This Week in Virology

TWiV 1178 Clinical Update

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Guest: Daniel Griffin

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

(music)

From *MicrobeTV*, this is *TWiV*, *This Week in Virology*. Episode 1178, recorded on December 26, 2024. I'm Vincent Racaniello. You're listening to the podcast, all about viruses. Joining me today from New York, Daniel Griffin.

Daniel Griffin: Hello, everyone.

VR: Daniel, our last broadcast of 2024, right?

DG: This is actually an exciting one too, Vincent, because it's that weekend right between Christmas, during Hanukkah, Kwanzaa is starting, New Year's is coming up. You're going to have all the family together listening to *TWiV*.

VR: Yes, and exchanging their microbes.

DG: Exchanging their microbes and discussing all the topics that we discuss.

VR: Speaking of microbes -

DG: Donations, donations. Don't forget that, Vincent.

VR: Oh, yes. They'll be writing their checks. It looks like you have some bacilli on your tie. Am I right?

DG: This is the waterborne pathogen. There's a whole bunch of different microbes.

VR: Do I see some rods down there at the bottom?

DG: Yes, some gram-negative rods. It's even like a little round, probably sporidium.

VR: Is there a cholera on it?

DG: I actually just recently saw a gentleman in southern Zanzibar with cholera, where they still have cholera outbreaks. There should be cholera on there. There should be norovirus, winter vomiting disease pathogens. All right, let's jump into it. I was thinking about this earlier today. We've done over 300 quotations. Did you know that? We've been doing this-- it's coming up on five years. Here's one that I recently ran across.

VR: You could write a book, *Daniel's Quotations*.

DG: Someone could do that. Someone could compile that. Yes, that would be great if someone wants to do that. All right, but this is a Richard Adams. It's from *Watership Down*. I have to say, what a great book. Even there's a Donnie Darko connection there. “Many human beings say that they enjoy the winter. But what they really enjoy is feeling proof against it.” No one likes actually being freezing cold. But there's something about being dressed warmly or maybe warming up by a fire.

VR: I think there's nothing good about winter except snow.

DG: I was thinking today about this, and we try not to be political. I was asking my wife, if we move the elections to the spring, like would it affect the outcome of elections? We vote in the beginning of November. It's starting to get dark. We're losing daylight. No one believes in global warming. If anything, we're wishing maybe global warming would help us a little bit in the dark, cold days of November here in the northern hemisphere. If we voted in like, June on a nice spring day, maybe in August when it's oppressively hot, it might actually affect our voting.

VR: It might. Although which way? Who knows?

DG: Maybe a little bit of optimism. I always feel a little bit more optimistic and positive on a warm spring day.

VR: Definitely, definitely. Snow is very nice as long as you're warm.

DG: Well, it was very nice for us this year. It's been a while since there's been snow on the ground during the winter holidays.

VR: White Christmas. I haven't seen one in ages. I even went and looked up the lyrics of the song to see what that was all about.

DG: I've been dreaming about it.

VR: I've been dreaming of a white Christmas just like the ones we used to know, implying that we don't have them anymore. That's pretty much true. I can't even remember when. When I was a kid, there was always snow on the ground, it seemed.

DG: Yes. I wonder how much of that is our memory because just think about when that song was written.

VR: I like the line that goes, "May your day be merry and bright and all your Christmases be white." I like that. Have a merry and bright day. Isn't that great?

DG: That is nice. I like that. All right. Well, we've got a lot to cover today, and we're going to be talking about whooping cough. That is pertussis. It's the same thing. Polio made it on the docket right at the end. Bird flu, a little bit upsetting news there. Actually, a lot about vaccines and Long COVID. This will be a chance for everyone to have those discussions gathered together as a family. Yes, whooping cough or pertussis, they are the same thing. We read the headline, "Whooping Cough Cases Reach Highest Level in a Decade."

The U.S. has recorded over 32,000 whooping cough cases this year, compared with around 5,100 as of mid-December last year. That's a big change. That's a six-fold increase. I've got a nice chart here from NBC News. Really, numbers had come down sort of mid-15,000 range. Then we have this drop in 2020, 2021. What do you think was going on there?

VR: Pandemic.

DG: Exactly. Wearing masks, a bunch of other things are going on. It really has come back to over 30,000 this year.

VR: Daniel, I told you my story. When I was 8 years old, I went to Italy and visited my father's parents in a very remote little town. They made me sleep in the room with a kid who had whooping cough. They said, "It's OK. You're vaccinated. You'll be fine."

DG: You'll be fine. All right.

VR: The cough was unbelievable. I've never heard anything like that.

DG: Oh, yes. It is. It's a characteristic. It's not diagnostic. There's a characteristic whoop to this cough. The coughing gets so severe, you can't even get a breath in. Next thing you're vomiting, this post-tussive vomiting, which is suggestive, I should say. What's going on? We don't have complete data for this year yet, so you have to go back a little and see what's going on. One of the things I was looking at is, one, and I think this is really important because we're going to talk about vaccines a little, is who gets pertussis and who ends up hospitalized for pertussis.

I was talking to the best man for my second wedding, which I guess implies I was married once before that. Tony Doing, who's a cardiologist, was saying, "Everyone's so concerned about vaccinations. Why don't we just wait a little?" I was like, "Well, one of the problems, as we see here, is if you look at the reported pertussis cases and percent hospitalization by age group, we actually see the highest burden, so the highest number per 100,000, is actually in the less-than 6-month-old kids and about one in five, so over 21% of those kids end up in the hospital."

It's really a problem. We recommend starting and getting those kids vaccinated for diphtheria, tetanus, and pertussis. It's that diphtheria, tetanus, acellular pertussis, so the DTAP. You start at 2 months and then 4 months and 6 months. You're trying to really start getting the immunity in there because if you wait, it's a problem because it's the youngest kids that are at the highest risk. The highest percent are going to end up in the hospital, so it's 2 months, 4

months, 6 months. Then you get another boost or 15 to 18 months and another four to six years.

That's one of the issues with waiting, and do vaccines work? I think you can also look at the same data. I'm going to leave a link in to this. If you look at, what percentage of these folks affected actually have completed that primary series. By 6 months of age, you should have completed that if you follow the recommendations. Only 28.9% have actually completed that primary series. Even when we're looking at 6 to 11 months, 38.2% were looking at 1 to 4 months. Most of these kids that are severely affected, they're not vaccinated. They're not getting those vaccinations.

Just a couple issues, vaccines work. Why there's this encouragement to really start protecting as kids enter this world? Now, the Nexus recently was sent my way. Couldn't have come sooner because it was yesterday morning. We're recording this Thursday, so it was Wednesday morning that this was announced, that an Israeli teen diagnosed with polio, Health Ministry investigates. What I really liked actually sort of did a screenshot of this from jpsost.com.

“The primary way to protect children from paralysis is through the inactivated polio vaccine the Health Ministry stated.” I like that Vincent, why weren't they just pouring in some more of the vaccine for polio?

VR: OPV causes polio, IPV is the way to go for sure. Israel has done IPV only for quite some time now, like many other countries. They don't tell you what serotype was in this child, right?

DG: I don't know if we know yet, and actually that was what they were saying. They're doing testing, so we have a case of polio, which means that this individual has some degree of paralysis, so we don't know the degree yet of the flaccid paralysis. We also don't know, and we suspect this was another case of vaccine-derived polio because they've been administering a lot of the vaccine in the region, in Gaza. This child was unvaccinated, which is a recipe for disaster here. Yes, so thoughts Vincent?

VR: Well, it's not surprising. The child was probably not vaccinated or under-vaccinated, I would guess, because if you're vaccinated with IPV, you're protected against paralysis. I think it would be really interesting to see what virus this is. I would suspect it's derived from nOPV2, which was given in Gaza, remember, back in October-November for trying to prevent paralytic cases.

More recently, environmental sites in Gaza have tested positive for polio too. I think if it turns out this is OPV-derived, it gives more ammunition to the idea of admitting that nOPV2 is no better than OPV2, and that we should move over to IPV, because the OPVs don't prevent transmission, and so we might as well use IPV.

DG: I got to say, people who are not swayed on this, we keep introducing this. What a bad situation where a child ends up vaccinated, and then this is now in the community. I think we do know this was an unvaccinated 17-year-old who's now got some degree of paralysis. We're introducing this instead of - I think it's one of those, what is it, penny-wise, pound-foolish, not really switching over to IPV and just making this happen throughout the world.

VR: It's hard for them to admit that they made a big mistake, and they're wrong.

DG: That might be the hardest thing. Yes. I was watching a video just yesterday that someone sent me, sort of just how wonderful the oral polio virus and how much better it is now that we have this novel one, but we're still paralyzing people.

VR: That's all fallacy. That's all wrong. It's not so much better.

DG: Got to stop. All right. Well, I also want to share, I don't know if you saw this, Vincent, but we have this new HHS, Human Health and Services, Let's Get Real campaign. I'm going to leave in a bunch of links. "

“HHS Launches Let’s Get Real Campaign to Highlight Facts About Childhood Vaccines and Share Stories from Confident Parents Who Vaccinate Their Kids." There's a news piece, and then there's a link to the actual Let's Get Real campaign.

In the news piece, they explain that the percentage of U.S. kindergartners with an exemption from at least one vaccine increased in the 2023 to 2024 school year to 3.3%, the highest percentage ever reported. One takeaway I'll take from that is this is still a fringe movement, by the way. 3.3% is certainly not mainstream. You read the media, you think everyone is stopping vaccinating, but 3.3% in the 2019/2020 school year, only three states reported vaccination rates below 90%. That sharply increased to 14 states in the 2023/2024 school year. We're starting to see this, anti-vaccine spread.

VR: Daniel, once a vaccine scientist told me that the medical exemption rate should not exceed 1% in the U.S.

DG: It really shouldn't.

VR: Yes. 3.3% is wrong.

DG: Now, and this is, we'll read on further, I really like this because it gives some numbers. If parents stop vaccinating their children, preventable diseases typically not seen in the U.S., they say they're going to come back. It's not a question of can. They will come back. They highlight measles, where they say measles, for instance, is extremely infectious and potentially very serious illness. Before the measles vaccination program began in 1963, an estimated 3 to 4 million people got measles in the U.S. each year. About 48,000 of them were hospitalized and 400 to 500 each year died.

These numbers dropped dramatically after widespread measles vaccination and prevention efforts. Despite the success of the measles vaccine, measles cases are increasing again because of declining vaccination rates. In this year alone, there have already - I put already - 283 cases of measles in the U.S. reported to the CDC. As we mentioned, these are in children, and the majority of those children ended up in the hospital. They've got some great - I love the graphics of the cute little girl there with her purple Band-Aid on from where she got her vaccine.

Of course, she's smiling. I don't know if that was staged. My kids usually never smiled right after they got a poke in the deltoid. I particularly like, they've got a bunch of pages you can

go into. I particularly like, “The Real Science Behind Childhood Vaccines.” A couple of things we talked about today. We started with the fact that you really got to start young because if you wait, you're going to miss that window when kids are the most vulnerable and when they really need this protection, so that less than 6 months period of age.

We won't talk about it today, but, hepatitis B, this idea that, oh, let's just wait. We tried that. Let's just wait and target risk groups. About a third of the hepatitis B cases were being missed with that. Don't try to reinvent the wheel. Just ask what have people done before. One of the big arguments you hear is, "Oh my gosh, all of these different vaccines," and they start counting on their fingers. This is this question about multiple vaccines being safe at the same time.

They point out here that, "Every day your child will encounter as many as 6,000 antigens just by being a kid." Put that, it's like, oh, my gosh, you're going to be overwhelmed by all these vaccines. Even if your child got four vaccines at once, they talk about this 276 antigens. Just put the 6,000 just by being alive and being a kid out there in the world. Then we're talking about 276 antigens from the vaccines.

VR: Such a nonsense argument. Such a trope. These anti-vaxxers, too many antigens, just shows ignorance. The fact that most people are not going to challenge that statement, right?

DG: It sounds like and I think that's what you really have to watch as they say, "Oh, well, I've seen kids and they were beautiful and wonderful and then they got the vaccine and now we see these problems." Kids develop problems at certain ages. They're much more likely to develop problems if they don't get these vaccines. We've talked about hundreds of kids now, getting measles, ending up in the hospital. Now we're talking more and more about children being paralyzed because they're getting polio, something that used to just be such a terror throughout the world, which we're at risk of.

Yes, these numbers. “Oh, well, maybe we should wait.” We talked about the risk there. “Maybe we should give smaller doses.” That just doesn't work. You have to actually get the right dose. Think about antibiotics like, "Oh, we're just going to give tiny doses." Well, that's a recipe for disaster. The vaccines, the actual dose has been studied and the dose is appropriate. The timing is appropriate. Really be careful about, what sounds like, "Oh, I just want to be safe versus I'm just using rhetoric to undermine confidence in vaccines and public health."

VR: I don't know who's going to be the director of HHS, but I hope whoever is leaves this up, right?

DG: I think that's the challenge. What's the timing here? What motivated? This should have been going on all the time, by the way, HHS. I'm glad you've awoken from your dogmatic slumber to making friends there. OK.

Avian influenza. This I found quite upsetting. This was a headline, "20 big cats die from bird flu at a Washington sanctuary." Then more of half of the cats at the sanctuary in Shelton, Washington, died of the virus over the past several weeks.

Really what got me was - maybe I'm an animal lover, but I'm sure a lot of our listeners are. We read in this article, in addition to the half-Bengal tiger named Tabbi. In the article linked, you can actually watch some archived footage of Tabby animal enrichment with this ball and the water feature. In addition to the half-Bengal tiger named Tabbi and four cougars, Hooligan, Holly, Harley, and Hannah Wyoming.

VR: It's a take on Hannah Montana, isn't it?

DG: I think it's a play. “The dead included an African caracal, named Crackle; two Canadia lynx cats, Chuckie and P’uch’ub; a Geoffroy’s cat, Mouse; I guess, a Bengal cat, Pebbles; a Eurasian lynx, Thumper; and four bobcats and five African servals, according to the sanctuary’s statement."

VR: It's too bad. These are very nice animals.

DG: They're beautiful animals and you could just - here's a - I've got a picture of them. This is Blondie, an African serval. You just sort of - look into the eyes of this little cat there. People keep asking, "Should we worry about avian influenza?" Yes. We'll talk a little bit more about how they're dealing with the millions of chickens out in California. If the way they're disposing of those is safe.

VR: I don't know if most people like animals or not, but you should, it's part of the ecology of the planet. These were sanctuary animals, but nevertheless, when you say no one is safe until everyone is safe, I think we should include non-humans as well.

DG: I certainly do when I say that, just think of, think of like people, their dream vacations that go somewhere, maybe like I recently came back from Africa, and seeing giraffes and lions and zebra. I think most of us really enjoy animals and just knowing that they're out there.

All right, well, for the human animals, acute respiratory illness activity, we are in the thick of it. In most of the country, we're at moderate or high. Only a few areas where the acute respiratory illness activity is not at those levels. Let's break it down.

Flu is here. Influenza A is here, and we really - we have influenza A high activity throughout the country. Looking at wastewater data, you can see a lot of areas. Some areas where it looks like we're high or very high, so really full-fledge. The influenza maps I show from the CDC are always a little bit behind, but you can see out there in the West Coast, we're at high or very high activity areas in the South. Basically, the activity is on the way up all across the country.

I do want to talk about this article, which I think is very telling because it's always important to ask, does this match what I'm seeing? Anecdotes can be a challenge. This is the article, "The Burden of All-cause Mortality Following Influenza-associated Hospitalizations: Influenza Hospitalization Survey Surveillance, 2010-2019," and this is published in *CID*. This is one of those things, practicing clinician, for instance, taking care of patients in the hospital with flu, has a certain experience, oh, maybe one in 50, maybe 2% of my patients die, and then I send them home, and "they then do well."

Is that the case? We've talked a little bit about this with COVID, where you may send them out the door, but what happens in the next month, two or three? People are often interested

in how deadly different infections might be, and I remember lots of discussion about what the infection fatality rate was versus the case fatality rate with COVID. This is this distinction, someone gets infected with COVID, we may or may not recognize that, and they may or may not get a diagnosis. They may not be recognized as a case.

Then you have recognized cases where they've actually been diagnosed, they had a test done, and then what's the percentage of the cases that ended up dying, so there's a little bit of a difference here. Then we're talking here about not only cases, but recognized cases that required hospitalizations, these folks end up in the hospital. Here, these investigators are looking at how many people who ended up hospitalized die from the flu, and not just while they're in the hospital. Let's go through the data here.

Here, the investigators looked at 121,390 cases hospitalized with laboratory-confirmed influenza over nine seasons. What percent died? 5.5% of these folks end up dying. That seems like a lot. It seems like more than 1 in 20. Let's start here. We have a case fatality rate of 5.5%, but then we're going to look a little more closely. They report that 76% of the cases, most of the cases, were in patients aged 65 years of age or older, 71% were non-Hispanic white, 34%, about a third, had four or more underlying medical conditions.

This is where it gets interesting and what I was sort of wanting to discuss. Among all the persons with an influenza-associated hospitalization who died, about half, 48% of deaths occurred after hospital discharge. The median number of days from discharge to death was nine. These people, they're in the hospital, we send them out, and an average of nine days later, just as many people as died during the hospital stay are going to die post-discharge.

Now, the post-discharge deaths more often occurred in older patients, and among those with underlying medical conditions. Of 37% of the patients who died, only 37%. Only about a third of these people actually were attributed to influenza on their death certificates. Sort of an interesting issue. A lot of these folks, we've talked about this, they were in the community, they got flu, they ended up in the hospital. What's actually happening, about nine days after they end up out of the hospital, they end up having a cardiovascular event. That's actually what gets coded if you don't look very closely at the cause of death.

VR: It just underscores the fact that when you talk about case fatality, you have to always take into account the sex of the person, because for COVID, men died twice as often as women, and the age, it goes from very low to very high. Where you are. In China, for example, early in the pandemic in Wuhan, you have very high fatality rates, whereas outside Wuhan, it was lower because the hospitals were not overwhelmed and they could take care of the patients. All these, nuances factor into it, there's not one CFR.

DG: That's really a challenge because people always want to know and there were, all these Hopkins trackers that people were following. It's really tough. Yes, what is the case fatality rate? What is the case fatality rate in hospital? What's the case fatality rate if you follow these folks out another month or two? What's the case fatality rate whether you're in surge conditions or not? Even some of the issues with the different variants.

Early on, when folks were using hydroxychloroquine, we saw about a 20% mortality raise because we were doing harm with that medication. We saw steroids being used at the wrong

time in the wrong doses. We saw then when the Omicron hit Hong Kong in this largely unvaccinated population, we saw about a 4% case fatality rate within 30 days, which was as high as it was getting anywhere during - so yes, always really tough to track down and compare these.

VR: This is a very good point. Hydroxychloroquine killed a lot of people, and a certain individual forced the FDA to license that, and there are no consequences for that behavior whatsoever.

DG: A certain person published a fraudulent article, which we talked to last week, some of the co-authors withdrew, the data was fudged, it was manipulated.

VR: Still no clinical trial was done in the U.S., and it was approved by the FDA. A dark spot on their history.

DG: Yes, no, clearly a dark spot. All right. If flu wasn't enough to get you, and I was consulted on a couple flu admissions today, so we are seeing this. Also got some calls today to see some folks with RSV. RSV activity is also high, and a couple different ways to look at this. One is the most up-to-date wastewater tracking where it's high. You can also look at hospitalization rates per 100,000. We're clearly on that exponential rise at the moment. Activity has followed that typical pattern of being high, sort of sweeping up from the South.

COVID, oh my gosh, three things at once. This is a triple-demic, or whatever they want to call it, SARS-CoV activity in the most recent updated wastewater is actually high across the country. We're even, I always think of this as a late indicator, but we're already starting to see certain states with a 2% to 4% of all the deaths are already due to COVID. We see that out in - is that Arizona and up there in Minnesota, so sort of follow that over time. Even the sort of delayed wastewater from earlier, mid-December from CDC, we're already seeing exponential rise in most of the country. We're headed well towards another peak, as one of the two of us predicted in January, so to say.

VR: It's delayed. At least it's delayed.

DG: At least it is. Yes, at least it's a little delayed. Unfortunately, everyone's all gathered around right now, so the perfect storm. You know what, Vincent? The only reason this is happening, this has nothing to do with human behavior and the fact that it's winter, it's all about the variants, isn't it?

[laughter]

VR: Yes. Of course.

DG Yes. I say that tongue-in-cheek because the variants are doing what they're doing. Not much really going on there, KP.3.1.1 is being slowly outpaced by XEC. No, this is really, as we've tried to reinforce over and over again, it's behavior, this is falling into this by seasonal peaks.

VR: Flu does the same thing. Variants take over from season to season. Similar pattern, right?

DG: Yes. Really similar. All right. Vaccines. I mentioned we're going to be talking about vaccines and apparently, childhood vaccines have become political. I joke about that because, yes, clearly. This week we have the article, "Initial Effectiveness of mRNA-1273 against SARS-CoV-2 Infection and Hospitalization in Young Children," published in, yes, one of my favorite journals, *Open Forum Infectious Diseases*. The objectives of this study were to assess mRNA-1273 - it's Moderna - vaccine effectiveness against symptomatic SARS-CoV-2 infection, and COVID-19-related hospitalization among children aged 6 months to 5 years during the initial five months of the vaccination campaign, as well as to determine whether the vaccine efficacy varied by age group. Six months to less than two versus 2 to 5 years. Here they included 572 test-positive cases and 3,467 test-negative controls. Receipt of the Moderna vaccine was associated with reduced symptomatic SARS-CoV-2 infection, which we care a little bit about, maybe me more than Vincent, but a 90% reduction in symptomatic COVID in these kids, and an 82% reduction in COVID-related hospitalization.

We've talked about thousands of kids end up each year hospitalized with COVID. This study, as they conclude, shows that Moderna's mRNA-1273 vaccine provided strong initial protection against symptomatic COVID-19, 90% vaccine effectiveness there, and against hospitalization, 82% vaccine effectiveness in children aged 6 to 5 years, once you start looking seven days after that second dose.

All right, and testing, just a little bit of a pause here on testing, right? It's the holiday season, you get cough, you get sniffles, you've got what you think is a viral syndrome, as we've been commenting for a while. The only way to know what viral syndrome that is, is testing. There are no symptoms that are clearly discriminatory. Yes, if you lose your sense of taste and smell, and you're not congested, that might be COVID. You might retain your sense of taste and smell, that might be COVID. It might be a cough, it might be a sore throat, it might be GI distress. Unless you do that flu or that COVID testing, you don't know. A lot of situations, it's really incumbent on patients to, unfortunately, inform their healthcare provider what that viral syndrome is through home testing.

VR: Daniel, shouldn't we have a test that would simultaneously do flu, COVID, and RSV?

DG: We do, we have that, and actually, we have that in a lot of our urgent cares in the region. There's also the LUCIRA combination flu/ COVID test that a patient can do themselves. They can pick that up at Walgreens or some of these other places.

VR: The urgent care test is a PCR test?

DG: Most of the one we're using is actually an antigen test, but a lot of our hospitals have a rapid molecular test, give us an answer in 90 minutes.

VR: It would be nice to have a rapid antigen trio test.

DG: I think it would be great if we had that for consumers. The LUCIRA is actually molecular, it's one of these isothermal tests. I think that, it really changes everything. I recently saw this when you're in Africa and someone comes in and they're sick. If you don't have the ability to do diagnostic testing and you're relying on just your clinical judgment, you're wrong way too often. Really, yes, providers really need help. We really need access to testing, even here in the U.S.

All right, so let's say you do that testing and you test positive. I'll continue to leave in the links to the guidelines, but number one, we are still recommending Paxlovid. Remember, based upon that EPIC-HR randomized control trial, 86% reduction in progression in unvaccinated individuals back during Delta predominance and about an 80% reduction in progression to severe disease. Currently, Omicron vaccinated individuals, we have over 800 real-world efficacy studies there. If you're over the age of 50 or if you have any risk factors for progression, why not reduce your risk of progression by 80% and in some cases, consider it for prevention of Long COVID.

All right, number two, remdesivir, that's based upon the PINETREE data. That's also about 87% reduction of progression if given in the first seven days. It is IV, so you may have to go to a place to get that. Molnupiravir, Thor's hammer, a little less impressive, but another option if they're drug-drug interactions or other issues, convalescent plasma in certain contexts. Remember, germ theory. If you've got acute COVID, you can spread it to your friends. Same with the flu. You show up at that holiday gathering and you're sick, you feel crummy, pretty soon everyone else will feel sick and crummy as well.

We're trying to prevent progression to the second week, that early inflammatory phase where, in certain situations, folks end up in the hospital. This is when there might be a role for steroids, anticoagulation, pulmonary support, remdesivir, immune modulation. Unfortunately, we're still, as I mentioned, seeing folks progress here. Last year we averaged over 100 deaths a day.

All right. A bunch today on COVID, late phase, PASC/Long COVID. In the *MMWR*, we have, “Notes from the Field, Long COVID and Significant Long COVID-associated Activity Limitation among Adults by Jurisdiction - United States, 2023.”

Here, CDC analyzed data from the 2023 Behavioral Risk Factor Surveillance System. They give a nice acronym, BRFSS. I don't know, but large population-based cross-sexual survey of non-institutionalized U.S. adults aged 18 or older. These BRFSS sample participants used random-digit dialing of mobile and landline telephones. They're getting self-reported information here. Age, sex, previous COVID-19, current Long COVID, significant activity limitation due to Long COVID. Here, Long COVID was defined as self-report of any symptom lasting for three or more months at the time of interview that were not present before having that COVID-19.

When they do the survey in 2023, 6.4% of the U.S. adults reported experiencing Long COVID when surveyed. It's not great. It's actually a lot of adults if you start, taking 6% of the 350-plus million folks in the U.S., and you get different ranges. Long COVID-associated activity limitation ranged at 12.8% in District of Columbia. You see a 29.4% in Puerto Rico. Among the seven jurisdictions with current Long COVID prevalence of greater than 8%, Idaho, Puerto Rico, and West Virginia were also in the highest prevalence quartile for significant Long-COVID-associated activity limitation.

I have a nice graphic here of an individual, huffing and puffing, trying to make it up the stairs. I got a woman here just trying to work on the computer and just not able to. Of course, the poor dad. His kids want to play with him and he's just sitting on the floor, just not able to even participate.

All right. 2024 update of the Recover Adult Long COVID Research Index published in *JAMA*. Many people remember this. This is this index that can be used to really discern which symptom clusters are coming from Long COVID to help us identify folks with this.

I won't go into too much, but it's really just an update where they compare this index, the 2024 and now updated to the 2023, assigning different points, things like loss of smell or taste, the post-exertional malaise, the brain fog, chronic cough. I'll leave a link into that as well. There was also a really nice piece in CIDRAP. I don't know if people listen to the CIDRAP podcast. I was listening to it today. This is out of University of Minnesota. They covered why do so many different studies give us different numbers on how many people are suffering from Long COVID, and a lot of things they talk about that might play into that.

They have a few nice quotations from Ziyad Al-Aly, who's the Chief of Research and Development at the VA St. Louis Healthcare System. I'll just read these off: Variation in incidence and prevalence estimates generally stem from variation study designs. Are you using surveys of self-reported Long COVID versus cohort studies? The definition of long COVID, is it narrow versus broad? What population is being studied? Predominant variant, vaccination rates, et cetera. "I also note lack of any information on infection," he said in an e-mail, “because most people abandoned testing.”

We talked about that. A lot of people get COVID without knowing it. They subsequently develop health problems that could be post-COVID conditions and cannot attribute them to an infection, and won't be able to identify them as post-COVID. He concludes, we entered a phase where post-COVID conditions now intermingled with baseline disease. Consequently, it has become harder to detect through these kinds of surveys. All right. A few more. A lot going on here in the Long COVID section.

Since we're still limited in terms of managing Long COVID, the best thing we could do is prevent it in the first place. We have the article building on this literature, “Real-World Effectiveness and Causal Mediation Study of BNT162b2 Among COVID Risks in Children and Adolescents,” published in *eClinical Medicine*. The Pfizer-BioNTech vaccine. Here, we have the results of another real-world vaccine effectiveness study. They use data from 20 health systems in the RECOVER PCORnet electronic health record program.

Three independent cohorts were constructed, including adolescents, 12 to 20 years during the Delta phase, July 1, November 30, 2021. Children, 5 to 11 years. Adolescents, 12 to 20 years during the Omicron phase, January 1, November 30, 2022. The intervention is first dose of the Pfizer-BioNTech vaccine in comparison with no vaccine. The outcomes of interest included conclusive or probable diagnosis of Long COVID following a documented SARS-CoV-2 infection. Body system-specific conditional clusters of post-acute sequelae of SARS-CoV-2 infection, PASC, such as cardiac, gastrointestinal, musculoskeletal, respiratory, and syndromic categories, end up with pretty large numbers here.

You've got 112,590 adolescents, 88,811 vaccinated, included in the cohort for the analysis against Delta, 188,894 children. With 101,277 vaccinated, 84,735 adolescents, 37,724 vaccinated when they're looking at analysis for Omicron. What do we end up with? During the Delta period, the estimated effectiveness of the vaccine against Long COVID among adolescents was 95.4%. During the Omicron phase, estimated effectiveness among children

was 60.2%, and then 75.1% among adolescents. Really some compelling differences here between the protection against Long COVID that we're seeing in children and adolescents.

What I really think is a big thing here, we already talked about the fact these vaccines can keep the kids out of the hospital. What are most parents most worried about that their children will have lingering after-effects of getting that COVID infection? Here, these are really dramatic reductions.

VR: They're very impressive. People should not question vaccination when you get numbers like this.

DG: This is interesting. this is a population which is clearly under-vaccinated. A lot of parents don't appreciate the protection that they can offer their children.

VR: One of the nominees for one of these healthcare positions has stated long ago that kids don't need to be vaccinated against COVID. This is just uninformed.

DG: I think the tough thing is you can't just have an opinion and then just stick with it. We didn't know a lot many years ago when one of these individuals was writing the Great Barrington Declaration.

VR: Yes, that's what I'm referring to. [laughter] The thing is, you go with what you have. You don't make stupid proclamations based on nothing, which is what you're saying, right?

DG: Yes. These are big numbers. These are great studies. Vaccinations in the kids can actually, it can keep them out of the hospital or it can keep them from requiring medical attention, which over 100,000 kids last year. It can keep all these kids from ending up with Long COVID and all the horrible impacts.

VR: If you were unsure, if you don't have the data, you go to the default, which is to treat, which is to vaccinate.

DG: Yes. One of the most effective, safest introductions in modern medicine. Just a couple more to finish this off before we get to our e-mails. Two more articles, the article, “Personality and Neuropsychiatric Symptoms in Individuals Diagnosed with Long COVID,” published in *BMC Infectious Disease*, where we read about the results of, this is an online survey with 114 participants diagnosed with Long COVID, high rates of depressive disorders, 46%, generalized anxiety disorders, 21%, sleep disturbances, 76%, and not surprising reported cognitive changes, 95%.

The article, “Post-COVID Condition Risk Factors and Symptom Clusters and Associations with Return to Pre-COVID Health - Results from a 2021 Multi-state Survey,” published in *CID.* Here they reported, again, the high rate of Long COVID in people who are infected in the pre-Delta period and a high percentage that still have not returned to their prior health.

I will finish off, as I've been saying for a while, no one is safe until everyone is safe, and I'm going to include the animals. I do want everyone to pause the recording right here, go to parasiteswithoutborders.com and click Donate.

I have to say, I've got to thank everyone who's done that, everyone who listens. This is a joint effort. It's not just me and Vincent here. It's all the people that help us find the important articles to discuss. Without your support, we couldn't continue. We're going to continue our fundraiser, November, December, January, and we're hoping to get up to a potential maximum donation of $20,000 for *MicrobeTV*.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Brian writes, "I work at a landfill in California. We are receiving truckloads of chickens that have been ground down into a fine material to make transportation easier. It's called detritus. This, of course, makes it easier to become airborne when it dumps out of the truck. We then spread this material with Caterpillar dozers, and mix it with other garbage into our landfill cells before covering it in dirt. I'm concerned for me and my fellow workers. Should I be concerned? Does H5N1 die quickly after the bird is killed?

Anyone know how long it survives outside a host? Sound like we should, at minimum, be wearing N95 masks when these trucks arrive and offload the dead bird detritus."

DG: What a frightening - I feel like this is a sci-fi film in the making here, Vincent, right? Just imagine these trucks and this cloud, the plumes. There is data. We have data. It's a little bit dated, but on H5N1 on poultry feathers. They do a lot of these, we'll call them fomite studies. I don't know. Is a bird ground like this? Is it a fomite? Does it fall into that category? No, it can last. It's temperature-dependent. Of course, the colder it is, and it's getting colder in places, the longer that you can actually have a viable infectious virus.

Yes, this just sounds like a recipe for aerosolizing and getting that into folks' eyes and lungs. Vincent, thoughts from you? Would you wear an N95?

VR: I would. I definitely think they should be wearing N95s. Yes, because this is being aerosolized. You don't know if it's infectious, but you should just be careful because it's a perfect scenario for getting infected The truck drivers, the people at the landfill, when they dump it, and I don't know how long, I guess when they cover it with dirt, then you're probably OK, but you should be wearing these masks. Totally.

DG: Yes. I'm just thinking like, how do they make the detritus? I'm just thinking of the process of grinding these chickens. Oh my gosh.

VR: Wherever that's done, they should be wearing masks too.

DG This is one of those, yes, I would err on the side of wearing an N95.

VR: Tom writes, "Is doxycycline a medication that qualifies as obfuscation of ‘symptom-free’ for COVID-19 infection in the same way that acetaminophen complicates the notion of fever-free? A friend was prescribed doxycycline, (RAT negative), based on painful sinus congestion and a history of hard-to-control bacterial sinus infections. The anti-inflammatory quality of the drug was prompt and effective in reducing symptoms with the exception of a cough,(post-nasal drainage). However, 36 hours later, tested RAT-positive for COVID. I expect that Hickam might remind the patient to keep taking and finish the antibiotic. The prompt improvement in sinus discomfort derailed discussions with the doctor about Paxlovid. A persistent cough and respiratory infection is 'trouble' in my opinion. What to watch for? How should doctors

respond to cases where symptom progression is very effective but the underlying disease progression is unknowable as a result?"

DG: This is great. Tom, I love that $10-word obfuscation. What a wonderful word. It's up there with crepuscular and a few of my others. That's always a challenge. We always say, are you fever-free without antipyretics? Are your symptoms improving without some sort of an anti-inflammatory? One of the challenges with COVID is it's like pancreatitis, it's like sepsis. The reason we recommend early treatment is that we have recognized that there are certain individuals, certain parameters that put a person at risk of progression. You don't just say, "Oh, you seem like you're fine."

I remember the acute pancreatitis cases, you'd tuck them at the end of the hall and they would not be alive the next morning. That's this issue with the second week of COVID. Yes, this is a challenge. I think you point out some good things. If this is an individual who is high risk of progression, you certainly want to have that Paxlovid discussion.

VR: Do you like the word bespoke?

DG: That's also a nice word.

VR: Yes, we had that in the title of a paper we did on *TWiV* last week.

DG: Oh, I like that.

VR: They made bespoke bat antibodies.

DG: Oh, I like that.

VR: You have a bespoke suit made in Hong Kong, you can make bespoke bat antibodies. [laughter] Ellen writes, "My grandsons, aged 2 with a cold and an ear infection, age 6 with a persistent wracking but unproductive cough, were prescribed amoxicillin by their pediatrician and both broke out with a red body rash. I understand that this may occur when there is a concurrent viral infection. What is the connection between the antibiotic and the virus? Is it just this particular antibiotic that produces this non-allergic reaction?

Their pediatrician stopped the amoxicillin after seven days and is prescribing a different antibiotic which the parents are ignoring. Texas Children's Hospital website encourages continuation with amoxicillin and advises against switching to a different antibiotic as, 'This can lead to the physician labeling them as allergic thus leading to the patient being given different antibiotics potentially causing more harmful side effects.' What is the standard of care in this situation?"

DG: Yes. It's really interesting and we've been seeing this for a while and unfortunately, I think what you point out is this is true. These kids often get labeled and so the kid has a viral thing, classically it was mono or Epstein-Barr and then they get the amoxicillin and this rash develops. It's not an allergy. It's not a reason to avoid amoxicillin in the future, and it might be a reason for you to say they may not have needed the antibiotic even to begin with. The mechanism, that I don't really fully understand. What is it about the amoxicillin, how does it trigger this rash with the viral syndrome?

Maybe some of our e-mailers know the etiology there, they can let me know.

VR: Karen writes, "I'm 67, I had COVID three times. First two times I took Paxlovid, both illnesses were not horrible but I was definitely ill. The third COVID came at an interesting point. A family friend, physician, four months older than me, just had COVID and advised not taking Paxlovid. He and his spouse both had COVID and did not take Paxlovid. Their illness, of course, did not seem any worse than mine. I recently had my annual physical. My doctor also had COVID, did not take Paxlovid, and suggested I really did not need to take it given my lack of comorbidities beyond age.

I planned to get the vaccine shot but another friend came for dinner and brought not only wine but COVID. This third time I did not take Paxlovid, the course of illness was not better or worse. My post-COVID experience seems no better or worse since I'm edging toward elderly. (Some say I am firmly in it.) My memory isn't what it used to be. My trouble with finding nouns, always every present, seems no better or worse, et cetera. A long message for which I apologize. I'm not sure what my question is as well; possibly, 'To Pax or Not the Pax, that is the question'."

DG: The guidelines are To Pax. Why do we say that? Again, every time you get COVID, it's a roll of the dice, it's a Russian roulette. I was fine the first two times, I was fine the first three times but what happens that next time? There also is a bit of an issue, you bring it up, is with age. We talk about the risk starts to go up at age 50. Let's say you use under 30 as your baseline. If you hit 50 or in your 50s, 28-fold increased risk of going to the hospital. Now you move into your 60s, your 70s, it really goes up dramatically as we get older.

The other, and this is really interesting, and this is some stuff that I was reviewing in a study in Taiwan, is that in younger individuals, there really is this growing immune memory. When we get older, part of immune senescence is that we don't actually get that protection. We may actually over time get knocked down. What we were seeing there in Taiwan was that the more senior individuals with repeated infections, their risk of bad outcomes was actually escalating as opposed to going down, which we have experienced in younger folks.

Yes, about an 80% risk reduction of progression of severe disease if you take Paxlovid. You're going to use a risk calculation here, a number needed to treat, you mentioned no comorbidities, hopefully, you're active and ideal body weight, throw that in there. Also, potentially we might have some impact upon long-term consequences.

VR: Finally, Gary writes, "I'm watching Episode 1176 and I'm still confused about my own polio vaccination. I'm a 73-year-old male, I remember receiving oral vaccine as a young child along with my siblings and parents. I never received IPV. Given concerns about vaccine-derived viruses and wastewater, more international travel in my retirement, and nut cases like RFK and his supporters who want to eliminate vaccines, should I consider a booster with IPV to reduce my risk?"

DG: All right, so maybe we'll each take turns here. Gary, this is an interesting issue. What is the current recommendation? The current recommendation is you go through your series that we've talked about several times. Then if somebody is going to be traveling to what's considered a high-risk situation, it's a recommendation for a one-lifetime booster with IPV.

What is this based on? We've talked about this a little as well. Back when there was some circulating polio, people would get their shots, they would be protected, but maybe there was some kind of a boost in some of those earlier studies.

The thing I have to say is, I've looked for and kept my eyes out for do we ever see anyone in their 70s, 80s, 90s end up having waning immunity and get polio? I haven't seen that. Maybe I'll let Vincent jump in.

VR: All right. The recommendation is when you're young, you get a four-course of IPV, right, Daniel? Four shots. If you haven't got a full course, either three of OPV or four of IPV, you should consider finishing it. That's the CDC recommendation. If you got the whole thing, unless you're going to an endemic area, as Daniel said, you don't have to worry. Both IPV and OPV give similar durability of immunity to paralytic disease. Remember that. It's not to infection. It's to paralytic disease. If you travel to Afghanistan, Pakistan, Sub-Saharan Africa, if you are traveling to those zones, you need a booster, but not the Europe or South America.

You don't need a booster. Now the U.S. is free of paralytic disease, but not virus. When you say polio, it's very confusing because you can mean poliovirus or poliomyelitis. You have to be really careful. You have to specify your terms. The vaccines, IPV and OPV, prevent disease. They do not prevent infection. They do not prevent transmission. We've known since 1928 that the polio vaccine - or that there was no vaccine in 1928 - but infection can be followed by another infection, but you don't get paralysis. It really depends on what you have had, if you can remember what you had.

I have records of having three doses of IPV and three doses of OPV later on. I'm good to go. If you haven't, you should consider following CDC guidelines. Does that sound good, Daniel?

DG: Yes. It's interesting because we bemoan the fact that they had COVID-19 as a disease and SARS-CoV-2 as the virus, and couldn't it? There's certain vanished names as we see here, right?

VR: It's true. We do have poliovirus and poliomyelitis. The problem is they both share polio, so people like to shorten it to polio, and then you don't know what you're talking about. You have to specify it, right?

DG: Yes. They need to just say, because they always talk about we're going to eradicate polio. It's like, you're going to eradicate poliovirus, which you don't seem to be doing each time you keep dumping all these doses of vaccine-derived poliovirus into the community. Are you trying to eradicate poliomyelitis, the disease?

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

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

VR: Happy New Year.

[silence]

[01:00:51] [END OF AUDIO]