This Week in Virology

TWiV 1230 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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VR: From *MicrobeTV,* this is *TWiV, This Week in Virology*, Episode 1230. Twelve thirty, recorded on June 26, 2025. 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 was going to say what's on your tie, but first, are you happy it's cooled off a little bit, Daniel?

DG: Oh my gosh, yes. I've been having that air conditioning saga where the air conditioning broke right after we recorded. It was last Friday. Then, I called, I was like, "I've got a contract, and you have to come out in three hours. Don't worry, my wife and kids are out of town." This is just reminding me of growing up on the South Shore without air conditioning. Then they did show up, and they're like, "Yes, we can't fix that." I'm like, "Oh, no, my wife and kids are coming home. Now it's a problem." [laughs] I'm very excited it's cooling off.

VR: What's on your bow tie, Daniel?

DG: What do I have on the bow tie here? Let me take a look. I'll bring this over. Oh, I think it's HIV. Interesting enough, it's a Thursday, and I've got a sexually transmitted infection on there.

VR: You can do it two days in a row. No problem.

DG: Tomorrow I'm doing syphilis [laughs]

VR: Oh, you gave it away. OK, that's fine.

DG: All right. I'm going to start off with my quotation, Mark Twain, "It's no wonder that truth is stranger than fiction. Fiction has to make sense." Those of you that feel like you're in a *Dr. Strangelove* movie, let's start off. I have quite a section here on the attack on science. It carries into several areas. I want to give people a link to a resource here. It's a project led by Jake Scott, and it's actually a spreadsheet of all the randomized controlled trials, RCTs, that have ever been conducted for licensed vaccines. Since late April, this infectious disease specialist at Stanford and his colleagues have been volunteering their time on this project to create this spreadsheet.

The idea actually hatched on a social media site, X, and was prompted by responses to an old video of current DHHS secretary, RFK Jr., in which he claims that none of the vaccines mandated for U.S. children have ever been tested in preclinical studies against placebo. Last time I checked, 340 trials there. Just a resource there for folks, and I'll leave in the links.

VR: Problem is, Daniel, he's going to say they're not saline placebos. That's what he wants. He wants saline placebos for everything.

DG: Yes, he's got all his ideas. I don't know what you've been doing the last two days, but I've been watching the June 25/26th ACIP meeting, the Advisory Committee on Immunization Practices.

VR: I couldn't bear to watch it.

DG: There were some times when I just had to like go out for a run and clear my head. The meeting started with the new chair, Dr. Kulldorff, a statistician and epidemiologist, announcing that there will be changes to the membership of the CDC's 11 different vaccine working groups, and that two more working groups will be added. These will both be anti-vaccine working groups. Just wanted to point that out. They've been characterized as the new working groups will focus on boilerplate topics of vaccine critics. One group is going to do this cumulative effects of vaccines on the CDC's recommended schedule for children and adolescents.

If you're listening, this keeps coming up as, “well, we may have studied the vaccines individually, but have we studied them all together?” If you actually listen to the discussion, the CDC people brought up the fact that, yes, we have. The other working group will examine vaccines that have been used for more than seven years, such as hepatitis B vaccination at birth and the use of the MMRV vaccine in young children. We're going to circle back to that in a moment. Just give people a sense of like, well, what's supposed to happen here? How has this been working for - the ACIP is 50 years old, Vincent. It's not as old as you or I, but it's been around for a while.

The way things are supposed to work is that here in the United States of America, we start off with the FDA, which reviews safety, efficacy data, and then approves, licenses products. Can it be on the market? Then, the ACIP, so the Advisory Committee on Immunization Practices, we'll call them ACIP from here on out, they have these working groups. The working groups have particular topics to consider. They consider them, they meet, they look at the FDA-approved products. Then the working groups then make recommendations to the larger group.

This has actually created a little bit of an issue because people were hoping we'd get a COVID vaccine recommendation. With all this disruption, the COVID vaccine working group didn't get a chance to meet June 12, so we didn't really get that. If we listen to the meeting today, I'm going to bring up several of the anti-vaccine talking points that came up. One of the ones is, which I just mentioned that they're going to form a new special work group on, is this concept that certain individual vaccines are well-studied, but the entire vaccine schedule has not been well-studied. That's one of their suggestions.

The other, and this came up repeatedly, that our current monitoring systems for vaccines are flawed. That VAERS, for instance, is only picking up about 10% of adverse events with vaccines. That we need more study of long-term immunological impacts of vaccines, such as

immunoglobulin class switching. Members of the panel raised concerns about what they saw as weaknesses in case control, test negative research study designs. I will point out that the CDC people were good about responding directly to these and saying, "This 10% is not close. This 10% is not accurate. The majority of significant and severe, 70%, 80% or more, are picked up with the current systems."

This 10%, it's basically you get a vaccine and your arm's sore after the injection, that doesn't get reported to VAERS. They say, "Oh my gosh, can you believe that?" The point was that's not what VAERS is about. VAERS is not about my arm was sore after I got an injection. I think the CDC people did a really good job of very respectfully, very professionally responding. Then, this is where it gets really shocking, there was a presentation on thimerosal by Lyn Redwood, who reported that she was speaking as a citizen, not representing any organization. Who is Lyn Redwood? Former leader of Children's Health Defense, an anti-vaccine group that lists DHHS secretary, RFK Jr. as a founder.

This was like a Make America Healthy Again fiasco. They post the slides online Tuesday. They cited a 2008 study in the journal of *NeuroToxicology* by Berman RF, et al. ,called, "Low-Level Neonatal Thimerosal Exposure: Long-Term Consequences in the Brain." The presentation claimed that results from a study in newborn rats suggested long-term "neuroimmune effects." The citation refers to Dr. Robert F. Berman, a professor emeritus at the University of California, Davis. He told CNN, "I don't have a publication in *NeuroToxicology* by that title."

Again, this was an AI-generated presentation where they started with their conclusions with the ideology, and then they invented references. Redwood's presentation was taken off the CDC website later Tuesday. They replaced it with a version where they take out this citation that never existed. Then we go ahead and we hear this very one-sided, scientifically inaccurate presentation. Really nice after she closes, Cody Meissner responds, basically starts going through a lot of the inaccuracies in the presentation, a lot of the chemistry is off. He also talked about the impact that decisions around thimerosal in the U.S. would make on vaccine access throughout the world.

Others asked about, normally, we have a process here where we have a working group, we get a scientific presentation by someone from the CDC who's a subject matter expert with peer-reviewed publications, referenced rather than just opinions from a self-described citizen with no advanced degree, not claiming any affiliations. Really concerning response from Martin Kulldorff, who basically said, "I find this insulting, and I want to let you know that in the future, the committee will be listening to lots of people with lots of things to say, and I don't think it's important that the person have any advanced degree or be from the CDC."

VR: Oh, really? You can just make up references, and that's good enough, Kulldorff? What an idiot.

DG: Currently, you can take time from this ACIP meeting and our taxpayer, and he can just have like a buddy of RFK Jr. with no advanced training present an AI-generated, misleading, and no preamble, no subject matter expert, no working group. Then, as you're going to see, they're going to vote on this. People ask, "Hey, before there's a vote on this, are we actually going to see the real peer-reviewed science?" One of the things that was pointed out is this is a non-issue that you're all worried about thimerosal, but thimerosal it's mercury preserved, is not in any of the routine childhood vaccines. Why is ACIP even spending any

time on this?

People are saying this is a question that has been asked and answered. It's a non-issue here in the U.S.

VR: Daniel, it's something that they've got a bug in their butt for years and they just want to show that they can win finally. It has nothing to do with science or safety whatsoever.

DG: Yes. We're going to circle back to the vote on that, but let's go through. You can go on YouTube, you can listen to these now, you can listen at 2X, maybe that's less painful. The American Academy of Pediatrics pretty much boycotted ACIP's meeting, saying that ACIP's meeting doesn't reflect a gathering of experts to inform the future of vaccines and the AAP will continue to recommend its own childhood vaccine schedule just as we have since 1930s. That was met by a little bit of negative response from the committee who said, "They're acting like children," which I thought was really cute, the American Academy of Pediatricians. It's cute.

Anyway, there were a few votes. The first vote, ACIP voted 5-2 to recommend the new passive vaccine, the new monoclonal clesrovimab, so Enflonsia by Merck, that was just approved by the FDA June 9, for infants age 8 months and younger who are not protected by a maternal vaccine. There was a second vote where the committee voted in a unanimous fashion to update the Vaccine for Children program to include clesrovimab. We're going to have clesrovimab, we're going to have nirsevimab, so we're going to have two passive, and we're going to have the RSV vaccine for moms in the last trimester.

Now, there were some more votes, and these were interesting ones. One is influenza vaccine vote, recommendations for influenza vaccination for 2025 through 2026, so the next winter. Here's the question, "ACIP reaffirms the recommendation for routine annual influenza vaccination for all persons aged equal to 6 months or older who do not have contraindications," and they voted "Yes." That carried. This new anti-vaccine, anti-science group is actually saying that they recommend it.

Here's where it got painful. Now they go after thimerosal, which is really a non-issue, it's a distractor, but they basically are saying ACIP recommends children 18 years and younger receive the flu, the seasonal influenza vaccine, “but only in a single-dose formulation that is free of thimerosal as a preservative.” Despite decades of evidence that this is not a problem, also the fact that it actually isn't really an issue, they vote -

VR: These supposed experts, who are not experts at all, could just waltz in and say, "We don't want thimerosal," not show any data why it should be taken out, right? This is what I'm hearing.

DG: That's basically the deal. You can have an AI-generated opinion piece presented by, clearly a citizen with no advanced degree, no respected subject matter expertise, just say, "Get all this stuff here, and I think thimerosal should be out." They had some talks about, "If we get thimerosal out, well, then people trust vaccines more and we'll get more vaccine uptake." They brought up, they're like, "This is really not an issue in kids. This is something like maybe in nursing homes. It's something overseas where if ACIP makes this recommendation, it's going to have this fallout where things are more expensive, where you're going to limit access."

It's just they seem to have this thimerosal issue despite decades of data. This question answered not - nothing new here. They get it out of that. They also asked about the other pregnant women. Again, same thing. Go ahead with the vaccine, but we're recommending that it be free of thimerosal. Then the last one, what about everyone else? All adults should get that seasonal flu vaccine, but they should be single-dose formulations that are free of thimerosal as a preservative. Those are the recommendations. If we stick with the normal process, then the CDC director will review the recommendations and decide whether or not they're going to be the CDC, because it's just an advisory committee.

These folks don't get to actually make the recommendations or get to actually make the guidance from CDC. They are merely making recommendations for the CDC director. Who is the CDC director, Vincent? I don't actually know. I tried to look this up. Now, the CDC's current nominee for director is Susan Monarez, and she became acting director January 23, 2025, but then she stepped down March 24, 2025 when she was nominated for the director position.

Now, on May 14, RFK Jr. said that lawyer Matthew Buzzelli is the acting CDC director. However, the CDC website does not state the acting director's name, and Matthew Buzzelli is listed as the office of the chief of staff. I'm going to leave in a link to the hierarchy organization of the CDC. He's off here as one of these side categories, office of the chief of staff, on par with, I don't know, 12 other folks. He's not the director. I'm not really sure what happens next, because usually it's the same day we hear from the director of the CDC what they think about these recommendations.

VR: That's what I've heard that Monarez is the nominee, right?

DG: Yes.

VR: Maybe Buzzelli is acting, but she seems to be OK. She says vaccines work, that they don't cause autism, and so forth. She seems to be at least reasonable at the face value, I don't know.

DG: Hopefully, we'll get her through and she can actually do something about this mess.

VR: Daniel, could the CDC director say, "There's no evidence to say we should take thimerosal out, we're not taking it out"? Could she say that?

DG: Yes. She could just negate this. She could say, "All right. I agree with your recommendation. Everyone should get the flu vaccine. That's great. This thimerosal business, you're going to have to revisit that." Hopefully. Fingers crossed.

VR: Waste of time.

DG: I'm also going to leave in a link because hopefully people are aware that childhood vaccines and schedule are on the radar for these folks. There are several articles in that. I want to point out that being anti-vaccine, it's a fringe viewpoint. This is not mainstream. We have a recent survey fielded by the Harvard Opinion Research Program and it's U.S. adults view on routine childhood vaccination. I'm just going to go through what are we finding? They ask a bunch of different questions. I'm going to jump right into - there's this question too where they ask these questions.

"I think routine childhood vaccines are effective in protecting most children." 98% say "Yes." "I think routine childhood vaccines have been proven safe because they've been around for decades." 94%. "I think routine childhood vaccines have been proven safe because they've been well tested." 96%. "I think requiring routine vaccinations for most children is important to protect children who cannot get vaccinated for medical reasons." 96%. I'm going to jump back to “E” in a second. "I think diseases like measles will come back if routine childhood vaccines are no longer required." 97%. "I think getting routine childhood vaccines is part of a family's responsibility to keep school environments healthy for children." 98%.

The only one that's a little bit of an outlier at 82% is, "I trust the government agencies that approve routine childhood vaccines."

VR: Wait until this agency operates for a while. It will be even less.

DG: The interesting thing is this was just done. I might be in that, “I'm not sure I trust them at the moment.” Maybe a little nuance, and, "Have you trusted them? Did that just change?" Really, this is disheartening. We're going to get into some peer-reviewed publications soon, but this just attack on science is more than distracting. U.S. withdrawal from Gavi. This is devastating. We already have children dying from the destruction of USAID. After targeting vaccines in the U.S., RFK Jr. is now working on undermining vaccination programs in the rest of the world.

I watched this YouTube video. I will leave a link to it. Really, it's mean. There's really a mean tone to this. It's not a, "Let's work together to make people healthy." Mr. Kennedy said the United States would withdraw its financial support for the group's purchasing vaccines for children in poor countries. A few excerpts here. He says, really mean tone here, "When vaccine safety issues have come before Gavi, Gavi has treated them not as a patient health problem, but as a public relations problem." In the video, Mr. Kennedy accused Gavi's leaders of being selective in their use of science to support vaccine choices and said that the United States would not deliver on its $1.2 billion pledge.

"We made a pledge for $1.2 billion, just no, we're not going to do that." Then, of course, he takes this moment to say he suggests that the diphtheria-tetanus-pertussis vaccination, the DTP vaccination, kills more children than it saves.

VR: Did he show the chart showing the data for that?

DG: No. He just says that when the science was inconvenient, Gavi ignored the science.

VR: He's just making it up. If people listen to him, they're out of their minds. Unbelievable. You know that the senator from Louisiana, Cassidy, didn't want this meeting to go ahead. He tried to stop it.

DG: Yes, he did. He said, "Let's wait until we actually have a panel of some experts here." I'm going to leave a link into polio and other vaccine-preventable diseases. This is a summary of the recent *Lancet* paper, “Global, Regional, and National Trends in Routine Childhood Vaccination Coverage from 1980 to 2023,” with forecasts to 2030. Really not looking good. Really substantial increases in coverage are necessary in many countries and territories, with those in sub-Saharan Africa, South Asia facing the greatest challenges as we're withdrawing support. If anything, we've actually had declines, and recent declines, really need to be reversed.

The studies here, they talk about the findings here, underscore this critical need for targeted, equitable immunization strategies and strengthening primary healthcare systems, addressing vaccine misinformation and hesitancy, and adapting to local contexts as essential to advancing coverage. There's a link in here, also. There's a polio outbreak in Papua New Guinea, where less than half of the population is immunized. Then in the last week, Pakistan, 47 wild polio-positive environmental samples.

VR: Gavi supported polio vaccination. Hopefully, they can replace the money from someone else.

DG: It is crazy. Bill Gates has said his organization will give a few hundred million, but it's not $1.2 billion, and that's in line what he's done. The UK has bumped up their contribution a little bit, but not -

VR: We need to go to Warren Buffett. Who are the other billionaires? Jeff Bezos.

DG: Bezos should kick in. We're not even going to mention the other names, right?

VR: They should give money for this, because they have more money than they're ever going to need.

DG: They really should, yes. Bird flu. Oh my gosh. We're not hearing much about this in the mainstream media. We won't speculate why, but Cambodia has now reported its sixth case and fifth death from H5N1 avian flu this year. The latest person to die was a 52-year-old man. He had handled sick and dead poultry two days before experiencing fever, cough, shortness of breath, difficulty breathing. Three children and another adult man have also died from H5N1 infections in Cambodia. The non-fatal infection occurred in an adult woman who did not report handling sickened poultry.

We read in Reuters that the USDA is considering vaccinating poultry against avian flu. Nearly 175 million chickens, turkeys, and other birds have been culled in attempts to contain outbreaks since 2020. I want to say, while not being discussed, we are currently in the middle of the nation's worst animal health emergency.

VR Yes, we've discussed before why vaccination is not a great option.

DG: I don't know. It's interesting. They vaccinate the poultry against so many other things. It would be just adding this to the vaccine schedule for the poultry. The big issue that they seem worried about is that if we vaccinate the birds, will they have asymptomatic infections, and you won't be able to sell the birds to other countries? That's not an issue at the moment. The issue at the moment is we don't even have enough eggs to meet our current needs and we're importing them from around the world.

VR: That's making America great, Daniel.

DG: Measles, right? It's still going on. More cases. I've been following this over time. 31 jurisdictions, 33, 34, 35, and now we're up to 36 jurisdictions and 1,214 confirmed measles cases so far this year. We're getting pretty close to setting a record since we thought we were out of the woods with measles.

VR: It's interesting that it's still continuing. It's supposed to stop at the end of May. Didn't they get the email?

DG: [laughs] It is interesting. It was funny because I know Paul Offit was the one that talked about the seasonality, and Mike Osterholm was like, "People think there's a seasonality, but there's no seasonality." [chuckles] People travel in the summer. It would be interesting to see. It looks to me like we're seeing some seasonality here. When it comes back, we'll have to see. Usually, it establishes peaks and then you can see a lower level in other times of the year. Canada is a mess. There are another 221 new measles cases, 3,381 measles cases so far this year. Really, continuing to go on with the measles.

We'll be discussing, I guess, at future ACIP meetings whether or not we want to still immunize against measles. I will point out, maybe just to give a little bit of clarity here, because when I saw the MMRV on the agenda, I was quite concerned. The head of the committee did a brief because they were all off with time and stuff, a brief discussion that - really what they were talking about is should the MMR be given at the same time as the chickenpox vaccine? Be given as a MMRV versus an MMR, and at a separate visit, get the chickenpox vaccine. It is about a signal where we're actually seeing an increase in febrile seizures.

It wasn't really a, "Let's get MMR off the schedule." It really at least was a discussion of, "Should we be separating the timing to try to reduce that signal that's been picked up?" All right. We are currently out of the flu season. Unfortunately, pretty close to a record here at about 250 pediatric deaths this last winter as the tallies come in. We probably will set a record for the most number of children who died in a non-pandemic year. As was brought up at the ACIP meeting, 90% of these kids were not vaccinated. The majority of the kids that died had no pre-existing medical problems.

The idea about targeting flu to only certain kids, not giving it to "healthy kids," that is not based on any science. RSV, the good news is we not only have nirsevimab, but we also have the clesrovimab. We still have Pfizer's ABRYSVO as the vaccine given during that third trimester. COVID update, multi-colored curves, Vincent, what are you thinking?

VR: I think they're flat, Daniel. I don't think that that one there is doing anything but oscillating. If you look at the past - like last November, it never got below low. It never went into the very low category, and that's where we are.

DG: We usually get a little bit of a gap there. We will see. We'll keep following. Right now, in most regions, we're in the low level with COVID.

VR: Are you seeing infections still in hospitals?

DG: Yes. We saw a number recently, but it may just be a blip. We've got a few cases that came in. I'll be covering what? This weekend, I'm covering Columbia. Next weekend, I'm covering out here on Long Island. Give everyone a little bit of updated data in both contexts. SARS-CoV variants, the Nimbus has taken over. That's our buddy up in Canada who names the variants. I remember he got really upset when I took issue with him calling it the Kraken. I was like, "If you call it the Kraken, that's going to make it sound like it's really bad. You call it Nimbus, and it sounds like some fluffy cloud and no one's worried about it." We'll see. We'll see what happens with Nimbus. It's in the JN.1. Be great to hear what we're supposed to do as far as vaccines next year. Hopefully, that working group can get together.

Children, pregnant individuals, other vulnerable populations. Just wanted to - a few reminders here about risks in children. I was listening to a recent CIDRAP, the *Osterholm*

Update. I thought Mike Osterholm did a really good job looking into the relative risks of vaccine versus getting an infection without the protection of the vaccine. I'm going to leave in a link to that. If people want to listen, about 27 minutes in, he reviews the early data from the three-month study showing Moderna's phase 3 clinical trial, suggesting that vaccines were associated with about 65 cases of myocarditis per million doses, resolving within one to three days, and that no one at any time was seriously ill.

In a study of 18-to-29-year-olds, there were 22.4 myocarditis cases per million vaccines. There were warnings on the vaccines about this for 18-to-24-year-olds, and now they're making a big fuss over changing that to 16-to-25. He points out that the risk of myocarditis from COVID without the protection of a vaccine is seven to 16 times higher than this risk, and in this context, much more severe and actually associated with deaths. Since the longer period between the first and second doses were recommended, we really have seen almost no myocarditis in vaccine recipients. If you really want to lower the risk of myocarditis in this population, ongoing COVID vaccination is safer than not vaccinating, and particularly if we separate that out a little bit.

He also points out that the risk of severe disease requiring hospitalization in the youngest children - this came up in the meeting as well, if you look at the kids' risk of ending up in the hospital due to COVID in the zero to 6 months, it's the same risk as people 65 to 74. If you look at 6 months to 2 years of age, it's the same as 50 to 64. The youngest kids really have a similar risk. Also, as we mentioned, half of the children who ended up in the hospital were otherwise completely healthy, challenging this recent limitation on pregnant women getting a third-trimester vaccine because, listen, those first 6 months of age, you can't protect them. There's no vaccines for them.

The way you protect them is mom gets a COVID shot during that last trimester. Now we have this proclamation that people at the meeting were saying, "You really have to address this. How are we supposed to protect those kids in the first six months if we don't vaccinate moms?"

VR: We should send this to Makary and Prasad.

DG: If they would listen, right? It's a really good podcast here, and of course, referenced, if you can imagine that, with real studies that actually took place. Starting with the investigation and then having your conclusion, not starting with your ideology and then having a chat-something invent references.

All right. We also have another article, “Children with Post COVID-19 Multisystem Inflammatory Syndrome Display Unique Pathophysiological Metabolic Phenotypes,” published in the *Journal of Proteome Research*. Here, the investigators conducted metabolic profiling of 147 children's serum samples, looked at acute COVID patients, MIS-C patients, healthy controls.

They use nuclear magnetic resonance spectroscopy, liquid chromatography, mass spectroscopy. They measured 1,101 metabolites, a really robust data here. The results revealed distinct metabolic profiles in acute COVID-19 and MIS-C patients, with significant alterations in lipids and increased serum inflammatory markers. They point out that despite milder clinical respiratory symptoms, children's metabolic disturbances mirrored those seen in severe adult COVID-19 patients, indicating the shared inflammatory response to SARS-CoV-2. They actually say this suggests potential long-term health impacts, underscoring the

need for continued research into the metabolic consequences of COVID-19 in children.

In the last line of the conclusion section, we read, "The persistence of inflammatory and cardiovascular markers post-infection raises concerns about long-term health impacts underscoring the need for vigilant monitoring, potential interventions, and further studies to understand the lasting effect of SARS-CoV-2 infection on pediatric health." Now, I want to point out, I'm reading in the study design that the samples were collected in the acute setting of SARS-CoV-2 infection. I'm really not sure actually, how long these changes actually persist. I feel like maybe they stepped beyond the data here. It'd be interesting to see, like, "Let's check a month. Let's check three months. Let's see actually if these are persistent," because it looks like it was acute.

VR: Yes. It's not persistent at all, is it? [chuckles]

DG: Yes. I'm not really sure where the conclusion followed. It's all exciting. All right. COVID early viral phase. We still have our guidelines, early antiviral, Paxlovid, remdesivir, molnupiravir, in some cases, convalescent plasma, early inflammatory, steroids, anticoagulation, pulmonary support, remdesivir, in some cases, immune modulation with things like tocilizumab.

Now we have a little bit here in the late phase. We have one article and a concept that I wanted to introduce to our listeners. This is all the excitement around this potential intervention called, “Stellate Ganglion Block for the Treatment of COVID-19-Induced Parosmia: A Randomized Clinical Trial*,”* published in *JAMA Otolaryngology Head and Neck.*

Here they're asking the question, "Does stellate ganglion block improve COVID-19 induced smell distortions, parosmia, symptoms, and disease-specific quality of life compared to placebo?" A little bit of background, and maybe we'll get this up for our YouTube people, but you can always follow the link. What is a stellate ganglion block? I'm going to leave in a nice webpage from the Cleveland Clinic, actually a great resource, with some pictures. The stellate ganglion is a bundle of sympathetic nerves located in the front of your neck near your first ribs. It's right actually, about C7, T1. You have one of these ganglion on each sides of your neck. A ganglion is a collection of nerves.

The stellate ganglion is shaped like an oval, but it also can look like a star, thus the stellate, because you sort of have this oval with the wiring coming out of it. Think of it that way, because it's nerves. We've talked before about this balance of parasympathetic and sympathetic nervous system, and these concerns that post-COVID you have issues with not enough parasympathetic tone and too much sympathetic nervous system activity. We've talked a bit about trying to improve that vagal tone with active breathing and maybe transcutaneous vagal nerve stimulation.

This is really - approaching from the other side, maybe we can block the sympathetic tone. You lie down, they use ultrasound or x-ray, and then they're going to inject an anesthetic medicine like bupivacaine. It's like a lidocaine type, but longer acting. They're going to put a needle there. They get the ultrasound, making sure the needle's in the right place. The whole procedure takes about 30 minutes. It might take a few injections. Sometimes the first one doesn't do it. You do a first one, you do a second one. Sometimes it takes a while. Then it works for periods of time. Different people respond and have an effect for longer. Some of the other studies, since this is blocking sympathetic, you'll see a drop in heart rate and a few other things.

Here, in this article, they conducted a randomized double-blinded placebo-controlled clinical trial, October 2023 to September '24, at a single center study, so Washington University at St. Louis, Barnes-Jewish Hospital. They start off with a volunteer sample of 192 individuals that they screen, and they end up excluding a whole bunch. Really, at the end, you've only got about 48 participants. Some of them had actually already gone ahead and tried this, or maybe they didn't have the parosmia from COVID. We end up with 48 participants, 32 get the block, and then you've got 16 that get placebo. What was placebo? It was saline. Someone will be happy here. They do the ultrasound guidance. They put a 21-gauge ultrasonography needle into this area. They advance in plane in the prevertebral fascia along the longus colli muscle.

Then they're going to inject 6 to 8 milliliters of, in the active group, mepivacaine or saline in the placebo group. They're going to inject that around the stellate ganglion. Now, I got to say, the first thing that came to me was, I understand sort of a sham in making believe, but I don't know if saline injected around the ganglion is going to have some kind of impact, because you're going to inject it, there's going to be pressure. I wonder if that's the right. I must have wanted a group where they put it in, and it was a sham, but you didn't actually inject anything.

This will come up in a second because the groups were pretty well matched. Then they get really good response rates, 43% in the stellate ganglion, but they got 38% in the placebo. It's an interesting issue. Is it really a placebo? Is it really an incredibly potent placebo? Because, theoretically, putting this needle in, suddenly everything smells just fine in about 40% of the people, whether it's the saline or the active. They conclude that basically it's the same. We don't know whether the stellate ganglion block with mepivacaine is really helpful. It doesn't look here to be superior to placebo, but there was actually a pretty profound placebo effect. Really interesting.

VR: People didn't know what they were getting, did they?

DG: No, it's blinded. They don't know. Did you get saline?

VR: Maybe you inject something into that area, maybe it just causes some inflammation, and it resolves it. Who knows?

DG: Yes. I'm curious, actually, because we've done studies where we do sham injections into joints where you can inject saline or you can inject steroids and then people actually with the steroids, they get worse and then they get better with the saline. They seem to just get better, but I don't know. It's like giving more fluid into a joint. It's a challenge here. I know there are a lot of other studies looking at a stellate ganglion block for other Long COVID issues. We'll follow that. All right, Long COVID. Now moving into low and middle-income countries. No one is safe until everyone is safe. I feel like the world is becoming less safe as we undermine vaccines and health around the world.

We're going to keep doing, and "We," I mean the global *TWiX* community here is keep doing everything we can. May, June, and July, we're doing our foundation, International Medical Relief of Children fundraiser over there in Uganda, doubling your donations, hoping to get up to a maximum donation of $20,000. Go to Parasites Without Borders, pause your recording, click the Donate button. Even a small amount helps.

VR: It's time for your questions for Daniel. You can send yours to Daniel at microbe.tv. Justin

writes, sends a link to an article, “HIV Post-treatment Controllers Have Distinct Immunological and Virological Features.” Justin writes, "Daniel, is this actually a thing? Namely, there are people that can stop antiretroviral therapy and yet maintain low viral load? Reason I ask, believe it or not, there are a substantial amount of people online that totally deny the existence of viruses at all. Are they pointing to personal testimonials from people who have stopped ART?" You can see where this is going. “In effect, they are telling people nobody needs ART, which is absolutely insane and dangerous.” Justin.

DG: There is a subset of individuals who actually off ART stay with these low levels. We call them these long-term controllers, and I've taken care of a number of these individuals over time. It's really something going on where maybe they were treated early, maybe there's something about their genetics where you could stop the ART, and they end up with this low level. They really don't get the huge surges, but it's rare. We were really excited early on. Maybe these individuals, these long-term controllers can tell us something about how we can cure and help all these other people. They're out there. It's a thing, but it's uncommon. We don't really understand fully the mechanism.

VR: Marshall writes, "First, let me say that I felt your podcast was incredibly important during the pandemic. However, maybe it's even more important now in the current political situation. Listening to the last clinical update and the latest *TWiV,* I wanted to provide some context for the latest Moderna vaccine approval. To be clear, my understanding is that the new Moderna vaccine is approved in addition to their previous vaccine. The newly approved vaccine would also likely have to be updated for strain-specific substitutions in the sequence of spike on a yearly basis, even though I understand the trial was done with BA4/5. This is not yet entirely clear to me.

The new vaccine encodes a significantly shorter spike than Spikevax, which includes a portion of the N-terminal domain and the receptor-binding domain, as well as the heterologous transmembrane domain. It lacks the S2 domain, meaning there need not be the proline-stabilizing substitutions. This allows for a much shorter mRNA encoding the antigen, and therefore, a lower dose can be used, apparently resulting in less reactogenicity. Just thought I'd weigh in, since it didn't seem clear from the previous episodes what the new vaccine entailed. Love discussions, and I will continue to listen in support."

DG: All right. Now, Marshall, these are some good subtleties you bring in, and there's a couple interesting things there, yes. Now we're going to potentially have two vaccines. It'll be a question of which one do we go with? The other is, it's interesting, you got away from the stabilizing proline substitution. I guess our buddies Jason and Barney were involved in discovering that. They also have a patent or a licensing thing there, so maybe Moderna can save some money and not have to pay that licensing fee. No, good to have more options, and I think that was part of the issue, too, is maybe better immunogenicity with less reactogenicity, which is always great.

VR: Colleen writes, "I want to first thank you for being such a wonderful, compassionate doctor. I know you aren't seeing Long COVID patients anymore, but I credit you for the improvement of my quality of life that I've gotten back. Still a long way to go, but I see hope. Here's my question, which I'm not sure if you would know the answer to this, or maybe I'm just crazy and this is coincidental, but I feel compelled to tell you this possibly interesting correlation. Last PEMGARDA infusion was October 24, and after I was able to eat food again and digest it, then I was due for another infusion in January, wasn't able to receive it, began

having the severe diarrhea again, became severe in February and March, multiple times a day, unable to eat solid food, continued every day.

Then, June 25, I received the PEMGARDA infusion, insurance finally resolved, and about two days later, I was able to eat a turkey club sandwich. I actually ate four of them. I've eaten solid food every day since without diarrhea. I even gained a few pounds. I'm just thinking, is there any way this is correlation? I know it's been only a few days, but I had not gone one day without that severe symptom after eating. Maybe it's coincidence, maybe I'm crazy, but I thought you'd find it really interesting, and maybe there is some mechanism. Thanks again. I also can't wait for America to be sane again."

DG: [laughs] I guess we should make MASA hats, Make America Sane Again hats. They'll be blue or something. No, this is interesting, actually. This is the way I think science is supposed to work. Interesting observations. Are we seeing this in other people? Is there something going on here? No, thanks for sharing this, Colleen.

VR: Daniel writes, "Listening to clinical update this morning, I have a correction for you. While FDA approved Moderna's mNEXSPIKE vaccine based on the non-inferiority trial versus SPIKEVAX, Moderna still has to do the randomized superiority trial versus saline in adults 50 to 64 at low risk. Read the full FDA letter to see the post-marketing commitment." Gives a link for that.

DG: Thank you for that clarification.

VR: Steve writes, "I recently contracted COVID on a trip to Alaska by ferry. After I tested positive, I had a conference call with my family physician. She prescribed Paxlovid and also a prescription called metformin for two weeks. She said the metformin may help to prevent Long COVID. I've listened weekly to *TWiV* with Dr. Griffin, but I've never heard of any mention of metformin. Can you tell me about it? Is it worth taking? Are there downsides? This is my second bout of COVID, and it's been almost four weeks, and I'm still not fully over it. Nasty bug. Thank you."

DG: All right, so Steve, the study was - this was part of the COVID-OUT trial, and this was in part actually supported by UnitedHealth Group. Dr. Boulware was involved. Some of my colleagues, Dr. Cohen was involved, Ken Cohen. They had four groups here where they looked at treating people at different things. Now, the metformin, one of the challenges here was initially when we were looking at setting up this trial, when this trial was being set up, was the idea of just putting people on metformin, but it was so poorly tolerated that there became this very complicated, starting with the low dose and then over a period of days, escalating this complicated escalation dose of metformin.

I think it was David Boulware, one of the authors on the study, who was basically suggesting this was like a poor man's alternative if you couldn't get Paxlovid. That's where this came out. In the metformin, so the four different groups, there was a really high incidence or low incidence in the placebo relative to what was seen in metformin. If you compared metformin and the Long COVID to some of the other groups, it wasn't really clear. It's sort of left in this. It's complicated, requires this complex uptitration, never been studied in people that got Paxlovid. We're not really sure where this fits in Long COVID. Mentioned it in the past, but really hasn't become a standard part of the recommended treatment of acute COVID.

VR: Metformin is for diabetes, right?

DG: Exactly. Yes. Interesting enough, it might have some antiviral, anti-inflammatory impacts.

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

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

[music]

[00:49:28] [END OF AUDIO]