This Week in Virology

TWiV 1032 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.

[music]

VR: From MicrobeTV, this is *TWiV*, *This Week in Virology*, Episode 1032, recorded on August 2, 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 have an easy question for you, Daniel.

DG [laughs] Really, an easy one? That always gets me worried, but please.

VR: Is the COVID-19 pandemic over?

DG: That's not an easy question, Vincent. We're going to end up right into the COVID update right after my quotation, but when I showed up at the hospital on Monday, a quarter of the folks that I saw were hospitalized due to COVID, not just with COVID. Our local positivity rate, 28%. There's a lot of COVID, there's a lot of people ending up in the hospital. We'll talk a little bit. Words matter, I think we may have entered a new phase, but COVID is here to stay. COVID is -

VR: I'm sorry, COVID is here to stay, that's a good way to interrupt you.

[laughter]

These individuals who are in the hospital, are they older people? Are some of them unvaccinated? Do they have comorbidities mainly?

DG: I think the data shows this nationally, it's mainly older individuals. It's individuals with comorbidities. We're not seeing a bunch of folks, healthy young people in their teens or 20s or 30s. This is, "What's the biggest risk factor for a bad outcome with COVID?" It's being over the age of 50, over the age of 60, and then having comorbidities like diabetes, carrying that extra weight, heart disease, hypertension, cholesterol issues.

VR: OK. All these people in the hospital have been vaccinated then?

DG: It is interesting because if you follow the mainstream media, you almost think there's like this huge proportion of our country that is to the point of anti-vax where they're not getting vaccinated, but the majority of Americans went ahead and got vaccinated. May have been a little bit upset about mandates and people telling them what to do, but it is pretty hard to find someone who is not vaccinated, or, if they weren't vaccinated, who hasn't had like three doses of COVID at this point. The very few non-immune people showing up.

VR: All right. The point here is very important, the people who are getting hospitalized for COVID are vaccinated but they're older and have comorbidities.

DG: You know what the biggest common denominator, is they're not getting treatment during that first week. We keep harping on this. COVID can be managed. We have a medicine that, add that on top of your 90% reduction in a bad outcome from immunity, we can drop you another 90% if you get appropriate treatment in that first week.

VR: These individuals who are hospitalized don't need to be if they had been treated early.

DG: It's tough because part of COVID goes against the common sense. People are like, "Oh, I'm not feeling that bad. Why don't I wait and see how I do?" You can't. You can't wait and see how you do. What predicts your second week, your "rebound," is your age, your comorbidities. It's not how you feel during that first week. I was communicating with actually a physician today who was asking a question then he was like, "OK, I'll be honest. I'm asking about myself." It was, "I am three days into the Paxlovid, that bad taste is really getting me down, maybe that's enough. Maybe I should stop."

I said, "Listen, what you're doing right now is reducing your risk of next week ending up in the ER, the hospital, in the ICU, or no longer being one of my partners." That's what we're doing during that first week. It's not a wait-and-see. It's not we'll see where it goes because once you get to that point where you're feeling bad in week two our options really drop. The window really closes.

VR: Now, let me put it this way for people who don't understand, you have an exam next week, you say, "I'm not going to study, let's see how I do."

DG: I like that. Then you get about 10 questions in and you realize, "Wow, I really should have studied," so you raise your hand and you say to the teacher, "Is it OK if I take a little bit of a break and study?" They say, "Sure, take a couple of hours, and then when you come back, the exam will be over and you'll have failed."

VR: There you go. It's too late. Exactly right. I should tell people that back in November, after returning from ASTMH, I started to have respiratory symptoms. I tested positive. The day after the symptoms began, I gave myself a rapid antigen test. It was vigorously positive, whatever that means, right?

DG: [laughs] Vigorously?

VR: Well, the band came up in seconds.

[laughter]

I don't know if that means anything. I called Daniel, I said, "Should we wait and see?" He said, "What? Are you crazy? Haven't you been listening to me?"

[laughter]

I actually wanted to see how I would do with the realization that it could be too late, but Daniel said, "No, no, no. You have to take Paxlovid." I did and the next day I felt better.

DG: It would've been very interesting to see what the natural history would be in you, Vincent, but then again, it might've been quite sad because then who would be doing these podcasts with me?

VR: I think I'm a healthy 70-year-old. I don't have any known comorbidities, but I don't think it's worth risking, right?

Daniel: Yes. That's the tough thing, right? You're 70 years old, healthy, you throw that in, but it's the being 70, so your risk of a bad outcome is not zero. Maybe it's one percent. Maybe it's 1 in 100, but that 1 in 100, when it happens to you, it's -

VR: I could have antibodies to type-I interferons and not know it, right?

DG: Yes.

VR: I think it's unlikely because I've never had a serious infection of any sort my whole life.

DG: At some point, we'll have more information, maybe it'll be week two and we'll say, "Oh, let's do a blood test and see if you need treatment or not." We're not there yet. Right now, it's a probability game. We say, "Here's your chance, you have a non-zero risk. We can get that almost down to zero." My less-than-sensitive comment to my colleague was, "OK, you think the taste of Paxlovid is bad, wait till that plasticky taste of the ET tube."

VR: Oh boy.

DG: Endotracheal tube.

VR: That's a tough comment. You shouldn't make that to just anyone, Daniel. [chuckles]

DG: I think as a colleague.

VR: Yes. [chuckles]

DG: Because that's the choice. I know it's a bad taste and it's that metallic and you don't like it, but come on, if it's next week, my options are pretty limited, so let's take care of it when we can.

VR: I have to tell you the bad taste is no big deal.

DG: OK.

VR: Just five days and then you're done, so don't worry about it.

DG: OK. All right. Throw the quotation right in the middle. "Science is founded on uncertainty. Each time we learn something new and surprising, the astonishment comes with the realization that we were wrong before." That's Lewis Thomas. A little bit of a difference in educational style. In the PhD training, it's all about being wrong. It's all about putting out a hypothesis saying, "Well, I think this might be the case," doing your experiments and then realizing, "Eh, it was not quite right," and learning from it. It's tough, I think, for a lot of us clinicians to admit that we don't know, that we're uncertain and that we're waiting to find out. We'll get into a bit as far as some of the science, particularly about Long COVID as we move forward.

VR: What's the bow tie today, Daniel?

DG: The bow tie is HIV.

VR: All right.

DG: OK

VR: That pandemic is still ongoing, wouldn't you say?

DG: Yes.

VR: OK.

DG: Last week I discussed the paper "Predicting COVID-19 Incidence Using Wastewater Surveillance Data, Denmark, October 2021 through June 2022," published in *Emerging Infectious Diseases*, where the Danes found that data from a large-scale wastewater surveillance system can serve as a good proxy for COVID-19 incidents. This week we have the article - a couple of articles you'll find out this week. The first one "Use of Wastewater Metrics to Track COVID-19 in the U.S.," published in *JAMA Network Open*.

Now, these are the results from an observational cohort study with a time series analysis conducted from January to September 2022 in 268 U.S. counties in 22 states participating in the U.S. CDC and P National Wastewater Surveillance System. Participants included the populations of those U.S. counties. In the first quarter of 2022, use of the wastewater percentile detected high reported case and hospitalization rates. Now, the percentage change metric performed poorly for reported new cases and for hospitalization across the first three quarters of 2022.

The performance of the wastewater percentile declined over time for cases in the second quarter and third quarter of 2022. Really critical here is that after the introduction of vaccines, we are seeing a significant disconnect between wastewater surveillance and disease. Is wastewater surveillance still helpful? Can it help us prepare for those high-risk people, as we've been discussing, that still might end up requiring hospitalization?

The article "Wastewater-based Epidemiology Predicts COVID-19-induced Weekly New Hospital Admissions in over 150 USA Counties," was published in *Nature Communications*.

Here the investigators evaluated the feasibility of using wastewater-based epidemiology to predict the COVID-19-induced weekly new hospitalizations in 159 counties across 45 states, so getting pretty close to the 50 there in the USA, covering a population of nearly 100 million, about a quarter of Americans.

Using county-level weekly wastewater surveillance data over a period of 20 months, they developed models. The wastewater-based epidemiology models accurately predicted the county-level weekly new admissions, allowing a preparation window of one to four weeks. In real applications, periodically updated WBE-based epidemiology models showed good accuracy and transferability, with a mean absolute error within four to six patients per 100k for upcoming weekly new hospitalization numbers. They conclude that this study demonstrated the potential use of WBE, wastewater-based epidemiology, as an effective method to provide early warnings for healthcare systems.

VR: I think I'd like to go back to that previous article where you say, "After the introduction of vaccines, there's a disconnect between wastewater surveillance and disease." That's really important because people are still getting infected, but they're not getting as much disease. That's why we find virus in the wastewater, because the infections are ongoing. Very important point.

DG: I think these are both important papers. One is that disconnect. Our immune system, it does work. We have changed the face of COVID-19, but we're still seeing folks end up in the hospital and we still can use that wastewater results to be ready and tell us what's about to happen. As we mentioned early on, increasing test positivity, increasing hospitalization rates, and boy, what started going up a few weeks ago? It was the wastewater levels.

All right. Now, a couple fun ones here. I've got this article "Association Between Duration of SARS-CoV-2 Positivity and Long COVID," right here in the testing section. This article was published in *JID* and looked at 1,293 healthcare workers previously infected with SARS-CoV-2, of which 34.1% developed Long COVID. A pretty high percent in this cohort. I'm going to go straight to the data because what they're looking at here is what was predictive of ending up with Long COVID.

Female sex. You're almost twice as likely to see this in women as you do compared to men. Also, interesting enough, allergies. I thought that was interesting, to see about one-and-a-half-time people who have allergies. Then they actually looked at the different waves and the number of doses of vaccine. We saw here some interesting - This is really the beat of the paper, which is the duration of test positivity.

I think there may be some interesting insights in here. Particularly folks that continue to test positive 15 to 21 days, or I'm even going to go out, more than 21 days, 15 to 21 days, four times as likely to end up with Long COVID. More than 21 days, 5.39 times more likely. Something interesting about our immune system having issues handling and clearing the virus associated with the risk of Long COVID.

VR: I thought this was a good study. You want to see other studies, similar studies, with more numbers in different populations to see if it holds up, but I think it was intriguing.

DG: As you could point out, we're looking at a little over 1,000, about a third of them, so we're talking about a few hundred that we're looking at. Yes, it would be nice to see this repeated. Also, it'd be nice to really understand, at an immunology level, what exactly is going on. Why are they continuing to have test positivity?

All right. Now we have the article "Rapid Direct Detection of SARS-CoV-2 Aerosols in Exhaled Breath at the Point of Care," published in *ACS Sensors*. I don't think I've ever quoted from this journal before. Lots of cool cartoons. In brief, this is a point-of-care testing platform that directly detects SARS-CoV-2 aerosols in as little as two exhaled breaths of patients and provides results typically in under 60 seconds. I have these nice pictures where you've got this hand-held breath aerosol collector. You breathe into it, and it uses llama-derived SARS-CoV-2 spike protein-specific nanobodies.

If people know, but llamas, camels, that whole group have a very different way of making antibodies. They've got these nanobodies bound to an ultra-sensitive micro immuno electrode biosensor. It actually detects the oxidation of tyrosine amino acids present. They detect that the electrochemical biosensor directly detects the virus itself as opposed to some sort of surrogate or signature or volatile. It's sensitive in this report down to as little as 10 viral particles in a sample. They reported a sensitivity of about 78% very high specificity. They actually say that this platform potentially could be adapted for multiplex detection of different respiratory viruses.

VR: Well, those llamas should know that they're contributing to healthcare.

DG: [laughs] They are, all of them camelids. Thank you. All right. We're going to move on to the early viral upper respiratory non-hypoxic phase. We hammered in this a little. This is that first week. This is that viral symptom phase. This is when you feel crummy, you get a fever, a sore throat, other things going on. What are our options? What we're trying to do is about 20% of people, 10% to 20% of people are going to feel better and then feel worse during that second week.

During that second week, some people are going to end up in the hospital, some people are going to end up quite sick, some people are going to progress. During this first week, this is our window of opportunity for decreasing the risk of a bad outcome during week two. Still can have week two, but you can have week two at home, in the discomfort of your own home versus the discomfort of a hospital or facility.

Number one, we've been talking about Paxlovid. Number two, remdesivir. What about head-to-head? Which is better? I know everyone likes to bet, so we have the article "Effectiveness of Oral Nirmatrelvir/Ritonavir versus Intravenous Three-Day Remdesivir in Preventing Progression to Severe COVID-19: A Single-Center, Prospective, Comparative, Real-Life Study," published in the journal *Viruses*.

These are the results of a prospective observational study conducted in a tertiary care hospital from the first of January, 2022, until the 15th of March, 2023, during the prevalence of the omicron variant. Important is that they included 521, so mainly immunocompromised, 56% of patients in the analysis. Sixty-eight percent received the three-day remdesivir, about 32%

received the Paxlovid. Overall, 2.9% met the primary endpoint of hospitalization at 30 days. That was 2.8% in remdesivir. That was 3% in the Paxlovid. Really pretty similar.

They conclude the choice of treatment did not seem to affect outcomes. They did find that one or two vaccine booster shots seem to reduce the risk for adverse outcomes. Remember timing on this. Maybe we'll talk a little bit about that. They conclude that in this patient population of high-risk, mainly immunocompromised, vaccinated patients, during the prevalence of the Omicron variant, both Paxlovid and the three-day remdesivir seem to be equally effective early treatments for the prevention of hospitalization and/or death. All right. Number three, molnupiravir, Thor's hammer. Convalescent plasma for specific situations and avoiding doing harmful and useless things.

Then the second week. Now, I know I've been quite annoyed that they call it Paxlovid rebound, but it is this second-week, early inflammatory phase. This is when people start to feel better and then they feel worse. Maybe it's good that this is out there, that people recognize that you have to be watching to see what happens during that second week because this is when some people may become hypoxic. Oxygen saturation is less than 94%. You're going to jump in with steroids, pulmonary support, anticoagulation, maybe remdesivir, if we're still in the first 10 days, immune modulation, and not jumping in with those harmful things.

Now, much to do today is going to be about the late phase or Long COVID. I was delighted with the announcement that the NIH has launched several Phase 2 Long COVID treatment trials. Put the emphasis on the word "trials," because it seems, talking to a lot of my patients, that their family members seem to think these are Long COVID treatments as opposed to trials to find out what the treatments need to be. The NIH launched and is openly enrolling folks for Phase 2 clinical trials that will evaluate at least four potential treatments for Long COVID, and then pretty soon, we're going to get up to seven in the coming months. Let's just run through a few of these.

First, RECOVER-VITAL. This is going to initially focus on treatment targeting the hypothesis, the idea of SARS-CoV-2 persistence. A lot of people just take this to be true, the idea that the virus is staying in the body and that's driving things. The first intervention will be to test a longer dose regimen of the antiviral Paxlovid, seeing if this improves symptoms in patients with Long COVID.

Now, they say in this announcement the first trial sites have been activated and are enrolling, but I do just want to give a little context here. We've been talking about the fact that Stanford, Duke, Yale, several places have been starting to look at this. We discussed the Stanford trial, but I just want to remind people what happened there. They stopped enrolling after an interim analysis found, as we have heard, inconclusive evidence to support this intervention. Just leave some links there to the Stanford study, as well as the news a little bit about that.

Second, RECOVER-NEURO. We've talked quite a bit about the neurological impacts. RECOVER-NEURO will examine accessible interventions for cognitive dysfunction related to Long COVID, including brain fog, memory problems, difficulty with attention, thinking clearly, problem-solving. What are they going to do? Well, they're going to use a web-based brain training program called BrainHQ. I want to try that for myself. This is developed out in San Francisco.

VR: It's too late for you, Daniel.

DG: Oh, Vincent.

[laughter]

This has been used to improve cognitive function. They're also going to use the PASC-Cognitive Recovery. It's a web-based training program developed by Mount Sinai here in New York City. This I thought was the most sci-fi here. They're going to use a home-based transcranial direct current stimulator developed by a company out there in Jersey that they claim has been demonstrated to help improve brain activity and brain blood flow. All right.

RECOVER-SLEEP. We've talked a bit about a lot of individuals having sleep disturbance issues. They're going to be having studies looking at hypersomnia, excessive daytime sleepiness, wakefulness-promoting drugs, and then they're going to look at others that actually help people sleep better, regulating their sleep patterns.

RECOVER-AUTONOMIC. I was just listening to the David Tuller episode where a little bit of discussion about the postural orthostatic tachycardia syndrome, the POTS, and all the many autonomic impacts that we are seeing.

They're going to be having different treatments used for immune diseases versus placebos, not just your standard autonomic treatments. The second arm is going to evaluate a drug used to treat heart failure in individuals. A lot of interesting things in the first four. Now, the fifth is what I'm most excited about, but it's not quite ready for prime time. This is going to be a platform focused on the exercise intolerance, fatigue/debility. I feel like fatigue just doesn't do enough. Once they get this put together, we're going to have a fifth platform, and then a sixth and seventh are going to roll out soon afterwards.

Really encouraging. I know a lot of people are a little frustrated with how slowly this has been moving. I also wanted to mention a couple of things. I'm going to close this out here today. I'm hoping that if we keep these shorter, we don't go too far past that 21-minute attention span that people keep listening. I want to direct people to an article by Ed Yong that many of my patients have told me they appreciate it. I don't know, Vincent, if you got a chance to read "Fatigue Can Shatter a Person: Everyday Tiredness is Nothing like the Depleting Symptom that People with Long COVID and ME/CFS Experience."

VR: I do have a subscription to *The Atlantic*, so I'm going to read it.

DG: Unfortunately, it's behind a paywall. I wonder if they shouldn't, every so often, an article as important as this. Actually, I think Ed Yong is leaving *The Atlantic*, so maybe as a farewell, they could, for 30 days, lift the paywall, because I think a lot of people have really found comfort in just how much he appreciates the impact here. I don't know if we have any Physics Girl fans currently listening. I'm going to leave a link.

As her fans and some of our fans may know, Dianna Cowern, Physics Girl, is suffering from a really severe case of debilitating long-COVID, basically making her bedridden and very limited. I've been working with Physics Girl on her long-COVID recovery and just recently started

working with her husband, Kyle Kitzmiller, and Space Gal, Emily Calandrelli, an aerospace engineer, to help create a video about the impact of long-COVID, what it's had on Physics Girl.

I think there's something really compelling about seeing how a disease can transform the life of a person from being so full of life and energy to being so compromised. When the live stream airs and the video becomes available, I will certainly share that. In the meantime, Vincent, I don't do picks of the week or talk about the weather, but perhaps my one and only pick of the week will be Space Gal. I'll leave in a link to her YouTube channel. I actually subscribed myself earlier today. You might remember her from *Bill Nye the Science Guy,* who I like to remind our listeners has only an honorary PhD, unlike the one that Vincent and I have, which are real PhDs.

All right. We will close with low and middle-income countries. No one is safe until everyone is safe. Let me start with a thank you for all of our listeners and contributors. We just finished our Foundation for International Medical Relief of Children fundraiser. We just squeaked in, we made our goals, so we're going to be sending them a check for $20,000 to support the tremendous work they do. We are now starting our Floating Doctors fundraiser, where for August, September, and October, we will double 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@microbe.tv. Dee writes, "My daughter's college roommate tested positive for malaria on an international service trip this summer. She may have received some initial treatment overseas. What would be the protocol for re-entry into the U.S.? Would she pose a risk to her roommates in a dorm setting? What recommendations and/or precautions are advisable?"

DG: This is a great question. As we know, in the news, this actually just recently came up at the hospital where I work, where a nurse was asking some returning traveler with fevers. The malaria workup was ordered and they wanted to know what isolation precautions. Now, you don't get malaria through direct contact. An individual with malaria has to be bitten by a mosquito. There's a sexual cycle of the parasite in the mosquito, and then that low likelihood event, but in certain settings, it is happening, where a second bite gives it to a second person. Really, there's no significant concerns here in the dorm setting.

What would you do for this individual? Well, clinicians are going to review, were they fully treated; assess whether or not further treatment is required for the person, but no, not a risk for having them return to the dorm.

VR: Anne writes, "I went to an urgent care center on Thanksgiving Day last year with the worst cough of my life. The doctor took an X-ray. He said it was bronchitis, likely caused by RSV, which was quite prevalent in our area last fall. I am 69, recently finished with breast cancer treatment, and eager to avoid getting RSV. However, my doctor is hesitant about my getting this new vaccine, and the CDC is equivocal about which elderly persons should get it. Here's my question: If I did have RSV last fall, am I now immune, or does it morph like the flu or COVID and attack again? Should elderly people with compromised immune systems get the RSV vaccine?"

DG: Unfortunately, RSV is something that we see repeated infections, so it's not a one-and-done. I wish it was. That would be ideal. I understand, and as we've talked about this, shared decision-making with your provider, balancing risks. This is a brand-new vaccine, we have pretty robust studies, but we don't have that real-world experience of millions of people getting it to really have a risk profile. It is interesting when you talk about shared decision-making. It's not really supposed to be the doctor's decision-making. It's supposed to be the doctor getting a sense of your risks, also your risk tolerance, and helping you to make your decision.

I often see a lot of doctors and they're really imposing their value system on the patients, but that's really not what our oath is supposed to be. Our oath is that we're supposed to acknowledge the goals, desires, the risk for a particular patient and help them make the decision that's best for them.

VR: Nick writes, "My mother-in-law is a 20-year kidney transplant patient in her late 70s, who is still mostly avoiding close contact with people after three years of COVID. Is there any news about how COVID is affecting immunocompromised transplant patients like her? According to the Labcorp COVID-19 Semi-Quantitative Antibody Test, she managed to make decent levels of antibodies after several boosters."

DG: This is a challenge. As we've talked about, these are the individuals that are ending up in the hospital. These are the individuals that are having the bad outcomes, people of older age, people who have comorbidities, people who are immunocompromised. A kidney transplant person is not going to have that robust immune system to protect them, so this is a challenge. This is someone that if they get COVID-19, you want to jump in and get that extra 90% reduction in progression by early treatment.

VR: Fernando writes, "Thanks in part to your advice, I managed to stay COVID-free until now, but my luck ran out last weekend, likely thanks to several busy events at work. Just finished my Paxlovid course, feeling totally normal, testing negative on NAAT, but our very attentive and knowledgeable doctor warned me to look out for Paxlovid rebound. Knowing your stance on that concept, I wanted to offer a hypothesis on why the concept is sticking, even with good clinicians, and certainly with friends and family who experienced it.

Any of us who've had a bad cold or flu can recall the experience of feeling better after a few days, possibly going back to work, and then starting to feel worse again, maybe with a hacking cough and fatigue for another week or longer. However, the contrast between the first phase and the second one is not extreme in terms of symptom intensity. With an effective antiviral like Paxlovid, the contrast between the first phases and feeling absolutely fine after a few days and the second is a lot more pronounced, making that 'rebound' feel different in quality than those in our early viral experiences that did not involve antivirals.

In other words, post-Paxlovid rebound feels that much worse because Paxlovid was so effective at squashing first-phase symptoms. Just thought I'd put this speculation to your consideration, trying to reconcile the objective data you present with the subjective impressions that dominate the discourse."

DG: Actually, I like that. I like the way - because part of this "rebound" is subjective, is how are you feeling? There is growing evidence that Paxlovid actually decreases the duration, the severity of symptoms during that first week, potentially creating more of a contrast. The "viral rebound," the idea of a negative antigen test, now, a positive antigen test, we're not seeing a rebound up into the millions. We're just seeing a low-level detection of either viral antigen or viral RNA during that second week.

Unfortunately, we've had "role models," in addition to experience, go out there and take a second course of Paxlovid during that second week, despite so much evidence that an antiviral is not helpful to treat inflammation during that second week. Continues to be a challenge. The plural of anecdotes is not data, but I understand that some people find that hard to accept, not trusting your own eyes, trusting science, trusting properly done trials to really get at the answers. No, I think what you bring up is super helpful.

VR: If I've learned anything during this pandemic, it's that it is not possible to get all the clinicians in the U.S. on the same page, Daniel.

DG: Nor all the scientists, Vincent.

VR: That too.

DG: [laughs]

VR: We already knew that. In the old days before communication, when someone figured something out - Who was the physician who figured out you had to wash your hands before surgery?

DG: That did not go over well. [laughs]

VR: It took a long time for that news to spread throughout Europe. Nowadays it doesn't take a long time, but still, it doesn't stick. People still are giving people azithromycin for COVID, right? I just don't -

DG: Unfortunately, these are true things. One of the tough things is the idea of washing your hands, really that was considered offensive. That was this whole idea that you're blaming doctors for illnesses, "As if their dirty hands are the cause. How dare you?" That actually was met with really a lot of negative impact for that individual. Here's a challenge, people get into a habit. There's a lot of eminent people that don't want to say, "OK, I was wrong and the science showed me."

I still remember the days of my training, I was considering doing family practice and I was quoting some data during rounds. One of the chief residents of family practice said, "Daniel, you really have to stop this. You're upsetting the community doctors. You are suggesting that a really good trial is more important than their 30 years of experience."

VR: [laughs]

DG: I said, "I'm sorry. Not only am I suggesting that, but it's true."

VR: Dr. Semmelweis was the father of hand hygiene. That's *TWiV* weekly clinical update with Dr. Daniel Griffin. Thank you, Daniel.

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

[music]

[00:36:48] [END OF AUDIO]