TWiV 1366 Clinical Update

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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 1366, recorded on October 14th, 2026. 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: Back to New York, Daniel?

DG: We are back to New York. I miss Colorado a little. I spent 20 years of my life out there, so it feels like home in certain ways.

VR: I can imagine. Speaking of home, what's on your bow tie today?

DG: Actually, that's perfect. *Giardia*, beaver fever.

VR: [laughter] Wonderful.

DG: All right. Well, hello, everyone. Let's start with our quotation. We got a bunch to cover today. We're going to cover viruses and diseases, not aspen groves, but talk about that, too. Bertrand Russell, "The whole problem with the world is that fools and fanatics are always so certain of themselves, and wiser people so full of doubts." I don't know if that's the whole problem, but it is a problem.

VR: Yes, I agree.

DG: All right. In our news, couple of things. Hand, foot, and mouth disease cases spike at Penn this fall. This is University of Pennsylvania. They've seen an increase in hand, foot, and mouth disease among undergraduates this fall. What is hand, foot, and mouth disease? This is a disease due to Coxsackievirus. They give a little bit of background. Now, the problem with Coxsackievirus, very contagious. It's in the nose. It's in the throat. You get these tiny little blisters on your hand, feet, your mouth.

There's virus in the fluid and all these blisters everywhere. There's virus in the feces. Now, usually, you don't see it in these populations. You usually see it in little kids. Then their parents get it because there's been a certain period of time since they had it. I don't know if you remember when your kids were little, did they give you hand, foot, and mouth disease,

Vincent?

VR: No, never had it because I used to work on polio, so I had immunity.

DG: Actually, yes, that's a good comment.

VR: Well, I don't know if it's - There may be cross-reactive immunity. I just don't know. I had a lot of immunity to polio virus, having worked on it, but I'm very familiar with this because I used to think about Coxsackieviruses all the time. They are highly related to polio virus. What's going on at Penn? What's the reason? Do we have outbreaks now and then like this in a university setting?

DG: Not commonly. This is a little bit uncommon, as they point out. It's tough, too. They make us like, "Oh, no touching and kissing." I'm like, "Oh my gosh, it's college. There's a lot of that stuff going on." This is not an enveloped virus, right?

VR: No.

DG: This is an unenveloped virus. I can't imagine those hand alcohol things are going to work very well.

VR: No, hand alcohol, not going to do it. No.

DG: You got to just, unfortunately, you're going to get it. You'll get through it. All right. The article, "HIV Service Delivery after the PEPFAR and USAID HIV Funding Withdrawal in Uganda and Zimbabwe: An Interrupted Time-series Study," was published in *The Lancet Global Health*. This is not good news. The study used data from four non-governmental organization, NGOs, in Uganda and Zimbabwe that had received PEPFAR funding for HIV services and work with high-risk populations.

Researchers found that the number of people receiving antiretroviral therapy dropped by 31.5%. We used to talk about this 90-90-90, diagnose 90% of the folks, get 90% of them on medicine, keep 90% of them with viral suppression. The real reason we want to do that, well, several reasons, but ART turns HIV from a fatal disease into a chronic one, it prevents transmission. If you treat these folks, it keeps it from transmitting.

Now, overall, in addition to what we're hearing here, the preventive services that complement antiretro therapies, such as condom distribution, that's down by 62.7%. HIV testing is down by 63.8%. Among the three NGOs that provided data on use of pre-exposure prophylaxis, PrEP, that is down by 71.6%.

VR: This is just so unacceptable that every Republican went along with this and didn't challenge it or try and reverse it. There is no reason to remove this funding. Remember, it was DOGE that did this, this is Elon Musk genius.

DG: Yes. This is going to snowball. You can think about people have HIV, they're not treated, they're spreading it to others, then they're not being tested, they're not being treated, they're spreading to others. We are just talking about thousands and thousands of human beings dying because of these decisions. Everyone, think about that when you make decisions.

VR: People, you need to just object to this. You cannot keep going like this. It's not humane.

DG: All right. Let's switch gears a little bit because this is a fun article. You get your vaccines, and there's a whole discussion about, "Oh, I had a really bad reaction. I had a fever. I didn't feel well." We always try to tell you, "Oh, that's a good thing." Well, here is the article, “The Human Gut Microbiome Primes Fever After Vaccination,” published in *Science*. The MicroHEAT, this is the Microbial Human Ecology and Temperature Study, HEAT, I guess the and gets an A, where they longitudinally tracked 171 healthy young adults receiving basically their COVID mRNA vaccines thrice daily, so three times a day.

They're doing oral temperature recording. They're looking for fever. Also, fecal and serum samples were collected for microbiome and immune profiling. Now, these investigators found that fever had very little effect on the microbiome, but fever-positive participants displayed chronic low-grade intestinal inflammation and a microbiome characterized by high expression of bacterial flagellants both pre- and post-vaccination. The idea here being that the microbiome might predict and may even have a causal connection with why you have a fever.

Microbiomes from fever-positive participants induced heightened inflammatory responses in human colonic organoids and exacerbated acute vaccine responses when transplanted into gnotobiotic mice. This was dependent on sensing of bacterial flagellin through host innate immune receptors. Moreover, microbial flagellin production was modifiable by diet. Dietary additives increased bacterial flagellin production in vitro, and a Western-style diet exacerbated vaccine reactions in mice.

Consistent with this, fever was associated with dietary and metabolic markers in humans. Although interventional human studies are needed to establish causality, this suggests that diet modification could be a viable strategy to influence microbiome-dependent vaccine responses. They've got a really cool graphical abstract, but just to run it through one more time. Fever risk, whether or not you're at risk of having a fever, folks that have fever, tended to have a low-grade intestinal inflammation, increased abundance of flagellated *Lachnospiraceae* bacteria, increased flagellate expression pre-vaccine.

Consistent with this, human fever risk was associated with, this is where it gets exciting, self-reported diet metabolic markers. We've got this Figure 2 where you can see that the vegetarians had less fever.

VR: All right, I'm not a vegetarian. I don't have any fever when I get vaccine, so it's maybe not universal. I agree it's interesting, but we don't know the whole story yet. Maybe my gut is not inflamed for other reasons.

DG: It's really interesting. Well, the caveat, too, because we always said, and that was the, I think it was the gamma interference study we talked about, where if you had more reactogenicity, you tend to get higher immune responses. Here, the vegetarians had less fever, but same antibody levels.

VR: It doesn't matter if you have fever or not, basically, but if you'd rather not have the unpleasant fever, you've got to switch your lifestyle.

DG: It might be true, but now we've got it. This is science. Now we've got to do it prospectively. We've got to get the meat-eaters to become vegetarians, and what's going to be harder, we get the vegetarian start eating meat, and then six months we got to, or maybe next year we vaccinate them again.

VR: Do you eat meat?

DG: I try to eat mostly a plant-based diet, but when we were out in Colorado, I had what, the buffalo empanadas, and I had the elk ragout, so I will occasionally eat meat.

VR: Do you have fever when you get vaccinated?

DG: [laughs] I don't, actually. I don't think I ever have.

VR: There's got to be something else.

DG: My wife is listening. Remember, if my wife is listening, every time I get a vaccine, oh my gosh, for a day, I just need to lay on the couch with the dogs. It's a terrible experience for me.

VR: Does she eat meat?

DG: No, I'm joking. I feel -

VR: Oh, you're joking about yourself. Yes, of course. [laughter] I just think that this is a nice study, and it's a nice correlation, but look at Figure A there. Look at the how overlap you have in the dots.

DG: Yes, there's a lot of overlap there. It would have been nice if there was a real, this is like a statistician can tell us. All right, another fun one. We got to throw fun stuff in because, oh my gosh, there's a lot of not fun stuff going on in our world, but in *CIDRAP,* we read, "Raw Milk Poses Serious Infection Risks with No Added Health Benefits, Pediatrician Group Warns." Now, what do we have here?

Now, last week, we had our first-ever Parasites Without Borders retreat up at the Mount Hayden Backcountry Lodge outside of Ouray, Colorado. Apparently, that's how you pronounce it, just like hooray, but Ouray, Colorado. There was a discussion about raw milk, and right on the heels of that discussion comes the American Academy of Pediatrics consumption of unpasteurized raw milk and milk products by pregnant people and children policy statement, here we have it. Because what was it, Chuck Knauss, was saying, well, it's anecdotally true, as Dickson would say, that raw milk makes you feel better and healthier.

Well, is it actually true? Sales of unpasteurized raw milk and milk products remain legal in at least 27 U.S. states. Unpasteurized milk and milk products from cows, goats, and sheep continue to be a source of infections attributable to several virulent pathogens, including *Listeria, Campylobacter, Salmonella, Brucella,* and *E. coli* O157. These infections can occur in both healthy and immunocompromised individuals, including older adults, infants, young children, pregnant people, and their fetuses, potentially resulting in life-threatening illnesses and fetal miscarriage.

Pasteurization of milk products greatly reduces risk of illness. Efforts to limit the sale of unpasteurized milk products have been met with opposition from proponents of unpasteurized milk's alleged health benefits. Now, we get this. These purported benefits have no evidence base and do not outweigh the risks of unpasteurized milk consumption. Substantial data suggests that pasteurized milk confers equivalent health benefits compared with unpasteurized milk without the additional risk of infection.

The purpose of this policy statement is to provide evidence for the risk of infection from unpasteurized milk consumption, along with the severe illness and infectious complications that occur, especially among pregnant people, infants, and children. Now, in the *CIDRAP*, we read that from 2013 to 2018, there were 75 known outbreaks linked specifically to consumption of unpasteurized milk products that resulted in hundreds of illnesses, about 100 hospitalizations, and two deaths.

VR: Daniel, do you think it should be outlawed?

DG: It's interesting. I'm always of the approach of educating people so they can make smart decisions, and hopefully that's what we're doing here. I feel like legislating something is really a last resort. Unfortunately, we're living in this world where people are misinforming. Unfortunately, you end up, we have people ending up in the hospital and people dying, then sometimes maybe legislation is required.

VR: Well, people have a right to die. It's, in a sense, callous, but the thing is that they don't want to believe that there's no health benefit to drinking raw milk. That's the problem. I have a quote here by Neil deGrasse Tyson. I'm reading one of his books. He says, "When people believe a tale," and this is a tale, "that conflicts with self-checkable evidence, it tells me that people undervalue the role of evidence in formulating an internal belief system."

They don't want the evidence. They have this belief that unpasteurized milk is good, it's the tale, and they believe it no matter what you tell them. They will keep drinking it and get sick. The question is, do we want to legislate away this illness, or is it your choice? I know what I would do. I'm not going to drink unpasteurized milk ever, and neither are you. What do you do?

DG: It's really easy to just heat it up. It does not take much. Just bring it to a boil. Boom. Not for very long. This is not like you've got a rolling boil for minutes. It's really just a very quick. We'll leave in a link to *Dairy Digressions*, the monthly podcast of the American Dairy Science Association. This is Episode 38, The Science and the Stakes of Raw Milk Consumption with Pam Ruegg, Nicole Martin, and Daniel Griffin.

VR: Is that you?

DG: Yes, that's me. I talk about it. Sometimes, if you legislate against the sales, what you can actually do is you can get rid of a profit motive. Then people can drink raw milk if they want, but they'll own a cow as part of a cooperative. It won't be a large herd. Maybe there can be certain testing requirements. There are ways that if people really want to go down this road, that maybe we can make it safer.

VR: I think it's an interesting title, *Dairy Digressions*. I like that.

DG: [laughs] All right. This is exciting. I have to say, it's taking me a little while to unpack this. Maybe, Vincent, you can tell me. From *Epic Research*, we have, “First Birth Cohort Eligible for Chickenpox Vaccine Has a Sharp Drop in Shingles Cases.” This is post on October 2, 2026. I'm going to tell up front, the unpacking issue for me, I would have thought it was a much sharper drop. Let's walk through this.

Shingles, or herpes zoster, is a painful rash caused by reactivation of the *Varicella-zoster* virus. This is that virus that causes chickenpox. We should call it the chickenpox virus. Now,

this virus remains dormant in nerve tissue after, for most people, a childhood infection. Now, it might surprise people to hear that without vaccination, about one in three people in the U.S. develop shingles in their lifetime. It's a really high risk. I don't know if a lot of our listeners knew, one in three. Getting shingles is really common. Now, the risk rises with age and with conditions that weaken the immune system. Women are more affected than men.

Now, the chickenpox varicella vaccine was introduced in the United States in 1995. I had finished my medical training. I finished medical school before this came out. Actually, there were some folks at NYU working on this when I was at medical school there. People born from the mid-1990s onward are the first to reach adulthood largely in the vaccine era. This is an attenuated replication-competent vaccine. You can potentially get shingles from the vaccine. That's the idea.

Here they examine the records of more than 85 million U.S. adults from two different angles. The first describes how common shingles diagnoses were across adult birth year cohorts, calculating the rate of patients diagnosed with shingles during the study period by their birth year. This is Figure 1. It's really interesting. If you start with the '68 to '75 and you start moving down, you're already seeing a reduction before we introduce the vaccine.

VR: That's what I'm worried about here. Maybe it would still go down without the vaccine.

DG: It's kind of an issue, because it's going down, it's going down, it's going down. We start off with 181.9. These are all per 10,000 then. 181.9, 116, 97, 76, 45. Then we get the vaccine introduced in 1995, and then it's 17, it's nine, it's seven.

VR: It's hard to argue that this is a vaccine effect.

DG: Right, It was going down.

VR: Yes. RFK would say this is not proven to be a vaccine effect. I hate to agree with him, but you don't know.

DG: I feel like Figure 2 is maybe a little bit better because you can see it really is going down if you're looking at the folks that are in the vaccine-eligible age groups. Because it was about 31 years ago that it got introduced. There was a little bit of a catch-up that occurred. I really would have expected it to be so much closer to zero in vaccinated folks.

VR: Yes. Nine per 10,000, seven per 10,000 is pretty low. Although when you have millions of people, I guess it's significant.

DG: Yes, you certainly see it a lot.

VR: Are there bad consequences of shingles?

DG: Yes. There are some horrible consequences. You can go blind. It can damage your brain.

VR: All right. Now that we have Shingrix, which is not replicating at all, and it also reduces dementia and probably other things, you should definitely get a shingles vaccine.

DG: You definitely should. I guess what we're seeing here is that even if you got the chickenpox vaccine as a kid, it looks like these folks are probably also going to be eligible for a Shingrix vaccine when they get older.

VR: Why was it declining from '68? Do we understand?

DG: Part of it's interesting. I think that this is a hard way they're displaying the data. You need to then repeat this in five years, because the birth-year cohort also corresponds to older people. Older people get it. Younger people don't. It's really hard the way they did this study. Because people birth year '68 to '75, those are folks in their 50s. Then folks in their 40s, 30s, 20s. It's hard the way they put this data together.

VR: If you're born in, let's say, 1970, then by 2020, then you're 50, right?

DG: Yes.

VR: This isn't right. You have to look at that group when they're susceptible to shingles, which is not on this graph.

DG: Yes, you need to look at the birth-age cohort at the same age, because you don't expect kids that were born in 2007, who are 20 years old, you don't expect a lot of shingles.

VR: Well, if you're born in '68, I have this graph, birth year '68, and then that year there are 181 shingles cases. It has nothing to do with the people who were born in that year.

DG: It may just be you're over the age of 50.

VR: No, it says birth year. Is this, I'm not sure, adults diagnosed with shingles between 2019 and 2026. They're looking at 2019 to 2026, and they're looking at their birth year. The shingles diagnosis was 2019 to 2026. That's OK. We were looking at the birth year correlating with the number of shingles, but the shingles didn't occur in that birth year. It occurred many years later. That's fine.

DG: Here we're basically seeing people in their 50s get shingles. Not so many in their 40s, not so many in their 30s, 20s, on down. I'm not sure this is a great design.

VR: The problem is that they have birth year 2006. Those people in 20 -

DG: Are 20 years old.

VR: Are only 20 years old, so no wonder it's low.

DG: It should be lower in my mind. That's what I'm concerned about. Why isn't it lower?

VR: Well, they're only 20 years old. Oh, you think it should be lower than six per 10,000?

DG: I thought we vaccinated them. I guess it's amazing to me that the vaccine is still either allowing them to get infected with non-attenuated chickenpox virus, we'll call it that, or whether or not the attenuated virus is triggering the shingles in these young folks.

VR: I think there's some, but it's pretty rare that happens. I don't think it would account for this.

DG: It'd be interesting to actually do sequencing and look at, OK, it's 6.9 for 10,000. Is that reactivation of the vaccine, or is it that the vaccine just isn't good enough and maybe we need to switch over to Shingrix?

VR: If you're getting a reduction in shingles, then you would also have to have a reduction in chickenpox itself, right?

DG: You certainly have a huge reduction in chickenpox, yes.

VR: I'm a little puzzled by this. I don't get it.

DG: All right, the article, now, we all hate AI, but sometimes AI is good stuff.

VR: I don't hate AI. I find it useful. [laughs]

DG: [laughs] I do, too. Full disclosure. When I'm driving along, it's like a verbal Google search for me. "Hey, look this up for me. Hey, look this up for me." I've got some idea, Vincent, that AI is going to solve fusion, and in eight years, we're going to have fusion, and that's going to solve our energy issue. Then we won't care about all the energy use of AI because AI will have figured out how to take care of its energy needs. Anyway, the article, "Accelerated Discovery of Thermostable mRNA Lipid Nanoparticle Vaccines Using Data-Efficient AI." It was published in *Nature Biotechnology*.

Now, the instability of the mRNA lipid nanoparticles, the current ones that we're using, has necessitated ultra-cold storage, limiting global distribution, and their broader application in advanced delivery systems. Now, this was, this is a big issue for those COVID mRNA vaccines with everyone buying freezers and the stuff shipping in these pizza boxes, and you had to keep it minus 80, minus 20. Now, solid-state, water-free formulations enhance thermostability and enable integration into emerging delivery modalities such as these microneedle patches.

Wouldn't that be great if you had these solid-state, water-free, thermostable mRNA lipid nanoparticle vaccines that you could put on these patches? Then you don't even need needles. You just stick the patch on somebody, and now they're vaccinated. Previous efforts to stabilize the mRNA-LNPs were constrained by narrow formulation scope, low-throughput screening methods, but here they introduce, I love the algorithm, Algorithm-Guided Experimental design for lipid Nanoparticle Thermostabilization, which they call AGENT. A-G-E, I'm not sure how they get the NT, but nanoparticle thermostabilization.

It's an artificial intelligence, AI-driven framework that couples high-throughput experimentation with Bayesian optimization to identify thermostable mRNA-LNP formulations. This AGENT extracts maximal information from sparse experimental datasets, enabling efficient formulation optimization in six iterations completed within one month. Now, results, proof is in the pudding, they were able to stabilize mRNA vaccines with two clinically-relevant LNPs representative of the Moderna and the Pfizer-BioNTech compositions into solid-state formulations that retained 100% bioactivity after storage at 37C. That's like human body temperature for more than two months.

In rodents, non-human primates, thermostable solid-state vaccine formulations induced antigen-specific immune responses non-inferior to those elicited by intramuscular delivery of freshly-prepared soluble vaccines.

VR: What does it mean, solid state?

DG: It's a little bit odd. I think it's an odd description. We would think of things like

lyophilized.

VR: Yes. Is that what it is? Is it freeze-dried or something like that?

DG: Water-free. It is lyophilized.

VR: Then when you use it, you add water. You reconstitute it, right?

DG: I don't know if you need to, actually. That seems to be part of the idea that you could maybe somehow put this stuff on those microneedle patches. You may not even need to reconstitute it. By just pushing it through the skin, that might be enough to activate it.

VR: Is that what they did here, or did they reconstitute it?

DG: Let's see. I guess that's an issue. When they actually did the rodent and non-human primates, did they actually put it back into suspension? I'm not sure.

VR: Well, the two months at 37 is fantastic.

DG: That is. Even if you need to add a little bit of diluent, that's fine.

VR: That's not a problem to reconstitute it. That's really good. Then you don't have to ship it in those bloody dry ice containers.

DG: Oh, and just think of the millions of dollars that were spent on all those freezers that now are just sitting there. We don't need them anymore.

VR: Well, you'd have to do a clinical trial with this, wouldn't you?

DG: You do. You do. Yes. Hopefully, we live in a world where, like they did with the rodents, non-humans, you can just do an immunobridging study where you show that, "Hey, this gives us the same T-cell, the same antibody responses, so surrogates." All right. We're seeing more screwworm, but the big thing that really, I have to say, I'm really worried about this, is that Ebola, we're up to 9,166 total confirmed cases, 4,413 total confirmed deaths. The largest Ebola outbreak in West Africa, that was, I'm going to say, only 11,000. We're headed towards halfway.

Now, there's an article. I've worked in Congo for decades. I've never seen an Ebola crisis like this. We read, even now, more than 140 days after the outbreak was declared, most new cases are appearing outside the chains of transmission that healthcare workers are tracking. Between one-third and two-thirds of deaths are occurring not in treatment centers, but in people's homes and communities. The threat is spreading. Last week, Kenya reported its first Ebola case after a man who had traveled there through Uganda from the Congo, died of the disease.

VR: Do we have a graph anywhere that shows the rate of new cases?

DG: If you follow our link to this Ebola, let me go to that now. We can maybe, while people are on YouTube, we can have David take a look at that.

VR: This is the CDC page.

DG: If you go to this link, yes, the CDC page. I'm going to paste it in for you there, Vincent.

VR: Oh, I see it then there.

DG: You can see how you still have this really significant increase in trajectory.

VR: Yes, it's not plateauing either. That's the thing. That's what I was looking for. It's still going up.

DG: Yes, it is just rising. It's really got the same trajectory. We're not even seeing it starting to level. All right, well, Ebola in the Congo, and we've got measles here in the United States. The sixth person died. I just want everyone to think about this. I was listening to NPR, and people are talking about who they're going to vote for. Really, what's going on with public health in the United States is really a tragedy. We talked about this. Maybe people thought we were being a little dramatic, but Franklin County, Pennsylvania health officials announced the state's sixth measles-associated death in a 39-year-old woman who was unvaccinated against the virus.

What ended up happening is, the measles led to probably an acute cardiac event as her complication of measles.

VR: Folks, I understand everybody wants to vote based on the economy, but you ought to be voting on this. These guys are botching healthcare in the U.S. They're botching it, and they're killing people.

DG: They're botching the economy, too, Vince.

VR: I understand.

DG: Try to buy some gasoline or some diesel, or groceries. Oh, my gosh. I'm not sure what the upside is to this.

VR: Now, I don't know if you noticed, but if you go in the supermarkets, the beef doesn't tell you where it's from anymore.

DG: That's a problem. As we talked about, I'll eat elk, I'll eat buffalo, I'll eat beef, though I try to eat more of a plant-based diet, but when I eat beef, I want it to be from Texas.

VR: Not from Venezuela.

DG: Yes, I really don't want that.

VR: Really, folks, there's no reason for six people in Pennsylvania to have died of measles. There should be no measles in the U.S.

DG: There certainly shouldn't be people dying. There shouldn't be hundreds of people ending up in the hospital.

VR: No.

DG: Little kids, who down the road are going to end up with basically encephalitis and dying because one in every 600 kids is going to get that as a complication. Even if they survive, they've got this ticking time bomb down the road. Measles is a bad disease. It always has been a bad disease. Just people seem to have forgotten that. All right, and the number of

cases, we're up to 4,267. That's an extra what, 250 cases just in the last week. If you look at Pennsylvania, and most of them, 157 were in Pennsylvania. Pennsylvania alone, 1,136 total cases. We've blown by that 2,242 that we had last year.

VR: These blue dots are getting bigger and bigger, and they're filling up parts of the U.S. now.

DG: Yes, they really are. A little exciting from Gavi. This is, “Made in Africa: New Measles Rapid Diagnostic Tests Mark Breakthrough for Vaccination Efforts.” Gavi, which is the Vaccine Alliance, announced a major milestone for measles surveillance with approval to deploy first-ever measles rapid diagnostic tests. I love this. I hate when it's hard to make a diagnosis, when you've got to jump through hoops to get access to the testing, and you've got to make phone calls. If you're thinking it's measles, you want to know. You don't want anyone to stand in your way and say, "Well, are you sure? Should we even test?"

Now, the breakthrough is the result of longstanding cooperation between Gavi, the World Health Organization, UNICEF, the Gates Foundation, and other partners to advance measles surveillance and support faster outbreak response. These new measles diagnostics are the only rapid test to meet required performance criteria following a rigorous evaluation process conducted by WHO and partners. It's manufactured by DIATROPIX of the Institut Pasteur de Dakar, in Senegal. Represents important technical breakthrough in the fight against measles and underscores the growing strength of African manufacturing.

Up to 500,000 tests are expected to be deployed each year once the program is up and running, with first rollouts expected to begin in Senegal later this year. Gavi investment in these tests forms part of a larger U.S. $43 million funding package provided by the Gavi Board in 2025 to find diagnostic kits across a range of diseases. All right. This actually just came up at work today. People were asking about measles. In New York State, we have a New York State dashboard. We have an emergency declared in New York for measles. We're up to 126 cases in New York and seven confirmed cases in the city.

All right, flu, we're just starting to get some activity of flu there. You can just start to see Alabama, South Carolina, Florida, just starting to get into that minimal, but rising. The epidemic trend. I've got this epidemic trend for the CDC. You can actually start to see the flu. What's really probably better, if you look at the yearly trend lines, the number of positive specimens, we're going up earlier than we did last year, for instance.

If you look last year and they number the weeks, it was really about week 44 that you saw stuff start to rise, and really, it's 33, 35, so about 10 weeks early. All right, so get those flu shots. Get those flu shots. You've got a lot of choices out there. RSV, still rather quiet. COVID, what happened, Vincent?

VR: Where's my COVID graph? There it is.

DG: There it is.

VR: It's going back up. I told you last time that these peaks go up and down.

DG: [laughs] This one. It matches, I head over to the hospital this morning, and I've got two new COVID cases to consult on in the ER, so yes, we're seeing cases, we've got a few in the hospital.

VR: The previous year, '25, it really went down by mid-October and then went back up again in November, it looks like.

DG: We had a little reprieve. I don't see a reprieve.

VR: Maybe we're not going to have a reprieve. Maybe we're going to have an outbreak just from October through March.

DG: That's quite possible. I suspect, if you look, it's really spotty. Florida has very high activity. There's high activity like Texas, New Mexico, California. There's high activity in Massachusetts, Connecticut, so maybe the people, they went up, spent a weekend in Connecticut, didn't realize how risky it was up there breathing in stuff.

VR: You think Florida is high because of the senior population?

DG: They are more susceptible, so.

VR: I just don't know what fraction of the population are seniors.

DG: I should probably throw in, because we haven't mentioned it in a while, transmission. This came up recently. I had a gentleman who I'm treating with IV antibiotics for a bacteremia. He's home. Then, boom, the wife gets diagnosed with COVID. What do you do? He's like, I'm in the home. We're going to be sleeping in the same bed. I'm like, OK. Xocova, ensitrelvir. We do have post-exposure prophylaxis. We've got the XPA-C. You take three pills on day one and then one pill a day for several days after that, 50% reduction in household transmission.

VR: Florida has about 20% seniors, which is one of the highest in the country. Maine and Vermont also have comparable percentages of seniors. I don't see -

DG: They're doing OK. They're low at the moment.

VR: That's not it.

DG: All right. We have a few papers here in the long COVID section. Start off with the first one. The article, “Characterizing Sleep Disturbance Phenotypes in Long COVID: An EHR-based Study from a Safety-net Hospital,” published in *Academia Medicine and Health*. These are results of a retrospective chart review of 496 adults evaluated between 2022 and 2023 at an urban safety net hospital's Long COVID clinic. I think it's really important to have that context. These are people attending a Long COVID clinic. We're looking at the reported sleep disturbances of people attending a Long COVID clinic.

Structured intake forms, provider documentation, captured things. They're really capturing this through structured intake forms and provider documentation. Then they're going to look at different types of sleep phenotypes. They're going to look at insomnia, hypersomnia, and mixed. Some people can't get to sleep, some people can't wake up, and some people can have a back-and-forth. Sleep disturbances were very common, reported by 71.8% of folks. Insomnia, about a third of the time. Mixed, 20% of the time. 10%, it was a back and forth.

Insomnia and mixed types were associated with preexisting cases of anxiety, depression, chronic pain. Use of benzos, beta blockers, and muscle relaxants. Mixed type was associated

with chronic heart disease. Actually, odds ratio of 5, really associated. Obstructive sleep apnea, odds ratio of 3. Chronic pulmonary disease, odds ratio of 2.8. Now, hypersomnia was not linked to prior medical or psychiatric history, but was predicted by past symptoms of post-exertional malaise. Odds ratio of 10.4. Fatigue, odds ratio of 6, and dysautonomia, odds ratio of 5.6. Gait instability, odds ratio of 9.2.

The reason I want to talk about this is just to mention. A lot of these folks, you think, "Oh, Long COVID, we don't understand what causes it, we're not sure what to do." If insomnia is going on 72% of the time, this is definitely something we can try to work with our patients on.

VR: You can deal with insomnia?

DG: We really can. Some of the easiest and ways that we talk about are just improved sleep hygiene, but also the studies on melatonin having both a beneficial effect on the insomnia folks, the mixed folks, and some ongoing inflammation. Remember from the studies, it was five milligrams was the sweet spot. Too low or too high actually might make things worse.

VR: This could improve fatigue, right? Because that's another common component of Long COVID.

DG: Yes, sometimes these folks, if you actually-- I remember early on when we started doing sleep hygiene, and we started doing the melatonin, I was thinking, "Oh, well, you're sleeping better, that's why you're better." To some degree, that's true, but things like the melatonin may actually help with some of the chronic ongoing inflammation as well. All right. The article, Sputum and Oral Microbiota Profiles are Associated with Long COVID Severity and Phenotype Post-hospitalization: A UK Multi-center Prospective Cohort Study," published in the *European Respiratory Journal*.

In this study, adults were prospectively recruited to the longitudinal UK post-hospitalization COVID-19 study, the FOSCOVID study. Patients were grouped by previously described severity clusters of ongoing health impairments and symptom subgroups. Oral and sputum microbiota at six months post-discharge were characterized through 16S ribosomal RNA gene amplicon sequencing, and microbiota diversity was assessed. 771 participants had their microbiota assessed. Participants with oral rinses and severity cluster assessment, mean age 57.5, and 38.5% were women. It's interesting because most of these clinics are usually predominantly women.

Now, the very severe cluster in which disease was predominantly pulmonary in nature was associated with a distinct microbiota profile post-COVID-19, reduced lung function had its distinct oral microbiota profile. Persistent neurocognitive symptoms had a distinct oral microbiota profile, while GI symptoms had a distinct sputum microbiota profile. Microbiota keystone taxa shifted to a high prevalence of lactic acid bacteria associated with worse outcomes. Lactic acid bacterial abundance was associated with elevated blood inflammatory proteins. I'll leave a link because I didn't go through all the different subspecies and taxa of the microbiota diversity there.

VR: I wonder if any of these have an inflammatory bowel thing which would predispose them to fever, right?

DG: Yes. I wonder if you could shift this if you were a vegetarian, right? Maybe that would

help with some of the information.

VR: Every cluster is different. I don't know if it's correct or if it is that it's really difficult to treat.

DG: The authors talk about this like, is this what made these people susceptible to certain phenotypes, or did the phenotypes themselves drive?

VR: Of course. We don't know if it's driving or not. Absolutely.

DG: Somehow you've got to change the microbiome and see if that impacts symptoms. Still a lot of research to do in this area. All right. "Microtesla Magnetic Therapy for Cognitive Impairment in Long COVI: A Randomized Pilot Study," published in *Brain Communications*. You guys probably talk about studies from *Brain Communications* in *TWiN,* right, *This Week in Neuroscience*?

VR: I don't think we ever did this one, no.

DG: Here we got a couple of cool photos. You got this guy wearing this Microtesla Magnetic Therapy device. It's this transcranial. Basically, you put this thing on your head, and low-amplitude radio frequency magnetic fields are generated. There's some past stuff where there might be anti-inflammatory, neuroprotective effects in some preclinical models. They had this idea this might help in Long COVID. Here we have the first randomized controlled trial of MMT, Microtesla Magnetic Therapy for Long COVID Cognitive Impairment.

They evaluated the feasibility and safety of at-home MMT in individuals with objective cognitive impairment from Long COVID. They got 30 folks, and they're randomized two to one to active or sham MMT in self-administered 15-minute treatments at home twice weekly for four weeks with remote monitoring using a head-worn device delivering a non-thermal radio frequency magnetic field to the whole brain.

Feasibility was completing at least 80% of the treatments. Safety was assessed looking at adverse events. Cognitive function, self-reported mood, and quality of life were exploratory outcomes assessed at baseline, week four, and week eight. Feasibility was high. All patients who completed the study adhered to 100% of treatments, and usability ratings were strong. No device-related adverse events occurred. Compared with sham, active MMT folks showed significantly greater improvement from baseline to week eight in the Wechsler Adult Intelligence Scale Digit Span Sequencing, the Hopkins Verbal Learning Test-Revised Total Recall, and the Delis-Kaplan Executive Function System Color Naming test.

These are all less than 0.05. Other measures of attention, processing speed, and executive function did not differ between groups. Emotional well-being actually improved more with active MMT. Depression and anxiety decreased in both groups, but the anxiety reduction was greater with active treatment. Interesting. Improved working memory, improved emotional well-being, improved processing speed, improved verbal learning. I'll leave a link into this article if people want to look at this device that they're using.

VR: I wonder how it works.

DG: Unfortunately, it costs $1,000 for one of these things. I don't know. Do you just use it for four weeks? Is that enough? Is this something you would use on a regular basis? Still, a

lot of work to do.

VR: This electro-radio frequency magnetic field, that's basically what MRI does at a higher intensity. Right?

DG: It is funny. We joke about this. Sometimes patients in the hospital, we don't know what's going on. Let's get a scan, and then they're better. We joke the scan made them better. I think we're still joking. [chuckles]

VR: It's the same radio frequency magnetic field. That's how MRI -

DG: Therapeutic MRI.

VR: These radio frequency pulses tip the hydrogen nuclei in your tissues, and that's how you get the detailed diagnostic images. That's the magnet in the thing is making all that noise.

DG: Yes. Donk, donk, donk. All right. That is the end. Before we get to our emails, I want to thank everybody who's supported us so far. No one is safe until everyone is safe. This is a cooperative effort. We all got to look out for each other. We are right now in our American Society of Tropical Medicine and Hygiene fundraisers. We're getting near the end of this. Right?

It's August through October. There's only a couple weeks left to get to our goal because we really want to have enough funds to support this five-year Dickson Despommier One Health lecture series, which, positivity here, we are going to announce that at the annual meeting next month. Go to parasiteswithoutborders.com and click on the Donate button.

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Connie writes, "Thank you so much for your reassuring answer to my question last week about whether we elderly, I'm 77, need a measles booster if we're going to a place with an outbreak like Pennsylvania. I'm wondering what the actual basis is for this universal recommendation?

Is it because prior to vaccination in the U.S., it was observed that elderly people did not get measles because they'd gotten it as kids, or is there a theoretical explanation for measles immunity lasting longer than, say, immunity to COVID following an infection? I tried to look this up on PubMed but didn't find any literature. I would just like to understand the evidence behind the recommendation."

DG: Yes, Connie, this is a great question. I think the simple answers are wrong. I'm just going to give a little bit of a deeper response. It really came from the observation that people who had measles as kids would not get measles when they were adults. There was this observation of lifetime protection after an infection. That's not true with all infections, right? As we've seen with coronaviruses in general, and more specifically with SARS-CoV-2. You get an infection, a year later, you can get an infection again. Not all infections give you lifelong immunity. Not all live vaccines, for instance, the measles vaccine, right?

We're seeing that not everybody gets that long-lasting protection. Mumps, another example of a live vaccine, replication competence virus, that for a lot of folks you need to do a second shot. Really, the actual is this was observed. It wasn't so much theoretical as observed that this particular infection gives you lifelong protection. We did not see measles

cases in older folks. I have to raise the issue that one of the concerns that's being raised now is maybe there was a background amount of measles that they were exposed. Maybe it wasn't just the one infection. Maybe it really was more than one boosting after the initial prime. Yes, that's how we understand measles. Any comments?

VR: This comes from this beautiful epidemiology study in the Faroe Islands. There was an outbreak of measles in 1846. Peter Panum, a Danish physician, was sent there to study it. He found that anyone who survived the previous outbreak in 1781, 65 years or more, were completely immune to measles, that outbreak in 1846. It was perfect.

DG: That's beautiful.

VR: People who had no immunity, everybody was susceptible, no matter what the age. If you had not been infected before, you were susceptible. He figured out the incubation period, the effect of quarantine, et cetera. This was a classic study. That is how we understand measles to this day, lifelong immunity. Susan writes, "Thank you for doing *TWiV.* It's great. I listen almost every week since COVID. I'm a retired pediatrician.

The question and the problem. My daughter, who is a pediatric fellow, 33 years old, had two documented MMR vaccines as a child. She has negative titers for measles and mumps. She has Crohn's and is taking Remicade, so she can't get boosters for live vaccines. She also is IgA deficient. In the past, the rates of measles have been low, but now due to lack of herd immunity in many places, she is potentially at higher risk.

If she is exposed to measles, can she get immune globulin post-exposure prophylaxis with her IgA deficiency? I've read that there's a contraindication due to that. What do you advise, since there's probably a good chance that she can be exposed to measles in the future? Do you have any suggestions? As a pediatrician, I'm a strong believer in vaccines, and I'm very upset and concerned about what RFK has done to support the anti-vaccine group and beliefs. He has destroyed the CDC. Children have already died unnecessarily."

DG: Yes, Susan. This is a complicated situation here. First, we'll start off with your daughter, who had two documented MMR vaccines and negative titer for measles and mumps. That does not mean that the vaccines did not work. That doesn't mean vaccines don't work. Part of that is that we're not looking at the T-cells. It is quite possible that your daughter, with two MMR vaccines, despite the negative serology, may still have protection against measles and mumps. That's really important because if she's on biologics that prevent her from getting replication-competent live vaccines, then you're not going to go ahead and give a third dose.

You also raise a pretty important challenge as well. What about folks with IgA deficiency? The measles immune globulins, actually, this is considered a contraindication to get immunoglobulins because there's an elevated risk of anaphylaxis. The whole idea is that people with IgA deficiencies have not seen IgA. You expose them to IgA and the immunoglobulin, and then they'll make antibodies and potentially react to the IgA. Yes, she's going to have to exercise some caution. I do think that it isn't as though people with negative MMR titers are necessarily susceptible.

VR: It depends also where she's working. She may be in a place where there's not measles at the moment, right?

DG: It also really matters where you work, yes.

VR: If she is in an area where there's a lot of measles and is working in an area with potentially infected patients, she should wear a mask, right?

DG: She's also a pediatric fellow, so if there's going to be measles, they'll be the ones seeing them.

VR: Don't you think a mask would be a good idea?

DG: A mask would be reasonable, yes.

VR: Patrick writes, "I really enjoy listening every week. I'm a 38-year-old nursing student who discovered *MicrobeTV* while in my microbiology prerequisite class. My question is regarding the severity of illness for measles. Is it possible that the modern strain of measles is more dangerous to humans than what was floating around in the U.S. in the 20th century?

I'm not sure if it's a different strain. That's beyond my pay grade. I'm guessing different strains of the virus have different effects in terms of their ability to make people sick. I suppose this could be seen when you talk about different Ebola strains and the percentage of mortality from them. Thank you very much. I enjoyed the Voltaire quote this week."

DG: Patrick, I don't think there's any evidence that there's a modern, more virulent strain of measles that is more dangerous. Measles is bad. Measles has been bad. Measles continues to be bad. Vincent, any comments on this?

VR: Yes, I agree. There's no evidence that there's any change in virulence, no. Ellie writes, "When I told my cousin in Rhode Island that I was getting my COVID shot, she said, 'I heard from a doctor of mine that COVID shots cause cardiomyopathy if used long-term. Annual shots are one of those money-making deals.' I told her that I rely on *TWiV* for vaccine facts and that, from what I recall, cardiomyopathy is not caused by the vaccine, but if you get COVID, it is a possibility. Did I get that right? I also told her that COVID can cause many long-term health conditions. Thank you for keeping those of us who listen safe and well-informed."

DG: All right, Ellie. We did see, particularly, there was adolescents, so particularly boys, so late teens, early 20s. It was maybe about one in 10,000. We would see some short-lived, usually less than a day. Very rarely was it very severe. We haven't really seen that in the future iterations of the yearly COVID shot. It's gone away, which is really nice. It is not a money-making deal. Yes, COVID itself is actually a significant cause of cardiomyopathy. It also increases your risk of getting diabetes, of having a stroke, of having heart disease. COVID's bad. You get a COVID shot, and it reduces your chance of getting the disease by about 50%. It's really recommended, and it's worth doing.

VR: Pamela writes, "Your discussion on *TWiV* recently about typhus made me realize that I don't really know what it is, how it's transmitted, et cetera. Of course, I can look around online, but it would be great to hear from you about some of these legendary ailments that are coming back to us. Last summer, six airport workers in Frankfurt, Germany, came down with malaria from a traveling mosquito, and two of them died. It was mentioned that they died because the medical staff didn't realize what disease they had. Even though airport

workers at Frankfurt had contracted malaria in the same way two or three years ago.

More recently, another traveling mosquito arrived at that airport and managed to travel five kilometers, where two unrelated people were infected with malaria, and one of them died as well. Tell us about typhus and dengue, dysentery, and maybe even the plague so that we can be forewarned. I've read many historical novels and descriptions of yellow fever epidemics, and death by tetanus are quite vivid. I'd rather we not go back to those days, but here we are."

DG: All right. This is fun. We'll finish off with a little bit of fun. There's different types of typhus. Usually, when people say typhus, they're referring to the epidemic louse-borne typhus, which is a Rickettsial disease. *Rickettsia prowazekii*. The vector, the reservoir, the body louse. This is probably stuff you saw in the trenches. Then there's actually a endemic typhus, also a Rickettsia, but this is *Rickettsia typhi*.

This is fleas as opposed to lice. Then there's scrub typhus. This is my favorite. This is the bacterium *Orientia tsutsugamushi.* That was actually something I saw a bit of when I was in India. A little girl, eschar under her chin. I made her lift her chin. I saw the eschar. She cried, but we got her better. I don't know. There actually are some other spotted fever, Queensland tick typhus, and things like that. Now, you also want to know about dysentery, right?

That's the bloody diarrhea, a bunch of different causes, bacterial and amoebic bloody diarrhea, and plague, right? We're still waiting to find out what's going on over there in Russia, but *Yersinia pestis*, the black plague. We see about a dozen cases in the American West every year. It's the fleas that are on those prairie dogs. When you're jogging along, and the prairie dogs run across your path, you try to really jump nice and high not to - When your cat starts coughing, the cat can spread the plague as well. All right, there you go, Pamela.

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

DG: Oh, thank you, and everyone, be safe.

[music]

[silence]

[01:01:45] [END OF AUDIO]