This Week in Virology

TWiV 1174 Clinical Update

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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 1174, recorded on December 12, 2024. I'm Vincent Racaniello, and you're listening to the podcast all about viruses. Joining me today from New York, Daniel Griffin.

Daniel Griffin: Hello, everyone.

VR: Welcome back from your travels.

DG: Thank you. I am just back from Tanzania. At the end, when we talk about no one is safe until everyone is safe, I'll talk a little bit about that trip. There's a lot going on, so let's jump right into it, Vincent. You're down there in Princeton, I guess.

VR: Yes, I'm down in Princeton working on the virology textbook.

DG: All right. Are people still going to read those? That's still going to be OK? [laughs]

VR: Probably the last one we're going to do.

DG: All right. Let me start off with a quotation. It's interesting. I think it's interesting. It's a quotation, but it's a song title from Wasis Diop. It is, *Everything is Never Quite Enough*. This song, actually, there was a *New York Times* piece where the title, the song is discussed, and it's a lot about the warning of the perils of modernizing African life and holding on to a dream. I'll leave a link into that. Quite a contrast to come back from some of the areas where I was in Tanzania with the Maasai, with the Hadza tribe, and then being back in New York.

A lot of comments from people. "What's going on, Dr. Griffin, in the DRC? Why didn't you talk about this?" I know a lot of people are disappointed that I did not discuss this last week, but

you know what? No news is actually no news. At the time, I really didn't have much news other than just there's a mystery disease. We're still trying to unravel this. I've been following this as best as I've been able with pretty limited access to the internet until really today when I got back from Tanzania.

A couple sources. Something that people may subscribe to is the ProMed service where you get these emails, and there'll be half a dozen or so different updates on things that are going on. We did get the ProMed most recently undiagnosed deaths, Democratic Republic of Congo, Congo logistics, second possible traveler case. Why are we still in the dark? Just reaching the epicenter of the outbreak of this disease, the affected area, can take about 48 hours by road from the capital, Kinshasa.

It's also the rainy season, which I was experiencing recently in Africa. That really slows progress getting to and from this site, getting testing kits, getting medical supplies. This is a forested part of the country. There's no laboratories in the province that can adequately test or diagnose these samples. Therefore, they're trying to get all these taking two to three days by car to get to Kinshasa.

We still do not know the cause. Over 400 people sick, dozens of deaths, lots of speculation. Could be malaria, a viral illness, or influenza. Then we hear about a returning traveler who came back, ended up in Cosenza, Italy, ill. Now, we know a little bit. I'm trying to tease something. According to the AP, most of the cases and deaths are in children under 14 in this remote area. Symptoms. Symptoms are fever, headache, cough, and anemia. Experts from the National Rapid Response Team, the WHO, have taken samples. Even more samples are being sent.

Now, we heard from the WHO that of the 12 initial samples collected, 10 tested positive for malaria. They say, although it's possible that more than one disease is involved. I want to point out that it's rainy season. Actually, you would not be surprised if a lot of people have positive malaria smears. A challenge in Africa, we've talked about this a lot on *This Week in Parasitism* is, is a person sick with malaria, or is a person sick because of malaria? I just want to point out that that really is not clinching the story for any of us.

VR: I was just going to say, Daniel, put on your *TWiP* hat. Fever, headache, cough, anemia. Anemia doesn't sound like anything in a viral illness, right?

DG: Not necessarily. A lot of these individuals, these are malnourished children. A lot of them are anemia at baseline. How much of this is a change in the level of the red blood cells? We're still in the dark. As we know more, we will definitely share that with you.

VR: Presumably, this returning traveler to Italy will get into a hospital and get tested. We'll find out what's going on with him.

DG: Apparently, they're already feeling better.

VR: OK.

[laughter]

DG: They really didn't get the mystery solved there yet for us. We will get more information. I'm not thinking this is just malaria because it does sound - Hundreds of people are ill. We've got a much higher than expected number of people dying. It's about 10% mortality that we're hearing so far. We'll see.

VR: You could have more than one illness, Daniel, right?

DG: Oh, my gosh. [chuckles] That is true. Vincent, I put a lot in for us to discuss today about polio. I was in Tanzania recently. We'll get back to details in that. I was with a group of doctors, most of them German-speaking, as in all of them except for myself. We're talking about polio.

First, I threw in the *MMWR*, "Progress Toward Poliomyelitis Eradication - Afghanistan, January 2023, September 2024." My subtitle, or lack thereof, where we read that since the global polio eradication initiative began in 1988, wild polio virus types 2 and 3 have been eradicated, and annual polio case numbers have decreased by greater than 99.9%. Wild polio virus type 1 transmission remains endemic in Afghanistan and Pakistan, two countries that share a 1,600-mile or 2,600-kilometer border.

During 2024 through September 30, Afghanistan reported 23 wild polio virus 1 cases, the highest number in four years. Polio virus vaccination campaign coverage improved markedly with house-to-house vaccination. However, we discussed before, local authorities have reinstated restrictions on house-to-house vaccine administration.

Just to give us some information on the numbers, we mentioned Afghanistan and Pakistan, I'll give you numbers on Afghanistan here, from the WHO, we just had an update this week. Since the last emergency committee meeting, 51 new wild polio virus 1 cases were reported, 17 from Afghanistan, 34 from Pakistan, bringing the total to 62 in 2024. This represents a 283% increase in paralytic cases in Afghanistan and a 550% increase in Pakistan compared to all of 2023. Is that all accurate so far, Vincent, according to these folks?

VR: It's accurate for Afghanistan and Pakistan, but in the rest of the world, there's large numbers of vaccine-derived type 2 poliovirus outbreaks. We're going to probably talk about that. That's really problematic.

DG: Wild polio types 2, wild polio type 3, gone? Do you trust that data?

VR: There are no more cases of polio caused by those that we know about. The assumption is the virus is gone, but I'm not sure you can even say that because you can't sample everywhere. As we'll see, the more we sample, the more we find the virus.

DG: We will move right into that. This is what triggered the conversation in Tanzania or Tanzania, depending who you're having pronounce that. Polio virus keeps popping up in European wastewater, perplexing and worrying scientists.

Now, this is an article that was in *Science,* and I have to say, I was a little curious about why the scientists were so perplexed and worried, [laughs] but maybe they don't listen to *TWiV.* I don't know. We read all the newly spotted isolates are vaccine-derived strains known as circulating vaccine-derived polio virus type 2. There's a little acronym for that, which are, I love this, spawned by the live attenuated virus used in the oral polio vaccine, OPV. They're

descended from the Zamfara strain, which emerged in Nigeria several years ago and has spread widely across Africa. The closest matches to the strain now circulating in Algeria, Guinea, and Mali.

This is from Robb Butler, the director of communicable diseases for the WHO European region. After detection of vaccine-derived polio virus type 2 in Barcelona in mid-September, we have had vaccine-derived polio virus type 2 detected in a sewage sample collected October in Warsaw, Poland.

Next, I like to say it showed up in Germany, but it was detected in Germany. The vaccine-derived polio was detected in Germany and samples collected over two-weeks' span in Munich, Cologne, Bonn, Hamburg, Dresden, Dusseldorf, Mainz, it's everywhere. Then wastewater samples in England's Leeds, London, and West Sussex in November tested positive. Just this week, Finland reported isolation of vaccine-derived polio type 2 in wastewater in Tampere.

Here, I think someone put in a little note, interesting that the, and this is little "c" circulating vaccine-derived polio virus 2, so VDPV2, was found in Tampere by Merja Roivainen, Tapani Hovi's wife, many years ago, and they were recombinant from immunocompromised individuals.

VR: Daniel, I don't know why these scientists are perplexed because Germany, the UK, Spain, they all use IPV, which does not protect the gut against infection. Someone comes into the country shedding vaccine-derived polio from an OPV, they will get infected, and they won't get polio because they're vaccinated with IPV, but the virus will end up in sewage. I can tell you can find this most likely in every country in the world, including the U.S., but here we don't look for it. [chuckles]

DG: I have to say, this is one of the best examples to reinforce the point you just brought up, is that vaccines protect you against disease, so you get your injectable polio virus vaccine, your chance of getting the disease, polio, is reduced almost to zero, basically, but it doesn't protect you against infection. That's really what we're seeing. You keep putting the oral polio vaccine out there, and people are going to shed that, and then people travel.

VR: That's the problem. OPV has not eradicated poliomyelitis. All it does is keep introducing virus into the environment, and then it circulates in Germany and Spain and the UK. People freak out. It's time to give up on OPV and switch to IPV globally, and we won't have this problem.

DG: All right. I'm going to leave in a link to the WHO polio page where they list a number of the different vaccine types. IPV, inactivated polio vaccine, or injected inactivated polio vaccine, giving protection against polio viruses type 1, 2, and 3. Trivalent oral polio vaccine, which protects against polio virus type 1, 2, 3. Following the OPV switch in April 2016, this trivalent, or TOPV, is no longer in use.

There's the bivalent polio vaccine, which protects against polio virus types 1 and 3, and then we've got the monovalent oral polio. We've got the OPV1, oral polio virus 1, the OPV2, and the OPV3. Those are all, little "m", monovalent OPV3. Then there also are some of these hexavalent and pentavalent vaccines that are available in Europe.

VR: Just remember, no OPV is licensed in the U.S. Why? Because it causes polio. We don't use it. The rest of the world shouldn't use it either by that logic.

DG: I'll also say, we're in a time where people are getting more and more sensitive to vaccines causing problems. Really, we need to move away from a vaccine that paralyzes a certain number of children. All right. Any other thoughts on polio, Vincent?

VR: We have a letter coming later, and we'll have more thoughts then.

DG: OK, let's do that. All right, avian flu. There's a lot going on. Hot off the press from CIDRAP, "Avian Flu Suspected in Cats that Drank Raw Milk as Virus Kills Animal at Arizona Zoo." I'll leave a link. We hear from LA County health officials that two cats developed symptoms after consuming milk from raw farms. Apparently not just people, Vincent, but they're giving the raw milk to their cats. The cats developed appetite loss, fever, neurological signs, and then both died after their symptoms worsened.

Testing revealed influenza A, which really is not common in cats. These are suspected H5 avian flu cases. There's some confirmatory tests that will be done. Officials noted that in earlier U.S. dairy farm outbreaks, cats were known to be infected after drinking raw milk from the infected cows.

Maricopa County announced that it is working with state and federal partners to respond to an avian flu outbreak affecting a number of animals at the Wildlife World Zoo near Phoenix. Animal deaths include a cheetah, a mountain lion, swamp hen, an Indian goose, and a kookaburra. An infected white tiger appears to be improving after treatment.

VR: Daniel, this is in response to people who say, "Is it OK if I drink raw milk?" or RFK Jr., who says, "Drink raw milk." Look what can happen. Don't be stupid.

DG: I'm going to leave in a link here, Vincent. I was in Tanzania listening to *TWiV 1173*: *Holy Cow! Convergent Evolution*. I wonder who came up with that title. Right at 25:09, discussion of the article, a human isolate of bovine H5N1 is transmissible and lethal in animal models.

This is a little disappointing, but also mpox, I remember when we were having this big outbreak and we're all excited. Even I love Rich Condit's take on this. "Mpox Trial Stops Enrollment after TPOXX," tecovirimat, "Fails to Speed Clade II Mpox Healing or Pain Relief." It was just this understanding or this idea that, oh, we all know tecovirimat works, but let's do a trial just because we want to really have some evidence-based guidance here.

We were leaving a link in. My friend, Jason Zucker, colleague at Columbia, MedPeds ID fellow, was helping with this trial. This was a study of tecovirimat, an antiviral for mpox, randomized control trial. After an interim analysis, really showed that this drug didn't speed lesion healing, didn't speed pain relief in folks that had mild to moderate clade II mpox that were on low risk for severe disease. The study sponsor, the NIAID and the TPOXX developer, Siga Technologies, basically halted this. No safety signals. were detected, but basically they looked at the data and said, "There's less than a 1% chance that the study is going to demonstrate efficacy if enrollment and follow-up were completed.

They also closed enrollment in an open-label study arm for patients at high risk for severe disease, which was not designed to estimate TPOXX's effectiveness, more of an access thing there. A little disappointing because I think a lot of the pox virologists were like, "Oh, obviously this works," and we're not really seeing the data here. I think I shared on an earlier *TWiV*, so far disappointing when it comes to the current clade 1B that we're seeing in the DRC in parts of sub-Saharan Africa.

VR: Remember, this drug was developed for smallpox, so didn't have to work for mpox. They were trying to find out if it did. It doesn't. It is disappointing, but we need to move on.

DG: All right, and move on we will, to flu. All right, influenza. It looks like flu activity is starting to rise in a lot of the Southern states. The data here for the flu map that I always share for the CDC is always a little bit old, so I've started also sharing right away a map looking at some wastewater data. There's wastewater data from the CDC, but I'm also going to share some other wastewater data as we move into RSV.

We are starting to see pretty high activity for flu down in Louisiana, out there in Arizona. California is in the moderate range. District Columbia is getting pretty hot. You got a bit going on there in Jersey, Vincent. It's in the moderate, almost high already. Then if you look at wastewater, you can actually see very high wastewater activity in California, and actually pretty high here in New York and some other spots. It looks like the flu is here just in time for everyone to come home for the December holidays and spread it to every other part of the country. That window is closing for you to get that flu vaccine, which will not keep you from getting infected, but can keep you from getting severe disease.

RSV. I'm going to use this new link for the wastewater because it's a little bit more up to date, and hopefully David will be putting these up for folks who are watching on YouTube. Following this new link from Wastewater SCAN, you can actually see we're getting pretty high activity for RSV in most of the country, except for the upper Midwest, so the North Dakota, Minnesota, Wisconsin, down to Missouri. It's still low, but then you look at the rest of the country and we're really seeing pretty high activity for RSV. The other map data we have, you can see a lot of activity, particularly very high down in the Southeast.

All right, COVID, Vincent. Interesting. It took us a little while to get to COVID this time because we had so much up front. Across the country, the only place, Maryland, is in that 2% to 4%. Everybody else is in the less than 2%. Now let's look at wastewater, because we've been watching this for a while. If we follow what we've always been following, that sort of up and down graph from the CDC, there's still a little bit behind us in time, and it still was looking really low.

If we go to the more up-to-date wastewater from wastewaterscan.org, we're actually seeing high activity through much of the country. Medium activity up here in the Northeast, low, basically, west Colorado, New Mexico, Wyoming, Montana, and west California. The rest of the country, we're actually starting to see high wastewater activity. What will be really interesting, and I think this is what we're hoping, is will this translate into increased hospitalizations, increased mortality? Or are we really getting to that point where our immune system is starting to protect us from disease?

I will move only a few new things for us to talk about here in the COVID realm. One is, I just wanted to revisit this topic again and just hammer this home. Last time, I brought up the article," Relative Effectiveness of Homologous Novavax-CoV2373 and BNT162b2 COVID-19 Vaccinations in South Korea," published in the journal *Vaccine.* This is basically head-to-head looking at Novavax versus the Pfizer-BioNTech vaccine in preventing SARS-CoV-2 infection, which we care a little less about, but we care about, and more importantly, severe COVID-19 disease during the Omicron variant dominance in South Korea.

What did they see? Head-to-head, you're going to compare Novavax to the Pfizer-BioNTech and you're going to look at day 180 post-vaccination, where we've seen-- particularly with the mRNA vaccines, starting to see a contraction in those antibody levels, so far, looking like you're losing a lot of that efficacy. When you get out to this time point, so six months out, you're seeing about a 10% reduction for laboratory-confirmed and about a 35% lower severe infection rate in the folks that got Novavax versus the mRNA vaccination.

I just want to say, this is the thing about science. You cannot hang your hat on just one study, because there's always this idea, "You told me here and then you told me there." There's also a link to the article, which looks at a number of other vaccine trials. It's a meta-analysis, and this was published back in February at *BMCID,* and that's, "Comparative Efficacy and Safety of COVID-19 Vaccines in Phase III Trials: A Network Meta-Analysis." As I said last time, Novavax is a great and an underutilized option for people with concerns about mRNA vaccines, less reactogenicity. We don't really know what the best vaccine is at this point, but we still have a lot to learn.

Pemgarda still out there as a prophylactic monoclonal treatment, and that's at every three-month passive antibody approach. When it comes to acute COVID, still same algorithm, number one, Paxlovid, and those who are at high risk of progression. As we've discussed some data that there may be some benefit for Long COVID, but remember, this is the compelling evidence-based recommendation for high-risk individuals, and this is decreasing the risk of progression to severe disease. Number two, remdesivir, which is a three-day IV. Molnupiravir, convalescent plasma. I think there was an updated FDA there. Then isolation guidance.

This is the article, which I figure you're going to like this one, Vincent, "Respiratory Equality: Let's Stop Playing Favorites with COVID-19 in the Healthcare Setting," published in *Infection Control & Hospital Epidemiology*. We read here that the CDC, HCP, that's healthcare provider, RTW, return-to-work guidance, last updated when? Late 2021. Come on, CDC. Continues to treat COVID-19 differently from other endemic RVIs, respiratory viral infections, with significant clinical impacts such as influenza and RSV. This exceptionalism causes healthcare provider confusion and poses barriers to practical healthcare delivery without enhancing patient safety. This also presents a lost opportunity to apply lessons learned during the COVID-19 pandemic regarding respiratory virus transmission in a more standard manner across RVI, respiratory viral infection, prevention. This letter provides insight into how leaders in healthcare epidemiology, including members of SHEA, COVID-19 return to work in this evolving landscape.

Now, the existing CDC guidance, as I mentioned, not updated since 2021, some places follow this, recommends a 10-day isolation period. Healthcare workers, you do the right thing, you get that test, you call up your employee health, you say, "Hey, I tested positive. What should

I do?" According to CDC, 10-day isolation, no work, no seeing patients. Now, you can return to work seven days after symptom onset if you're afebrile for 24 hours, you haven't taken any antipyretics, things like ibuprofen or Tylenol, symptomatically improved and negative test results within 48 hours of return to work, which is, as we've discussed, in no way evidence-based. [chuckles] The problem is the current healthcare provider return-to-work guidance contrasts with the CDC's updated community guidance from March 2024, which adopted a unified approach for all respiratory viral infections, including COVID-19, emphasizing, "Stay home while ill, followed by five days of additional protective measures, such as masking." A June 2023 survey found that only 16% of hospitals were following the CDC's healthcare provider return-to-work recommendation.

I don't know if the CDC folks are still listening to us anymore. You really got to update this. You can't just forget about it because it's sitting there and, well, 16% of hospitals are still following those guidelines. If anything, we're struggling to adequately staff the hospitals. I have to say, what, day eight, day nine of this isolation period, you're not at risk of transmitting this to your patients.

VR: I think this is a great article because they're right. Why should you treat COVID-19 different from flu and RSV? We've talked about this many times. You test positive for COVID, you stay home. Flu, RSV, "Eh, I'm going to work."

DG: Which is crazy. There may be a higher number of deaths still from COVID, but COVID, RSV, influenza, they continue to kill tens of thousands of folks here in the U.S. every year.

All right. COVID, the early inflammatory phase. Remember, for a lot of folks, you get a little better and this can be that bad week. Starts at the right time and the right patient at the right dose, anticoagulation, pulmonary support, maybe remdesivir if still in the right window, immune modulation. I'm going to close out with the late phase PASC/Long COVID. We have a link to the post-acute sequelae of COVID, also the number and the link for the Long COVID Treatment Center at Columbia, where you can schedule an inpatient or hopefully telehealth appointment if the telehealth access is renewed.

I'm going to say that's a call to people to reach out because I think a lot of people have really become accustomed to the convenience and the improved access with telehealth. That's going to expire here in New York in just about three weeks unless something is done.

Low- and middle-income countries, no one is safe until everyone is safe. Our listeners may know that I am just back from Tanzania. I was hanging out with our buddy, Kay Schaefer, Vincent, who joined us on *TWiP* one time. He, 30 years ago, started this program, Tropmedex, where he describes it as a working holiday where we travel around an international group of doctors, I have to say, by international meaning mostly German speakers, and go to a number of different healthcare settings.

We spent a day at a remote Maasai hospital. We had to go in four-by-four vehicles through the Ngorongoro Conservation Area. This is a very remote hospital that takes care of pretty much the Maasai. You see a lot of brucellosis because they're living intimately with the cattle. Cattle get repeatedly infected because it's a bacteria, so it's not something that gives you

lifelong immunity. The people keep getting repeatedly infected, so you don't see lifelong immunity there.

Saw the Hadza, which are a very subsistence-based group. We were mostly above the malaria zone, high enough in the mountains above the mosquitoes, which was nice for us. Then spent the last week in mostly the southern part of Zanzibar, where there have been some pretty major problems with cholera. I didn't throw this in this week, but maybe something we'll discuss on the *ID Puscast*. Starting to see increasing drug resistance in our cholera cases, and so we saw a gentleman there with presumed cholera, waiting for the test results to come back. They're usually using rapids, but they're out of the rapids. They've burned through those.

Really a great trip. A little bit of a shout-out, the importance of going out to these areas, making these connections, really the hardworking providers in these areas doing the best that they can. We will continue to support that work, but we're also going to support microbe.tv. This is Vincent's favorite time of the year. If you go to parasiteswithoutborders.com and click on Donate, we will double that, November, December, and January, up to a potential donation of $20,000 for *MicrobeTV.*

VR: It's time for your questions for Daniel. You can send yours to daniel@microbe.tv. Gail writes, "How often would you recommend that someone who is over 65 and immunosuppressed, but able to mount an adequate antibody response to vaccines get additional 2024/25 COVID vaccines?"

DG: Right now, our recommendation is every six months. The immunocompromised, you may want to actually think about adjusting that a little bit, depending upon the degree of immunosuppression, maybe even depending on the age. The other, we keep talking about, does it make sense to start thinking about using a protein-based, like a Novavax, maybe some more durability.

VR: If someone had a unique transitory side effect to 30% of the COVID mRNA vaccines they've had, Pfizer and Moderna, how likely do you think they'd get a similar side effect to the Novavax? In case this is relevant, the side effect had to do with sporadic swallowing issues, which started the night of the vaccines and lasted around two weeks to a month.

DG: This is a great question. I keep bringing this up, I was coming home today from Tanzania and driving past pharmacies, and you see in the window, Moderna vaccine, Pfizer-BioNTech vaccine. I'm like, "Where's the Novavax vaccine thing sticking in the window?" No, did not see a single one. They really have not done a great job of getting the word out.

Clearly, in the studies that we have, clearly in our experience, which is consistent with those studies, the reactogenicity with Novavax tends to be less. We've always been very clear about the fact that the reactogenicity, the side effects, the safety profile does not mean that vaccines are 100% safe. We do see side effects periodically, a certain percent of people will have adverse reactions, but Novavax tends to have the lowest.

VR: All right, brace yourself for this next one, Daniel.

DG: A lot of ivermectin I see.

VR: G. Baydon writes, "The following was sent to a healthy living WhatsApp group I follow. My eyebrows were slightly elevated while reading it, and I thought I'd send it to you for fact checking. As an ID doc, what's your take on these claims? Is there any evidence to back this up? I was especially interested in the point about disorders like ankylosing spondylitis and Crohn's disease, as from what I know from friends with the disorders, they're treated with chemo, not ivermectin." This is a list of 23 ways that ivermectin helps you and includes, did you know that it treats herpes simplex and herpes zoster, Daniel?

DG: How would that work, Vincent?

VR: [chuckles] It improves the immunity of cancer patients. It helps traumatic and orthopedic injuries. It strengthens muscles and has no side effects like corticosteroids. It's anti-neoplastic, it's anti-microbial. It regenerates nerves, it regulates glucose, insulin, cholesterol, liver fat. The only thing that I can see is right, and you can correct me, number 12, ivermectin is anti-parasitic. Daniel, do any of these look accurate?

DG: It's pretty amazing. I'm looking through, it seems like it does everything. I'm trying to figure out if it's something that if you take it, it'll prevent conflicts with the in-laws over the holidays, and I didn't see that it does that. It's absurd. This is like the snake oil. This is like, they have found a magical drug that treats anything you can think of.

VR: Listen to this one point. It treats coronavirus. Unproven efficacy is not of ivermectin, but of vaccines. How many clinical trials have we talked about here about the efficacy of COVID vaccines preventing disease? This is an ignorant statement, right?

DG: Science is nothing mysterious. Basically, we just ask, we say, "Hey, does this work?" Which seems like a very valid question and not asking for your anecdotes. I was on the island of Zanzibar just recently. It's really interesting because when I learned about the spice trade, I was under this impression that it - I was basically miseducated, Vincent. It was, "Oh, well, see, when we had the spice trade, then suddenly your meat and your fish wouldn't go bad because they could salt it." I'm like, "I don't think that's really what was going on."

Now I learn that a lot of the spice trade was based upon the idea that these spices were felt to be great treatments for all kinds of maladies. There was the idea that there was a certain spice that you could buy in Zanzibar that would cure the plague. You can imagine a third of Europe ends up dying from the plague, so there's this massive appetite to get this. Here we are in 2024 and we're still being sold snake oil. Now the snake oil, it's not nutmeg, it's ivermectin. A lot of it is this challenge. You really got to ask the question, does it work?

My wife was saying like, "Oh, well, it was very obvious that nutmeg would not work to cure the plague." I said, "Actually, think about it this way. The people that could afford nutmeg tended to be wealthier, tended to have better nutrition and actually were less likely to die of plague. The people who could not afford the nutmeg tended to be less economically advantaged, tended to not be eating as good a diet, tended to be malnourished and have a weaker immune system. If you looked around, it seemed like the people eating nutmeg were doing better."

You have to be careful and not just string a bunch of anecdotes together and really ask these questions. All the stuff I'm looking here, "Ivermectin protects the liver exposed to insecticides," they're just making stuff up.

VR: Ivermectin has been tested as an antiparasitic. It works, right?

DG: It does. That's what it's great for.

VR: It was tested as an anti-COVID and it didn't work, right?

DG: Yes, we looked. We were not conspiring to see ivermectin, fail. Actually it would have been great for me because I have to say prior to COVID, prior to 2019 in the U.S., I was one of the probably most prescribers of ivermectin because I actually treat people who have parasites. It would have been great. Just think of all the money, Vincent, I could have made traveling the world talking about ivermectin as a cure for COVID if it was true, but I will not claim it's a cure for COVID if it's not true.

VR: All right. Muhammed writes, "I hope this email finds you in good health. I'm Muhammed. I'm from Lahore, Pakistan. I enjoy *TWiV.* Provides invaluable information on recent advancement in the field of virology research and clinical cases related to viral infections across the world. I just have a simple question about polio vaccine. Since OPV is no longer used in the U.S., our government is still administering this vaccine to children. Why should children be constantly vaccinated against polio virus? Why they receive multiple shots if it's live-attenuated, why a single dose cannot provide lifelong immunity?"

DG: Vincent, this seems like it's right up your alley. I have to say I was in Zanzibar and it is amazing how many doses of OPV these kids are getting. They're getting a shot, meaning these little drops in the mouth at birth. They get half a dozen doses of the OPV. What's going on?

VR: All right. Let's go into this. There are three serotypes of polio, 1, 2, and 3. Both IPV and OPV used to be all three. In 2015, IPV was added to routine childhood vaccination schedule in preparation for the global switch from trivalent OPV to bivalent, which only includes type 1 and 3. Today, the routine childhood vaccination schedule against polio in Pakistan is one IPV and at least one OPV. However, Pakistan is one of the countries in which wild type polio 1 is endemic. Consequently, additional OPV doses are used in supplemental immunization activities.

Originally, both vaccines, IPV and OPV, were developed as monovalent vaccines, meaning you were given three different shots to get an immune response against each serotype. Development of the trivalent vaccine, which has each of the three serotypes, occurred later because it was not practical to vaccinate children with three different shots for the same virus. However, the immunogenicity of the serotypes is not equivalent.

Type 2 is more immunogenic, which is defined as type 2 immune interference than type 1 or 3, meaning that if given one shot of trivalent IPV or OPV and asking, are neutralizing antibodies against type 1, 2, and 3 elicited, the answer would be no. The antibody response against type 2 would dominate. Consequently, to get a detectable antibody response against the serotypes, you have to get more than one vaccine. This is called vaccine take or

seroconversion. It's influenced by human genetics and the physical environment that you live in.

Many vaccine guidelines are based upon the temporal climate and sanitation public health conditions of the U.S., but this is not right for the rest of the world. OPV take is less efficient in warmer climates and those in which public health conditions are compromised. Consequently, additional doses of the vaccine are needed for high levels of seroconversion. An example of this is how India achieved "virus-free" status. Children were given numerous doses greater than four of OPV for many years. Once the differences between the physical environment in the U.S. and India were recognized and India switched to IPV, was the country able to achieve virus-free status.

Jacob Johns was the architect of the eradication program in India. While it's believed that polio infection and vaccination confer lifelong immunity, those studies, the Inuits, Native Americans studied in the '20s and '40s, were done when the virus was circulating. It could be acting like a boost. Since most polio infections are asymptomatic and there are reports of reinfection of individuals by the same serotype in the 30s and 50s, it's not clear that you have lifelong immunity against infection. What you have is lifelong protection against virus neuroinvasion and the development of paralytic polio.

DG: Interesting. Here in the U.S., you get your IPV, so your inactivated polio virus vaccine series, as a kid. In most cases, that's the end of it. Now, in some parts of Europe, including, this was this recent change in Germany, they're recommending you get an IPV update every 10 years. It's this idea that you're not getting any kind of environmental boost, so you're not seeing -

VR: The situation has changed with polio. There's much less virus circulating, at least we think. Susan writes, "I was about to get the current updated vaccine when I got sick. I got COVID 17 days ago, took Paxlovid, now I'm testing negative. I have some symptoms, sore throat, productive cough, fatigue, no fever. I have a visit scheduled with family in two weeks, including a 10-month infant. Do I put them at risk? Should I take the current vaccine now or wait three months? Is it best to cancel the visit and avoid contact with family members?"

DG: OK. Let's see. I'm looking through, is there any kind of immune compromise or a kidney transplant, anything like that I'm not seeing? Seventeen days ago, you're not contagious, so you are not a risk to your friends and family. Go enjoy your time with them. You should wait three months from when you got COVID before you get your booster. Pretty straightforward.

VR: Rich writes, "After listening to your comment about nasal antihistamines, what is your opinion of using nasal neomycin for prevention of respiratory viral infections?"

[laughter]

DG: All right. That really is, I got to say, a reference to the Akiko publication that we talked about, where they did those studies where, you put neomycin - Initially, the earlier studies were neomycin in the vagina, and then there's, put neomycin up your nose, and basically, it's going to trigger a bit of an inflammatory response. I'm not recommending that. Also, at this point, I'm not sure what to do with the nasal antihistamines, but thank you for your questions.

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

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

[music]

[00:49:25] [END OF AUDIO]