**This Week in Virology**

**TWiV 1068 Clinical Update**

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Aired 9 December 2023

pdf of this transcript available (link)

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

[*This Week in Virology,* Episode 1068, Clinical Update with Dr. Daniel Griffin]

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**Daniel Griffin:** Hello, everyone. This is Dr. Griffin coming to you from Uganda, actually Eastern Uganda, and pretty close to the Kenyan border, up here at Mt. Elgon. I've been working at the FIMRC Clinic for the last week, so this is a special episode as I'm recording this solo and then Vincent will piece it together as best he can. Let us get going, start with our quotation. "Education is the ability to listen to almost anything without losing your temper or your self-confidence." That's by Robert Frost.

We will start off with malaria, seemed very appropriate as I'm recording this in Sub-Saharan Africa. According to a recent WHO report, a World Health Organization report, we are losing ground and adding about five million cases per year. Progress has stalled since 2015 with the rising drug and insecticide resistance. "Progress towards the 2025 milestone is 55% off track," the global health body said, and will be missed by 89% this year if the trajectory persists, and I'll just read a quotation.

"This year's report includes, for the first time, a dedicated chapter focused on the intersection between climate change and malaria. As described in the report, climate change is one of the many threats to the global response to malaria," and I will leave a number of links in our show notes. RSV, still with the shortage of Beyfortus, and, unfortunately, as many of us have moved from shared decision-making to really trying to get the highest-risk individuals vaccinated, we are just seeing that less than 20% of the high-risk adults are taking advantage of the protection of vaccines.

We'll talk more about that next week, but I just want to really point out to people that if you look at RSV, we're really there. The numbers have really shot up through most of the U.S. You wait much longer and you're going to miss your opportunity to protect yourselves, so let's really take advantage of these tools. Influenza, right? This is due to a virus, not the influence of the planets, just by the way. Weekly activity update is really that the alerts are going out. Hospitals, I guess, that otherwise hadn't, are saying, "Let's get those masks on, let's make sure everyone has been vaccinated."

We're really seeing that this has risen. It is mostly influenza A. There is some influenza B, and I wanted to give an update from a comment I made last time. This is really all Victoria lineage. The Yamagata sequences that were reported? Looks like those were sort of added from probably a number of years back. Currently, according to the CDC, as far as isolations this season, most of it is influenza A, but if you're getting into B, all Victoria lineage.

All right, COVID. The wastewater numbers are rising just in time for the holidays, as predicted, and really shooting up across the country, but particularly in the Midwest and the Northeast. Let's jump into children. This is really, I think, an important article here. The article, “Developmental Impairment in Children Exposed During Pregnancy to Maternal SARS-CoV-2: A Brazilian Cohort Study,” published in the *International Journal of Infectious Diseases.* These are the results of a prospective cohort of babies exposed to SARS-CoV-2 during pregnancy compared to a control group of unexposed babies in a low-income area, Brazil.

They looked at the children's neural development. They followed 127 children for one year, 69 in the COVID-19-exposed group, 60 in the control group. All the mothers were unvaccinated, right? So the children are not getting that passive protection that we've talked about. All the mothers were unvaccinated at the time of cohort inclusion, and maternal demographics were similar in the two groups. Twenty percent of the exposed children, compared to 6% - 5.9% - of the control group, received a diagnosis of neurodevelopmental delay within 12 months of life. Then they followed out, for the exposed group, the prevalence of neurodevelopmental impairment was 35.7% at four months, 7% at six months, 32.1% at 12 months, so depending when we're checking, we're getting different numbers there.

All right, just some reminders about transmission. Remember, this is really not contact. Keep washing your hands, keep doing that, but, remember, this is being around an individual who is exhaling, who's coughing, who's singing, who's talking, and this is you inhaling, right? Remember that as we get closer to the holidays and we're spending more time indoors, improved ventilation, distancing, et cetera. Let's get into, just a reminder, again, COVID, early viral phase, Paxlovid, remdesivir, molnupiravir, convalescent plasma, isolation for the infected, and let's not keep doing those harmless - harmful and useless things.

Unfortunately, some people are still progressing. We're still seeing people ending up into the hospital, and those numbers are predicted to be increasing as we move forward here, in coming weeks. For those folks, if you end up in the hospital, oxygen saturation's less than 94%, so right patient, right time, Dexamethasone, easy to remember, 6 milligrams a day times six days. Forget about what your IT folks put in the computer, do what's evidence-based.

Number two, anticoagulation, and we have guidelines from a number of organizations. I'm going to be talking a little bit more about that next week as well. Pulmonary support, remdesivir, if you're still in the first 10 days, immune modulation. Mainly tocilizumab, and next week, I'll talk about, is there's still really a role for baricitinib? Again, remember, let's avoid those unnecessary antibiotics as unproven therapies. Great to see, here, in Sub-Saharan Africa, all these signs like antimicrobial resistance, everything we need to do to prevent that. Last thing we want to do is lose our tools by using them inappropriately.

All right, COVID, the late phase, PASC, Long COVID. We have a couple - well, more than a couple, a few articles here. This will be the bulk of what we talk about today. I'm going to try to keep this brief. Just want to make sure I check in with everyone this week. Number one, the article, “Vagus Nerve Dysfunction in the Post-COVID-19 Condition: A Pilot Cross-sectional Study,” published in *CMI*. Now, here, the authors tell us that they evaluated the structure and function of the vagus nerve and evaluated the structure and function of respiratory muscles in a cross-sectional pilot study in subjects with post-COVID, PCC, post-COVID conditions with symptoms suggesting vagus nerve dysfunction.

Remember, they're targeting. They're not saying, "Everyone's got this," they're saying, "We only got 30 individuals," and they're going to compare those to subjects fully recovered from acute COVID and individuals never infected. That's going to be an N of-30 that they think have this vagus nerve dysfunction. They're going to look at acute COVID, that's without, those will be 14.

They're going to look at individuals never infected, that's going to be 16. It's a small study, but what did they find? Participants were mostly women, 80%. The median age was 44 years. The most prevalent symptoms were cognitive dysfunction, 25/30, so 83%. Dyspnea, about 80%. Tachycardia, 80%. Remember, that's sort of a circular here because that's how they're starting to think these folks might have vagal nerve dysfunction.

Compared with COVID-19-recovered and uninfected controls, subjects with post-COVID conditions were more likely to show thickening and hyperechogenic vagus nerve in ultrasounds, right? They're not biopsying, they're looking at ultrasounds. Reduced esophageal-gastric-intestinal peristalsis, more gastroesophageal reflux, more hiatal hernia. I thought that was interesting, and, "Subjects with PCC showed flattened hemidiaphragms and reductions in maximum inspiratory pressure, indicating respiratory muscle weakness."

All right, so after the vagus nerve, we have the article, “Humoral Immunity to an Endemic Coronavirus is Associated with Postacute Sequelae of COVID-19 in Individuals with Rheumatic Diseases,” published in *Science Translational Medicine*. Here, I thought those prior infections with common coronaviruses were just helpful, but let's see what we find.

Here, the authors performed comprehensive antibody profiling against SARS-CoV-2, a panel of endemic pathogens, and a panel of routine vaccine antigens in cohorts of patients with pre-existing systemic autoimmune rheumatic disease who either developed or did not develop PASC. "A distinct qualitative shift observed in the Fc binding was observed in individuals with PASC. Specifically, individuals with PASC harbored weaker Fc-binding anti-SARS-CoV-2 antibodies, and stronger Fc-binding antibody responses against the endemic coronavirus OC43," one of my favorites, Old Cow 43.

"Individuals with PASC developed an OC43-S2-specific antibody response with stronger Fc-binding linked to cross-reactivity across SARS-CoV-2 and common coronaviruses." As these authors conclude, "These findings identify previous coronavirus imprinting as a potential marker for the development of PASC in individuals.

Now, the article, “Incidence and Burden of Long COVID in Africa.” How appropriate that this came out this week while I was here in Uganda, while I am here in Uganda.

The article was published in *Nature.* Let's talk a little bit in terms of background. The authors start by saying that the epidemiology and burden of post-COVID conditions in Africa are unclear. These are the results, not original research. They didn't go out and do anything prospective. This is a systematic search in several databases, and they include observational studies from African countries reporting the cumulative incidence of Long-COVID science and symptoms. Only studies conducted in African countries were included. Several sensitivity and meta-regression analyses were performed.

Among 1,547 patients' papers initially screened, 25 were included, consisting of 29,213 participants. Well, they go ahead and they estimate the incidence of any Long-COVID symptomology and find that psychiatric conditions were the most frequent, particularly post-traumatic stress disorder. They find that a higher age and hospitalization were associated with a higher frequency of Long-COVID. They suggest that Long-COVID poses a significant burden in Africa, particularly concerning psychiatric conditions.

This is really a challenge. There are numbers in here which actually seem pretty high, and I think that's a lot of what the press is picking up on, very high incidence of Long-COVID, of post-COVID conditions in Africa. Hard to know exactly the numbers, right? We've talked, previously, about this. Some of the numbers in Egypt are very high. Some of the numbers are lower in other areas. Really, the thing to point out, this goes back to something I've been saying for a long time, no one is safe until everyone is safe. Very clear in places like the United States, Western Europe, other areas where we have really good data on this, that a lot of people who get acute COVID continue to suffer and have issues for really quite a while afterwards.

Really pointing out that here, in Africa, this is not something that we can just say, "We're done with this, wash our hands." A number - over 1,000 papers here, and then almost 30,000 participants in the final papers that they're looking at, really seeing a high incidence of post-COVID conditions, and, really, probably troubling to me is that a lot of these are psychiatric conditions. Clearly, in a lot of the world, and I'm going to just include the U.S. here right up front and say mental health is something that really is neglected, not prioritized, not screened for, underdiagnosed, undertreated, so really concerning here that we're seeing this.

Probably should comment, here I am in Africa, "What are we seeing?" I guess I'm going to say, the same thing: that neglect. Not a lot of questioning, not a lot of probing. When a woman has a child, does postpartum depression occur in Africa? Well, it depends who you ask, and probably the person to ask is the moms who have the babies in the first couple of weeks afterwards because the answer from them will be yes, but the answer in the literature may not be. This is really, I think, something that, going forward, we need to keep our eye on.

Let me finish off that section with, as I've been saying for a while, no one is safe until everyone is safe. I'm glad I have this ability to check in with everyone. Next week, I will be in a remote island off the coast of Panama. That may also be another one of our briefer sessions, but then I will be back in New York in time for the end of December when we will catch up on, really, a lot of exciting literature coming out.

In the meantime, no one is safe until everyone is safe. I do want everyone to pause the recording right here and go to parasiteswithoutborders.com and click ‘Donate.’ Every small amount helps. Right now, we are still in our MicrobeTV fundraiser. For the months of November, December, and January, we're hoping to double those donations. We will double those donations. We're hoping to get up to a maximum donation of $20,000 for MicrobeTV*.* If you like what we do, if you don't like what we do but you want us to keep doing it, then jump in there and help us. Thank you, and, everyone, be safe.

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