This Week in Virology

TWiV 1044 Clinical Update

Host: Vincent Racaniello

Guest: Daniel Griffin

Aired 16 September 2023

pdf of this transcript available (link)

Vincent Racaniello: *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 1044. Recorded on September 14, 2023. 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, should everybody over 6 months of age get the new booster?

DG: Well, we will certainly be discussing that.

VR: All right, I can't wait.

[laughter]

DG: I'm sure you're waiting for my sage advice, Vincent. Let's start with my quotation, "Let us remember one book, one pen, one child, and one teacher can change the world." That's by Malala. For a lot of folks, it's back to school, and so I thought that was appropriate for this time of year. Also, what else is on everyone's mind, influenza, I'm sure. I actually really like this. I don't know if our listeners have heard about the Wild to Mild campaign for flu vaccines. I'm going to leave a link in, but Brenda Goodman wrote a really nice piece about this in *CNN Health*. I'm pleased to see the messaging is much better here.

Just let me read the beginning of this piece because I think this really - We've missed the point on I think a lot of communication. Some Americans have given up on flu shots because almost everyone remembers the season when they got one and then got sick anyway. Now the U.S. CDC wants to reset expectations about what these annual vaccines can and can't do. It's rolling out new ads it hopes will increase confidence in the vaccines with a clear, straightforward message, "The flu vaccine won't keep a person from getting sick, but it will tame the infection, taking it from Wild to Mild."

They've quoted Bill Schaffner. He's an ID doc down at Vanderbilt, "With these respiratory viruses, flu included, the vaccines aren't very good at preventing mild disease. They're much better at preventing the serious complications, and I think we have not been very clear in presenting that information."

VR: I agree. Perfect. The same would go for COVID vaccines, right?

DG: Yes. Bill, why didn't you mention COVID? Let me rephrase that for you, "With these respiratory viruses, flu, COVID, RSV, the vaccines aren't very good at preventing mild disease, but they are better preventing serious, severe disease." That's always the thing I say to patients who get the flu, I say, "OK, you may have gotten the flu, but did you die?" They have these great ads where you've got this ferocious tiger, now it's being transformed into a kitten or it's a great white shark transformed into a goldfish.

I think this is great. This is the messaging. If we had had this messaging at the beginning of the COVID vaccines, just how much grief we could have saved.

VR: I agree. In hindsight, it's always 2020, right?

DG: We were not hindsighting. You and I were talking about this in 2020. [laughs]

VR: True. It's true. You're right.

DG: All right. Here's another one, I think, which is really important, going to help people with a question on the horizon, the article, "Immunogenicity and Reactogenicity of Coadministration of COVID-19 and Influenza Vaccines," published in *JAMA Network Open*. They look to address a simple question: Is the coadministration of COVID-19 vaccine with the seasonal flu vaccine safe and efficacious? Can you just go get those two shots at the same time?

They performed a prospective cohort study that included healthcare workers at a large tertiary medical center in Israel, who received the flu shot and the COVID, it was actually the bivalent vaccine, or both. Vaccination began in September 2022, and data was collected until January 2023. Vaccines were offered to all employees and were co-administered or given separately. They reported then both the reactogenicity, that's that reaction you get from getting your shots, and the immunogenicity, and really basically found that it was unchanged whether they got them both at the same time, or whether they got them separately, so fine to get both those shots at the same time.

Vincent, do those flu shots even work? We're actually in a fortunate situation here. The *MMWR, "*Interim Effectiveness Estimates of 2023 Southern Hemisphere Influenza Vaccines in Preventing Influenza-Associated Hospitalizations, the REVELAC-i Network, March-July 2023," is now available. The nice thing is we get a peek how well are those flu shots doing in the Southern Hemisphere that gets a flu season prior to us. We could say, "Oh, is it going to be worth it?"

In this report, the vaccine efficacy against what? Influenza-associated hospitalization, was estimated using a test-negative case-control study designed to compare the odds of vaccination between hospitalized patients with a positive flu test and patients with a negative

flu test. Overall, the vaccine efficacy against an influenza-associated hospitalization was 52%. I thought this was interesting, the vaccine efficacy was highest in young children, where it was 70%. Flu shots seem to be turning the wild into mild.

VR: At least if you're young. If you're older, not as good. 50% is not great, right, Daniel?

DG: Yes. 52% is not great. Actually, if you looked at the oldest adults, it was only about 38% reduction.

VR: Maybe getting two shots per season might help that number.

DG: I think that's an interesting issue. We always talk about timing, right?

VR: Yes.

DG: A lot of folks are lining up already to get their flu shots. Let's say you did get a flu shot the first week of September. September, October, November, December, whoa, you're pretty much you've dropped off. What do you do in January, February, March? I think that would be great to have a study looking at getting that second shot, particularly in the highest-risk individuals.

VR: The question is, Daniel, if you are in the older group, and this number is 37%, why would you get it then? Is that better than nothing?

DG: Certainly, better than nothing. If you take a 38% reduction of a big number, let's say your chance of ending up in the hospital was like 10%, now you drop that, that's worth it. Also, if you end up in the hospital, it may not be as severe. Then what I always like to point out is the majority of people that die did not get that flu shot. We're not actually even seeing the mortality reduction here. Lots of good reasons to get the flu shot.

Then, the other thing, to be honest, which will come up again, is this is the public health. The more people that get flu shots, the less cases of flu, the less hospitalizations. If you end up showing up at that hospital, and everyone's done their part and jumped in, you're not waiting eight hours to be seen, the hospital capacity is somewhat impacted.

VR: All right. You don't have to convince me, I get my flu shot every year.

DG: [laughs] OK. RSV. Lots of discussion about RSV lately, with all the new active and passive vaccines available. One big challenge, and I think it's important, RSV seems to affect everyone. It's not just something that we can ignore because our child or an older person is otherwise healthy. People always have that idea like, "I don't have to worry because I'm not the kind of person who would get sick."

Here the article, “Genome-wide Association Study of Susceptibility to Respiratory Syncytial Virus Hospitalization in Young Children Less Than 5 years of Age,” was published in *JID*. This is really robust. Here the investigators conducted a genome-wide analysis study, or GWAS, on two large cohorts with 134,234 individuals. Then the controls were randomly selected among the entire Danish population, with really the only inclusion criteria being that you are born to

a mother with a Danish social security number and being alive and residing in Denmark on their first birthday.

Despite being the largest GWAS of severe RSV infection to date, they didn't detect any genome-wide significant loci. The challenge here is that RSV can lead to medically attended lower respiratory infection in anyone when clearly seeing that you're genetically at risk, so your otherwise healthy child could end up in the hospital. We now have the tools to transform what happens this coming winter. Big issue is, will we use them?

All right. COVID. I want to remind people how to use those rapid tests. I just want to review an article that I think we've talked about before. This is the article, “Performance of Rapid Antigen Tests to Detect Symptomatic and Asymptomatic SARS-CoV-2 Infection: A Prospective Cohort Study,” published this July in the *Annals of Internal Medicine*. They really have two great figures, Figure 2 and 4, that really help, I think, understand what to do here. This is a reminder of how to use these tests.

The first day, that day zero, "I'm starting to not feel so great," that's not the time to do the test. Wait until the next day in the morning and do that test. Now, that first day, our sensitivity is going to be about 75%. That sounds great until I say, "Wait, I'm going to miss one in about every four cases." If I'm working at an urgent care, someone comes in, "I started getting sick yesterday," if we're doing this at home and the rapid test is positive, you've got COVID. Pretty good. Not only do you have COVID, but you probably have a lot of RNA in your nose, probably already contagious at this point.

Now, if that test is negative and you work in an urgent care, send out the PCR, because you're going to miss a quarter of the people. If you miss those people, they're going to go to work. They're going to go hang out with their friends. They're going to go infect their elderly parents. If you're at home, you can wait 48 hours, you repeat it. If it's negative at 48 hours, we've reached that sensitivity of greater than 90%. If you're going to do the rapid tests, do them right.

VR: We also covered that on a *TWiV* after you had covered it as well, so we got double coverage.

DG: [chuckles] All right. Like the second test, right? Look at that.

VR: That's right.

DG: All right. Good reminder there. All right. These are the questions this week, Vincent. Lots of questions about boosters. Actually, they're not calling them boosters, they're calling them updated vaccines. Let's go through. Tuesday, September 12, 2023, the question put before the advisory group. Should 2023-2024 monovalent XBB containing COVID-19 vaccines authorized under EUA or approved by BLA be recommended for use in persons 6 months, greater than or equal to 6 months of age?

That's a question. You don't get to jump in and change the question. The vote was 13 to 1 in favor of recommending the vaccines. The boosters are FDA-approved. Actually, the updated vaccines from Moderna and Pfizer-BioNTech are approved. We're still waiting on Novavax. The boosters, the updated vaccines, are now recommended for everyone greater than 6

months of age or older. A little bit of science and then I will promise to give you my sage advice. I know you and Vincent are waiting for that.

[laughter]

Let's start off with a little bit of science. Get everyone in the mood. This is like that mood music they play at church if you go to church. Recently, I discovered my children think that they don't hold services in the summer because I asked my son, "Oh, are you going to go to church?" He's like, "Oh, it's the summer, dad. They don't have church in the summer." I'm like, "Yes, OK. We just don't go in the summer."

Anyway, so you've got your mood music. Here we go. The preprint, "Safety and Immunogenicity of XBB.1.5-Containing mRNA Vaccines," recently posted on *medRxiv*. These are the results of an ongoing phase 2/3 study where participants were randomized one-to-one to receive the 50 microgram doses of the monovalent or the bivalent administered as – are you ready for this? - fifth doses to adults who previously received a primary series, third dose of an original mRNA vaccine, fourth dose of a bivalent. Interim safety and immunogenicity data 15 days post-vaccination reported.

This is all pseudovirus neutralization data. They report both the new monovalent booster and this bivalent booster increased neutralizing antibody titers against all variants tested at day 15 post-booster compared to pre-booster levels. Geometric mean fold-rises from pre-booster titers after the monovalent booster were numerically higher against XBB.1.5, XBB.1.16, the D614G, remember that one, higher than those of the bivalent booster, and were comparable against the BA.4/BA.5, and BQ1.1 variants.

The monovalent vaccine also elicited neutralizing antibody responses against the Omicron XBB.2.3.2, EG.5.1, FL.1.5.1, and the BA.2.86, which were similar to those against the XBB.1.5 looking at a subset 20 participants. No safety concerns. They report that the occurrence of adverse reactions/unsolicited adverse were really pretty similar. Just to focus on the new Moderna booster that people can now schedule to get, the XBB.1.5 containing monovalent updated vaccine elicited potent neutralizing responses against variants of the Omicron XBB lineage, and as mentioned, XBB.1.5, XBB.1.6, XBB.2.3.2, the EG.5.1, and the FL.1.5.1, as well, don't forget, the recently emerging BA.2.86 variant.

The safety profile has been consistent with prior vaccines. Some really nice figures where you can actually look at the pre- and post-results for each of the different variants. Not only in all participants, but they're even looking at boosting in folks that had a prior infection. All right. Back to our questions that everyone's been waiting for. Who should get the updated vaccine and when should a person interested get the updated vaccine?

I want to comment first about the political implications of the advisory board decision. When they go ahead and they answer that question we talked about before with a yes, should this updated vaccine be authorized for persons 6 months of age and over? If they say yes to that question, then that's going to basically provide access and coverage for these vaccines for lots of people, but it doesn't necessarily get into the nuance of, "OK, are you going to make an equally strong recommendation for a healthy 22-year-old, a 17-year-old, a 70-year-old, or let's say, an 85-year-old with multiple medical problems?"

A couple of things that we're going to be talking about. I'm going to jump right to the IDSA chiming in. The IDSA gives a little bit more nuance here. What they say, "The ID Society of America supports recommendations made by the CDC's advisory committee that will allow access to updated COVID-19 vaccine boosters to all people 6 months of age and older. This recommendation will allow individuals who choose to receive vaccines to do so under public or private insurance, removing an important barrier to access." This is where they give us the nuance.

"It should be noted that the most important people to receive this new vaccine are individuals at increased risk for severe COVID-19 infection, including people 65 years of age and older, and those with underlying medical conditions. IDSA strongly urges these individuals to receive the new vaccine." Then I'm going to say I woke up Wednesday morning to see a really nice guest essay in *The New York Times* by the CDC director, Mandy Cohen, entitled, “The CDC Director Explains Why You Should Get the Latest COVID Booster.” I just want to go through her comments. Vincent, I want you to jump in as well. Not like I'm going to be able to stop you, but I'm encouraging you. [laughs]

VR: Tony Fauci said, "Let's simplify it and say everybody needs to get this." He said, "We needed one message," and he said, "I don't care what the science is because you may be right, but I want one message for everyone." That's not a bad argument, right?

DG: It's not a bad. I might have worded it a little different than Anthony did, but I understand what he's saying. People are like, "Stop making it so complicated," particularly my pediatric colleagues. Let's go through. What does Mandy Cohen have to say? We'll start off. "While we would all love to leave COVID-19 in the rearview mirror for good, the virus is still here, and it will probably always be with us. The good news is that we have the tools to help people avoid serious illness, hospitalization, death, and Long COVID symptoms."

I like the change in the message. I feel like we're no longer thinking that COVID is going to go away. It's here to stay. We need to use the tools that we have before. The next, and I think this is really nice, we can minimize the virus's damage to our lives by using one of the most effective tools in combating the virus, updated COVID-19 vaccines. I'm not sure in all honesty that's the most. I think that vaccines have done a tremendous amount. I'm not sure the updated vaccines. I think the actual original three doses is probably the most effective tool. People sometimes put comments on our YouTube, "Why don't they talk about natural immunity?"

I think most people at this point are going into these next surges and waves with immunity. Some of those have been acquired through vaccination. Some have been acquired through repeated infections, those of you that have survived those. Really, I think the challenge is the people coming newly into this world, the newborns, where for them, this is, "Welcome to a world with COVID."

The next. Some viruses, however, change over time. Is coronavirus one of them? Only some viruses change over time, Vincent. Apparently, there are some that don't change.

VR: [laughs]

DG: We can word that differently. All viruses mutate, change over time, that's the deal. This coronavirus is one of them. It finds ways to evade our immune system by constantly evolving. I will avoid the anthropomorphism there. That's why our vaccines need to be updated to match the changed virus. Even though many Americans have been exposed to previous versions of the virus because they've been infected and protection decreases over time, this is partly why you can get COVID more than once and why you can still get very sick even if you had it before.

It's an interesting thing. I think we've all learned. Early on, I remember people saying, "Oh, you can only get it once." Do you remember our buddy Joe Rogan - Is he our buddy? He was on with some particular guest who was, "No, no Joe, you can only get it once." Joe's like, "I've had some." "Damn, Joe, you don't know what you're talking about." Anyway, no, you can get it more than once. I think we all know that.

Now, the other, and this is interesting -- Hopefully, this is said in a sensitive way because sometimes this - COVID-19 continues to pose a health threat, especially to older Americans. From January to July 2023, 88% of deaths from COVID-19 were among people who were age 65 years or older, those with certain underlying health conditions, and then I think this is what I like, approximately 70% of American adults all fall into that category of underlying health conditions and weakened immune systems, also are at greater risk than younger healthier Americans.

I think that's something to point out. None of us think we're older. I was talking to my wife about those RSV vaccines for people 60 and over and I started to realize that I'm getting pretty close to 60 and over. Hypertension, other heart issues, a lot of us don't even realize, but yes, being older, having hypertension, we're an individual with a comorbidity that puts us at increased risk. What's more, anyone who gets infected with COVID can develop long COVID. I like, "Studies have found that the people who may be more likely than others to get Long COVID were unvaccinated against the virus."

Doubling down on the growing data we have there that vaccines are an evidence-based way of reducing your risk of Long COVID. I think this is really important. Don't just put all your eggs in the spike vaccine basket. If you get COVID-19, remember that treatment is available. Paxlovid, pills you take twice a day for five days, can help reduce the severity of illness and may prevent Long COVID. It works better when taken or best when taken soon after symptoms develop. That's why people with COVID symptoms should get tested and ask their doctor about treatment. I think that's going to double down on that.

The more people who get the shots, this is interesting, the more people get the shots, the bigger difference it can make in how many Americans are sick and the ability of our healthcare system to handle influxes of patients. This is really that public health argument. Not sure how many Americans go for that, I do, but the more of us that are on board with vaccinations, this could be influenza, this could be RSV, this could be COVID.

Then really bringing it home, "As a doctor, a mother, the head of the CDC," Mandy Cohen's words, "I would not recommend anything to others that I wouldn't recommend for my own family, my 9- and 11-year-old daughters, my husband, my parents, and I will all be rolling up

our sleeves to get updated COVID-19 vaccines along with our flu shots soon. I hope you and the people you care about will do the same." All right. Any comments, Vincent?

VR: I don't know. I can say what I think, but -

DG: [laughs] You certainly can.

VR: Let me say, I'm not a medical doctor. I'm not a public health official. I'm a basic scientist and I'm looking at the data. We have neutralization data. It doesn't say whether this will help against severe disease, but what I suspect is that you'll get three months of protection against probably moderate to severe disease because your antibody levels will be high. That's a suspicion because we don't have any data because we don't have enough experience with COVID vaccines.

Then after three months, you're going to start to get a more severe infection and so the timing of when you get the vaccine is very important, and we don't really know when there's going to be a peak in SARS-COVID-2 infection, so that's one variable. If you're concerned about Long COVID, I think then you should get the vaccine. You'll be protected against that maybe for a couple of months. I think people who should definitely get it are over 65 with severe comorbidities of various sorts. I think that's a no-brainer.

Personally, I am 70, I have no comorbidities. I will take my chances and take Paxlovid should I test positive, but I don't see the evidence that this vaccine is going to be much benefit for me. I do understand the need for a unified message, that everybody get it instead of this and that, and the other. I get it, OK, but I just am in a special situation where I look at the science. Paul Offit agrees with me and a lot of people don't like that either, but you don't have to listen to me. That's just my opinion.

DG: All right. I like the way you seg into this. As we've talked about, timing probably matters. It's probably going to be a three-to-four-month boost here, so we're doing the Yogi Berra thing, we're predicting the future, the hardest thing to do. We're expecting maybe December/January to see the biggest rise in cases. Maybe end of October, early November is the best timing. Some people, unfortunately, are getting their natural boost all around us every day. Probably the big thing, and I'm really glad that Dr. Cohen put this in her messaging, she's talking about vaccines, but she makes sure to mention we can reduce the risk of progression by 90% with early antiviral treatment.

Really, I am glad. I hope that the messaging around the flu vaccine is starting to get people to appreciate what vaccines can and can't do, but we need better messaging around early antivirals. Recently had a story where an individual - we'll protect their private health information by just saying an individual - called me, sounded really raspy on the phone. "Oh my gosh, you don't sound well. How are you doing?"

"I'm not doing well. I've been diagnosed with COVID and my doctor sent in a script for Paxlovid but said not to take it unless my temperature gets above 102."

I'm not sure where that study is [laughs] where it shows that 102 predicts the severity of the second week, the early inflammatory phase, the cytokine storm. There is no study. The messaging has to be here, is we are not able to prevent the cytokine storm, but we can turn

wild into mild with antivirals. See, I'm stealing the flu campaign, and so during those first five days, why not reduce your risk of that cytokine storm being wild by 90%?

Let's stop using the word rebound. There's no rebound here. There is a second-week, early inflammatory cytokine storm. During the first week, the viral symptom phase, that's when, number one, we can jump in with Paxlovid, 90% reduction in that severe experience during the second week. Number two, IV remdesivir, three days. Molnupiravir, convalescent plasma, for a few select folks. Let's not do harmful things. I just hate to remind people, but ivermectin is not indicated for the treatment of COVID. Apparently, that came up again. Just because it appears on social media, there's no new science.

Second week, remember this is the cytokine storm week. We've been talking about this for four years. I just saw an individual hospitalized today. This individual was sick, started to feel better on day six, day seven, and then started to feel really crummy, checking his pulse ox levels at home that had dropped into the 80s. This person had not gotten antivirals. That's why I'm seeing them in the hospital, which is actually true for the majority of individuals that progress to the hospital.

Once they progress to the hospital, that's where, number one, we look at steroids, we look at anticoagulation pulmonary support, maybe remdesivir, if still in the first 10 days. Immune modulation, maybe tocilizumab or baricitinib in certain cases. Again, avoiding those harmful things. Here's a big thing that people ask about all the time. They're sick with COVID but what they really want to know is, "When can I get back to my life?" They usually ask the question, "Dr. Griffin, how long am I contagious?" What they really want to know is when can I stop isolating and get back to my life?

Let's discuss the article, “Timing and Predictors of Loss of Infectivity among Healthcare Workers with Mild Primary and Recurrent COVID-19: A Prospective Observational Cohort Study,” published in the *CID*. These are the results. You get it from the title of a prospective observational cohort study with serial viral culture, rapid antigen detection testing, and RT-PCR on nasopharyngeal specimens of healthcare workers with COVID-19.

Now, I want to point out, the primary outcome was viral culture positivity, which they pretty much equate to infectivity. Let's just pause there because we know that's not true, but anyway. [laughs] Because we have talked about transmission studies where people that are viral-culture negative, still we have contact tracing showing that there's transmission. Sorry, there's just a problem with sensitivity there. We also have situations where someone is exposed to someone who's viral-culture-positive, there is no transmission.

I just want to point that out because they are going to do predictors of loss of infectivity but they really mean viral-culture positivity, determined using a multivariate regression model. Then they're going to actually criticize the performance of the U.S. CDC criteria, fever resolution, symptom improvement, negative rapid testing to predict the negative culture results. Here are the results. We've got 121 participants. Actually, 79% of them were female. Average age, 40. Most of them had received three or more of the SARS-CoV-2 vaccine doses. I was surprised by how low. In this study, 16.5% had COVID-19 previously.

Viral culture positivity decreased from 72% on day five of infection to 18.2% on day 10. The investigators, as I point out, are equating positive viral culture with being infectious, and negative viral culture with being not infectious. I want to caution with regard to their conclusions. They do have an interesting and not unexpected result that they present in Figure 3. Participants with recurrent COVID-19 had a lower likelihood of a positive culture than those with primary COVID-19 at each follow-up day. Everyone had negative viral cultures by day 10. All those people with prior infection had negative viral cultures by day 10.

They report that independent predictors of a positive viral culture included, as we mentioned, prior COVID-19 and RT-PCR Ct value of less than 23. I think this is really important. Not symptom improvement and not a rapid test result, which I think is really interesting, because I've heard people start to say in certain parts of the country, "Oh, we're treating this like the flu. As soon as you feel better and you no longer have a fever, you're not contagious." I think this study is at least challenging that as a predictor of the positivity or negativity of the viral cultures.

All right. COVID, the late phase. Going to leave plenty of time for questions this week. The article, “Effect of Famotidine on Cognitive and Behavioral Dysfunctions Induced in Post-COVID-19 Infection: A Randomized, Double-blind, and Placebo-controlled Study,” recently published in the *Journal of Psychosomatic Research*. This is a randomized, double-blind, placebo-controlled study, but they're only looking at 50 patients with a confirmed diagnosis of COVID-19 and a score of less than or equal to 23 on the Mini-Mental State Examination, or a score of less than or equal to 22 on the Montreal Cognitive Assessment test, the MoCA.

A lot of headlines about this, but let's actually look at the data. These individuals were randomly assigned to either the famotidine, PEPCID, 40 milligrams twice daily, or placebo. The changes in MMSE or MMSE scores at weeks six and 12 were the primary outcome, while changes in other scales were the secondary outcome. We end up with a small sample size. They report that at weeks six and 12, participants in the famotidine group had a statistically significantly higher MMSE score and MoCA scale score.

They also looked at the Hamilton Depression Rating Scale at weeks six and 12, and the famotidine group experienced a larger reduction. Additionally, comparison of the HAM-A, Hamilton Anxiety Rating Scale, at week six and 12 showed a statistically significant larger reduction in the famotidine group. Now, before we all get too excited, I do want to point out that this statistically significant change in the MMSE at six weeks was about one point, and at 12 weeks about two points. If you were asked that really important question, the differences in the MoCA scores at six weeks were only about two and two-and-a-half points also.

This would be like if you were asked to remember those three things. Vincent, remember the three things? Man, woman, television?

VR: Yes.

DG: This time you remembered television.

VR: Maybe just vision.

DG: [laughs] Maybe just vision. A statistician might be happy, but I am clinically a bit disappointed. We're certainly using famotidine in some patients with Long COVID, but I'm a bit concerned that this data does not really support all these headlines. I will wrap it up there with, no one is safe until everyone is safe. Right now I'm going to ask everyone to pause recording, go to parasiteswithoutborders.com, and click on the 'Donate' button. We are continuing our Floating Doctors fundraiser for August, September, and October. You can also mail us checks. We're hoping to get up to a maximum donation of $20,000 to support the tremendous work that these folks are doing.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Lauri writes, "I have recently been treated with oral budesonide for an ulcerative colitis flare. Currently, I'm tapering off usage. If all goes well, I should be finished within two weeks. Total one-month treatment. I understand that steroids weaken the immune system, so my question is, how long after my last dose will it take for my immune system to return to its normal level of immunity? Is it OK to receive a flu vaccine and a COVID booster after steroid treatment?"

DG: Now, this is an excellent question. I'm sure this comes up for a lot of individuals. There's different half-lives. You can get into subtleties, but maybe I'm going to do the Anthony Fauci and just give a nice clean answer for everyone. Wait about two weeks. Actually, that should be good timing, because as we've talked about, timing matters. Probably, end of October, early November, great time for you to get both your updated COVID vaccine and your flu shot.

VR: All right. Virginia has a comment for us. Virginia retired from ID practice about a year ago. "I chuckled a few months ago when you and Vincent were joking about surgeons reading only the titles of articles. I thought how as a retired ID doc, I don't read the entire article, nor do I read just the title, but I listen to your podcast to stay up to date. I was interested in the discussion last week about having Paxlovid available when one travels abroad. This has been referred to as prophylactic. To me, a medicine taken prophylactically is meant to prevent disease.

In that case that Cathy mentioned, she wanted to have medication available. Should she develop symptomatic COVID then the medication is not prophylactic but rather treatment and thus would be used as intended by the FDA. I don't understand the reluctance of physicians and other providers to prescribe Paxlovid for patients to have when they travel. This is of concern to me as I am an avid traveler in retirement."

DG: This is actually a great point. I was thinking about this, because what is the FDA-approved indication for Paxlovid? It's for treatment of acute COVID. Those of us in travel medicine for decades, someone is going to travel and we will say, "If you get X then I want you to have this medicine available to you." Maybe we've got a person with recurrent urinary tract infections. Maybe we have an individual who's going to end up with traveler's diarrhea. They're not taking these medicines prophylactically. They're taking the medicine with them, so should the FDA indication arise, then they actually have access to the medication.

I actually think this is a good point, because yes, we're actually prescribing the medicine in accordance with the licensing. We're just getting the prescription in the person's hand, getting the medicine in their hand, so should the approved situation arise, then they can take the medicine.

VR: All right. We have a question from Lauri who's a pediatrician in San Francisco. "Would love to hear your thoughts. A COVID booster 2023. No data except neutralizing antibodies, which I have learned from you all may or may not be relevant, but that's what we have. We have to order ASAP and we definitely will want Moderna for the littles, but for the bigs, flip a coin?"

DG: Yes, flip a coin. One of the things a lot of shops do is they will just pick one manufacturer because you can often get a better pricing if you negotiate it that way, but I don't think there's any data that we have that would say one versus the other. Whatever works out for you.

VR: "PCV15 versus 18, the Merck 15 claims to have superior coverage for serotype 3, but of course, the Pfizer 20 covers more serotypes. Any thoughts?"

DG: Yes. Most of us are moving to the PCV20. I think that's reasonable. Again, trying to standardize, trying to make things simple, trying to increase the number of serotypes that we're protecting against.

VR: All right. Kate wants to know. Her 83-year-old mother is living in a nursing home. She has been advised to decline a booster because the doctor suspects the cause of her low blood platelets has been a vaccine reaction. She wants to know if that's true or not.

DG: A rare side effect that has been described, that I've actually seen, is that people, they get a COVID, they get a vaccine, and then three weeks later they actually have thrombocytopenia. They have decreased platelets. Not knowing exactly the details and the timing, that is possible. It's not unreasonable. The big thing here for you, we've talked about this, is being ready to jump in with early antiviral treatment.

What is the med list? Are there things that can be changed? Are there things that can be paused? I would say I understand that concern there. We have talked about how really the first three doses are giving you that sustained protection against severe disease. How do you get another 90% reduction? You can safely do that with medications if you can handle renal function issues and drug-drug interactions.

VR: Bill writes, "Do you recommend using a high dose flu vaccine in a 40-year-old female with systemic lupus erythematosus?"

DG: It's interesting that last year, and I think I complained about the timing, it was like right after we all ordered, you got for the first time the CDC giving preferential recommendations for high-dose vaccines. Interesting enough, if you look closely at the data, if you're looking at people in the 40s, 50s, because we have this data looking at the UnitedHealthcare claims data, maybe going ahead with avoiding the egg attenuated and using a cellular-based flu vaccine might be a reasonable thing to consider in a situation like this.

VR: Ellen writes, "This is about RSV vaccine. My husband and I are in our upper 70s. One has mild COPD, the other well-controlled diabetes. It seems the Pfizer vaccine is somewhat less durable for the second year while the GSK had more serious adverse effects. Should we have a preference for one or the other?"

DG: You're basically describing two individuals who we would say, "OK, go ahead. At this point, the risk-benefit would favor getting the RSV vaccine." I don't really know if we have enough data from these trials to really say one vaccine is better than the others. A year from now when we have that post-marketing data, then I think we'll be able to comment. Is there really a difference as far as the durability? Is there really a difference as far as the reactogenicity or adverse events? Right now, I think either one would be reasonable.

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

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

[music]