This Week in Virology

TWiV 1010 Clinical Update

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Guest: Daniel Griffin

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

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From MicrobeTV, this is *TWiV, This Week in Virology*, Episode 1,010, recorded on May 24, 2023. I'm Vincent Racaniello, and you're listening to the podcast all about viruses. Joining me today from New York, Daniel Griffin.

Daniel Griffin: Hello, everyone.

VR: I could have said "ten-ten" instead of "one thousand and ten," there's a radio station, right? 1010 WINS, I don't know.

DG: Exactly. Well, hopefully, this is going to be a 1010 WINS.

VR: OK, let's hear it.

[laughter]

DG: I put in my show notes, a heads-up Vincent, I'm going to be hoping to pull you in for lots of discussion.

VR: Love it.

DG: I think there's a few discussion topics here and -

VR: All right.

DG: Yes, if you jump in, that's good. If you don't, then people know that - Anyway, OK let's start with our quotation. I'm wearing my coronavirus, my nice coronavirus bow tie here so people can enjoy that if you're watching on YouTube, but my quotation, "I do not believe in any wise man until I've heard him say, 'I doubt it,' three times and, 'I don't know,' two times." I think that's really important.

There's a lot of people out there who have just always been right and have not, so let's try to bring some humility. I think that's what science is about. Science is not about

confirmation bias, it's about learning, it's about discovery. I'm going to start right up front with HIV, and I'm going to start with the CDC *HIV Surveillance Report*. Why in a moment, I think people will understand why I'm talking about this right up front.

This just came out, and as we've talked about before, it takes a little while for all the data to be put together, but here we hear that we saw over 36,000 new diagnoses of HIV in 2021, just right here in the United States. Now, I read a few articles, really interesting ways that people are spinning this. This is up from 2020 by 5,000, so I did that 2020 there, 5,551, but down from 2016 by 2,655, so I've seen people spin it both ways there.

Now they say things like only about 20% of the new diagnoses in the U.S. are in women. Only 20%, one in five are in women, then still predominantly impacting those with male-to-male intimate contact, but about one in every three is outside this population. The majority of new diagnoses are actually now occurring in the U.S. South, so the majority, over 50% of the new cases, not California, not New York, but down in that Florida, Georgia, Louisiana, Alabama, Texas region, majority.

VR: Here's another way to look at it, Daniel.

DG: Yes.

VR: That's 98 new infections every day, or 4 every hour, one every 15 minutes. It's a lot.

DG: That's a lot. I put this right up front because I'm going to put forth this crazy idea that HIV AIDS is still a pandemic with an estimated 34 to 44 million people globally living with HIV, an estimated 1 to 2 million people newly infected with HIV globally each year, and somewhere between 500,000 and 1 million people dying each year from AIDS-related diseases. I want to talk a little bit as - because I'm going to be asking this question in a moment. What is a pandemic? Why do you call this a pandemic?

I want to share a story that I found quite upsetting, and this was actually early on in my time practicing clinical medicine at Columbia. It was started off with a young man who came in, freshman, at Columbia University, a student, he had met a girl. This was his first physical intimacy experience of his life, but he was having a number of issues and as part of a screening, he had actually had an HIV test and tested positive. He was completely shocked. Then turned out his girlfriend with which this was his first and monogamous sexual experience, she also tested positive, this was her second sexual exposure, so obviously her first exposure.

He was just shocked, as was she, and just, "What is going on? Why did I not know that I should be aware of this? " I remember at the time trying to get one of the major newspapers to do an article just on the fact that we are still in a situation where unprotected sex can carry this risk with it. Here's the issue. What is a pandemic? Here is the problem as I see it and hoping Vincent will have some comments as well. I see you getting ready to jump in.

VR: Well, we had a nice discussion with Maria Van Kerkhove and Kanta Subbarao, right? You probably heard that.

DG: Well, I heard that. I'm actually responding to that. [laughs]

VR: OK.

DG: I will say that because of poor communication, for most people, the HIV/AIDS pandemic has not changed the way they live, work, and play until they're actually surprised by a new diagnosis for themselves, as I just described, their daughter, their son, their friend. I don't think the definition of a pandemic should be contingent on successful education that results on the degree of understanding that triggers a change in the way people live, work, and play. Maybe a pandemic is just a widespread occurrence of an infectious disease with significant impacts around the world.

Now, the problem as we see with the HIV/AIDS pandemic is unlike pornography, not everyone recognizes it when they see it. We were well into this COVID-19 pandemic of March 2020, and some people then and even afterwards never really decided that they were going to change the way they lived, worked, or played. I pasted in a little bit of a graphic just showing over time, this 30,000 to 40,000 person new diagnoses here in the United States.

VR: Well, at the beginning of the SARS-CoV-2 pandemic, I was telling reporters, "Did you know there's another pandemic ongoing?" and they didn't know that, that there was an HIV/AIDS pandemic. I've always felt that there is one. Then my definition is it affects everyone without infecting everyone, and people say, "Well, how does HIV/AIDS affect you?" Well, first of all, it took a lot of grant money from other viruses, that's affecting me, but also it bothers me that this is happening and we can't understand it and we can't fix it. We can't prevent it. We can't make a vaccine. We can make great antivirals, but I learned recently that they can make you really sick too, right, Daniel? These antivirals.

DG: Yes. Actually this week we had an issue where it was a young dental assistant who was assisting and ended up getting a needle-stick injury. It was a bloody needle, went through the glove, actually penetrated the skin. They were started on post-exposure prophylaxis. We're all thinking this is good within the first 48 hours, but then they developed this really horrible chest pain. The call I got was from an urgent care provider saying, "This young lady will not take any more of this. It's just the pain is so severe. What are our options?"

Yes, those of us involved in different areas of the medical profession, there's always a risk. In this case, it was a person who was newly diagnosed, so probably had an incredibly high viral load, so making this a higher-risk setting. When I practice in Africa, a lot of places I go, 10%, 15% of the community is infected. Tremendous impact on the economy, tremendous impact socially, all these children who have lost their parents. We talked about direct impacts of HIV, but what about the increase in cardiovascular disease, significant increase we're now seeing in cancers?

Yes, this is an ongoing pandemic. A lot of people are ignoring it. I think as we move forward, that was, Tedros was saying, "We're saying this health emergency is ending, but we're not saying forget about it. We're not saying ignore this. We're not saying just move forward and dismantle all the systems you put in place, because COVID-19, it's here to stay."

VR: Daniel, so is there a hepatitis B virus pandemic currently?

DG: Interesting. The only challenge I would say there is how global, right? Because they're certain areas of the world that are not, and I think this is important in defining the pandemic, certainly in parts of Asia and China, it is a tremendous burden. You get into like, does it have to affect everywhere for it to be a pandemic?

VR: How about seasonal coronaviruses? They infect almost everyone, right? Is that a pandemic?

DG: I think this is sort of this judgment when we talk, when we use the word significant impact. There's certain sort of background that we live with and there's times it rises above that. It's going to be interesting to see going forward what is the level of ongoing activity of SARS-CoV-2 relative to those seasonal coronaviruses. No, I think most of us do not consider - I don't think it would be appropriate to consider the seasonal coronaviruses as pandemic.

VR: Would you say there is a global pandemic of heart disease?

DG: I think yes. I think that's an interesting way, right? We normally think, and I have my blinders on. We use infectious disease to talk about pandemics, but we've applied the word crisis, the word pandemic to opioid issues, which people are not changing the way they live and work, and play, and they probably should. Cardiovascular disease, cancer, yes, I think this is tough.

VR: Even the WHO people had trouble defining it, right? It's not easy. I don't think that we can restrict it to infectious diseases. I think it's any global condition, which, heart disease, diabetes, obesity in certain countries can be extremely disruptive, let's put it that way for -

DG: Yes, the term obesity pandemic, I think is appropriate. I think it communicates a significant clear and present danger to the health of human beings throughout the world, and a problem that's growing.

VR: Do we have a stupidity pandemic, Daniel?

DG: [laughs] No doubt. No doubt. All right, let's move on to some good news. [laughs] RSV, right? We've been talking about RXV, and now we're going to talk about RSV. On Thursday, May 18, an advisory panel of the FDA voted in favor of approving the Abrysvo vaccine by Pfizer to prevent severe respiratory virus that is a potentially deadly threat to infants, right?

The last time we talked about protecting those 60 and up, right? Saying that you end up in the hospital with RSV, you're twice as likely not to survive an influenza hospitalization, Ten-thousand, 20,000 deaths per year here in the U.S.. What about those kids who flood into the hospital? This vaccine would be the first to protect babies from RSV. Really, as mentioned, this is the reason many infants are admitted to children's hospital each year. This virus kills several hundred under the age of 5 each year.

Fourteen agency advisors unanimously agreed that the vaccine was effective. The FDA typically follows the recommendations of its advisory panels. Now, we discussed the data that led to this recommendation that was published in the *New England Journal of Medicine.* That was the MATISSE trial where there was an efficacy of around 82% in reducing medically attended severe lower respiratory tract illness due to RSV that occurs

within 90 days after birth. The idea here is that an individual gets the vaccine in the last trimester of pregnancy, and the infants then have this robust protection during that most critical period of time.

VR: And then by 6 months, when antibodies from the mother have lowered, the babies have probably made their own because they've been infected, is that the idea?

DG: That's going to be the challenge because this is only going to last maybe three to six months, right? That's what we think with the maternal antibodies. Now, if you continue to breastfeed, will you continue to provide some benefit? That's something we'll have to follow. What do you do from 6 months to 5, are we going to have some sort of an infant vaccine on the horizon?

VR: Interesting times where we have two RSV vaccines, one for older people, one for people to be. [chuckles]

DG: Yes. [laughs] Good times, I dare say. All right, now let's move right into COVID and I'm going to jump in on testing. I really like this. We're not going to keep you here too long this week. It's going to be Memorial Day weekend when this drops. We answered some emails last week where it was discussed that many people don't want to test. This is true. Many do want to go into settings where they might get COVID. Maybe this is like getting on an airplane, and not wanting people aboard with things that might harm you and others.

Is there a way to do this? Is there a way to make these areas safe without sticking swabs up people's noses or other places like in their mouths? The article, "Canine Olfactory Detection of SARS-CoV-2 Infected Humans - A Systematic Review," was recently published in *Annals of Epidemiology*. For background, several diseases are known to produce specific scents in affected individuals excreted as volatile organic compounds, which can be easily detected by dogs within seconds.

Now, I was reading this and it reminded me of a primary care physician who I saw when I was young, who claimed to be able to smell if a person had strep throat, thus saving us all the trouble of testing. Maybe he was smelling the methyl mercaptan, I don't know. This article is a systematic review that evaluates the current evidence for using dogs' olfactory system as a reliable COVID-19 screening tool. They identified a number of studies with low risk of bias and high quality. They also found some studies that were not so great.

The six high-quality studies revealed sensitivity ranges of 82% to 97%, and specificity ranges of 83% to 100%. We discussed one of these studies where the dogs actually just were walking past the children actually right behind them. You weren't putting gauze in cones or anything like that. Just interesting thinking about how this might play a role in the future.

VR: Maybe Daniel, if you have dogs, you could get them trained to sniff COVID, and then you could have a test every day.

DG: [laughs] I have to say this really. I spend a lot of time, and by the way, people read this article, it's great. It is amazing how many different breeds of dogs can be trained to do this. It's not like one specific breed. I was amazed just the numbers of different dogs. Now, we, as you may know, we actually help foster and train service dogs. A couple of them have gone

on to be hearing dogs, right? They actually hear things, and they have paw signals for individuals who are deaf. Ones that help. We actually have an active serviceman who had some trauma overseas. The dog goes into his house, turns on all the lights, and lets him know it's safe to enter, allows him to continue to function. These dogs are just amazing. Excited to see that they might have an opportunity.

All right, let's move into vaccinations. I'm going to start this section with the article, “Safety of the BNT162b2 COVID-19 Vaccine in Children Aged 5 to 17 Years,” published in *JAMA Pediatrics.* These are the results of a cohort study of more than 3 million children, aged 5 to 17, who received the Pfizer-BioNTech COVID-19 vaccine through mid-2022, using data from three U.S. commercial claims databases. Only myocarditis or pericarditis met the statistical threshold for a signal after the vaccination. Now, both myocarditis and pericarditis is a rare post-vaccination event giving us an incidence of about 39 cases per million doses administered in children aged 5 to 17. They're looking at that post-vaccination period.

They did not, I think this is really important, they did not detect a signal for myocarditis or pericarditis in the younger children, those aged 5 to 11, which is consistent with reports from other surveillance systems. I think just more and more when we're having discussions with parents when we're having discussions about vaccination in the youngest among us, we really, as we talked about last time, we can reinforce messages that are persuasive. This is a safe, well-studied vaccine. We have lots and lots of experience. This is a safe, effective vaccine, and I think we're all supposed to show in, “all the cool kids are doing it,” those that you trust, I vaccinated all my children or I should say all my children were vaccinated. It was a mutual decision. I will also throw in, no more J&J vaccines in the U.S. All remaining doses here in the U.S. have expired after about 19 million people in the U.S. received this vaccine. Now, we're going to get into some discussions soon. We're going to be hearing more on vaccine compositions, June 15, from the U.S. FDA but we do have some recommendations from the WHO.

First off, we have the, “Statement on the Antigen Composition of COVID-19 Vaccines,” from the WHO. This is that 1,616-words document that is suggested to take six minutes to read. I encourage, take the six minutes, but a few bullet point takeaways. Here's what they have to say. Despite increasing gaps in genomic surveillance globally, the available sequencing data indicates that the index virus and the other earlier variants, so Alpha, Beta, Gamma, Delta, are no longer being detected in humans.

The trajectory of further SARS-CoV-2 evolution indicates that XBB will likely be the progenitor of SARS-CoV-2 variants in the near term. There is invitro evidence, and this can be interesting, that immune imprinting, which is a phenomenon in which B cell memory recall responses towards previously encountered antigen reduce the response to new antigens, may be occurring, however, based on observational epidemiological studies to date, the clinical impact remains unclear.

I'm amazed at how much mileage people have made of what you can see here is a very qualified statement. Preclinical data shared confidentially with the TAG-CO-VAC by vaccine manufacturers show that vaccination with XBB.1 descendant lineage containing candidate vaccines elicits higher neutralizing antibody responses to currently circulating SARS-CoV-2 variants compared to responses elicited by currently approved vaccine.

Here are the punch: One approach recommended is the use of a monovalent XBB.1 descendant lineage such as XBB.1.5. Now, I do want to leave in an extra link here to *Immune 68: Sins and Blessings of Immunity*, certainly worth listening to, and then even going on to read some of the linked articles, maybe a discussion about original antigenic sin and what we know versus what we think we know. Maybe I'll pause here for a moment, Vincent, if you want to comment because you were involved in that discussion on *Immune*.

VR: Yes, so that's original, originally – heh heh, originally. It's described with influenza virus where your first encounter with a virus, that's what you make an antibody response to when you get subsequent infections until such time that the virus changes substantially and then you make a new response to that new antigen and so this is going on with SARS-CoV-2. People who are infected with say XBB.1.5, right? Any XBB.1 lineage, they're mostly making a response to the ancestral virus which is no longer circulating and those antibodies don't neutralize infection very well.

That's I think what original antigenic sin is or imprinting, and some people are concerned because you want to make antibodies that neutralize what's ever around but as they say in this statement, and as Paul Offit has said, the clinical relevance isn't clear because in the WHO presentation, Kanta Subbarao who is on the TAG-CO-VAC, this WHO advisory committee. She said, "We're erring on the safe side, we're not sure that declining neutralization is clinically relevant but if in certain people, if you allow infection to go more than it normally would, that's a problem for them."

It's not a problem for everyone, it's a problem for certain people, and they're erring on the side of caution. That's what they're doing here. She admitted it's totally on antibody neutralization data, no T-cells and I asked to see another person on the committee, "What about T-cells?" and he said, "We know they're there. The epitopes don't change, what do you want to know?" Oh boy. OK. I touched a nerve or something like that.

DG: It is interesting. They would say, "Oh, but they're so hard to measure," but I think the consensus is that the T-cell protection, the T-cell memory is durable, and I understand, and I think this is maybe the important distinction that we need to get people's heads wrapped around, is that if we're trying to boost and get three to four months of neutralizing high-level mucosal antibodies, it doesn't make sense to use something that's not going to provide a neutralizing antibody at those sites.

The other question is, how important and in whom do we need to keep updating and doing this? It's going to be hard if we say, "Oh, we're erring on the side of caution in such a way that we're not going to get the science. We're just going to keep rolling the dice in a way that we think is so I'm a little bit concerned about the - [crosstalk]

VR: Yes, that's a problem because we still don't know the correlates that prevent severe disease, so antibodies are part of it, but there's also non-neutralizing antibodies with FC functions, there's T-cells, as you say, there's probably complement, so you would like to have a better understanding - for flu, we have a good understanding when the neutralizing antibodies drop below a certain level, we change the vaccine because we know that's accompanied by more severe disease.

We don't know that yet for SARS-CoV-2. They're saying, "OK, let's use a vaccine that at least induces antibodies to the currently neutralizing variants, circulating variants, and it's hard to argue with that but who should get it? That's the problem. My feeling is, well, you know best, people with health conditions, people over 70 or so, but a 25-year-old, that's already had an infection and a couple of vaccines doesn't need an XBB.1.5.

DG: I think the challenge is still that Long-COVID out there, as we're still seeing that and we just had a rather prominent scientist who, he's been vaccinated to the hilt, everything's great, two months later, having cognitive issues and actually someone that I rely on for their opinion, so I'm a little bit disturbed that, yes, they didn't end up in the hospital, they didn't die but yes, they're having word finding and memory and. That's our big thing is, it would be nice if there was some way to not get infected but I think there's still a lot of science here that we need to sort out.

All right, so what happens, you get infected still number one, Paxlovid, but we have a little bit of an update here. We have a new resource, the dosing and prescribing reference guide from Pfizer, I'll leave a link here, and this actually links to a nice resource, including an FDA Paxlovid Patient Eligibility Screening Checklist Tool for Prescribers, leave the link for that as well, it's nice.

You go through a checklist, what's the age, comorbidities, OK, this is a candidate, then you can go through renal function and then they have a really nice color-coded, what medicines are they on and how do I navigate these waters because remember, this - and we'll talk about this maybe in future episodes, but you can't put all your eggs in the vaccine basket. There's individuals who get infected even though they've been vaccinated. We still have over 1,000 people here in the States dying every week, more when you look around the world. This is another tool to jump in with.

Number two, remdesivir when you can get it, molnupiravir, convalescent plasma in certain settings and remember, let's not do harmful things. Moving into the second week, the cytokine storm, the lower respiratory hypoxic phase in some folks, the early inflammatory, that's when we talk about steroids, anticoagulation, pulmonary support, immune modulation and I will then move into very briefly the late phase Long-COVID. As a teaser, I will say that next week I will be discussing a *JAMA* article on PASC that is still under embargo at the time of this recording, so I can't mention it yet but it will be off embargo and ready for discussion next week and I expect there to be a lot of strong reactions to this publication.

No one is safe until everyone is safe. We're going to hit some emails here in a minute but pause right here. Go to parasiteswithoutborders.com and click ‘Donate,’ every little bit helps. We keep talking about the importance of education, but we can only do what we do with your support. Right now, we're having our Foundation for International Medical Relief of Children fundraiser. May, June, and July donations made to PWB will be matched and doubled up to a potential maximum donation of $20,000.

VR: It's time for your questions for Daniel. You can send them to daniel@microbe.tv. Robert writes, "I'm 83, recently came down with shingles despite being fully vaccinated with Shingrix. It was a horrible experience, months of pain, fatigue, loss of appetite, weight, et

cetera, have not yet fully recovered. In the news I read that Senator Feinstein was also vaccinated against shingles and, according to news reports, at 89 had a much worse outcome with shingles than I did. Could you comment on these apparent failures of the vaccine to do much to mitigate shingles' disease course?"

DG: Yes, I think this is actually, it's a very timely discussion and so hopefully, this is going to trigger a bunch of people to go out there and make the right decision with their health regarding the Shingrix vaccine, the shingles vaccine. We have a couple of iterations of the shingles vaccine. You get chickenpox when you're younger, your body keeps them under control for a while, and then about 50% of individuals at some point in their life will have reactivation of that virus and will get shingles.

The current vaccine is a protein-based vaccine. It's almost like a Novavax for shingles and it has varying degrees of efficacy. The overall efficacy that we suggest is about 85% but then maybe this is easy to remember, only about 80% if you're over 80, so run the numbers. You go into this world with a 50% chance that you're going to have shingles after that chickenpox, you get a vaccine that's 80% effective, you still have a 10% chance that you're going to end up with the shingles.

Unfortunately, as you describe, as we hear with the senator, shingles can be bad and particularly if it involves dermatomes up in the head, in the face. I recently, unfortunately, had a gentleman in his 70s who started off with facial shingles, actually became encephalitic. Otherwise, had no other medical problems, ended up going down the comfort care route and died despite being on antiviral medication. You're going to take your 50-50, you're going to drop it down to maybe a 5% or 10% risk depending upon your age when you get the vaccine, other problems, but no, these vaccines are not 100%.

VR: Alex writes, "I'm wondering what your thoughts are on the new mpox outbreak in Chicago, specifically that a majority of the patients received both shots of the vaccine and it seemed we were largely able to beat the virus back. How do you think we should interpret these events in terms of the potential for wider spread and what is responsible for this resurgence?"

DG: This is great. These are great discussions, so thank you for emailing in and bringing these up. I don't think we have any vaccine out there that's truly 100%, maybe Vincent knows of one. If you're in a situation where a person is going to be repeatedly exposed to a pathogen, we can dramatically reduce your risk of having severe disease. We maybe in many cases can reduce the severity of disease should you get infected. We've always talked about vaccines don't prevent infection. They might reduce the risk for a period of time.

Now, in this case, were those diseases less severe? It's always hard to know in a little group of five or eight or 10. Was it reducing? How bad would the disease have been? The disease was horrible in a lot of cases. What I worry about is going into the spring and summer when there's potentially going to be a lot of exposure. Have we vaccinated enough people? What are we going to see? I have to say all the data we are seeing is really encouraging with regard to the efficacy of these vaccines but no, they're certainly not 100%.

VR: I think in some of the trials, the HPV vaccines in certain age groups were close to 100% at protecting against cancer. That's the best. All right. Clark writes, "We are two physician spouses, 60 years old, and without other risk factors, traveling for two weeks in the Mediterranean. We continue to wear N95s, eat meals outdoors, and endeavor to be judicious regarding crowd density.

One of us contracted our first case of COVID and started Paxlovid. The second of us turned positive a day later, also began Paxlovid. Are there special precautions we should take to protect one another's full recovery as we pass the five-day isolation period and make our way through the subsequent five-day masking only, or until two consecutive negative tests separated by 24-hour period? For instance, should one of us isolate from the other for a specific number of days, or is there a reasonable chance that the one continuing Paxlovid and still within the five-day period could reinfect the other?"

DG: In the story you lay out, and this is a story we saw many times played out, most likely you both were infected from a common source, probably have the same variant. I would not be particularly concerned that you're going to be passing it back and forth reinfecting one another. Your immune system is starting to respond. The medication is playing a role here. In general, our advice is if you wind up in a situation like this, you just weather the storm together. I wouldn't recommend any special precautions sort of protecting yourself from one another.

VR: Ann writes, "Just got my first COVID diagnosis, tested positive a day after symptoms. Assumed getting Paxlovid would be pretty straightforward, but the covering doctor at my medical group flat-out refused. His statements justifying his decision, he claims “Omnicron,” that's his term, doesn't affect the lungs in the same way. He claims Paxlovid triggers a rebound, not my understanding from your podcast. He also claimed that five days after my first positive test, I could consider myself non-contagious regardless of my COVID test, also not my understanding. Has something changed recently? I no longer listen weekly the way I did the first few years of the pandemic or am I talking to the wrong doctor?"

DG: Yes. You're talking to the wrong doctor and I'm hoping something will change in the near future and is that you will actually get a competent clinician to take care of you. You can imagine how frustrating this is. With over 1,000 people dying every week still, what is a common denominator there? At this point, there's all a level immunity. The common denominator is these individuals not getting offered that early treatment. I'm hoping that's going to change once this medication is fully licensed, once we can rely on better education but no, this is a misinformed, poorly educated clinician offering horrible advice.

VR: Finally, Mary writes, "During *TWiV 1*008, you answered Roland's question about using Symbicort inhaled steroid during the first week of COVID infection by saying it's the systemic steroids that should be avoided. This caught my attention because Paxlovid is in my plan should I contract COVID. My doctor agrees I should suspend my use of Flovent inhaled steroid for asthma as soon as I start taking Paxlovid since it is on the list of conflicting medications with Paxlovid. I'm elderly, have suffered pneumonia several times in my life, so I am super careful to avoid contracting COVID. I want my plan to be sound as I'm pretty sure I'll be experiencing COVID cough if I do get it."

DG: Great. Thank you for sending in that email. That is an interesting little thing that I am glad you bring up, is you do always have to be careful. There can be drug-drug interactions with the Paxlovid and some of the inhalers that folks are using. Yes, that was the really big distinction in the science. People that are getting systemic steroids, so people getting prednisone, dexamethasone, et cetera, those Medrol Dosepaks which cost a ridiculous amount when someone could just get prednisone in a situation like that.

Those are increasing the risk of progression by five- to six-fold, increasing the risk of mortality by about 35%. That's bad. We did study the inhaled steroids and the inhaled steroids didn't offer any benefit, but they were not associated with that harm.

VR: I want to just go back to Ann's email. She says she hasn't listened every week like she did at the beginning of the pandemic. I would say you ought to because just think how smart you're going to be if you listen every week. That's the best way to learn, to listen to things over and over, and you never know when something new is going to come up. I don't see any negatives. Do you Daniel?

DG: No. I only see positives. Education is a positive thing. We encourage you to listen every week.

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

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

[music]

[silence]

[00:37:37] [END OF AUDIO]