This Week in Virology

TWiV 1128 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 1128, recorded on July Fourth, 2024. 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 guess you don't have a Fourth of July tie on, do you, Daniel?

DG: No, I probably should have found one that had a lot of blue and red and white and all that stuff. I actually am not sure what this bow tie is. My son Barnaby tried to use a Google program where you look at stuff and it tells you, it doesn't know what it is either. It's some sort of microbe and people who are on YouTube can see this. Yes, let me know. I don't even remember what this was. I knew at some point.

All right, let's jump right into it. It's July Fourth. I'm not going to keep people too long. No promises, of course, but let us start with our quotation. This is from Sir David Attenborough. "People must feel that the natural world is important and valuable and beautiful and wonderful and an amazement and a pleasure." It made me think of just science. What is science about? Science is about understanding and exploration and staying curious and just appreciating just how complex and beautiful and intricate this world we live in is.

When I hear a lot of this sort of anti-science, like basically, "Don't look there, don't touch that, don't do that," it's just antithetical to this whole, just nature and everything around us is amazing and wonderful and fascinating. We are explorers. We are curious creatures. I hope the politicians don't succeed in reining in our curiosity.

VR: They're doing their best to try, Daniel.

DG: They can try, but I think the human spirit will prevail. Speaking of the human spirit, well, this is not a proper segue, but let's just call it that. Bird flu. CDC reports fourth human case of H5 bird flu tied to dairy cow outbreak. This is a press release. I'll share a little bit of the CDC press release. Just came out yesterday, July 3. A human case of highly pathogenic avian influenza, HPAI. I want to point out highly pathogenic in avians influenza, H5 bird flu virus

infection. United States has been identified, in the state of Colorado. This is the fourth case associated with an ongoing multi-state outbreak of the avian H5N1 in dairy cows. First in Colorado in a person.

Previous cases were reported down there in Texas, which is sure hot this time of year, up in Michigan, which actually is particularly nice this time of year, particularly up in the Upper Peninsula. We read that, as with previous cases, the person is a worker on a dairy farm where the cows had tested positive for the avian H5N1 virus. The person reported eye symptoms only, got some Tamiflu, they got better. The CDC just lets us know that they're watching their surveillance systems closely, particularly in these affected states. Again, nothing to worry about here as per the CDC.

VR: Daniel, it's interesting that a couple of years ago, there was a case in Colorado of a worker who had been assigned to cull chickens. There was an outbreak of H5N1 in chickens, and he got it. They treated him with also Tamivir and he was fine also. [crosstalk]

DG: OK. Yes, I remember that, actually. Yes. All right. A little plug for *CIDRAP*. I don't know if you subscribe to *CIDRAP*, Vincent, but it's worth doing. C-I-D-R-A-P. There's a link where we read about this case. We also learn, unfortunately, about the, I'm going to say, low level of education when it comes to pasteurization of milk. What is that about? From the *CIDRAP*, you can actually link to this Annenberg poll. What's up with this?

For context, I want to point out that raw milk, drinking of the raw milk, it's a thing. Actually, according to the Associated Press, it's becoming more of a thing. Weekly sales of raw milk are actually increasing. Late March up 21%. Mid-May, they grew 65%. This is becoming more and more of a thing. We've talked a little bit about it. There's this special opinion panel omnibus platform. That's where this survey stuff is coming from. Let's go through. I'm going to leave in a link so you can actually look. What do people think?

The first question, and the questions are key, is raw milk safer, less safe, or just as safe to drink as pasteurized milk? This seems like a no-brainer. Everyone's going to say, of course, pasteurized milk is safer. Everyone's going to say that, but no. 47% say less safe. It should be closer to 95%, I had wished. About 30% are like, "I don't know, not sure." 15% just as safe, and 9% say it's safer to drink.

Now, the next is, does this stuff work? Did Louis Pasteur come up with a good idea? How effective is pasteurization? Only about half the people, only 54%, recognize that it's very effective; 22% say, yes, it's somewhat effective. Another 20%, not sure; 3%, not too effective. Then 1%, it doesn't work at all. What do you think, Vincent? We've got some education to do.

VR: I think this is crazy that we have H5N1 in cows, in cow's milk, and people are drinking more raw cow's milk. It doesn't make any sense, right?

DG: What are they teaching in the schools these days, right?

VR: Forget about the schools, they're not teaching them any good science in the schools. Oh my gosh. H5N1 may not be a problem in raw milk, but there's other stuff in raw milk, as you know, that's why Pasteur invented pasteurization.

DG: Yes.

VR: Oh my gosh.

DG: If you go on and read more from *CIDRAP,* you find out how many - like over 400 different pathogens you can get from the milk. We've talked about the fact that it's not that you can't drink raw milk, but if you're going to do it, you have a little bit of education, understand you want to -- If you're going to be doing this, you want to be doing it from these operations that actually have certain standards. They make sure that the cows are germ-free so that the milk is safer. If you don't have all that stuff in place, and who do we trust these days, just get the milk pasteurized. Get it heated up to a certain temperature. Make it safer to drink.

Moving back into COVID, and Puerto Rico is still yellow. It's still in that 4% to 6%. Here in New York, we see 2,000 to 3,000 people die every week, and only about, say, 1% or so of those deaths are due to COVID. Well, actually, it's less than 2%, so it's actually above 1%, so that's not great. I could do the math. Let's see. 3,000 died this week, 2% from COVID. That's about 60 deaths. Puerto Rico, where we see about 600 deaths, we're seeing about 5%, so 30 deaths in a much smaller population per week. The rest of the country is all in that either less than 2% or the less than 1%.

What about wastewater? Remember, wastewater is a way to track. You're not getting it from the wastewater, except for Dickson. [laughter] Really, the West is where we're really seeing that big rise. We're seeing a little bit of a rise in the South. We're leaving a link so you can look and see what happens over time. There tends to be this pattern. Interesting enough, I got sent this link from the CDC. COVID-19 can surge throughout the year. This just came out from the CDC, and it was - a communication came out yesterday. There's a summary, and in the summary, the CDC says what CDC knows.

The United States respiratory virus illnesses typically peak during the fall and winter. These peaks are due to several factors, including human behaviors and environmental conditions that affect the ability of viruses to survive and spread. Since the start of the COVID-19 pandemic, infections with SARS-CoV-2, the virus that causes COVID-19, have peaked during the winter, but also surge at other times of the year. These periodic surges are due in part to new variants, decreasing immunity, and because the evolution of new variants remains unpredictable, SARS-CoV-2 is not a typical winter respiratory virus.

What's nice, I'll leave in a link. You can actually look since early 2020 and you can see that the percentage of these positive SARS-CoV-2 percent tests reported to the NREVSS, the National Respiratory and Enteric Virus Surveillance System. You see this pattern, and I like the way they color code it, because they've got the December, February, and that's in this like teal or turquoise-type color, and you see that's when we see these big peaks. July, September, you see these rises, sort of this biphasic pattern, but it tends to be, in general, a more significant rise in the winter. For instance, last summer, the July-September rise was actually right up there with the winter rise in percent positive tests.

VR: This doesn't make a lot of sense to me, because influenza viruses undergo antigenic variation, and sometimes the vaccines do well, sometimes they don't, but it is seasonal. That's the point with influenza. It's winter disease. I don't understand why SARS-CoV-2 is different.

DG: I have some ideas, but that's all they are, is ideas. One is, as we've seen, if you get a particular type of influenza, let's say, in December, you're pretty much good. You're not going to get that same influenza in the next three to four months. With COVID, we see people get COVID in October, and then February, they've got COVID again. There seems to be - when you get infected, it doesn't give you that, I don't know, six, nine, 12-month protection. I think it was Jeff Seamus, is that who -

VR: Jeffrey Shaman, yes.

DG: Yes, Jeffrey Shaman. Really, after nine months go by, boom, you're getting it again. If you get infected with SARS-CoV-2, if you get infected with the coronavirus, you don't really tend to have the same durable immunity. Also, is this an mRNA vaccine issue we talked about last time? We just don't have this durability. Maybe this fall, when people get more Novavax, we might see a little bit of a change in this pattern.

VR: A couple of things. First of all, I wonder what the ages are, because I wouldn't be surprised that older people do not make a durable response to anything. It would be nice to stratify these numbers by age. The other thing is, people are getting infected, they should have durable immunity to infection. Even with a variant, you're still going to have T-cells that hit the cross-reactive epitopes that prevent severe disease. Maybe what we're seeing here, these are just positive tests, maybe a very small fraction are severe disease, so it doesn't really matter.

DG: Yes, and there's a disconnect here, because if you looked at this last July 2023 into September, the peak of percent positive tests was actually even slightly higher than we got winter, but that did not translate into hospitalizations and deaths, yes, so we will keep an eye on this.

An update when we get to COVID passive vaccination. I was on a call last night with the folks from Invivyd. I don't know how we pronounce that, but I-N-V-I-V-Y-D, the company that makes Pemgarda. Pemgarda is the new prophylactic monoclonal treatment. You get this 4,500 milligrams, you get it every three months, and it basically is going to protect you, it's going to give you these monoclonal antibodies. Right now, there's an EUA for Pemgarda. Apparently, people took issues when I said this is the replacement for Evusheld because that company is working on their own replacement.

While we don't have Evusheld, we have Pemgarda, which has an EUA, so it's emergency-use-authorized by the FDA for pre-exposure prophylaxis of COVID-19 in certain adults and adolescent individuals, 12 years of age and older, weighing at least 40 kilograms, who are not currently infected, who have not had a known recent exposure, and who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments, and are unlikely to mount an adequate immune response to COVID-19 vaccination.

I think I bemoaned in the past when I first came up the infusion center locator. I didn't think it was working. Part of it not working may be that the locations are limited, but the center is working. Yes, the locations are still limited, so this is going to be a call to arms for the providers out there wanting access for their patients to reach out to Invivyd. You can also email us at

daniel@microbe.tv, and we'll send you - Basically, I'm going to get you in touch with the company, and let's try to have more places where we can send our patients.

If you're a patient wanting access to this, ask your doctor, say, "Hey, let's try to increase the infusion centers that offer this." Apparently, there's the right billing codes, and this is not an altruistic thing. The infusion centers can make money providing this useful therapy.

COVID, early viral phase, you test positive. What to do? I will keep sending out those links to the guidelines so people can follow those guidelines. Number one, Paxlovid, two, remdesivir. Number three, molnupiravir. What about molnupiravir? I had a patient this week, got acute COVID, ended up on molnupiravir for some drug-drug interaction issues. We have the article, "Effectiveness and Safety of Molnupiravir in the Intended-use Population: An Observational Cohort Study," published in *CMI.* These are results of a retrospective cohort study on folks that were in the Israel's Clalit Health Services, CHS, from January 16, 2022 to February 16, 2023.

We've shared data from this health services group before. The effectiveness outcome was the incidence of hospitalization or death due to COVID-19. The safety outcome was the incidence of all-because mortality within 35 days of infection. 49,515 patients met the criteria for eligibility. Of them, 3,957 molnupiravir-treated matched to 19,785 untreated. In the molnupiravir-treated patients, we had 5.1 per 10,000 person-days experienced COVID-19-related hospitalization or death compared to 10.4 per 10,000 person-days. A relative risk, 0.50. A 50% reduction in folks that ended up hospitalized or not surviving.

What about mortality? All-cause mortality was also lower and similar. About a 50% reduction in all-cause mortality. Dropping that from 6.1 per 10,000 person-days down to three per 10,000 person-days.

VR: That's very impressive, Daniel.

DG: It's much more impressive than I think people realize. It's not that 80%, 90% we might get when monoclonals were working, that we get with Paxlovid, but it's a big difference from doing nothing. When the whole - This is an easy lift. There's no drug-drug interactions. There's no kidney issues. This is just a really easy, four pills twice a day, five days, you're done. Yes.

VR: For people who can't take Paxlovid, this is a reasonable alternative.

DG: Exactly. Don't want to give this to pregnant folks, don't want to give it to young children, but yes, a lot of our high-risk folks can benefit from this. All right, convalescent plasma, certain context. Remember, you are still infectious. You still get COVID-19. You still spread that SARS-CoV-2 virus to other folks. COVID, the early inflammatory weeks. This is the second week. First week, viral replication. Now the immune system kicks in, viral replication is on the way down.

Just remember, antivirals treat viral replication, they don't treat inflammation. We've looked at five, we looked at 10 days, extending that Paxlovid with some data at CROI, just five days is where you get it. Even at 10 days in a high-risk population, just not doing much. Here we are, second week, but what are we doing during that second week? Steroids at the right time, in the right patient, at the right dose.

We have a, I thought it was a really interesting article, “The Life-saving Benefit of Dexamethasone in Severe COVID-19 is Linked to a Reversal of Monocyte Dysregulation,” published in *Cell*. Now, we all wave our hands and talk about how steroids calm down the cytokine storm and rein in that overly exuberant immune response, but what's actually going on? Why do steroids at the right time in the right patients save lives, keep people off ventilators, and decrease the risk of Long COVID?

Here these investigators identified patients treated with and without dexamethasone according to criteria of the RECOVERY trial during the first months of the COVID-19 pandemic from a large observational cohort study. They generated single-cell omic profiles from peripheral blood-derived immune cells. They tell us they deciphered the cellular, molecular, and functional changes to dexamethasone treatment and linked the observed changes to clinical outcomes. Let's dive a little bit. They found that dexamethasone specifically reverses the dysfunctional molecular phenotypes associated with severe COVID-19 in monocytes of patients with a clinical response to treatment, but not those that went on to die, not those with a fatal outcome.

Based on these outcome-specific single-cell gene expression data, they generated these transcriptomic signatures that they transferred to whole blood transcriptomes of two independent COVID-19 cohorts, demonstrating their potential as predictive biomarkers for treatment response in clinical studies. They made the discovery, and then they actually looked at it as predictive. They report the molecular hallmarks that are linked to the life-saving effects of dexamethasone, and they actually go ahead and show that you might be able to use this to do this in vivo drug target assessment.

The whole idea is they've identified the responders, the non-responders, and you can see what's going on here. I have to say, full disclosure, this is a *CELL* paper, lots of data, where, oh, you're allowed to have so many figures, but each figure can have 12 different panels. There's a lot of data here. I have to say, this treatment is a bit, well, it's more than a bit. It's very simplified. They look at B cells, they look at T cells, and neutrophils, and cytokines, and heat maps. We've got this holiday weekend. For the brave, it's worth spending some time with this open-access paper over the weekend and enjoying all this.

VR: The interesting point is that the target of dex is the macrophage.

DG: I really thought it was interesting that it was monocytes. You would have thought it was the activated T cells and all this other. I don't want to be too monofocused. I was thinking of a good pun there, monocyte-focused, monofocal. Anyway. [laughs] All right, and anticoagulation, pulmonary support, remdesivir if you're getting in there early enough, immune modulation, and the late phase, PASC/Long COVID. I might, as a teaser for next week, Vincent, I might do an update on where we are with Long COVID, and diagnosis, and testing, and treatment. We have one, two, couple of articles here before we go to our emails.

The first one is interesting. The article, “EEG Signatures of Cognitive Decline after Mild SARS-CoV-2 Infection: An Age-dependent Study,” published in *BMC Medicine*. This is a cohort study where they conducted pre- and post-infection EEGs, 185 participants, 181 structured questionnaires of long-term symptoms across four distinct age groups. Cool, right? You've got an EEG pre, and then you've got an EEG and these questionnaires. The goal was to

comprehensively evaluate the impact of SARS-CoV-2 infection across different age demographics. They're going to analyze the EEG across these different age groups.

Now, interpreting EEG data is not something most of us do. We stand next to the neurologist, and they point at these squiggly lines, and they make a lot of interesting comments, and we say, "Uh-huh, uh-huh." They found that children and adolescents exhibit smaller changes in brain network and microstate patterns post-infection, implying a mild cognitive impact. They do these sequential linear analysis that they say show us that SARS-CoV-2 infection is associated with a marked rise in low-complexity synchronized neural activity within low-frequency EEG bands.

They go on to say sequential nonlinear analysis indicated a significant reduction in the Hurst exponent across all age groups, which I don't know what that means, but they say this points to increased chaos and complexity within the cognitive system following infection. All right, chaos and complexity. They go on to do further linear regression analysis and they establish a positive relationship between the magnitude of the changes in these neural indicators and actually the persistence of long-term symptoms post-infection.

We're seeing EEG changes. We're seeing this EEG disarray with complexity and chaos. Really interesting, and this is actually correlating with the cognitive decline that's being reported. SARS-CoV-2 messes with your brain.

The last one before we get to our emails, the article, “Tissue-Based T Cell Activation and Viral RNA Persists for Up to Two Years After SARS-CoV-2 Infection,” published in *Science Translational Medicine*. The title's great, but you're going to see they sort of - I don't know, maybe the reviewers got a little bit lazy, but there's a nice editor's summary, some colorful images. Here we see that these investigators performed whole-body PET scans, positron emission tomography imaging, in this well-characterized cohort of only 24 participants at various time points, ranging from 27 to 910 days after acute SARS-CoV-2 infection.

They used this radiopharmaceutical agent, this 18F-F-AraG, which is a selective tracer that allows for anatomical quantitation of activated T lymphocytes. Now, the tracer uptake in the post-acute COVID-19 group, so we're going to see those with and without continuing symptoms, was higher compared with pre-pandemic controls in many regions, including the brainstem. This is activated T cells in the brainstem, spinal cord, bone marrow, nasopharyngeal and hilar lymphoid tissue, cardiopulmonary tissues, gut wall.

The T cell activation in spinal cord and gut wall actually correspond, it was associated with the presence ofLong COVID symptoms. In addition, the tracer uptake in lung tissue was higher in those with persistent pulmonary symptoms specifically. Increased T cell activation in these tissues was also observed in many individuals without Long COVID, so it's not as nice a binary as we would like to see.

Now, since they see, so they say this, and who knows, they probably plan on doing this anyway. They say, given the high 18F-F-AraG uptake detected in the gut, they obtained colorectal tissue for in-situ hybridization of SARS-CoV-2 RNA and immunohistochemical studies in a subset of five participants with Long COVID symptoms. They identified intracellular SARS-CoV-2 single-stranded spike protein encoding RNA in rectosigmoid lamina

propria tissue in all five participants and double-stranded spike protein encoding RNA in three participants up to 676 days after initial COVID-19.

They suggest that tissue viral persistence could be associated with long-term immunologic perturbations, but we're still back to the issue with them not demonstrating replication-competent virus. A good question, is there replication-competent virus in these sites? Is this important? We need the reviewers to ask them to include whether they just try to do any assays, if these assays failed, rather than just let them speculate, because, dare I say, this is science here.

VR: Daniel, are there controls here where they don't find RNA persisting or they don't have those because those people are not sick?

DG: If you see here, so what they do is they say, "We took five participants with Long COVID," and they get the colorectal tissue. You want negative controls. Yes.

VR: Maybe everybody has RNA for 676 days. Who knows, right?

DG: Yes, they might. It's hard to say, "Look, this is the smoking gun," when you have no idea. Yes, you need that. You need those controls.

VR: We know that RNA can persist after infection for long periods of time. I don't doubt that these individuals have symptoms, but I'm not sure that the RNA is what's causing them.

DG: Yes, and we want to know, is the RNA causing it? Also, they're speculating it's viral persistence, but is it viral persistent? Is it RNA persisting? Persistent RNA could be triggering TLR3, et cetera. Yes, these are important questions. They throw a little bit too much speculation at the end for my liking and not of science. All right, I do want everyone to pause recording here. No one is safe until everyone is safe. We are in the middle of our Floating Doctors' fundraiser, May, June, and July. This is our last month. We're hoping to double your donations up to a potential maximum donation of $20,000. Go to Parasites Without Borders, click on that Donate button.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Mark Martin writes, last night, actually, on the live stream, he asked me to ask you this. “What do you think of the commercial ELISA kits that measure antibodies against SARS-CoV-2? Is it useful?” You can do these at home, apparently.

DG: Yes. I remember when they were first getting these into the country and there was this whole rush like, "Can we get these?" Because there was this whole idea. It was behind things like Survivor Corps, the idea that you would find out, "I already had SARS-CoV-2, I'm good to go, I can be out there," because, boy, no one ever gets re-infected, do they?

The other wrench to throw in here is that we've seen these abortive infections, where someone gets exposed, particularly people who've been vaccinated, and we can even see this signature at the local mucosal levels that there was this encounter, but even people that were PCR positive in one of the studies we talked about, it's like a quarter of them never got an antibody response. It's becoming less and less useful what to do with these results. Not really

sure that knowing antibody levels and knowing antibodies is particularly useful at this point in time.

VR: Lindsey writes, "I'm writing from Northern Illinois, near Chicago. Dr. Griffin, I've wanted to become an epidemiologist since I could read. My father passed away from influenza when I was 11 months old, which sparked my deep fascination with diseases of all sorts. However, no one in my family has a background in healthcare, so I didn't know where to start. I aim to enter clinical research. Besides applying to a college, do you have any recommendations? I'm 22, already have a degree in horticulture and two certificates. I can't express my gratitude in words. I've learned so much from MicrobeTV. PS, I almost cried when you quoted Peter Gabriel, *Don't Give Up*, in *TWiV* 1122. I've been a huge fan since I was a kid, saw him in concert in the fall of 2023. Truly made me admire you even more.

DG: Thank you, Lindsey. I'm sorry to hear about your dad, but excited to hear about your interest in becoming a future epidemiologist. I was thinking a little bit about this. There's a couple of different ways to do this, the traditional track is going to a place where you can study, and specifically finding opportunities where you can connect with, maybe even work with an epidemiologist, because that's really going to be the best way, is I get that mentor, make that connection, get advice from an actual epidemiologist. That would be my thought. Look at what are these opportunities, where might you get a little more, specific training, but more importantly, where might you get the opportunity. Maybe there's someone, they need some help doing their research. Best of luck, Lindsey.

VR: Jalna writes, "My friend's husband had his booster last fall, 10 days later had a TIA. She also had a friend who had a TIA after vaccination. Is this a true risk? She and her husband are in their late 70s. She believes in vaccines, but is concerned."

DG: Yes, there were issues, particularly with the J&J vaccine. They were rare, but they were certainly there. They were enough that, really, we're not doing the J&J in most parts of the world at this point. When it comes to the mRNA vaccines, when it comes to the protein-based Novavax vaccine, we've looked at this. Actually, it was a really good VA study, which we may have covered or not, I'm not sure, with about 30,000 folks in it, specifically looking is there an increased incidence of stroke or TIAs after vaccination? We didn't see that. There was not a safety signal here.

There clearly is an increased risk of stroke and TIAs after a COVID infection. That risk is actually reduced by vaccines. No, these are coincidences. This is what happens, is people have TIAs, people have heart attacks, people get in car accidents, people swallow marbles, lots of stuff happens. That's why it's important to look at the science, because, no, you hear this story. This is the stuff that someone who's anti-science will say, "I'm not going to believe you because of this," but no, we look. This is an important question. We've looked at it and we're not seeing this as a true risk.

VR: Daina writes, "Novavax got a lifeline earlier this year from Sanofi, who licensed Novavax protein-based vaccine alone and for development of a COVID flu combination vaccine. Sanofi will start commercializing the vaccine for the 2025 respiratory seasons, and I expect Daniel will have no trouble getting his protein vaccine then." Diana provides a link to a press release.

DG: Fantastic. Thank you so much. I look forward to my protein vaccination this fall.

VR: Jason writes, "At about nine minutes and 16 seconds in in *TWiV* 1122, you went over the CDC map of the percentage of provisional deaths due to COVID in the past week by state, territory, US, and noted that Puerto Rico showed 4% to 5.9% of all deaths due to COVID for the past week. I think it would be interesting to see in future examples for particular states what the percentage of provisional deaths due to COVID-19 represent in terms of absolute numbers. For example, what was the total number of deaths in Puerto Rico over the past week that COVID-19 represents 4% to 5.9% of all these deaths?

If there were 20 total deaths in Puerto Rico, then 5% would be one out of 20. In contrast, if there were 10,000 total deaths in Puerto Rico, then 5% would be 500. A big contrast. This type of comparison could also be made with total numbers of deaths contrasting largely between states and also affected by the differing populations among states. I know the CDC also has information on what is the percent of total emergency room visits for each week for each state due to COVID. However, I don't see any information on what the actual total number of ER visits are for each state over the past week.

If this information could be found, then the absolute number of COVID cases making people sick enough to seek care at an ER could be calculated and if we know approximately what percent of total COVID infections result in seeking ER care, then an idea of total cases could be estimated and this could be triangulated with wastewater levels and perhaps modeling of wastewater levels. Just a couple of ideas. I don't know where to find this information, but if you do and could include it in the show, I think it would give a better sense of where we are with COVID."

DG: Yes. Jason, thanks for writing in. I think probably I need to clarify. What we're talking about on this map we show is that in each particular, I will say, jurisdiction, it's what percent of the people that died, died due to COVID. It's not what percent of the deaths across the country. For instance, I use the example here in New York, 2,000 to 3,000 people die per week. When we see that it's above one and less than two, we're seeing somewhere between 30 and 60 people died from COVID here in New York of those 3,000.

In Puerto Rico, where the average number of deaths per week is about 500, which is a really interesting relative to population, so it's about 500, and what we're seeing there is that about 5% of those 500. That's about 25 deaths. Actually, this stuff's all available, so you can see what's the story, you can actually look up what's the deaths per week in different jurisdictions, and then you can look at our map that we share and say like, OK, of those 500 deaths, what percent were due to COVID? Of those 3,000 deaths, what were due to COVID?

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

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

[00:38:06] [END OF AUDIO]