

This Week in Virology

TWiV 590: COVID-19 and coronavirus update – we have mail

Hosts: Vincent Racaniello, Rich Condit, and Kathy Spindler
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VR: From MicrobeTV, this is TWiV - This Week in Virology, episode 590 recorded on March 7, 2020. I'm Vincent Racaniello and you're listening to the podcast all about viruses. Joining me today from Southeastern Michigan, Kathy Spindler.

KS: Hi, everybody. Here, it's a beautiful sunny blue sky day. I'm trying to get the temperature. 38°C, feels like 33°F, that would be - I'm using my Norwegian weather app for that.

RC: I'm going to guess 3-4 degrees?

KS: 4 - you got it. Yep.

VR: And joining us from Austin, Texas, Rich Condit.

RC: Hi, everybody. How ya doin'?

VR: SXSW - does that happen in Austin?

RC: Yeah, it's been cancelled.

VR: You don't usually go, right?

RC: No, all the locals leave town. (laughs)

VR: What is it? What kind of a festival is it? Is it a music festival?

RC: It's supposed to be music and art. It's been going on for 32 years. It runs for a week or ten days.

VR: When I came in November, something was going on. That was something different?

RC: There's always something going on. So this draws maybe 150,000-200,000 people. Sometimes more. And there's been a lot of discussion in the local news as to whether to continue it, or whether to hold it this year, and it starts like next week. Some people spend all year preparing for this thing. People have millions of dollars invested in making it happen, but big participants were dropping out and they just decided, ya know, err on the side of caution and cancel it so that's what they've done.

VR: Yeah, a lot of things have been canceled. Tech conferences, meetings, and I think it's a good idea, not to have a lot of people together. I have to say I was just in Ohio for a brief two-

day trip - and I'm apprehensive sitting on the plane because it's recirculation of air. Not that I'm scared, but it's recirculation of air.

KS: Actually, It's not really recirculation. It's fresh air on the plane. It's not all recirculated and they're filtering it.

VR: I think it also depends on the plane too. The newer ones are better than the older ones. The 787 is really good with air. This is out of my wheelhouse so I shouldn't talk about it, right? People get mad about it. I still felt apprehensive, but then in Ohio they have no cases yet and they said they're not even testing but the thing is they have 65k students on campus but they're all leaving for this week because of spring break and then coming back in a week, and they're going all over the place. This is going to be repeated many times on campuses.

KS: Yeah ours are all coming back today and tomorrow.

VR: Do you have cases yet in Michigan?

KS: No cases that we know of yet.

VR: So this obviously is a rapidly changing situation. Here we are on a Saturday, and it's not the normal TWiV. I was away, and I would have posted something different on Sunday but we're getting a lot of email so Kathy and Rich agreed to join me, because you don't want me just talking by myself. That would be weird. That's never happened on TWiV. The numbers we give are always going to be out of date by the time you hear this. But, we passed 100,000 total cases which is quite remarkable. Back in January, we wondered if this was going to go anywhere, right? When we looked at the first 41 cases in Wuhan. A lot of universities are closing... University of Washington, right? I heard Stanford is going to close. Twenty US states have cases. Washington and California have the highest. New York has 33. We have a case in I think New Rochelle, and that individual has been admitted to Columbia and now his family has been tested positive, and all their contacts are being monitored. If you hear Daniel Griffin this past week, he said that's all that's been announced, so it sounds like they're investigating many more. The US total though is 343, however there are lots of incubations going on. I'm sure it's going to go much higher. What do we think here? Any comments?

RC: I'm totally distracted here. I just sent you an email that's a chain that I've been having with Stacy Schultz-Cherry and it's absolutely fascinating. I was going to mention earlier that my son lives in Kirland, where the first gaggle of deaths and still most of them, are in the US. And my wife and I were supposed to travel to Kirkland this weekend, and you know, I was all set to go. But we decided to cancel, once again, err on the side of caution. My son, I think, justifiably, didn't feel comfortable having his aging parents around at the epicenter. Plus the fact that the area is kind of on alert, in a way, at least everybody's radar is humming, and so it wouldn't have been as comfortable a visit as could have been otherwise. They're on a "work from home" thing. Some of the schools are closed. They're kind of, like I said, on alert.

VR: It's nice they were concerned about you guys.

RC: Yeah - so much for all my bravado about how I'd go to Wuhan.

VR: You still might go, they have many fewer cases now. They still have 100 or 200 a day in China, I believe. I'd still go. In fact, in Ohio State, one of my hosts, Shan Lu Lu, who Kathy

knows, said they're having some virology meeting in Wuhan in 2021 and he would invite me, so I will hopefully go and talk with some of the principals here involved in this. Seems to be connected. That would be cool. Someone called me last night at the airport and said, "I have a plan to go to the UK for four weeks" and I said "Go. If you wanna go, go. The worst thing is that could happen is you'd be stuck there and that's not a bad place to be stuck". I would go. I would just be careful. I came into the office today and someone put two facemasks on my desk. N95's. They're in a ziploc bag. I haven't worn them. Here at Columbia, there's been cases. We have 33 cases in New York. Over 4,000 New Yorkers are currently being monitored. I think there are going to be a lot of cases here in New York City. A couple of other things. Let me just go through - two weeks ago, there was a joint WHO China report - a very long document, which we'll put a link for. But if you search WHO Joint China Commission on Coronavirus disease, you'll find it. Parts of it are good. It has some good summaries of what are happening so far. Parts of it are very party-like. "We have to confront this all together. Blah blah blah." It sounds more like China than WHO. There's lots of stuff about the disease here. As we said before, 85% of infections are mild or moderate, 15% are severe, 5% are critical. And this is interesting, progression - about 10-15% of mild-moderate cases become severe, 15-20% of severe become critical, and then we have some average times.

KC: Yeah the epidemic curve by system onset and date of report. So they have nice curves on that.

VR: Yeah the curves in the report are very interesting because at the beginning in January, Wuhan was very high and other places were lower and then they all reduced over time about a month later where they're very low and that just shows a number of things, that Wuhan was overwhelmed and also, they say in the report that they learned how to care for the patients as well. Okay, average times from exposure to symptom onset - 5 days after infection. From symptoms to recovery: for mild cases is 2 weeks, from symptoms to recovery for severe cases is 3-6 weeks, and symptom onset to death is 2-8 weeks. I think what is interesting is the symptoms - what can you expect? Typical signs and symptoms: fever (88%), dry cough (68%), fatigue (38%), sputum production (33%), shortness of breath (18%), sore throat (13%), headache (13%), myalgia or arthralgia (15%), chills (11%), nausea/vomiting (5%), nasal congestion (5%), diarrhea (3.7%), hemoptysis (0.9%), conjunctival congestion (0.8%). So the major ones are fever and dry cough.

KS: The symptoms that you talked about, time from onset of symptoms and so-forth also are repeated in the NY Times article, "The coronavirus by the numbers" that we have the link for that's a mathematician from Britain - it's very well-written and in fact, I saw David Quammen tweet about it and said, "This is really good. I'm going to read it again." The mathematician's name is Adam Kucharski.

VR: I know him. I met him in Glasgow. I did a TWiV with him actually.

KS: So, this article is really good. It's a question-and-answer format.

VR: Truly asymptomatic infection is unknown without serology, so right now we're guessing, but it appears to be a certain proportion, about 11%. Rare, using molecular testing is <1%, because I think up until now they haven't tested a lot of people just randomly. Just symptomatic people, which of course, is the opposite, and an estimated 70% of "asymptomatic" cases at time of report soon progressed to disease. Asymptomatic infections could be the infectious source but transmission capability weaker than patients with symptoms.

RC: Like as we've said, it's a numbers game.

VR: You're shedding less virus, so yeah. There have been two outbreaks in China with the first case of asymptomatic infection. Children tend to have milder disease, as we know. Virus shedding is highest early in the course of disease vs. SARS shedding which peaks at least 10 days post-onset. As Ralph said, at the peak of disease for SARS. Virus shedding can occur in the 2-4 days prior to symptom onset, and again, whether or not that transmits depends on how much you're shedding. Virus can be isolated from stool but there's no epidemiologic evidence of fecal-oral transmission. Virus shedding usually continues for 7-12 days in mild-moderate days and for over 2 weeks in severe cases. Patients who recover can be PCR-positive after symptoms resolve. Note: PCR positive. No infectious virus. Prospective studies of recovered patients need to be done to determine if virus can be isolated. Exactly. They can get virus RNA from urine, blood, and tear fluid. PCR again. Good stuff.

RC: RNA is like DNA. It's really a problem. It's everywhere.

KS: Right.

VR: So then there are a series of articles here where I think there have been some claims about different circulating lineages and what that means. Are you on this, Kathy?

KS: Right, so there was an article that I first saw in the LA times. Chinese scientists say 2nd coronavirus strain is more dangerous but in the article there's a link to virological.org and we talked about another article posted there a couple weeks ago and they really debunk this and they think this Chinese article about a second coronavirus should be retracted. It has two of the key claims that are reached by a misunderstanding and overinterpretation of data and an additional analysis suffers from methodological limitations, so this long thing on virological.org goes into the reasons why there is no real evidence for two different strains - a more severe strain and a less severe strain.

RC: it also provides a nice summary of the sort of variation in the sequence that's being observed in the virus over time.

VR: It's a good article. We'll put in a link. It's worth reading. But as everyone should know, these RNA viruses, every replication cycle, they sustain mutations in their genomes and the lethal ones are gone, the viruses don't reproduce but some of them stay and if they're neutral, they remain, and so they can be characteristic. And so the virus introduced into the WA area, it's a single introduction and it's spread and you can tell that because it has a unique set of mutations compared to the Chinese isolate, but it doesn't mean anything biologically. It's just markers, right?

RC: And the markers are really interesting though because they give you insight - the insight that I got from observing what came out of the Washington cases from looking at the sequence of the viruses they concluded that in fact the virus had been circulating for some time and they can even get a VERY rough estimate of how many cases might be out there based on the variation in sequence and the time at which the disease first showed up in a person.

VR: And I think there's some emails later about this. People are concerned that... and people suggest in these papers, at least the one here that we're being critical of that you know, it could

have evolved to be more virulent or more transmissible and there's no evidence of that whatsoever.

RC: This is the kind of thing that just won't go away.

VR: Oh it doesn't go away. Every outbreak, it comes back.

RC: And there's no evidence and people have looked at this. We've gone over this for several - Zika, Ebola, you know, where there has been a variation and people point to a particular variation and they say, "You know, this is going to make it more virulent or something" and then the experiments ultimately get done and no. It hasn't made a difference.

VR: Also, the issue of increased transmissibility. I think this virus is very transmissible as it is, and I think the mutations that made it effectively transmissible among humans which happened very early on, either in animals or in humans, early on before we knew about it. They're done. And it's going to be hard to know what they were, and you know, MERS-CoV has never acquired those high transmissibility changes and it keeps fizzling out and then you have another reintroduction from camels but this particular SARS-CoV-2 sustained them probably early on and it's a very good transmitter. It doesn't need to get better, at least from my anthropocentric view. We never really know what viruses are selected by, but I don't think there's any evidence and it's very hard to get the evidence. That paper tells you what you need to prove that mutations are doing something phenotypically. It's very hard to get that.

RC: It has occurred to me that people who don't think about this stuff everyday might be a little confused by this discussion relative to the discussion that goes on all the time relative to variation in influenza virus strains and new strains coming up and having to change the vaccine and stuff, but that's different. That's variation in the influenza virus that makes it evade the existing immunity, okay? And those sorts of variations arise, so you get circulation of viruses that you don't have as good an immune response to, but that's different than a virus generating mutations that makes it more virulent, so a different story.

VR: Kathy, you put something here about animal models?

KS: Right, so there's an article in Stat about the difficulties in studying the virus in animals and that's important of course for antiviral and vaccine testing and it describes a little bit about the history with SARS - that passaging could infect run-of-the-mill mice but only to a limited extent, so there were some developments of particular strains of mice - Stanley Perelman's lab engineered some mice to have the receptor that SARS uses, and they kept that going for a long time and then it seemed like a waste of resources because he said, "we kept it for an extra five years and we're not using these mice - you have to propagate them - there's animal facility costs - you have to genotype them so there's experiments you have to do on them, so they sent them to Jackson labs to cryopreserve. And then Lisa Gralinski is the person quoted and she's working in Ralph Barric's lab. They were preparing to do the same thing with mice leftover from SARS work and they were about a week away from killing all of them and cryopreserving them also, but they decided to keep the mice going and breed them up. And at Jackson labs, they're breeding up the ones that Stanley Perlman had cryopreserved there, so they'll have those mice but whether those will be useful for this SARS-CoV-2 remains to be seen. But it's difficult because you can't just start infecting animals and expect to get good results. You have to show that the animals are really productively infected.

VR: And then we have a numbers paper.

KS: Yeah, it's one that Lisa Gralinski mentioned on Twitter as being useful because it has some important information about co-morbidities and symptoms and lab results. Then I think one of the readers sent in a question that has a paper that I think maybe it's parallel but maybe with a different set of studies - this one shows people that died vs people that were discharged, and the age distribution, interval from onset to symptoms, and the laboratory parameters for the outcomes, so they measured different clinical things like IL-6, c-reactive protein, myoglobin, cardiac troponin, things like that. It's just a short little paper but people are starting to put out this sort of thing based on actual infected patients.

VR: So this is clinical predictors of mortality due to COVID-19? I'll put a link to that. And then we have something from Rich. NY Times article?

RC: The NY Times article that I think Kathy has already mentioned, but I think this is a great article that I think we should link to as well by Adam Kucharski, it's about epidemiology. He's a mathematician... how you calculate case fatality rate and what it means, and how you calculate reproductive rate, and what it means, and it's just very well-written if you want to understand all these. I just recommend it for that. One of the important bottom lines for me is that - this is from a couple of days ago so it's pretty current, he says his bottom line was: his best guess is that CFR in reality once all is said and done is somewhere between 0.5-2.0%. That's a very broad range but I think it's good to have that expert...

VR: And that's crude overall CFR...

RC: Crude overall, between 0.5-2.0% so I appreciated that. That would make it worse than seasonal flu. So I think that's what we're seeing. Granted, this is an average. And he goes over how it differs based on co-morbidities and age and etc.

VR: And depending on what country you're in. Look at South Korea - they're at 0.6%. They have 7k cases and 42 deaths... and if you compare to Iran, they have 4,700 cases with 124 deaths, which is much higher. So it depends how old you are, where you are, how good the health care is, etc.

RC: And a lot of those things that we're seeing now have to do with where it's breaking out and how it's being reported and how it's being tested, so we're not going to have a real good grip on this until long after it's over.

VR: By the way, when's it going to be over? Is this going to be a seasonal thing?

KS: Well, we have some evidence from pre-SARS, the coronaviruses that infect humans evidently according to Stanely Perelman do show seasonality, like a lot of other respiratory viruses, but we really don't know for this virus, so we just don't know if it's going to lessen in the summertime or not.

VR: And of course the original SARS went away after some months and never came back so we have no idea with that one either. We're in new territory.

KS: Another thing from this article from the NY Times with Adam Kucharski is how to know whether there's already community spread and he says that if the first case in the area is a

death or a severe case, that suggests that you had a lot of community transmission already. Suppose you just use a 1% fatality rate, then that means you probably had about 100 cases three weeks ago, which is when the person that's now the first case in an area has died. And when they got it was probably about three weeks ago, so in that subsequent three weeks that number could well have doubled, then doubled, then doubled again so you're looking at maybe 500-1,000 cases if there's 1 death, so he just does a lot of nice numerical calculations like that that seem logical and well-reasoned.

VR: Two more things and then we can get on to Stacy's email, Rich, in a moment. I just wanna mention two things. First off, the US has given 8.3b dollars to this coronavirus effort, a lot of which is going to public health measures and CDC which is great, 800 million is going to NIH for research and you know, if you work on coronaviruses, you can get some of that. If you work on something that is related to that, that's helpful. I heard at Ohio State that even though there are guidelines on who can apply, they're a little bit squishy. You can call your program officer and say, "hey, we have this cool thing that might be applicable" and they may say yes, so ya know, do that. I think this is great, however, it's like, after the horse has run out of the barn, we should be sustained high research support all the time and we would have been prepared for this. We would have coronavirus antivirals which are totally possible to have a broadly acting corona antiviral but that's the way it goes, I suppose. It's unfortunate. Now, Rich, tell us about Stacy.

RC: So, just this morning, I had an email exchange with Stacey Schultz-Cherry who's a flu expert at St. Jude's in Memphis. Kathy, I forgot that you brought this up a couple of weeks ago. Independently, my wife the other day was wondering... I was talking about how it's hard to tell whether the steps that are being taken, quarantine, travel restrictions, all the hand washing and stuff, what sort of impact it has on the spread of this and my wife says, "well could you monitor other diseases and could they serve as a control for this?" and so just a couple hours ago, I emailed Stacy and I said, "is it possible that flu and other infectious disease monitoring could serve as a control to understand the impact of CoV mitigation measures in controlling spread?" and she writes back right away and says, "Fantastic suggestion but could be difficult to interpret the data since we're at the natural end of flu season" and then wrote me back - I love it, this is the modern world just a few minutes later and says, "Discussed with my WhatsApp group of virology and epidemiology nerd friends and one of them gave me this new info from Hong Kong." And she inserts a chart. "Definitely highlights the measures taken to control CoV are not surprisingly helping with other respiratory diseases. Would be a great TWiV story entitled, 'Wash your damn hands!'" So I've just been looking at this chart and it's interesting. It's from Hong Kong - it's weekly positive tests for a wide variety of infectious diseases going back to the first week of 2019 and up through week 8, the end of February 2020. And sure enough, from what I can see, from week like 5-6, so that's the beginning to the end of February relative to the previous year, the reporting of several infectious diseases absolutely tanks. The flu crashes weeks earlier than it would have ordinarily and really impressive is rhinovirus- that crashes. Parainfluenza - that crashes. The others don't have real high prevalence to start with so it's a little harder to see but everything just goes down to baseline.

KS: And it's really useful because you can compare it to Week 8 from 2019, for example, what the levels were then, and how long it takes before they tail off, or not even tail off in the case of rhinovirus and enterovirus.

RC: Really interesting.

VR: Well so I guess the result is that we all need to stay home, then, right?

KS: Well, no... Or wash your hands.

RC: Wash your hands. Wash your damn hands! (laughs)

VR: That's pretty neat. Now of course those restriction measures there probably aren't gonna happen here, but the hand washing we could do.

RC: Well this was Hong Kong.

VR: Hong Kong didn't have much restriction.

RC: I don't know. I certainly don't recall reading as much about it.

VR: That was my initial impression. That's pretty cool. Speaking of hand washing, we have an e-mail here from Maxim, who writes "Dear TWIV team, As pretty much everyone knows, cleaning your hands regularly with soap or hand sanitizer is as far as I understand, the best way to prevent yourself from catching COVID-19 and a plethora of other diseases. However, I was wondering if bar soap is as effective as liquid soap in killing viruses that may be on your hands, especially in the context of the COVID-19 outbreak. I also wonder if bar soap "retains" microbes and viruses after washing your hands with it. The preface of this question is that my father only uses bar soap and refuses to use liquid soap, a remnant of him growing up in the Soviet Union where liquid soap was a rarity, and his stubbornness in regard to change. Right now the weather here in the Region of Valencia, Spain is a sunny 22°C / 72°F." I do not know about liquid soap. I haven't seen any studies comparing them. I'm sure they're out there.

KS: So, I pasted in a couple of things here about bar soap in particular, which really surprised me that they looked at the microbial content of 14 bars of soap in a household setting. They had some wet ones in one bathroom and dry ones in another bathroom, and they isolated *Staphylococcus* and *Enterobacteriaceae* and I wasn't able to get the digital version for this yet, even though it's a journal that the U of M has, and then another test of bar soap in dental clinics and they tested and found each bar soap harbored 2-5 different genera of microorganisms. Heavily used soap had more, and it was a mixed flora of Gram+, Gram-, aerobes, and anaerobes, so there are all kinds of bacteria and fungi, so knock me over with a feather. I had no idea that stuff could live on bar soap.

VR: These are bacteria and I guess there's some viruses but I guess they don't look at viruses. People say "wash your hands - it has a great effect" so how is that compatible with these studies?

KS: It's that it's mostly the mechanical and the water and the flushing. It's the soap to some extent but also the mechanics of doing it.

VR: As far as liquid soap, you didn't find anything?

KS: I didn't. I think I googled bar soap vs. liquid soap and then I got distracted and then I didn't pursue that.

VR: Maybe someone can help us out with that next time...

RC: This, by the way, is TWiV in real-time here. There's a lot of stuff happening as we record. This is great.

VR: Alright, Kathy, wanna take the next one?

KS: Sure. Patty Michelle writes, "Please always differentiate in your conversations between facemasks (surgical masks and N95 masks. There have been many recommendations that N95's do protect the wearer. Here in the US, 3M N95 masks are available before COVID-19 even in Home Depot and hardware stores for protection against dust. So the technology for good SARS-like protection has been widely and cheaply disseminated. Could this potentially have an impact on epidemics? Viven the numbers game, I should think so. This is important given the need to reasonably conserve the global economic output"

VR: I would say to preserve people's lives.

KS: So, then, Vincent, you put in something here about "At least for influenza, they're equally preventative" meaning face masks vs N95 masks.

VR: Yeah I found a study of nurses in a hospital where they had some N95 and some wear surgical masks and the rate of acquiring influenza was the same in both groups, but it was protective, so at least that one study, you know, says that they're both effective. The real key here is, "how does a surgical mask do?" And you know...

KS: Well that's what they're saying, is that a face mask is basically a surgical mask. That's what they're talking about.

VR: Right, so the N95's, the ones that are sitting on my desk, they're solid. Surgical masks are the floppy things, but this is a molded thing. It's solid. It does have a metal band over the nose that you can fit to your face. There are studies that compare them and the ones I've looked at say they're comparable. The real issue is overall, how do they work?

KS: So when you say they're comparable - comparable to what? What is comparable to what?

VR: N95 is comparable to surgical mask in the rate of acquisition of influenza infection, so that's one study I saw. However, they didn't have a control group who wore nothing, which I would like to know. They just said, "20% in both wearers acquired influenza infection," and so all that says is that the conclusion is that one is not inferior to the other.

KS: Well, and you said that was in a hospital setting with nurses, right? So there, they are probably trained even in how to take off a surgical mask so that they don't contaminate themselves and they don't lift it up and eat for a while and then put it back on, because that would go against all of the other advice from CDC and the WHO that the surgical masks aren't going to do anything to protect a wearer. They are going to be more important for protecting the population from an infected person who is sneezing and coughing.

VR: That's what Daniel said the other day, right? So I've looked for surgical mask trials, and there are plenty for influenza, and one I saw where they had identified families where one kid had confirmed influenza and then they had the family wear face masks and they looked at the rate of acquisition of influenza in the family, and they didn't wear it all the time but even with

wearing it some of the time - in some cases, the kid was sleeping in the same room as the adult. It was a 70-80% reduction in transmission. And they note that this is only in a family setting and it could be really different outside in a community setting, so... and so, you know, I really don't know. And there, you're right. The parents are wearing the face masks and they're being protected from acquiring it from the kid. The kid wasn't wearing the face mask. I think we just don't know and there aren't a lot of well controlled studies. If you want to wear a face mask and as long as you do it properly, I don't see that it can harm you, right?

KS: Right. But it might give you a false sense of security.

VR: Right. For sure. What we said last time, I think, I'm sorry - one more thing, Rich, I think it will stop you from touching your eyes and nose more, and mouth, and maybe that would help too. That's part of the protection. Sorry Rich. Go ahead.

RC: One of the things that comes up is that the rush on facemasks makes them less available for the people who really need them in the healthcare industry.

VR: Yep. Can you take the next one, Rich?

RC: Keanu writes, "Thank you very much for your highly educational podcast. They are utterly invaluable. My 12-year-old daughter, Melanie, who listens to your programs regularly, has a question for you." Far out. "Greetings!" This is Melanie, talking, I guess. "I would like to know if there are any projections as to the probability rate of mutation of SARS-CoV-2. Will most infected humans who recover develop immunity to this virus for the near future, or is it predicted that the virus mutates so rapidly that immunity even for the near future is not likely? In such a scenario, would a previously SARS-CoV-2-infected person get reinfected in the near future? Thank you very much in advance for reviewing my question." Great question, Keanu. You are right on the ball.

VR: Listening to TWiV! Way to go!

RC: This is great stuff! You guys may have more insight into this than I do, but I don't believe that there is any evidence that in coronaviruses there is the type of variation that would cause it to evade immunity, and my sense is that we will develop immunity to this and it will be a lasting immunity to this virus and I don't expect this thing to behave like flu and come up with another related strain that can evade that immunity. Am I on the ball here?

VR: Yeah, I agree. I agree.

RC: Great question. And from a 12-year-old. I love it.

KS: And to add on to that, even though RNA viruses do have a lot of mutations, as Vincent said earlier, most of them are gonna be lethal and many are gonna be neutral but the idea that a virus could mutate so rapidly that immunity for the near future wouldn't exist - it's not likely to happen that way.

RC: And then there's another whole podcast about the fact that although it's an RNA virus, coronaviruses have an unusually large RNA genome, which they can do because they have a proofreading function for copying the genome, so it's lower than the normal RNA virus mutation rate. Did I get that right?

VR: Yep, they do have a proofreader. Yep. We've talked about that in some episodes in the past. Now one of the things I'm thinking is that I should go back and I should clip out all the corona discussions. Gosh, it would take so long. I would love to be able to do it. I wish I could. Oh, someone volunteered to transcribe the last two TWiV's so that's cool. The Griffin and the one that Rich and I did, so that'll be out soon. Matt writes, "Thanks for the superior podcast," which is warmly appreciated. "It's a glorious pristine morning in these verdant Northern Californian foothills with a temperature of 52C. I notice a continued emphasis on handwashing recommendations for the general public, including the Times article discussion last week, describing its effectiveness during Chinese SARS outbreak in public schools. Let's supplement the recommendation for diligent handwashing to include face washing as well." And he has a lot of detail, which I will include, but it will be in the show notes and you can read it all, you know, so... not just your hands, but your face and eyes and even tear ducts. (laughs)

KS: Yeah, I talked to an ID doc and he said, "how do you even wash tear ducts?" and my fear is that you're going to do more damage and potentially make things worse, so I'm not sure that this is something that we really want to get into. I think we should stick with the CDC recommendation: "Cough into your elbow. Wash your hands, and don't touch your face".

VR: And then he ends with, "thanks again for setting the GS in medical podcasts. I will become a patreon subscriber later this week." Thank you very much. We have a lot of new listeners here. We really appreciate it. You should stick around, because if you just keep listening - doesn't have to be every week - you'll learn more virology and then in the next outbreak, you'll be in a better position, right?

RC: There's a surge, it seems to me, of greetings alternative to handshakes going around. There's the elbow bump - and I saw a great video the other day - of, I think this was made in China - all of the individuals in the broadcast were Asian, and this guy getting out of a minivan wearing a facemask and encountering all these other people wearing facemasks, and he declines a handshake, and they go through this whole routine of doing foot bumps. It resulted in something kind of like, a... it was obviously staged, but it was hilarious, and it was really kinda nice, because everyone was kinda dancing with each other.

VR: Yeah, so having gone to visit this week, everyone is kind of awkward. Some people just grab your hand and shake it. And some people say, "what should I do?" And some people give you their elbow. It's a very interesting cultural thing that's happening here.

KS: So I have a paper for later, I don't know if we're going to do it officially as a pick or in response to another reader, scientifically looking at hand shaking vs high-fiving and fist bumping. It's a nice study.

VR: So the preview for the next email is that on some previous episode we asked about cruise ships, and we thought, "Oh, there used to be someone who listened who worked in the cruise industry." And so, that's this. Kathy, that's yours.

KS: Vic writes, "Dear all. This is Vic, the ship's agent in Kristiansund Norway. First of all, of course I'm still listening. I think you could say I'm a TWiV womb to tomb listener. Secondly, what's happening in the cruise industry in the time of coronavirus? The answer would be, it doesn't look good. In the past 48 hours, one of my colleagues was the agent for a German cruise ship - the AIDA Aura which had a port call in Haugesund, Norway. On Monday, the ship

arrived in Haugesund and the passengers were allowed to go on land for tours of the local sights. During the day, two passengers received news from Germany that an acquaintance of theirs had tested positive for coronavirus. When they returned to the ship, they reported to the ship's medical personnel that they had had contact with a known carrier. Following this, these two passengers were quarantined in their cabin. The ship then contacted my colleague, the ship's agent, and informed her that they might have infected people on board. She informed the local medical authorities and one of their staff doctors went on board and took samples from the two quarantined passengers. These were sent to the pathology department for testing. In the meantime, all passengers and crew were confined on board the ship. No one was allowed to leave the ship and the ship was not allowed to leave the pier until the test results came back. My poor colleague now had to handle a storm of phone calls, e-mails, and messages from the media and all of the consulates of every nationality on board. Yesterday afternoon at 4:00 PM, Haugesund Medical Authorities held a press conference where they announced that the testing showed no signs of coronavirus infection. The two affected passengers were allowed to leave the ship and fly back home. However, the airlines would not allow them to travel until they could provide fit-to-fly certification from Haugesund hospital, which they subsequently received. The ship was then allowed to continue her voyage northward. According to my colleague, if the test would have been positive, then all passengers and crew that had been in contact with the two affected passengers would have been removed from the ship and placed in quarantine. This would indicate that the Norwegians have learned something from the mistakes made on the Diamond Princess in Japan. In general, the cruise lines are reacting to the current situation by requiring anyone, including us, the ship agents, to submit a recent travel history and have their temperature taken prior to boarding. I'm sure that the already vast number of hand sanitizing and washing stations in the ships has expanded. They are also plating and serving all meals, so no passengers are grazing along the buffet lines. However, this may all be moot if people get freaked out at the prospect of spending a week in very close proximity to potentially infected fellow travelers. We have not gotten any port call cancellations as of today, but I would not be surprised if we begin to hear that many many ships will not be coming to Norwegian waters this season. Love the show. Keep up the good work. Best, Vic."

RC: Great.

VR: That's great. Thank you so much. Now of course, there's another cruise ship off California where they have an issue. Sounds like they haven't learned from the Japanese...

KS: They're going to take them off some time this weekend to a non-commercial port, but that's all kind of vague. It seems like they're scrambling and they don't know what to do and you'd think they would have made some contingency plans before now.

RC: So, Vic, I'm sure you're still listening - I had heard that there was some sort of standing policy in the cruise ship industry to deal with disease outbreaks on board. This sounds like maybe not. I'm wondering if there is and what it has been and how that's been impacted by this whole thing. What do you do if there's a norovirus outbreak? I mean, they certainly deal with that, and they must have some sort of policy. I mean of course, that's a different kind of thing, but it would be interesting to know if there's a stock policy or if it's the same throughout the industry or if different cruise lines use different policies.

VR: Okay, Rich, you're next.

RC: Glen writes, "Love these podcasts. As a layperson with zero tolerance for second-hand spinning of data and "facts" by the mainstream media, this hour is invaluable as are the notes and links supplied for me to peruse on my own. Thanks for addressing the GI complications in this episode. My question is: why are masks not mentioned in safe practice guidelines or endorsed by you, panel, when it seems that droplets are the primary source of transmission when hand washing and proven hygiene are being utilized? I get that the virus particles themselves can easily pass through the mask but just considering the benefit on a particle to PFU ratio basis, it seems that restricting propagation to any degree would be beneficial. If not in this case, then why not? Thanks in advance, Glen." Well, the deal is, as I understand it, surgical masks - and we will make this distinction now - which are these floppy things that don't fit snugly on your face made out of regular cloth - because they don't fit snugly and also because people don't necessarily use them properly, are not a good barrier to respiratory droplets that transmit the disease. Stuff can leak in around the side, and etc. They do provide some protection if you are sick and you're coughing and etc. and it means that you won't spread stuff as far as usual, or as far as you would without the mask, but if you are well and just out in normal circumstances, a surgical mask is not a very good barrier. An N95 mask, if it fits right, and if you know how to use it and if you use it properly, can be a reasonable barrier but man, what a hassle to actually wear one of those all the time and use it properly. So that's why surgical masks are not among the safe practice recommendations.

VR: So I'm on the CDC page for recommendations. Question - should I wear a respirator in public? Umm... is that the right one? Let me see... respirator, face mask... yeah, this includes face masks... CDC does not recommend routine use of respirators outside of workplace settings. More often spread are respiratory viruses person-to-person happens among close contacts within six feet. CDC recommends everyday preventive actions to prevent the spread of respiratory viruses, which we have all talked about. And this includes N95 and surgical masks, so the masks will stop the particles, the droplets, which contain viruses, but they have to be worn properly and not everybody does that, and as Rich said last time, you can't take it off to eat your peanuts. That's one of the misuses of it, right?

KS: Well especially if you touch the outer surface of it, that's you know, where you're trying to trap things. You have to know how to use these things correctly. Put them on, donning and doffing procedures.

VR: So basically, CDC doesn't recommend them, but you can wear them if you can get them, and wear them properly, right? I think that's the message. Yuki writes, "Hello, my hero/heroine scientists. I'm Yuki writing from Japan and I was one of the first writers to TWiM if you remember I'm a freelance translator mainly translating adverse drug event reaction reports from Japanese to English for foreign pharmaceutical companies. Thank you for keeping me updated on COVID-19. In Japan, facemasks have vanished from drug stores and are hard to find. Demand greater than supply, but I can just calmly wash my hands frequently because I am your listener. In latest news, February 12th, we talked about a quarantine officer on the cruise ship, Diamond Princess, tested positive for COVID-19. I advertised TWiV with Diamond Princess hashtag on Twitter. I hope things are going to calm down with that. Any repercussions for the Tokyo Olympics/Paralympics? Looking forward to the next episode. Best regards, Yuki." Yeah. Thank you, Yuki. Umm... Kathy...

KS: Tony writes, "Hi TWiVers. I just came across the attached paper which I think sucks but that's beside the point. And I noticed the high degree of antibacterial use despite a low incidence of bacterial comorbidities in the cohort. In fact, the rate of antibacterial administration

outstrips the rate of antiviral administration. Although this cohort may have been studied because the causative agent was definitively identified. Are you aware of any research investigating the effects of antibiotic-mediated microbiome disruption on COVID-19 pathology? China's long been a known hotbed for misuse of antibiotics and it seems within the realm of possibility that overuse could affect a novel disease. Thanks." And he sends a link to, I forget if I even looked at this link... oh yeah. This is the other one that I think is kind of a case report. It's in Lancet Respiratory Medicine again clinical course and outcomes of critically ill patients in Wuhan - a single centered retrospective observational study. So it has again a lot of statistics and things, so it doesn't directly relate at all to the microbiome question, and I think it's just too early to have bonafide published studies on the microbiome and this disease pathology. And I did check but I didn't look specifically with the right search terms, but just look on bioRxiv for how many coronavirus papers are present on bioRxiv: 413. So if I put in "coronavirus" and "microbiome" on BioRxiv, it's loading... and just to remind you, BioRxiv is where people put stuff before it's been peer-reviewed, so there's 41 articles, but looking at the first several titles, they don't seem to relate specifically to the question that this listener has asked. I think it's just too early.

RC: Yeah.

VR: We have an e-mail later about comorbidities from a physician if we get to it, that talks about that but not microbiome. Rich, can you take the next one?

RC: Tim writes, "Dear TWiV crew, thank you for providing such an informative and accessible podcast. I always learn something new and interesting. It is -6C and cloudy here in beautiful Madison, WI this morning. I saw someone speculate that ADE (that is, antibody-dependent entry due to exposure to one of the common cold coronaviruses) might facilitate SARS-CoV-2 infection. I can't evaluate the plausibility of the hypothesis, as I have no prior understanding of ADE. If you have time, on an upcoming episode, a brief discussion of what ADE is and what viruses are advantaged by it, could be interesting at least for me. Thank you again for your wonderful podcast. Keep on TWiV'ing. - Tim." And yeah, we discussed this on the last episode, right, Vincent?

VR: Yep.

RC: In some detail...

VR: Yep. In 589.

RC: Yeah... that'll be enough. And basically there's no evidence that that's gonna impact on this infection at this time.

VR: David writes, "While we're on the subject of coronaviruses and their interactions with the immune system, persistent viral shedding by a significant number of COVID-19 survivors is being reported." Provides a newspaper link. I say newspaper I actually mean news source. I'm old-fashioned. "Would be very interested in the group's thoughts on the implication of this finding for vaccine and antiviral development. What underlying mechanisms may be involved allowing virus to evade immune surveillance to CoV's persistent protected immunological spaces, such as the eye and testis? As does EBOV. What other mechanism might be involved?" So this is an article where, okay so Kathy has nicely summarized it. The No. 8 People's Hospital found 13 discharged patients that tested positive again though none showed

renewed symptoms, nucleic acid tests for 104 close contacts all found negative results. The director of ID at this hospital said the positive results were all found from anal swabs, a method rarely used in other parts of the country. The results were in the weak positive range, so my interpretation is that there's a bit of NA in the intestine and this is from swallowing of mucus which we all do, which contains virus, and it's pieces of non-infectious virus, so without further information, I would say that there are no implications for vaccine/antiviral. It doesn't imply an immunoprivileged site at all, although that could change and that's what happened with EBOV. We found out many months afterwards that it was persisting in these sites but so far, I think that this is not the case. Everybody would buy that? Is that good?

RC: Yeah, I'm with you on that one.

KS: Yep.

VR: This is David from Ann Arbor. (laughs)

KS: Yeah.

VR: Professor of Human Genetics! At your place, okay! You don't know him, though, do you?

KS: I don't know him in person.

VR: That's funny. He could just go down the hall and ask you. Thank you, David. Kathy's next.

KS: Stephen writes, "Dear TWiVsters, I wanted to shed a little light on something Dixon mentioned briefly in the last episode. He talked about a story about a whole family he had seen that had died. It sounded like he was worried that that was evidence of higher mortality among younger people. However, I think I read recently about the same family," and Stephen gives a link. "The family in question is the standard nuclear family - a 55-year-old movie director, his sister (age unspecified), and his mother and father. While the youngest member is a little on the young side for the highest levels of mortality rates, this isn't a counter-example. In fact, the article also talks about how they could not find a bed in the hospital for the father and they ended up self-quarantining at home which undoubtedly put them at greater risk, so maybe Dixon's worries were unfounded about that being evidence for young people infections."

VR: Yep, in fact later in an email that kind of chides Dixon. You shouldn't chide Dixon.

RC: Be nice to Dixon. Well, this is a great example of how you can't trust anecdotal reports. You can't extrapolate them because they may represent an unusual situation.

VR: Rich?

RC: Matt writes, "Hello. I am a tourist in the world of virology who happened upon your podcast while looking for more information on, you guessed it, COVID-19." What - a virology tourist? What do you see in the landscape? Very interesting. "As best I could follow your convo in TWiV 588 about proximal origin of SARS-CoV-2, I was especially confused by one of the pieces of evidence presented in support of the virus having its origins in the wild, so to speak. It was said, "So let's say a human wanted to put a furin cleavage site here, they wouldn't put the proline upstream. It was also said that the proline allows the addition of O-linked glycans and that the sugars act as a shield for the immune response. Again, I knew none of these terms until today

so I'm clearly not challenging what you're saying. Rather, I'm trying to inform myself. Given that the proline allows the addition of O-linked glycans which acts as a shield to the immune response, why wouldn't someone insert the proline if the objective is to design a more infective virus? I should conclude by saying that one thing I've learned during my brief voyage of curiosity into this world of yours is that when assessing the virus' capability for devastation, it is of little relevance whether the virus is the product of a lab experiment gone wrong, or worse gone right, or a free-range organic virus. I also come away with a budding fascination of virology. With thanks, Matt." Yay Matt!

VR: I love that! Free range organic virus. That's great! That was a good question. So the thing is Matt, you put the furin site in it doesn't include the proline, but the proline is different. It's obviously in addition to what's present in the highly-related bat virus, so why is the proline there? So the authors speculate that this could lead to the addition of a glycan site and that would in fact, you know, shield the protein from the immune response, but that's really speculation. The point is that you wouldn't put a proline in. You would just put the furin site. And so their speculation is kind of to say, you know maybe the proline was selected for because it's shielding. It's all speculation, but the real issue is that if you were designing this, you wouldn't put the proline in because you'd just want a cleavage site.

It's not like it's common knowledge in this field that if you wanted to do this, you should put a proline there. What they're saying is it showed up, okay, and maybe it does this and maybe it does that but it's not like if you were, the point is that if you were trying to create it, you wouldn't necessarily know that you oughta do that.

VR: Yep.

RC: Therefore, the fact that it's there indicates that it came out of nature - a free-range organic virus.

VR: Mmm-hmm. You know, I wanna just comment, this world of ours, I understand what Matt is saying but I don't consider it our world - it's just the world we live in and we happen to be scientists that explore it a different way than lawyers or business people might.

RC: As you might imagine, I've been having a lot of correspondence with my son in Kirkland, and it's interesting that you know, now he's (although he's known that I'm a virologist for his whole life) and yet, this has caused him to look a little deeper into this, and he says, "It's still mind-blowing that any of this stuff works at all" like not only do we carry around detailed instructions for assembling tiny little machines that are capable of sustaining and replicating sentient living organisms but they're also short programs written in the same language that can hack the mechanism and make more of themselves. It's insane!

VR: Yeah, it's why people like virology. What were you gonna say, Kathy?

KS: I was just going to say, I think he's talking about the world of virology.

VR: I understand.

KS: The people who consider themselves virologists.

VR: I do. I think the point of these podcasts is that I don't want us to be insular. We want to be part of your world, and you should listen. Cuz It's cool. Alan writes, "Dear TWiVers, thank you for your informative and no-sensationalized information-packed geeky podcast. I discovered you only about a month ago in search for solid information. So glad I found you. I recommend you often to friends and strangers alike." Alan is in Dubai where it is the 29th of February and it is 26C. "We have just been told that schools will cancel and some after-school activities and trips as precaution. However, it appears the malls will remain open." (laughs) By the way, I met an Italian student at Ohio State and she said, "They're only letting two people into stores at a time but 100 people queueing outside"

KS: They're clustering. (laughs)

VR: So they're all clustered and talking to each other. (laughs) "My question is about the graphs that I see often that show total cases and total deaths. They're provided in both linear and log format. My question is not about how to read them but why they are posted this way. Scales make sense in both, but what is the reason for both? In terms of how to interpret the data, the actual number doesn't really change my view. Is one advantageous over another for reasons that are unbeknownst to me? Thanks and please continue to be the signal though the noise." Kathy, what did you learn?

KS: I think that Alan has picked up on a point that if you understand the numbers, you can evaluate the data in either linear or log format. So, our graduate student seminar meets on Fridays at noon and a now-retired faculty member would invariably ask a student who had a graph something about the graph and say, "well you have that plotted with the y-axis as a logarithmic scale and that can really influence how you consider the data", and then the next week, another student would have a graph and she would say, "you have that plotted with the y-axis on a linear scale and that could really influence how you look at the data." And so the point is, if you understand the numbers, the presentation is just sometimes a matter of convenience and be aware that what kind of scale you're looking at influences how you interpret the data. If it's a local scale and the numbers are close together, they could be numbers that are quite disparate.

RC: Do you remember from centuries ago cot curves? So I believe on those it's the x-axis that's logarithmic, and I spent a long time trying to understand - probably a whole day, maybe two, trying to understand why that would be logarithmic, and I came to the understanding that due to the wide range of numbers that in order to get it all in one graph, they present it as a log scale rather than a linear. There are other reasons for doing this kind of thing, but sometimes it's just a matter of convenience.

VR: Yeah, you have a huge range of numbers. That's absolutely right. The thing is, you may have an experiment where some of the data are huge ranges and then others are very small, and then if you put them on a log scale, the ones you can barely see and it's not worth showing that way so you really need to use a linear scale and sometimes you have to put a hash... you have to break the y-axis, and so forth.

RC: One of the most useful things about a log scale is that if something is a geometric progression, it shows up as a line on a log graph so that you can visualize that very easily so there are good practical reasons for doing that.

KS: If you google cot curves, you can instantly see that Rich is right. The x-axis has a logarithmic scale.

RC: So that was like 20 years ago.

KS: No, more than 20.

RC: Thirty? Forty? I was teaching it at the time! I didn't try to understand it when I was learning it.

KS: So Eric writes, "Hi Vincent and Go Blue to Kathy! I'm writing from South Korea where I work as a high school teacher. It is a hazy 2C with unhealthy levels of pm2.5 fine dust pollution. My question concerns the government response to COVID-19."

RC: That's a good one!

KS: Yeah. PM2.5.

RC: We haven't had a weather report that had dust pollution in it. That's a novelty. That's good.

KS: "South Korea is an interesting example as it has the most cases outside of China but has a democratic government much more comparable to the US. The spread here was accelerated by transmission within the secretive Shincheonji cult. CNN has a good brief summary here. About half the cases here are still linked to this religious group and the large majority are still in the city of Daegu. I was wondering if you could comment on the following South Korean government responses - how well they serve public health and whether they would replicate well in the US and other countries faced with similar outbreaks. Number one: Opening drive-thru COVID testing facilities and there's a picture in the article. Is this a good way to reduce the chance of virus spreading in hospitals?" Do we want to answer them one of the time or just go through them?

VR: Go through them.

KS: Number two: rationing face masks by limiting to 2 per person per week with the date you're allowed to purchase limited by birth year and requiring ID and using the drug purchase system to prevent repeat purchases. Three: using the cell phone emergency alert system to notify people of general hygiene recommendations and to inform us of the exact locations that infected people recently visited. Personally, I actually receive 25 emergency alerts in one day. They come from both local and regional governments and he's giving links for all of these. Four: maintaining a public website from the KCDC with twice daily updates. Five: Using military trucks to spray streets with disinfectant. He's got pictures. Six: Ordering all schools closed until March 23rd and limiting and closing other large gatherings. There are of course many other responses as the government has approached this with urgency, carrying out hundreds of thousands of tests and converting facilities for patients and even investigating the Shincheonji leaders. Personally, I've been impressed overall with the efforts but I'm concerned that the decentralized US system may not be as focused and I worried about what would happen if hospitals become overwhelmed in some areas as has happened in Wuhan. Also, a specific question for me - since it's impossible to maintain a supply of face masks to use daily due to the rationing, and it's impossible to go outside without one as people will yell at me, do you have any advice? I know it is dangerous to reuse these single-use masks but does it work if I for example use one mask for

each day of the week and when Monday comes around again, will any virus from a week ago be dead? Thanks. I've been enjoying your podcast for years and recommend them to my students who are interested in virology.”

VR: I didn't realize they were doing some of these things. I don't know. My thoughts are that first the drive-thru - not sure that would work here.

KS: No, because we don't have enough testing capability as it is now and people are going to go that aren't even showing any signs or symptoms.

RC: In the US, it's all about personal freedom, so there's going to be pushback to anything that's sort of potentially cramping your personal freedom so rationing face masks by limiting to two per person per week - with the date you're allowed to purchase limited by birth year and requiring an ID? I just don't see that happening here.

KS: No, I agree, but you could imagine that a particular store would limit an individual from buying up everything on the shelf...

RC: I could see that.

KS: So that could happen but nothing quite so regulated as he's describing.

RC: The cell phone emergency alert, I think your informance of exact locations that infected people recently visited... once again, that's going to be that's going to be a privacy thing that's going to come up and plus as he says he got 25 alerts in one day you become sort of immune to them. A public website...

KS: I wanted to channel Alan and say, “What could possibly go wrong with the alerts?” I just remember that that alert that went out to Hawaii about whatever it was, it was sort of a nuclear weapons thing.

RC: Maintaining a public website. I think you know I think good accessible accurate information is one of the best weapons we have and so I think that's important.

VR: I have to say this CDC website has a lot of good stuff but sometimes it's hard to find... you know, they divide it between healthcare people and everybody else and I'm not sure you know I want to see it all right but I do agree that a good website is great. The next one, I totally disagree with.

RC: So do I. I think spraying streets and other things with disinfectant is just not going to do anything.

KS: It's a waste of resources.

VR: You're not picking this up on the streets. By the way, back to the face masks... he asks whether... Is that right? Is this the same person?

RC: Later on he asks about... he gets to that. Are any schools closed?

VR: I mean we don't know.

RC: Most of these, we don't know their effect. I think, they're not bad ideas, for some of them anyway. In the back of my mind I keep coming back to that the number of flu deaths greatly outnumbered this so far. On the other hand of CFR for this could be greater, so we really don't know. So he brings up an issue that is really interesting. He says that if he doesn't wear a facemask outside, people yell at him... so this to me is a problem it becomes a sort of a social issue, the single-use face masks. If it were me, I figure that there's not going to be virus on my facemask, okay it's not like you're going out and breathing through a facemask the whole time and collecting a whole gob of virus on your facemask. If it were me, I'd have a face mask and I use it over and over and over and over again just so people wouldn't yell at me.

VR: You would be sensitive to people yelling at you? I don't know, Rich, knowing you...

RC: I could see how in some circumstances and in some cultures, if you look at the pictures of people in the street everybody's wearing a face mask. I've heard of this before. You get to a situation where if you're not wearing a face mask, you get abused, of one sort or another.

VR: I just don't know. I mean, he asks if the virus will be gone but I'm not sure that it would be in a week. That depends. Some last for a long time. Back to me? Kathy? Oh. Rich you're next.

RC: Nima writes, "Hi TWiVeraters - I love your podcast. My thought in question is, since CT scans can be used to diagnose COVID-19, why not do a study of lung CT scans for atypical pneumonia in January-February 2020 as a way to estimate the current community spread of CoVID-19?"

KS: So this is where I asked Vincent about using lung CT scans because it's not something that Daniel Griffin mentioned last week at all.

VR: Yeah, so I mean, Nima is asking just as a retrospective way of looking at the data right and you know, they had tried this in February in China and then that made a big spike in cases, right? And then they decided to go back to PCR.. and I asked Daniel, "Why don't we use it?" and he said, "We're discouraging this because it really increases exposure events." So I guess if you have a person who is potentially infected and you do a CT, there's a lot more potential for exposure, a lot of personnel and so forth... if it's already done I understand now that she's saying if we have the data why not look at it? That's not a bad idea, I think. But again, my problem is China abandoned it because they didn't think it was a good indicator.

RC: I don't know. Maybe you guys know but I don't know that you can actually discriminate between a SARS-CoV-2 infection and an influenza infection with a CT scan.

KS: Right, that's what I question and I also question the statement that lung CT scans can be used to diagnose CoVID-19 because again, it's not what Daniel mentioned as one of the criteria.

VR: Ok, Regula writes, "You and your team have probably seen this notice about the improving air quality over China. Thought it was amazing. Kind of reminds me of the reports of the ecosystem thriving in the Chernobyl area. Thanks for everything you do. I'm currently in the middle of a marathon training cycle and TWiV is my podcast of choice for long runs. Don't mind at all the episodes are 2+ hours."

RC: If you can finish your marathon before you're finished with a TWiV episode, then you ought to be a pro.

VR: "Airborne nitrogen dioxide plummets over China along with the Corona virus quarantine". Wow it's interesting and they have an atmospheric map of that.

KS: Yeah I think I had sent that by Slack earlier this week. It's really impressive and it also reminds me of how after 9/11 and all the air travel was shut down there were no contrails in the sky. Remarkable.

VR: Here it says the auto traffic has dropped off right and that's part of this, yeah... so like I said, we should all stay home, I guess. The washing hands wouldn't help with this, I suppose. Kathy?

KS: Kevin writes, "Great show, TWiV 589. Been looking forward to repeated exposure to rationality. Question - on various International newscasts (China, Japan, Germany, UK) there are video clips of space-suited Personnel spraying gray clouds of unspecified fumigant usually in outdoor locations. My brief literature search on the efficacy of this practice yielded a few references from an animal husbandry perspective. Is there any precedent or evidence that fumigation has any role in epidemic control? Thanks. PS. I will not compare thee to a bat pissing in a cave: "A SHAFT OF GOLD WHERE EVERYWHERE THERE BE DARKNESS." I don't know what that reference is but it's pretty funny.

VR: This is Kevin who always writes into TWiP with really long wonderful discourses. This is from Monty Python. I don't think there's any evidence. So the fumigants - someone wrote in and they said it's a bleach or hydrogen peroxide mixture. I don't know of any evidence that spraying the ground is going to do anything. I mean, even mosquito spraying, which is totally different, is of limited duration and effectiveness. So I don't think... do you guys think that the spraying... yeah, we just said that it probably doesn't do anything.

RC: Yeah. I don't think so. Wash your hands. Ben writes, "Hi Vincent, Rich, and Kathy. I am a relatively new fan of TwiV writing from my home outside of Philadelphia. I love the rational science-based nature of your podcast. Terrific resource. Please keep it up. I have two questions which I would love your feedback on. 1. I understand that from reading numerous reports that development of a vaccine for SARS-CoV-2 is only a matter of time, and that this could take upwards of 18 months to two years. As someone who is totally new to the vaccine development process, I was curious about the underlying reasons for the duration of this development timeline. In other words, is it a function of the capital to apply to the science? If capital was unlimited (for example, global scientist and bio pharmaceutical companies had as much money as they ask for) would this shorten the development time. If so, I wonder by how much? Would it cut it in half? I understand the human trials are highly complicated and take time but what are the other elements in the timeline of development? I'm very curious to better understand this at a granular level." Let's do that one first. I think you understand already the issues. Capital can be a problem. There can be a problem in getting anything off the ground and in the absence of an emergency because of the lack of capital for research or development of things that are not immediately profitable. Just the research to come up with something that has efficacy can be problematic and every creature is different. It's not like there's a rubber stamp method for making a vaccine for any given pathogen. They all differ. The clinical trials take an enormous amount of time and it's interesting that people are in a big hurry for vaccines and yet when you

have them they don't want to use them because they think they're not safe, okay... the reason it takes time is because we have to make sure they're safe! Okay, which means doing a whole bunch of trials and stuff in their Phase 1 to make sure on a small number of people that are safe and then there's Phase 2 which is a larger study to see if it's safe in a larger population and there's any efficacy, then there's Phase 3 which is a huge trial they're all enormously expensive and take a tremendous amount of time.

KS: I posted in a timeline from GSK for example of how we develop new vaccine and it shows the timeline for them and getting to the point of testing something is one thing and then getting to Phase 1 and testing for safety, and then clinical development and basically they show it as after phase 1 another 2 to 3 years (for phase 2) or and then another two to four years for phase 3... so that sounds like it's going to be accelerated greatly based on some of the things that we're hearing now for instance there was a story on NPR this morning about an NIH designed vaccine that's a DNA-based vaccine and they're going to start testing it for safety in a few weeks is what they said. And for that they're recruiting volunteers in Seattle but that person said we will not have a vaccine for a year-and-a-half.

VR: So are they bypassing preclinical studies with this DNA vaccine and if so why?

KS: They didn't discuss that. It may be that DNA vaccine preclinical studies for spike coronavirus have already taken place.

RC: By preclinical, what we're talking about is work in animals and cell culture to make sure that the vaccine can elicit an immune response, etc.

VR: So if you have something new you have to do that. There's an RNA vaccine also that was going into Phase 1 at NIH, I thought, and it's like an encapsulated RNA but unless you have information its going to work it's kind of on faith thinking it will and maybe they want to bypass that and just make sure it's safe in people... I could understand that, but it seems to me that if you don't have some information it's going to work and you go through all this, that's not good.. because then you can end up in Phase II or III even and it has no efficacy and that's really bad.

RC: It occurs to me that one thing I probably a lot of people don't understand is that there is no one cookie cutter method for making a vaccine, okay. In fact, I think that as a discipline we're kind of in an era of change because most of the existing vaccines that we have were developed in an empirical fashion where you took a virus and you passaged it in culture for a long period of time, and hoped that it got crippled and then hoped that that worked and so that's sort of a maybe-maybe not... or you make the normal virus and then inactivate it and inject and sometimes the inactivation makes it so it's no longer immunogenic... so it was an empirical very case-by-case, 'try this and see if it works' and so you don't know how long it's going to take for... every creature is different. We're entering a new era where there's more and more use of recombinant DNA techniques where we can take a protein from a given virus that we figure based on good information should be important in the immune response and put that into like a carrier vector virus and ask for expression and then test that, so that's a more programmed way of making vaccines but still that's more an art than a science at this point so there is no sort of "oh, I want to make a vaccine I got to do this and this and this and then it'll work". It's really an art.

VR: So in this case we have people have made MERS Coronavirus vaccine candidates - experimental vaccines - if you want to say just vaccine it should be approved in the end so let's

say experimental or vaccine candidate... and they put the spike glycoprotein into either or modified vaccinia Ankara or VSV vectors and we know that gives some amount of protection and so you could say, 'well let's just put this SARS-CoV-2 spike into these vectors' and so you could do a Phase I directly from that but I would certainly want to do some preclinical and show that it works on animals, 'cause you just don't know. Everything is different.

RC: And they're you're talking about these vectored vaccines and in one case, it's a vaccinia vector and although these are used in veterinary practice for a variety of reasons, (although they work), there's no licensed vaccine that uses that technology for humans. There have been some in trials for HIV but so far there's been no license back scene using the NVA/ vaccinia vector and the only example of a VSV-vectored vaccine that I know of is the Ebola vaccine... so at this point in time, this is not standard practice and so that's even going to ramp up the safety testing. Saying "oh, this is a new concept. Is this really going to be safe on a global scale?" So in the long run maybe we will develop something as if we have enough research money okay to actually do this properly maybe we can come up with something that's more like a cookie-cutter way of making vaccines so that we could cut out some of the research that's involved now but now, no.

VR: Good point, and the thing is just one more - if you make something and it backfires, then that puts a damper on the whole thing.

RC: So you have to be careful. So he has another question too. Along the lines of question #1, I wonder if there are opportunities for volunteers who want to be helpful in working on the many dimensions of this global health problem. Are you aware of resources that folks who want to get involved might be able to explore? For example, I have a background in engineering and computer science and decades of experience in data science / big data and would be happy to volunteer my time to help scientists to review data, do data entry, etc." what a nice question. I don't have an answer. "Thank you so much for answering my questions. -Ben." Where would a person go to volunteer time? Especially somebody like Ben with that kind of background?

KS: I don't know...I had someone who was very into social media and into virology and wanted to somehow parlay that into helping some entities with their public relations regarding social media and the coronavirus and I don't know.

VR: Yeah, these out-of-the-box ways we don't typically know much about, right? There have been standard ways of doing certain things but yeah you could you could explore on social media... and say, "I can do this. Does anybody need help?"

RC: This whole discussion emphasizes for me that this is sort of a teaching moment for the anti-vax movement, it seems to me, because you know there's been so much pushback on vaccines and so much anti-vax stuff out there and now all of a sudden everybody wants a vaccine and they want it now, okay? And this is emphasizes to me that making a safe vaccine is not a trivial task, alright, and it takes time among other things because we want to make sure it's safe.

VR: However, his point about resources would certainly apply to antivirals and we could have had antivirals against all coronas or many coronas if we had put the money into making it but there was no interest and therefore companies who need to make profits were not interested in pursuing them, but they could have been developed and been stockpiled and been ready so if you had infinite money and people you could say let's get a bunch of RNA polymerases from bat SARS-like coronaviruses and design something that will inhibit them all, I don't think it would

be that hard cuz they're very conserved but without the financial incentive... so an antiviral is kind of a different thing because you could develop them and bring them you could even do a phase 1 and then have them ready for actual testing when there's an outbreak. Alright, Emma writes, "Emma writes:

Hello TWiV Team!

I recently sent a long-winded email not related to the current coronavirus outbreak so I think it will take you a while to get there. However, I wanted to bring up something related to your most recent episode.

I would like to respond to the anecdote shared about being offered a facemask by a "perfectly healthy individual." While these masks of course would not be any more effective for someone with an underlying health condition, it is not possible for you to determine the state of a stranger's health by a simple look. I am 20 years old and have a condition that effects my immune system, but on the outside generally appear healthy. I will likely need to start using a wheelchair soon, but you would not be able to tell this by simply looking at me, since I am usually capable of walking short distances. While the health status of this individual was not at all the purpose of the anecdote that was shared, I wanted to bring this up with the hope that you could use your platform to share this message. You can not assess a stranger's health just by looking at them. This is particularly important to remember because people like me who appear young and healthy on the outside are often accused of faking or exaggerating our symptoms. Thank you for taking the time to read this, and thank you for all the work you do. I hope this is something that my fellow listeners will keep in mind going forward. Again, thank you so much for creating this podcast!" Totally appreciated and Emma, thank you for saying it nicely instead of getting mad at us...

RC: you know, that's a really good point, and this applies to... you know, I've had this experience of seeing somebody park in a handicap space and then jump out of the car and walk into the store, and I'm thinking, "Wait a minute", okay, but you don't know... you don't know what sort of issues a person might have... absolutely.

VR: Okay Kathy you're next.

KS: evin writes, "Hi. Got a question. After our children sports competitions teams will line up and all the players will high-five each other according to this it appears a high fives will transmit nearly as effectively as moderate handshakes. Should I bring this up with coaches to try to get them to switch to face bumps or would that be an overreaction? In case it makes a difference were in San Mateo California, one county North of Santa Clara County where there has been community spread of SARS-CoV-2." So, now might be the time for me to bring up this pick that I have. It's a two-page paper. My former student Nikki sent it to me. She has used it for teaching in class because as she says, "it looks at the aspects of scientific experimental design so students don't get bogged down in complex methods. Everyone can understand the different things that they're evaluating and measuring without a lot of scientific knowledge". So basically it's a one-figure, two-parts paper where they compare hand shakes to high fives to fist bumps and then they looked at several different parameters. They took people wearing disposable gloves and they dip them into a non-pathogenic E coli and then they had them do these various types of engagements - handshake high-five or fist bump - with another person with gloves and then they measured the amount of bacteria that was transferred and they also mention measured using paint how much contact area there was between the two and of course, handshakes had the most contact area and the most spreading of the bacteria, high five was next, and fist bump was lower. And then they controlled for the fact that a handshake would take longer than the average high five or fist-bump, so then they did a prolonged high five and a

prolonged fist bump and looked at how those affected things... and then they also looked at how strong the handshake was and so they used a dynamometer to measure the strength of the grip, and showed that a strong handshake gave more transfer than a moderate handshake and so forth, and so bottom line is, yeah they should probably stop doing the high-five. They can do a fist bump, or as Rich described earlier, they can do a foot bump or an elbow bump, but yeah definitely not a handshake and not a high-five.

VR: That's the paper that Kevin sent in fact. It's exactly that one.

KS: Oh, is it? I didn't know that.

RC: I don't think that's an overreaction. What the heck? Do a fist bump. I really like the foot bump because it really does evolve into a dance.

VR: Especially if you're playing soccer. Kathy, you're next.

KS: Oh so that's Ben? No, Michael. It's a different Kevin. Okay. Michael: "Thanks for your great podcast. There's community supported websites that are keeping track of the transmission in South Korea and are being utilized by the major media outlets." And he gives two where there's a corona map side with an English version that I think he has prepared, or maybe it's just in English. Okay. Yeah, and then he has a second one that's only in Korean but he has some charts. So again, we're starting to hear from Korea with some resources for Korea. "Always enjoying your podcast. Thanks - Michael."

VR: Rich?

RC: Gotta go back here. Maritza writes, "Hi TWiV-Team, huge fan! Thanks for all the knowledge you provide & insight you give. I've always been interested in epidemiology, even though I work in politics now, but I'm planning long-term to move more into public health communications. A question: How are people who are shedding SARS-CoV-2 but not showing any symptoms able to find out if they are infected, if that's possible at all without testing? I travel a lot, and the idea that I'm potentially and unknowingly spreading the virus – even if I wash my hands often, try not to touch my face etc – makes me worried for the people I interact with. This tweet by a Chinese reporter in particular made me think about the issue. Thanks and greetings from Goa, India (currently 32C), where I'm on vacation and where it's wonderfully sunny." I haven't looked at this. This is a tweet of some sort. "Scoop". So this talks about asymptomatic transmission. I wouldn't go on one tweet and from what we know so far, is it fair to say that asymptomatic transmission, if it occurs at all, is really rare? I wouldn't worry about it.

VR: Yeah, that's what we said at the top, from the report from China, it happens but it seems to be minimal so far, although that needs further study. Maritza wants to know about testing, and no. If you are an asymptomatic shedder, you have to have a PCR to see if you are shedding, there's no other way because you wouldn't have symptoms, right?

RC: And that's going to be hard to come by, probably.

VR: Ype, especially in Goa. Thomas writes, Thomas writes: I'm an occasional TWiV listener & of course a more regular listener at times like these.

Thanks very much for your service to us non-scientists. TWiV has made me much more interested in viruses than I once was. *If only my high school science education had been as interesting as you are...* My very simple-minded question: Is it likely that the coronavirus which is causing this pandemic is even now, as we speak, mutating and becoming something different? If this virus is mutating, will new cases of respiratory illness which doctors think was caused by COVID-19 be less capable of being treated with the drugs (such as remdesivir) that are now being tested? How long does it take for a virus such as COVID-19 to mutate into something substantially different — hours days, weeks?" Well, so it depends what you mean by something different, I asked. I assumed that you were talking about a phenotypic difference as opposed to the errors that happen with every cycle, right? And because as we mentioned earlier, these genomes are always mutating but often, that doesn't make any difference to the virus. It's likely that if Remdesivir works, there's already genomes with a resistance mutation out there that already are circulating in people and it'll just be a matter of time before resistant viruses are selected for and that's why we need to have more antivirals. With the first AIDS drugs, resistance was seen within months of use of AZT, so it can happen very quickly or it can take longer. If you use triple therapy, you don't see resistance very frequently so..

RC: But the important thing there is that in that particular case, you're applying a selection. Okay, you're administering this drug, and so that gives the drug-resistant viruses an advantage. Yes, there is variation in the virus but that doesn't mean that the virus is going to mutate to something substantially different just on its own. Now, the immune system is going to impose a selection that in theory, and in some viruses, could in effect select for viruses that can evade the current immunity, but I know of no evidence in the case of the coronaviruses that that sort of thing happens.

VR: Right. Okay, Kathy, go ahead.

KS: I was just going to insert something about the pronunciation because someone wrote to me very specifically and said that it's Remdesivir (slowly enunciates remdesivir) so there's four syllables.

VR: Remdesivir? It's like a fabricated word and they're telling us how to pronounce it?

KS: Well it's got four syllables. This is from an ID doc from another institution.

RC: Oh yes, that's where we should get our pronunciation from. I'm not being snarky. I'm just fooling. Alright, let's take... there's a bunch more. Let's do some rapid fire. These next ones coming up could be rapid fire, unless you feel that you wanna do more than that. That was Rich, right? John writes: Dear Twiv, HI my name is John a student at SUNY albany, a former student of Cara Pager's cell bio class. I was wondering how many of the current coronaviruses are infectious per 100 virus "cells". If you are exposed to the virus, like inhaled a sneeze or touched your mouth after touching someone with the virus, how likely the virus will surpass your immune system and cause the disease? - John." Well, we don't know. For some viruses like noros, it just takes 10 PFU to initiate an infection, typically more for other viruses. Thousands or tens of thousands. We just don't know what the infectious dose is, which I think is what John is asking here.

KS: He might also be asking about particle:PFU ratio, but when he says virus "cells" I think he means per hundred viruses.

VR: We just don't know. That's why you could get a package from Amazon China and it might have a little, 10 PFU of SARS-CoV-2 on it and that might not be enough to initiate an infection. We really can't do those experiments with this particular virus. Alright, Kathy.

KS: Steve writes: "Hi TWiV-cast, I have a question for you. You've mentioned a few protease inhibitors as possible antiviral (he means antiviral targets) for COVID-19, and I understand the traditional Influenza antivirals would probably not be effective since they are neuraminidase inhibitors but what about the newer anti-flu medication Baloxavir or Xofluza, since this is an RNA polymerase inhibitor? Thanks your for your passion and all you do. -Steve"

VR: So, Baloxavir is an endonuclease target which is part of the polymerase but it is not the catalytic subunit so the coronavirus does not have an endonuclease.

RC: By the endonuclease, that's the cap-snatching function?

VR: Yeah, so that Baloxavir wouldn't work either.

KS: So those are very influenza specific, in other words. One of the key things that we teach about viruses is that if you want to make a good antiviral you need to target a specific enzyme that the virus has that the cell doesn't have, and so that's why targeting a protease or the coronavirus polymerase could be effective strategies but they are going to be significantly different from the RNA polymerase that influenza has, for example.

VR: Rich?

RC: Cookie writes: You mentioned on your last show – when discussing the coronavirus transmissibility- to keep 6 feet between you and a visibly sick person....are you suggesting we bury the sick person?" (all laugh)

KS: We didn't mean six feet under.

RC: Good one.

VR: John writes:

I have relatives who work in emergency rooms, so I have concerns about his their safety in the case of a pandemic coronavirus. I had read about passive antibody in college, and found this reference on it. Is the use of passive antibody, so called horse serum, (although its probably bioengineered these days)," ABSOLUTELY "still something that people do for situations like pandemic flu or coronavirus, where there is no vaccine available. Would passive antibody work?" Good question. People are trying it. They have developed passive antibody treatment for Ebola viruses, for other viruses. Listen to Prometheus project. They're doing it for a variety of others. I'm certain that people are doing it for coronaviruses, so yeah, in the absence of a vaccine you could give an antibody and it should work.

RC: It should work.

VR: It should work, but you have to test it. Kathy?

KS: Adam writes, "Hi TWiV team. The Singaporean government has produced a fantastic data dashboard for Covid-19 cases in Singapore. I am particularly impressed by the information provided on each case and the graphic showing how they are connected

(<https://www.wuhanvirus.sg>). The actual statistics, and your podcast, are some of the very few places reporting without needless hysteria. Thanks, Adam. P.S Weather in Newcastle, Australia, is cool and wet. It is a comfortable 22C and we have had a drizzle of a couple of mm of rain today. Everything is green again after being brown two months ago.”

VR: It's a cool site.

RC: Very nice site.

VR: So Singapore is interesting. They have 138 confirmed cases. They have no deaths. Someone told me to have a really good health system there, which I don't know but I would.. You know, it probably is good. Umm Rich?

RC: Rebecca writes, “Group home residents are well known to be especially vulnerable to transmission. I have seen no guidance offered for reducing risk to residents. I have seen long term care facilities addressed in general, but usually in the context of a discussion of risk in healthcare facilities. Many group homes for people with mild to moderate intellectual disability are not healthcare facilities. The residents of group homes have high rates of diabetes, asthma and obesity. Many group homes are overcrowded, with residents doubling up in bedrooms designed for one adult. Staff are underpaid and are not adequately insured. Adults with Down Syndrome are especially vulnerable to pneumonia and in general are thought to have reduced immunity compared to the general population. What criteria can guardians of high functioning adults with developmental disability use to decide whether to bring their loved one back home with them to ride out the coronavirus? At what point would bringing a resident home not be considered over reacting? I'm asking because our 29 year old daughter with Downs lives in an overcrowded group home. My husband and I are searching for criteria to help us decide when it is reasonable to disrupt her routine and bring her back home to reduce her risk of infection. She lives about 45 minutes from recent cases in Illinois. Do we wait until there is widespread community transmission? Or should we act much sooner?” Wow. Heavy question. Umm, I'd frankly - you know, this is an important question from a person with a perfectly reasonable concern and I don't feel qualified to really advise in this situation. Personally, I don't know. I'd be waiting until there was a real threat at the home, like a case showed up or something like that. On the other hand, by the time that happens, based on what we know it might be too late. There might be a lot of circulation in the home, so that's a tough question. You guys?

KS: It's hard to know, which is why it's so distressing for us. How much is the disruption of the routine and how much of a burden is it? But based on that New York Times article about the numbers, if it's 45 minutes away already, community-transmitted, it seems like it's only a matter of time, and if you wait until you hear of something being there, it could be that you know, it could be too late. On the other hand, this person is 29 years old, so is on the young end of things, but it's...

RC: She points out that young adults with Downs Syndrome are especially vulnerable to pneumonia and generally thought to have reduced immunity, so the age thing is ...

KS: Yeah, it overrides it.

VR: These are all good concerns but you have balance it with: so if you take your daughter home, are you going in and out of your home and contacting other people or are you going to stay home? Because if you're going to work, you could bring it home and then you would, you know, be doing the same thing that you're trying to avoid... so I would say, if you were both staying at home and you can take care of your daughter without going out, that would be a good place as long as you think the disruption wouldn't be bad. Anyway, these are things to consider, but we can't really give you advice... but that's what you should think about.

RC: I think they're all legitimate concerns, cuz I mean as I think about this whole thing, group homes are an issue, because it's a dense population of individuals who are likely to be at risk so that's a problem and she mentions that this is an overcrowded group home so it's quite a legitimate concern, but I don't know how to answer it.

VR: It's a concern, even in a very expensive retirement home where you have elderly people who are interacting and as soon as you introduce the virus... Rich and I were in one 2 weeks ago. We walk in, there is a room full of people playing cards.. perfect way to spread the virus.

RC: You know the guy in Florida... The first case in Florida that showed up was a guy that caught it playing cards with a bunch of buddies in a club or something...

VR: Valeria said that's how they caught it playing cards up in remote Italian villages. Are you both okay with doing a couple more? Todd writes, "TWiV team, Good afternoon from Japan. It is currently 57 degrees F and mostly cloudy. I wanted to reach out and say THANK YOU for all you are doing in keeping up with COVID-19 as it continues to evolve. You are doing a tremendous public service, and it is greatly appreciated. Saying thank you does not do it justice. For context, I am in the medical field here in Japan, and we are doing our best to stay on top of the facts as this situation continues to change. Your subject matter expertise and grounded analysis is desperately needed so we can give decision makers good advice. This allows them to make informed decisions and keep the community apprised of the ongoing situation. Many of us are going from meeting to meeting regarding COVID-19 and thus can't devote the necessary time to keeping up with the constantly changing landscape, and without your expert team continuously reviewing the literature and giving it a critical peer review, we could not keep up and give our decision makers the input they need to do their job. THANK YOU! Much of what we are combatting at present is misinformation and speculation, so what you do is a great enabler to all of us in doing what is right for our team and our community. We have had a series of town halls to engage the public, and for my piece, I have used the information you provided to inform our team members about the virus and how this compares to SARS and MERS. On a personal note, I enjoy your podcast immensely and it allows me to stay current on virology even though I can't be at the bench doing what I love - virology research! I have also enjoyed hearing former colleagues on your show, like Dr. John Dye and Dr. Gustavo Palacios. I worked with them at USAMRIID, the US Army Medical Research Institute of Infectious Diseases, prior to my current job, and I look forward to working with them again when I return to USAMRIID this summer for my next assignment. I hope to meet you all at ASV this June, COVID-19 permitting, and sincerely wish to thank you in person. Keep up the great work and thanks again. V/r, Todd" Okay V/R - what does that mean?

KS: Don't know. We need Alan.

RC: Thanks, Todd!

VR: Yeah, thank you very much. Kathy?

KS: Wink writes, "Could you be overemphasizing hand hygiene? What is the data that the current coronavirus transmits as does rhinovirus? Why downplay a surgical mask? For all we know now, they may offer excellent protection. Daniel, EID 2004 reported that surgical masks protected Toronto nurses from SARS." Okay so I looked up that article and just now pasted it in, and they compared... Vincent, this might be what you were referring to earlier.. they compared the N95 and they said consistent use of the N95 Mask was more protective than not wearing a mask. Risk was reduced by consistent use of a surgical mask, but not significantly. Risk was lower with consistent use of an N95 mask than with consistent use of a surgical mask. We conclude that activities related to intubation increase SARS risk and use of a mask, particularly

N95 mask, is protective. So, to me, the devil is in the details of the sentence. Risk was reduced by consistent use of a surgical mask, but not significantly. That's like how people say, "You know, we got the result and it is trending because the P value is not 0.05. Trending? Then it's not real, so saying it's reduced but not significantly to me means that you can't say that it's reduced.

RC: And I would point out that that's in a setting where you have nurses dealing with people with SARS, so these are people in close contact on a regular basis with people with the disease, so that's a different situation than just walking around in public in an everyday situation.

VR: And here, they talk about the risks associated with intubation. Right, we have fluid spraying around, so that may be different from walking around... so I don't know. We're not overemphasizing hand hygiene at all.

RC: No, as a matter of fact, I would go to the top of the show with that data from Hong Kong, okay, that shows that generally, it's not just hand hygiene but the measures that are being recommended are in fact impacting all sorts of infectious diseases now...

VR: and hand hygiene is easy.

RC: And it's documented that contact with hands is the major spreader. Getting the stuff to your face from your hands.

VR: Rich?

RC: "Thank you very much for your recent SARS-CoV-2 outbreak coverage. Here in Ottawa (where it is -4°C and sunny)," These people pick up on the schtick pretty fast. "we haven't yet had a case, but I figure it's only a matter of time, and people here are trying to prepare. Several weeks ago, the Anglican Church of Canada sent out a statement to try and reduce the risk of transmission in churches. The statement emphasised that it is not strictly necessary to drink from the shared cup of wine, and the clergy in my church also drew our attention to existing hand sanitiser stations and encouraged us to try hands-free greeting methods during the Peace (it is traditional to shake hands at that point in the service). I have been of two minds about whether I should take extra precautions, like refusing to shake people's hands in church. On one hand, the congregation is quite elderly, and even though SARS-CoV-2 isn't here yet, there are plenty of other respiratory illnesses around. On the other hand, they all know that I'm doing a PhD in biology, and if they see me taking it too seriously, it could frighten them. As virologists, how do you balance this in your daily lives? Speaking of other respiratory illnesses, I remember you said that flu deaths are calculated by looking at excess pneumonia deaths in a given year. How will this new cause of pneumonia affect the accuracy of those numbers?" Okay, so you know, I think taking precautions in church is a perfectly reasonable thing to do, and the precautions they were talking about are not... they don't really cost you anything and I think as a virologist in a situation like that, you're setting a good example for, you know, hygiene... why not? Wash your hands. And I think, you know, over time maybe in certain circumstances, the elbow bump or fist bump will replace the handshake. Fine, you're still greeting someone so the sentiment is the same. That's fine.

KS: There was a feature on NPR this morning on just exactly this post - the sharing of the peace and the common cup and even the communion by intinction, which is where you dip the bread into the wine, and the concern there is that someone is ripping up the bread and handing it to you before you dip it in, and so how clean are their hands? So, they address some of those things and you can share the peace... the way that they describe on NPR was - you can just wave to people, you can do the two-finger peace... I know that you can do sign language peace

which is really beautiful, and so there's a lot of ways that you can avoid that hand-hand connection, and the bit about the communion and so forth, I don't know where I come down on that but I agree with Rich that I think it's wise for you to set a good example and have people see easy precautions that they can take that may be important.

RC: Actually I saw a bit today that I fully support, which is that really what we ought to be using is the Vulcan hand greeting, which is 'live long and prosper'. What could be better?

VR: The last question is good. I don't know the answer there. I suspect that the SARS-CoV-2 pneumonia deaths are going to be segregated, right?

RC: Yeah. I would assume so. It requires appropriate testing. But the flu excess pneumonia - those are people who, by some test are documented to have influenza-induced pneumonia correct? So you ought to be able to segregate out the SARS-CoV-2 tests.

VR: We actually have a letter from someone later which we won't unfortunately get to about just that - the excess pneumonia with flu. We'll get to that another time. Okay, I think we can stop there because we've gone two and a quarter hours and we have taxed many people's attention, but if you're training for a marathon this is probably good for you.

RC: We have many many more emails too. Wow.

VR: They may appear to just roll in and I don't want you to stop sending them in. Keep doing it. Now what we will do is next week, we have Ralph Barric on, so we should all go through and see if there's some things that we think he would be good at answering. We kind of know his strengths... and then we'll get back to the regular schedule after that... we'll just deal with these. I don't think they're going to go out of relevance anytime soon. I think they're all great questions and a lot of people are telling about their experiences in various places which is great, so keep on sending them in.

RC: People are coming in with good questions and good ideas and situations that we haven't considered that are worth discussing. It's good.

VR: This is really... I'm looking at the last line here. This is really the only place where you can get your questions answered. Lots of places where you can get news, but here on TWiV, we'll answer your questions. You could be part of the show, and you can find your questions and answers, by the way. Well, the answers are on the show but your questions are on Microbe.TV/TwiV. The show notes for every episode. We have a link there for all the letters and all the text of the letters and lots of good stuff, so we thank you for that. If you want to send a letter, Twiv@microbe.TV. If you enjoy what we do, consider supporting us (microbe.TV/contribute). Kathy Spindler is at the University of Michigan in Ann Arbor, Michigan. Thank you, Kathy, for doing this on a Saturday.

KS: Thanks. This was fun. I want to just include one other thing and that is ASM sent out a newsletter this week that included a Boston Globe article with a question-and-answer format. Most of the questions were answered by Stanley Perlman, who we've had on TWiV and he's a coronavirus expert, so you might also look there. If we can put that link into the show notes for some answers that we maybe didn't answer today and answered in the past, or that you might have thought of and they're useful from an expert.

VR: That's a good source. Rich Condit, Emeritus Professor, University of Florida Gainesville, currently residing in Austin, Texas. Thank you, Rich.

RC: Sure enough, and I don't mind doing this on a Saturday. Every day is Saturday.

VR: I'm Vincent Racaniello. You can find me at virology.blog. I decided to start using .blog. I thought maybe people think .ws is weird so virology.blog. I want to thank ASV and ASM for their support of TWiV, Ronald Jenkees for the music. This episode of TWiV was recorded, edited, and posted by me, Vincent Racaniello. You've been listening to This Week in Virology. We'll be back next week. Another TWiV is viral.

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Transcribed by Anna Fagre