This Week in Virology

TWiV 1182 Clinical Update

Host: Vincent Racaniello

Guest: Daniel Griffin

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VR: *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 1182, recorded on January 9, 2024. No, recorded on January 9, 2025. I'm Vincent Racaniello. You're listening to the podcast all about viruses. Joining me today from somewhere in South America, Daniel Griffin.

Daniel Griffin: Hello, everyone. What do you call that, Vincent? That's like date misinformation, getting the year completely off, we're all adjusting to 2025.

VR: That's right. I think that's the first time I made that mistake.

DG: That's OK. Hello, everyone. Yes, I am just about 30 miles north of Venezuela on a little island in the Dutch Antilles. We've got a lot to cover. Can you imagine that? I'm going to start off with a quotation. I think as we get into today's episode, the cat lovers will understand why I start with this one. "Owners of dogs will have noticed that if you provide them with food and water, and shelter, and affection, they will think you are God. Whereas owners of cats are compelled to realize that if you provide them with food and water, and affection, they draw the conclusion that they are God."

VR: That's great. That's just great.

DG: That's Christopher Hitchens. He's famous for his epistemological razor, which states that what can be asserted without evidence can also be dismissed without evidence.

VR: Basically, according to that, since the saying that SARS-CoV-2 came from a lab, there's no evidence for that, we can dismiss it without any evidence, right?

DG: When people, it's like, I believe the earth is flat. It's like, if you want to actually talk about that, there's going to have to be something there. You can't just make wild claims. I've got a nice little AI-generated picture of a black cat here eating raw meat, which we will get to in a moment. I just wanted to start off with mpox, a few things happening here. There's a couple articles, I'm going to leave links to these. One was "Mpox Vaccination Hesitancy, Previous Immunization Coverage and Vaccination Readiness in the African Region: A Multinational Survey," published in *The Lancet*.

Also an article, "Global Prevalence and Correlates of Mpox Vaccine Acceptance and Uptake: A Systematic Review and Meta-analysis," also published in - this is published in *Nature*. Really what we're seeing here in these articles is a description about a lot of actual vaccine hesitancy, which I thought, mpox is just such a horrible disease. We have no treatment for it that actually works, as we're seeing with the TPOXX studies. Who wants to get their - what is it, the natural immunity after being covered with these horrible - Apparently, thanks to social media and some individuals out there spreading misinformation, we're seeing actually vaccine hesitancy.

That is not serving the rest of the world well. This last week, France identifies first case of new mpox variant. The patient in this case is a woman. I want to point that out. I actually diagnosed it in a woman, northwest region of Brittany, at a hospital in Rennes, France. This individual probably was exposed to someone who had come back from where this was circulating. Also earlier today, we read about a cluster in China as well. This is that clade 1B variant, which is the new variant, which has actually affected a lot of children as well.

Avian influenza, Vincent. People, a lot of comments about this. Apparently, this is a hot-button topic. I don't know if you realize this, but the following article was published in *The New York Times*, "First Bird Flu Death in U.S. Reported in Louisiana." It comes with a subtitle. It just really got me bothered. The deceased was over 65 and had other medical conditions, state officials said. That's in the subtitle. I got to get that right in there. There's that wildfire in southern California. A couple people have already died, but it's OK. They're over 65 and had medical comorbidities.

It's not OK. Here they mentioned that the individual became infected with the bird flu virus H5N1 after exposure to a backyard flock and wild birds. They also mentioned the Canadian girl we've talked about. Note that both patients carried a version of the virus that is circulating in wild birds distinct from the one causing the outbreak in dairy cattle. Just a reminder of our discussion on *TWiV* 1180, not all bird flu is the same. We should be concerned about the different types for different reasons. Most cow infections are genotype B. Think genotype B for bovine, and for humans so far, fingers crossed, generally benign.

Not completely benign for cattle. If you care about cattle, if you like to drink milk, which, count me in both camps, cattle, we may see a low mortality, but significant drops in milk production in infected cows. Also, this genotype can kill cats and continues to infect humans, presenting an unprecedented opportunity for adaptation. Think genotype D for ducks or for directly from birds or D for deadly. This is what we have recognized for 30 years has spread globally in migrating birds. We talked about vaccine candidates. We talked about antivirals. I just want to point, we care about both types for different reasons.

This week we're going to care about it because of a *CIDRAP* piece that I'm going to link to. This is an image from CIDRAP. There are these two cats and they're at this bowl of what looks to be raw meat. They've got these evil looking cat eyes. I love cats, but man, these cats, I'm frightened just looking at them. The *CIDRAP* piece is titled, "California Probe Ties Cat Avian Flu Illness to Raw Pet Food." Let me just read. On New Year's Eve, the Los Angeles County Department of Public Health urged pet owners to avoid feeding pets raw food after tests found links between a cat's H5 avian flu illness and raw food sold by Monarch Raw Pet Food at California farmers' markets.

The announcement marks the second raw pet food company tied to a related illness in cats. There was an issue up in Oregon involving one type of frozen raw pet food from Northwest Naturals that was marketed nationally. In its statement, the LA County Department of Public Health said H5 avian flu from product samples of Monarch's Raw Pet Food have been found in an investigation into an illness involving a house cat with a lab-confirmed infection after consuming the product. Four other cats from the same household have presumed H5 infections after eating the same food.

VR: Daniel, what's the source of the H5 in the raw meat? Do they actually put chicken in that or is it something else?

DG: I'm trying to figure out. If you look at the picture, it looks to me like ground beef there. Is it related to the dairy? Is it somehow related to direct from avian? I think the point is it wouldn't actually matter. The cats are susceptible and can die from both.

VR: Do they know what genotype this is, the D or the B?

DG: I haven't seen yet.

VR: That would be interesting, because if it's the cow version, then maybe they have cows on the farms where they make this meat, and that's the source.

DG: Or even maybe there's some beef in there. People like to feed their - All right. Human metapneumovirus. Vincent, I was asked to be on the Bill O'Reilly show this week, but I couldn't because I'm down here off the coast of Venezuela. There might have been other reasons. Anyway, so human metapneumovirus. People had questions about this. Our listeners may have seen some of these headlines.

This is an evolving story. I'm going to give you the steps along. There was this piece in *The Guardian*. What is human metapneumovirus? What is HMPV virus outbreak in China? Raises alarm. This is in *The Guardian*. Viral video shows HMPV chaos at China hospital, raises alarm. “Is Human Metapneumovirus a New Virus? in *The Economic Times*? What we know about HMPV, the virus spreading in China, in *The New York Times*. Lot of this might border on a little bit of irresponsibility, Vincent, I'm going to suggest.

VR: I agree. This virus has been around for ages. They should know about it.

DG: It was identified in 2001. It's been around for six decades. We know a lot about human metapneumovirus. It's transmitted contact and respiratory particles. Here's probably the biggest thing. We see a little bit of this. Human metapneumovirus activity is low here in the

U.S. A couple cases I saw recently. Usually this follows the end of the RSV season by a couple months. As per the WHO, based on data published by China covering the period up to 29 December 2024, acute respiratory infections have increased during recent weeks of detections of seasonal influenza, rhinovirus, RSV, and human metapneumovirus, particularly in northern provinces of China, have also increased.

This is the observed increase in respiratory pathogen detections is within the range expected for this time of year. During the northern hemisphere winter in China, you ready for this? Influenza is the most commonly detected respiratory pathogen currently affecting people with acute respiratory infections. The WHO is in contact with Chinese health officials. We're really, as many headlines about human metapneumovirus, not consistent with the data we're actually getting out of China and from the WHO.

There you have it. Human metapneumovirus. It is not a new virus. We're very familiar with it. Some of our listeners may have remembered this historically had been one of my favorite viruses, because it would usually start showing up around end of March, early April and remind me that it was time to get the sailboat ready for the spring and summer. It's not any more deadly or scary than any other respiratory pathogen.

VR: Someone on the stream last night asked me, we have a vaccine for RSV. Why don't we have one for metapneumovirus?

DG: Probably next on the slate, it would be great. It's not as big an issue as RSV. We think about numbers of people that end up hospitalized, number of people that require medical attention, number of people that die, human metapneumovirus is definitely below RSV. Good news, I didn't really put this in, but we'll mention RSV in a minute. Really great protection of the infants with RSV so far this year. Doing well there. It's going to be interesting to see what happens with RSV hospitalizations in the kids. Influenza A is at high levels. If you look at the maps by the end of December, basically the whole country is on fire with lots of flu A activity. Really went up pretty abruptly.

VR: You got to watch out when you say "on fire", Daniel.

DG: Actually, with what's going on in Southern California, yes, definitely. Lot of influenza A activity. As we mentioned with RSV, we're also seeing RSV activity is holding at a high level. An upward trend in the last three weeks. You can see that that's most of the country. A few areas where the activity isn't as high as others. SARS-CoV-2, the activity is high. If we go back to our wastewater, you can actually see the Midwest is already above that peak we had end of summer, early fall. The rest of the country just rising exponentially.

VR: I was wrong. I thought there might not be a peak. I was wishful, but I'm wrong. I admit.

DG: It's a little unfortunate. This looks like we've now got another player in the game. It seems so far to be settling into this biannual peaks. Which makes sense as we talk about vaccine strategies, particularly in the most vulnerable. Everyone always plays it on the variants, but nothing exciting here. XEC is little bit, relative to KP3.1.1. At some point, I think people are going to have to look at this data and explain what fixation on the variants we really have.

Moving into COVID, the early viral phase. Unfortunately, we're still seeing cases. Number one, as per the guidelines, is Paxlovid. I'm going to talk about this article, "The Effect of Nirmatrelvir/ritonavir on Short and Long-term Adverse Outcomes from COVID-19 among Patients with Kidney Disease: A Propensity Score Matched Study." This is an *Open Forum Infectious Diseases* article. For context, there's a bit of hesitancy. It takes a little bit of thought to properly dose the Paxlovid in folks with kidney disease. Remember, patients with kidney disease are really at high risk for adverse outcomes despite vaccination.

Because patients with advanced chronic kidney disease and kidney failure were excluded from the registrational trials, the impact of protease inhibitor treatment with Paxlovid in kidney disease is unknown. Here we've got 1,095 Paxlovid-treated patients matched to 584 comparators. Patients who received the Paxlovid were less likely to be hospitalized within 30 days. We're seeing about a 56% reduction there. Actually at one year, you follow this out for a while, the Paxlovid-treated patients had a lower risk of hospitalization for major adverse cardiac events. That's 51%.

We're seeing a 63% reduction in death. We're not seeing any issues with chronic kidney disease. We're actually seeing a decreased risk of chronic kidney disease progression. In an associated *CIDRAP* post, they point out that 94% of patients had predialysis chronic kidney disease, 6% had kidney failure. Nearly all, 92%, had been vaccinated. Highly vaccinated population. Patients given Paxlovid were significantly less likely than comparators to be hospitalized within 30 days. Just to give you numbers here, without treatment, we're looking at 8% up and up in the hospital. With treatment, we dropped that down to 3%. As far as death, those that got treated, we saw no deaths versus about 1 in 30 who were not treated.

VR: Daniel, would you call these real-world results?

DG: That is the terminology. These cohort, these real-world trials. I think that's a [crosstalk] that's a spin.

VR: It's not a placebo-controlled double-blind trial, right?

DG: Yes. It suffers from some of those flaws. Like, what was the difference between patients that got treated versus didn't get treated? It's a lot of those limitations. Remdesivir, actually, which really would be an easier lift in these folks. Molnupiravir, another option for folks with renal issues. In some cases, convalescent plasma. Then not much here as far as the early inflammatory phase. Remember, that's that second week. That's a cytokine storm that we're trying to prevent. Steroids as an option. Right time, right patient, right dose. Anticoagulation. We have guidelines there.

We've talked about those. Pulmonary support, remdesivir. We're still in the first 10 days immune modulation. A little bit here in the COVID late phase, PASC/Long COVID. Really just two articles. The last one we're going to have a little discussion about, at least that's my hope. The article, "Epidemiological Insights into Chronic Urticaria, Vitiligo, Alopecia Areata, and Herpes Zoster Following COVID-19 Infection: A Nationwide Population-based Study," published in *The Journal of Dermatology*. Just in brief, the study aimed to estimate the incidence of the risk of chronic urticaria, that's being itchy all the time.

Vitiligo, there's those areas of depigmentation. Alopecia areata, that's areas of balding, and herpes zoster following COVID-19 infection. Only participants confirmed by real time reverse transcription PCR tests to have COVID-19 were enrolled in the COVID-19 group. The matched cohort without COVID-19 were enrolled randomly at a ratio of 1 to 1. Used to wonder where you find those folks.

The incidence and risk of chronic urticaria, vitiligo, alopecia areata, and herpes zoster were assessed in both groups. A total of 4,976,589 COVID-19 patients. This is 9.58% of the total population of South Korea. They've got an equivalent number of match non-infected control subjects. Yes, chronic urticaria, vitiligo, alopecia areata, and herpes zoster manifested at higher rates within the COVID-19 cohort, even after they did adjustment for all the potential confounders.

VR: What does higher mean? 1.5 -

DG: I was trying to dig through. I was like, is it statistically higher? Is it clinically significant higher? It was a little hard to actually get the raw data out of that. Good comment, Vincent. Last, we have the article, and this is, "Impact of Extended Course Oral Nirmatrelvir/ritonavir in Established Long COVID: A Case Series," published in *Communications Medicine*. Let's just be clear what this actually is. This is a shared case series of 13 individuals with Long COVID who initiated extended courses of greater than five days of oral nirmatrelvir/ritonavir.

They're going to look at this, 11 of them did it outside of the context of an acute infection, a couple did it within the context of acute infection. Really, if you go through the article, you're going to see each of the 13 cases and they're going to describe all about the patient, what they're experiencing, all the different therapies they've been trying, then the experience that they have during and after they get the nirmatrelvir/ritonavir. Then they conclude with, we really should study this. That's really where we're left with.

Yes, we should really study this. There's no ability here to sort out any placebo effect, any difference, relative treatment versus natural history. I think it's really important for us just to point that out. I expect this will get a lot of social media attention spread all throughout there, but that's all it really is just - by the way, we are doing those studies. One study was done out at Stanford. We have a few others ongoing at the moment. We will find out about the impact of extended Paxlovid in established Long COVID.

VR: This study is just too small to make any conclusions, right?

DG: It's really not a study. It's just a description of these 13 people and their experience. You don't really know what would have happened with or without. No placebo, no control group. There isn't even a natural history. There isn't even a random, hey - Then I am going to conclude, as we've been saying for a while, this seems very appropriate down here off the coast of Venezuela.

No one is safe until everyone is safe. I do want everyone to pause recording right here. I want to thank everyone for the tremendous generosity. We are finishing up our microbe.tv fundraiser where it looks like we're going to hit our goal, be able to give $20,000 to *MicrobeTV* to continue this science education. We'll be doubling your donations up to a potential maximum donation of $20,000.

VR: It's time for your questions for Daniel. You can send yours to Daniel at microbe.tv. Robert writes, "I'm a long-term listener and lover of science. Your weekly update has been a religious listening event for me. One of the most important aspects you have been consistently highlighting is to follow the science. While this is not so romantic in the eyes of some people, conspiracy theorists and anti-vaxxers seem to think every aspect of pathology is linked to a vaccine or just populating the 'COVID' or 'flu' box on a death certificate. I found this article posted by the McCulloch Foundation, which is run by Peter McCulloch, MD, creating an inflammatory base to question the recent death of a man in Louisiana.

They note the man had many comorbidities and that the cause of death cannot be solely linked to H1N1. That's just it. If you have multiple comorbidities, you have a higher likelihood of poor outcomes with viral infections. I'm very confused about how we as a society can trust and allow a platform that is spearheaded by physicians who are known to spread misinformation to gain followers and capital. Can something like this be brought to the AMA? Where does it end? This article was reposted to the McCulloch Foundation's LinkedIn profile and is gaining traction. The bias and disinformation are painful to read." You aware of this, Daniel?

DG: Yes. This is a really tough argument that we have to work with, where this idea, I guess, that if we don't have comorbidities, apparently we're immortal, and that it's a blame game. If you died from COVID, it's because you didn't exercise enough. You didn't eat the right foods. That really seems to go against the oath we take, the idea that we're there to take care of patients. We're not here to blame them. We're here to guide them, to work with them, to do everything we can. It's not like we write you off once you get diagnosed with diabetes, or we write you off because your life situation is such that you're not wealthy enough to go to the fancy gym and maintain that ideal body weight.

A number of the purveyors of misinformation, they do end up losing their board certification. I'm not sure how the AMA is supposed to enforce this conduct. You know what, Vincent, I'll just use this as a soapbox. Maybe we're not using the right selection criteria when we choose who gets admitted to our medical schools and who graduates from our medical schools. Getting a bunch of great grades in science classes really just does not weed out people who just don't have the integrity and the character to be honest and to put their patients in front of their own self gain.

VR: I totally agree with that. I just think just gauging it on grades is ridiculous, but that's what they've been doing for years. Daniel, let's say a patient comes in the hospital, has influenza and progressively gets worse, needs oxygen and eventually has a myocardial infarction. Wouldn't you put on a death certificate, cause of death, myocardial infarction, secondary to influenza, no?

DG: That would make sense. I think as we've like picked up, particularly on the ID *Puscast,* is there's really been a failure of an appreciation that, particularly for younger individuals, folks in their 50s, 60s, I'm going to call them younger because I'm in my 50s, they don't necessarily suffocate and die that way when they get influenza or a viral infection. It's really the next 30 days, the risk of a major adverse cardiac event doubles, and then they die. A lot of this United Health Group and all these other big insurance companies, they're trying to push those

vaccines because they don't want those young, otherwise relatively healthy folks dying in their prime when they still could be paying those premiums.

VR: Meredith writes, "I appreciate all you do to keep us informed about viruses. I turned 50 recently and received my first Shingrix dose. They told me to get my second in two to six months. I was wondering if later in that window is more efficacious. Does it make a difference?"

DG: We often talk about maybe a three-month gap, and that's just our basic understanding of immunology. That's what I did, got my first shot. You could probably jump in four or five weeks later, but I waited three months, because this really is a prime boost approach. That would be my advice.

VR: Gene writes, "I'm a long-term listener to *TWiV*. I have a quick question. I recently turned 65. Which pneumonia vaccine should I get? The options on the CDC website are somewhat confusing. This will be my first pneumonia vaccine."

DG: It's a great question. We spent a little time. They've updated the options and the recommendations here. Now there are two conjugate vaccine options, the PCV20 and the PCV21. Little discussion back and forth about which is better, the 20 or the 21, but I will tell you 90% of the places out there in the U.S. are offering the PCV20. That's the one I got. I think that's a fine, simple, straightforward option. Recommend that.

VR: Carson writes, "I'm curious based on the *TWiV* 1178 question about penicillin, plus other discussion around penicillin allergy. I had frequent strep throat infections as a kid, enough to warrant tonsillectomy when I was 8. I'm now 28. I was always prescribed amoxicillin and had no issues. Close to my surgery date, don't remember how close, but I assume a week or two, I got strep again. Instead of the usual oral amoxicillin, I got one IM injection because the doctor wanted to make sure the infection cleared up before surgery. I felt fine but immediately broke out in a rash.

The office gave me Benadryl and kept me for maybe 30 minutes for observation. Had no further symptoms, but was labeled as having a penicillin allergy. I still report that on medical forms. One additional detail, my mother is genuinely anaphylactically allergic to penicillin, which makes me hesitant to assume that I didn't develop an allergy as well. I'm not regularly prescribed antibiotics now, so it's not a huge problem, but I'm not sure what to do moving forward. Should I stop indicating that I have a penicillin allergy? Should I see an allergist? Should I just wait for it to come up in the event that I need penicillin and then discuss it with the physician?"

DG: This is a challenge, so I'll walk through this because I find this fascinating. First, I'm just trying to tease out timing here. It sounds like you got that shot. You're still in the doctor's office, because they're going to give you the Benadryl. It had to be a relatively immediate response. Yes, I do think that was an allergic response, but not anaphylactic. That's one of the things to point out, that if you are saying, I do have a penicillin allergy, it was immediate, it was rash, it's not anaphylactic, I didn't stop breathing, nothing like that. The reason I point out timing is that you've got sore throat, you get a positive strep test, which 20% of people have, independent of whether or not what's going on is due to strep.

We do worry about Epstein-Barr infection, which came up before, increasing our sensitivity and our reaction to things without a true allergy there. I think this is a penicillin allergy. Discuss it. If you're ever in the hospital, request an infectious disease consult, because otherwise you'll get labeled as penicillin allergy. You may get second-line inappropriate antibiotics, and that's associated with worse outcome. Get that ID doc involved, explain what's going on. Hopefully they can guide the decision to make sure you still get optimal antibodies.

VR: Carol writes, "My son is expecting a baby in August this year. I'm going to be a grandmother, yay. I am due for a Tdap booster. When's the best time to get the booster to optimize protection for the baby?

DG: I'll say about a month before the baby's due. You never necessarily know unless it's a scheduled C-section. About a month out, you should have great protection.

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

DG: Oh, thank you. Everyone, be safe.

[music]

[00:31:21] [END OF AUDIO]