the same, so a 42% reduction, so a hazard ratio of 0.58. Get a few other little bits of data. What if it's a little bit longer?

Let's say a little bit past, so 121 to 365 days earlier, you really were losing almost all the protection. Hazard ratio 0.92 for infection, 0.80 for reduction in ED visits. What about what we actually, we, I think I could say we, Vincent, and I care about, what about severe disease? You get an infection, maybe you go to the ED, but what about getting sick enough to end up in the hospital? Here, you're actually seeing, even if you look past the 120 days, folks that had gotten an updated shot, 120 to 365 up to a year before, there was a 43% reduction.

VR: This is a year ago till January, basically.

DG: They looked at last fall, winter, and they said, let's look at people that got a booster or didn't, and yes.

VR: What's circulating at that time, which variant?

DG: They say here it was the JN.1.

VR: The booster is XBB, which is different.

DG: Yes. Yes.

VR: OK.

DG: Interesting, right?

VR: Basically, you don't need a JN.1 update to get protection.

DG: Particularly when you looked about severe disease it looked like there was, yes, a variant. Yes, so, interesting.

VR: There's the risk of infection. I don't really care about that, but ED visits and hospitalization, and this is good that the previous booster will do it against the new variant, right?

DG: Yes. Yes. Yes. What we'll talk about, repeatedly we've discussed that immunity has really changed the outcomes with COVID-19. For most people at this point, this is a combination of vaccination and prior infections, hybrid immunity for most folks. Unfortunately, here in the U.S., we now have over 1.2 million individuals who died with their deaths attributable to COVID-19 on their death certificate. We're still seeing thousands of people end up in the hospital each week due to COVID-19, thousands of deaths. I don't want to leave this out, we also now have over a million individuals suffering from Long COVID here in the United States.

With that said, and the fact that getting vaccinated and getting boosted reduces an individual's risk of infection, the need for medical attention, a trip to the ER, hospitalization, death, and we're going to talk a lot more about this post-acute sequelae of COVID, Long COVID, how are we doing with people getting those boosters here in the U.S.? It must be lines like people wondering if a new *Star Wars* episode came out.

Everyone wanting to get updated vaccines? Apparently not. Here we have the *MMWR,* "Coverage with Influenza, Respiratory Syncytial Virus, and COVID-19 Vaccines among Nursing Home Residents - National Healthcare Safety Network, United States, November 2024." Of course, these numbers are going to be super high because these are the most at-risk individuals. Let's look at the numbers. For flu, only 58%, COVID-19, 30%, RSV, 18%.

VR: Daniel, obviously, the residents of these nursing homes have a say in whether they get vaccinated or not, right?

DG: If they're offered. I think that's the thing is the nursing home has to make it available. They have to offer it.

VR: Because this is the key population for these vaccines. Yet 30%, 18% is crazy. You think they're just not offering it?

DG: Yes. A lot of facilities are not making this happen.

VR: That's crazy. I bet this goes down next year even more.

DG: I think you're right. I'm a little bit baffled. We've been told, recently, don't say vaccines are safe, effective. You're supposed to be saying the risk benefit profile clearly favors vaccination. I'm not so sure about this. I put in this little section, trying to figure out the disconnect here. You and I are old enough to remember the 1980s. Remember when seatbelt laws were being introduced?

VR: Oh, yes.

DG: I remember. I distinctly remember Thanksgiving, where this was the heated topic of conversation. When these were being introduced in the 1980s, what percent of Americans at that time opposed enforcement of seatbelt laws? 65%. The majority of Americans. This is one of those minority of Americans are forcing this on us. I went through and looked these up. What are the arguments? What do people say? Number one, it's uncomfortable. It's cumbersome. It's going to wrinkle my shirt. This was the big one. This was the passion. It's going to make it difficult to escape a damaged car.

It's safer to be thrown from a car at 65, I think it was 55 back then, 55 miles per hour. If I get into a car accident, I want to be free of the seatbelt so I could be thrown through that windshield and end up on the side of the road safe and clear from the accident. Then the anecdotes about seatbelt injuries. I knew this guy and he was belted in, and he was in a crash and the car was completely mangled and he had bruising across his sternum.

[laughter]

VR: But he was alive, right?

DG: Yes, but he had bruising across the sternum.

VR: It's terrible.

DG: Then the last is how am I supposed to maneuver the car? That was the Volvo versus Subaru. Volvo was like, we're going to keep you safe and then the Subaru drivers were going to maneuver and not end up in an accident.

VR: Daniel, aren't airbags now mandated as well in cars?

DG: These coastal elite liberals, next thing you know.

VR: People don't object to airbags. They don't have any choice. They can't not turn it on, basically.

DG: I don't think there's quite as much of an anti-airbag. I've been like people worried about, I'm not tall enough, the airbags are one size fits all. I need to go to the dealer and have them disable my airbags.

VR: It's interesting. This law would never pass today.

DG [laughs] Definitely wouldn't pass in the next couple of years.

VR: I wouldn't be surprised if it were repealed by some wackos.

DG: I wonder if this isn't enough in the rear-view mirror that people aren't going to try to overturn and the libertarian wear your seatbelt if you want, a human being should have the freedom to drive around unrestrained. I remember when we were kids piled in the back of the station wagon, unrestrained, the good old days when America was great, when the way that we resolved sibling conflicts was when one parent would yell at the top of their lungs, "Don't make me stop this car."

[laughter]

All right, let's move on to the early viral phase. Now, unfortunately, someone has been breathing and someone else has been breathing in and we end up getting COVID. We still have our NIH treatment guidelines. We have our ID Society of America guidelines. I just renewed my membership. Hopefully that'll keep moving forward. Number one, Paxlovid that we've been talking about. Number one recommended, about a 90% reduction in progression. Also, as we've been talking about, if you use the umbrella of post-acute sequelae of COVID,

cardiovascular issues, et cetera, significant reduction. Number two, remdesivir. For those that say like, oh, this is not a big deal, remember thousands of people still getting hospitalized here in the U.S. alone.

Number three, what about molnupiravir? What about Thor's hammer? I will admit, I have never been too enthusiastic about molnupiravir once we got the full data. We do have the article, “Real Clinical Effectiveness of Molnupiravir against 30 Day Mortality Among 74,541 SARS-CoV-2 Positive Patients: A Nationwide Cohort Study from the Czech Republic,” publishing in *Open Form Infectious Diseases*. I wanted to start off by first, what is a real world effectiveness study? What is that?

Is this just a rebranding of the terminology, retrospective cohort study? A real-world effectiveness study refers to an observational study that examines treatment effectiveness in a typical clinical setting, often using readily available data, while a retrospective cohort study is a specific type of observational study where the researchers look back at data from a group of individuals where the exposure and outcome have already occurred, meaning they are analyzing data collected in the past. Essentially, a retrospective cohort study is a method that can be used to conduct a real-world effectiveness study, but not all real-world studies are necessarily retrospective cohort studies.

I'm going to say, yes, pretty much real-world effectiveness study is a bit of a rebranding of retrospective cohort study in most cases. The authors even challenge the respect we are giving to randomized control trials as they write in the background section. You ready for this, Vincent? Although RCTs, randomized control trials, are the gold standard for drug efficacy assessment, their findings may not apply to real-world populations because they usually focus on selected patients who differ from the real population in routine clinical practice.

VR: Daniel, isn't the trial population selected to try and be as diverse as possible?

DG: Yes, I just want to make sure that, yes, we just, yes. Here, they report the results of a population-wide retrospective cohort study in the Czech Republic. They analyzed 74,541 patients with an officially registered diagnosis of SARS-CoV-2 infection, January 1 through 31 December 2022, aged 18 and older. Primary outcome, 30-day all-cause mortality. The use of molnupiravir in adult SARS-CoV-2 positive patients was associated with a lower risk of both 30-day all-cause mortality, so about a 42% reduction, and 30-day COVID-19-related mortality, about a 50% reduction. They saw this regardless of sex, severity, hospitalization status, vaccination.

VR: If you can't get Paxlovid, this is not a bad alternative.

DG: Yes, if you can't get Paxlovid, if you can't access remdesivir, there might be some mortality reduction. The other, and this is the next article, “Time to Sustained Recovery among Outpatients with COVID-19 Receiving Montelukas versus Placebo.” This is this issue that maybe it makes you feel better. That's a thing that people have asked as well. Are we doing molnupiravir to make people feel better quicker? Are we doing it to keep people out of the hospital? None of those endpoints have been that impressive, but at the end of the day, maybe it's reducing your chance of dying.

VR: That's probably the best outcome, isn't it?

DG: It's a great outcome, but you want all the others, too. You don't want to end up in the hospital. You don't want to end up with Long COVID. Some fates are worse than death. For a lot of people, I have to say, with Long COVID, they are miserable. We've had some individuals actually take their own lives because they are.

VR: Yes. OK. We've taken.

DG: Convalescent plasma in some situations. Moving on to early inflammatory phase. As I mentioned, we're still in the U.S. seeing about 5,000 or 6,000 people being hospitalized per week with COVID, usually because they're in that early inflammatory phase. Sometimes it is in that first week as well. If they're in their early inflammatory phase, often during the second week, but COVID doesn't always respect that calendar, this one, people might become hypoxic, and steroids might be appropriate. We have anticoagulation guidelines, pulmonary support, and still, in some cases, there might be a window for benefit for remdesivir.

Remdesivir, first week, three days, remdesivir in people requiring oxygen support. We have the article, "Remdesivir for Treatment of COVID-19 Requiring Oxygen Support: A Cross-study Comparison from Two Large, Open-label Studies," published in *CID*. I have to say, we keep learning about remdesivir. For instance, we learned about it being safe to use in folks with renal failure. I'll also leave a link into efficacy and safety of remdesivir in people with impaired kidney function, hospitalized for COVID-19 pneumonia, a randomized clinical trial. Here, we actually are going to be looking at folks who are hospitalized. In general, we're using five days. Why five days? Why not 10?

That's because we have that *New England Journal of Medicine* article, "Remdesivir for Five or Ten Days in Patients with Severe COVID-19," where we actually saw that people did better. There's actually a trend towards five days as the optimum duration, a trend away from doing too much. Here, we actually find that whether they're just using nasal cannula, whether they're on high flow or non-invasive positive pressure support, whether they're ventilated, even whether or not they're on ECMO, we're actually seeing about a 50% reduction in mortality in all these contexts. In some contexts, immune modulations with tocilizumab. I'm going to wrap us up with two things.

One is the late phase, PASC/Long COVID section. To be slightly political, Vincent, I was a little concerned when I heard a nominee to one of our federal agencies say that long COVID was real but overplayed. For the millions still suffering from Long COVID, let me say, Long COVID is real, and if anything, has been underplayed. We have the article, "Neurological Manifestations of Long COVID Disproportionately Affect Young and Middle-Aged Adults." Here, these investigators sought to investigate neurological manifestations of post-acute sequelae of SARS-CoV-2 infection, so neuro-PASC, in post-hospitalized, so we have a post-hospital neuro-PASC, which is PNP, and a non-hospitalized neuro-PASC patients.

What did they basically find? There was a significant age-related difference in really a number of things. They divide the patients into those who are younger, middle-aged, older, and they found that fatigue, sleep disturbances, and higher impairment in quality of life among the younger patients. There were significant age-related differences in objective executive functioning and working memory with the worst performance coming from the younger group. I think I would say that, in general, the older you are, the higher your risk is of Long

COVID, but some of the most severe cases we're actually seeing in these young individuals, 18 to 44, and middle age, 45 to 64.

VR: By the way, I heard that Physics Girl is getting better.

DG: She actually is, and I'm going to hopefully jump on a call with Kyle and Diana Coward when I get back from Africa. Yes, I was delighted. I don't know if people are aware, but Physics Girl really has been suffering horribly from Long COVID, debilitated. She's now talking up to an hour a day. She recently recorded a video. Tremendous to see that there's some improvement there. I think there's been a bit of a fundraiser, and I talked to Kyle, and I'll talk to Diana, Kyle is her husband, about possibly what can we do to help with awareness and help support those. All right, a recap for any new listeners today, and also our longtime listeners.

It's been about five years since this virus crossed over from animals at the wet market in China and got into the human population before spreading throughout the world. I'll leave a link into the *TWIV* special, *How the Pandemic Began*. I give people permission to fight about this while gathered together for the holidays, because the lab leak conspiracy theory is not innocuous. I'll read from a linked article here. The unsubstantiated claims of the lab leak theory have provoked harassment, intimidation, threats, and violence towards scientists, which are often vile in the online space.

An article in *Science* reported that of 510 researchers who had published on SARS-CoV-2 or COVID-19, 38% acknowledged harassment ranging from personal insults to threats of violence, docking, and personal contact. A second survey, which included 1,281 scientists in a wide range of fields found that 51% experienced at least one form of harassment, sometimes repeatedly for years, most worrisome for future preparedness. The next generation of scientists has well-founded fears about entering fields related to emergent viruses and pandemic science.

As far as transmission, it's basically the same virus and just as easily spreads from person to person, but this virus is now encountering a wall of immunity that we have built with prior infection and vaccinations. We covered this by discussing those articles looking at secondary attack rates or the chance of people getting infected being around someone sick with COVID-19, and I'll leave a link into a few articles, but studies that show no intrinsic difference in the virus. Really, the difference that we are seeing is because of this wall of immunity.

As we've discussed again today, getting into a cadence of yearly boosters reduces an individual's chance of getting COVID, then based who you are, your chance of feeling rotten, your chance of needing medical attention, going to the ER, getting hospitalized, dying or suffering from Long COVID. If you don't like the mRNA stuff, we have the more traditional vaccine choice, Novavax. If you do get sick, we have highly effective medications. Call your doctor to see if that might be right for you. I feel like it's a commercial. If you do end up with Long COVID, we are learning more.

We do have evidence-based treatment and a growing number of Long COVID treatment centers, such as the one we have right here, I'm going to say right here at Columbia, and I'll leave in a link to that center. You can also call 877-426-5637. I will wrap it up as I have been for quite a while. No one is safe until everyone is safe. I want people to pause the recording,

go to Parasites Without Borders, click on Donate, every small amount help. We're going to continue to support *MicrobeTV*. We're in the midst of our fundraiser, hoping to get up to a maximum donation of $20,000 for microbe.tv.

VR: It's time for your questions for Daniel. You can send them to daniel@microbe.tv. Chris writes, "I would appreciate your opinion on the importance of fall boosters for kids 4 to 9 years old. My daughter-in-law says their pediatrician isn't recommending vaccines and is saying that they've all had COVID. Their risks of the disease are low as healthy kids. I do not agree, but don't know how to present it to my daughter-in-law. They have had only the initial three shots and do not have any health conditions that raise the risk of COVID illness. Thank you."

DG: What are we trying to prevent with the vaccines? We've been through this and with kids, we'll put it in context. Here in the United States, over 1,000 children died of COVID. I want to point out the majority of those children, not just a little over 50%, but 75%, 80% of those deaths occurred after Omicron. These are deaths due to Omicron, which is the current virus that they'll keep telling you is not a big deal, but it is a big deal. We have death. We also have Long COVID in kids. One of these federal appointees who claims that we're overplaying Long COVID was saying, oh, we only see it in 1% or 2% of people after infection.

1% to 2%, every time you get COVID, you have about a one in 50 chance that you're not going to be better in two to three weeks, that you're going to be sick for months. Vaccinations, clearly, and we're going to present about 50 studies next week about vaccinations reduce the risk of Long COVID, old people, middle-aged people, young people, young young people. Long COVID protection, protection against death, protection against getting sick. Also, we know that the duration of illness is significantly reduced. That vaccination for your child can get them back to life a bit sooner, get them back to feeling better a bit sooner. The big specter for the kids is Long COVID.

VR: Mary writes, "Thank you for your ongoing commitment to providing science-based information about COVID and other infectious diseases. The first thing I do on Saturday morning is listen to you and Vincent in Clinical Update, and it starts my day on a positive note. In the November 22 episode, you mentioned that you care for some people who have a long COVID-like syndrome after vaccination. A close friend had her life turned upside down after her second Pfizer shot. Her symptoms are similar to those of people suffering from PASC. She's having a really hard time getting sympathetic care here in our small town, Corvallis, Oregon. Are there any resources you could direct her to? I've done a lot of searches to try and find something, anything, without luck."

DG: This is a challenge. One of the nice studies that's based in Yale that we've collaborated with is the LISTEN study, L-I-S-T-E-N. Akiko is involved in that. There's also a connection with David Petrino down at Mount Sinai. This is a study where they're looking at people with Long COVID, but also people that develop similar issues post-vaccination and trying to understand, because sometimes there seems like a symptom overlap. A lot of times, some of the therapies that we use for Long COVID help people that have injuries post-vaccination. Feel free to look at the Long COVID paper.

A lot of times you need to go to more of a major center and then maybe continue to follow up afterwards with telehealth visits. This is really tough. Because we acknowledge and I think Paul Offit always has talked about this, vaccines are biologically effective agents. It might be one in 100,000, it might be one in a million, but when you vaccinate 300 million people, when you vaccinate billions of people worldwide, that one in a million, that 1one in 100,000, that starts to add up to a number of people that we really need to help take care of.

A nice thing, and this goes back decades, is realizing this, a fund was set up, 75% of every vaccine that's given out goes into this fund so that when people end up being adversely affected, there's a fund to help take care of these folks. Make sure that this is reported, make sure you work with your doctor. If this is adjudicated, if they establish this connection, which has happened for a number of patients I take care of, they can actually get support.

VR: Susan writes, "I had a preemptive kidney transplant five years ago. I am up to date with vaccines and boosters, 11 plus two Evusheld injections, three Pemgarda infusions. I had COVID two years ago and received Belatacept when it was authorized. When I ask my transplant center about treatments, they always say, well, the disease isn't so serious these days. No remdesivir if you're not in the hospital, and you could try molnupiravir if you don't want Paxlovid. My feeling is the disease hasn't changed, but we are coping with it better because of vaccines and acquired immunity from infections. Is my transplant center right?"

DG: It's troubling. You are right. As we've repeatedly talked about, the virus did not magically become something innocuous. It's this wall of immunity, and folks that have had transplants, and because of some of the medicines, don't have as great a wall of immunity. Those are the people that we're seeing in the hospital. Those are the people that are not surviving the infection. The most effective time to intervene is either before or during that first week. You want to find out, can I take Paxlovid?

Is there any kind of a drug-drug interaction? I think we covered last week that of the 15 million courses of Paxlovid given in the U.S., only about 500 individuals had drug-drug interactions or suspected drug-drug interactions. Tacrolimus, which you might be on, is one of those. That might interfere with your ability to take Paxlovid, which would be recommended as first line. If you can't navigate the drug-drug interaction, then you do want to look at remdesivir or molnupiravir, but you are right.

VR: Walter writes, "I have a question regarding Bronch-Vaxom (OM-85) and its use for preventing recurring respiratory tract infections. My primary healthcare provider, who notably does not recommend COVID-19 vaccines even for elderly patients anymore, yes, I know I may need to reconsider my choice of doctor, recently suggested Broncho-Vaxom to help with my recurrent RTIs, which I suspect are viral in nature. For context, I'm 40 years old, healthy male. Does this recommendation make sense given the evidence for Broncho-Vaxom's effectiveness, particularly in such cases? I'd greatly value your opinion."

DG: Broncho-Vaxom is an interesting product. It's like a desiccated, bacterial, outer coat product. I think it's actually licensed in Europe. Here you buy it from Amazon.com or something. We don't really know, but the idea is this gets some priming of the immune system so you've always got a little bit of inflammation going on. Then when you get some infection, you're more ready to go.

Really the outcomes that I remember for the Broncho-Vaxom was that people end up getting less antibiotics. I don't know if they end up getting less antibiotics because they're on this and people think, oh, I don't have to worry about antibiotics. The data is not the most compelling under the sun. It doesn't appear that there were safety issues with doing this. Yes, most important if your doc's not pro-vaccine, you may want to look into that.

VR: Finally, Zaharoula writes, "These comments are my own, do not represent my organization or hospital. I want to clarify something that was said in *TWiV 1168*. Parents have always had the consent for any type of medical treatment for their child, including getting vaccinations. I can't even give their child Tylenol without their consent. They also receive vaccine information statements from the CDC for each type of vaccine that their child is receiving at the time before the vaccinations are given. Federal law requires that health care staff provide VISs to a patient, parent, or legal representative before vaccinations are given.

This is required in both public and private sector health care settings. We as medical professionals do not make the decision to vaccinate children. Their parents do. It's always been the parent's decision to proceed with vaccination or not. However, paraphrasing Dr. Offit, there are no risk-free decisions. Choosing not to vaccinate your child is still a decision and one that carries extremely great risk. Nothing in life is risk-free, and choosing not to do something is still a choice, and all choices have consequences. I try to explain to parents that choosing not to vaccinate their child carries the greater risk of getting the vaccine-preventable disease, a risk that includes death.

Unfortunately, during my 32 years as a pediatrician, I've taken care of pediatric patients with polio who've lived in iron lungs, kids who have died of varicella pneumonia, pulmonary complications, kids who died of epiglottitis, respiratory failure, sepsis from *Haemophilus* influenza type B, kids who died from pneumococcal sepsis, babies who died from pertussis, kids who were not vaccinated with COVID vaccine and had MIS-C and needed critical care, kids in respiratory failure from flu infection, and countless other children with lifelong disabilities after having vaccine-preventable diseases. Parents have always had the right to choose to vaccinate their children.

They have always had the information about the vaccine given to them before proceeding with the vaccinations, and they have always had the opportunity to discuss the vaccinations with their pediatric provider. In addition, there are the post-vaccination safety monitoring systems, including the Vaccine Adverse Event Reporting System, V-SAFE, the Vaccine Safety Datalink, and the Clinical Immunization Safety Assessment Project.

I am confused as to what RFK Jr. thinks we have been doing all this time. I would also ask, in his career as a lawyer, how many patients has he treated? Has he actually sat at the bedside of an infant struggling to breathe with pertussis? Has he had to talk with a grieving parent after their child died from pneumococcal meningitis? I wonder, would he be willing to do that now? Thank you again for all of your efforts in educating all of us and for all the great science communication. I'm proud to be a *MicrobeTV* supporter, and in the spirit of Thanksgiving, I'm most thankful for all that you and the other hosts of *MicrobeTV* do.

DG: That's fantastic. Thank you for sending that email. Not really much I can add. I think you're basically putting it all out there. Everything you're saying is true.

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

DG: Oh, thank you. Everyone, be safe and enjoy the holidays.

[00:53:46] [END OF AUDIO]