This Week in Virology

TWiV Special: Coronavirus SARS-CoV-2 and COVID-19 Update

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Vincent Racaniello: From Microbe TV, this is TWiV - This Week in Virology, a special episode recorded on March 4, 2020. I'm Vincent Racaniello and you're listening to the podcast all about viruses. Today, we have a special coronavirus episode for you. We're going to talk about SARS-CoV-2 and CoVID-19, and joining me - my TWiV co-host Daniel Griffin. Welcome.

Daniel Griffin: Hello, everyone!

VR: Are you going crazy, Daniel?

DG: Yes, yes I am. I'm thinking this is one of those Marvel things where we cross-pollinate where you bring someone over from one of the other shows - the other universe, and now I'm here in the virology universe, which I feel like I am in the virology universe.

VR: I figured you're an infectious disease physician. Here we have SARS-CoV-2 coming into the US, probably big-time, and I thought, "perfect time to get you on" because I figured you'd be dealing with it somehow, right?

DG: Certainly. So yeah, Let me give our listeners - the TWiV listeners - I think our TWiP (This Week in Parasitism) listeners know me well - a little background and intro for our TWiV listeners. So I am a MD/PhD. I am a board-certified infectious disease specialist. In addition to my role at Columbia where I am part of the Infectious Disease department and also my appointment in biochemistry and molecular biophysics where I do a bit of virus research myself, but a lot of my time lately has been spent doing clinical work for ProHealth Care Associates. And I am chief of the division of Infectious Disease at ProHealth Care which is the largest physician-owned multi-specialty practice in the country with about 1,000 physicians and about 3 million patients, and I am the Infectious Disease physician on the core team, the CoVID-19 response team, that is helping our organization respond to and address CoVID-19.

VR: So is this organization New York state only or is it throughout the country?

DG: So it's in the whole tri-state area, so there are 240 practices, 24 urgent care centers, the physicians are at a number of hospitals in New Jersey, New York (in and outside the city), as well as Connecticut.

VR: So, how long have you been preparing for COVID-19?

DG: You know, in certain ways I think those of us in infectious disease have been preparing for years. I think it would have been foolish to not see this coming to some degree. I don't know if we've been preparing as long as I wish we had been practically, you know, for the disease preparedness level I would like us to be at right now.

VR: Never ready enough really...

DG: Um, we're definitely not ready enough, and we'll probably be talking I think about some of those challenges we're facing right now.

VR: So, tonight, I went down to Morning Side to teach and on the way back, I walked past the emergency room and of course there's a television crew waiting there (laughs) - I don't know what they're waiting for - for someone to come in? But one of the guys was standing there and he said, "If I get sick, I'm gonna be pissed!"

DG: (laughs) Ok. You know, it's interesting. Not only is the public concerned but a lot of providers are concerned, so I have been getting a lot of calls from providers at different centers trying to figure out how we respond, so, you know I also listen to TWiV. I've been listening to TWiV and I think really an excellent insight into the science and all the publications that are pouring out understanding the coronavirus and I've been doing a number of webinars where I get on the web and you know, a few hundred clinicians are listening in and we go through talking a bit about what we know about the virus, what we know about how we can respond, and hopefully how we can help our patients. You know, one of the things I remind people, I think it's a little reassuring is that we've known about coronaviruses since the 1960's.

VR: That's right. We have. Some people think they're new, but they're not.

DG: They're not novel, are they?

VR: Nope, we have had a lot. There still are a number of coronaviruses that cause common colds, but these epidemic ones (first SARS, then MERS, and now SARS-2) - they're relatively recent - 2003 and beyond, so umm… this is the effect of population growth, global migration, and the desire for exotic meats, I think.

DG: There's, you know, a lot of things have really come together, and I think you know, global travel - we are so interconnected now. Within 24 hours, you know, it seemingly takes me longer to get to and from Uganda, but other people seem to travel the world much quicker (laughs). But no, within 24 hours, you can get from almost one point on the planet to the other, which means that if you have been exposed to something and there's any sort of an incubation period, it's very hard for something to stay in one place.

VR: That's right, especially something like this which doesn't necessarily make you terribly ill. You can be mildly sick or maybe not at all, and therefore traveling and so it's insidious because SARS, the original SARS, was far more serious. You ended up in the hospital - over 50% of infections, and so much easier to contain because in a hospital, as you know, you can do better infection control than in a community.

DG: And that, I think, you hit the nail on the head with one of the biggest challenges for us here is that particularly early on the disease it is very hard to differentiate this from the flu, from a lot of the common rhino-, entero- winter viruses that we see, so we've been given a little bit of an algorithm to try to figure out how to address this, and the first two features are the clinical features, say, so you want to raise your radar when you have a patient who has fever and respiratory symptoms, and all the clinicians I work with say, "That's pretty much what I see all day every day".

VR: Right, right.

DG: And so the last piece was the piece where we're losing, which maybe we should have lost a little bit sooner, and we'll talk about why, was "Oh, has this patient either been in a place where there's active transmission, or was this individual exposed - and it's 14 days prior to onset of symptoms - to someone with laboratory-confirmed CoVID-19? And um, or, I guess we'll use the right language. They'll say "laboratory confirmation that they're infected with SARS-CoV-2 and that they have CoVID-19". And what we're seeing now just in the last few days and actually we can talk a little bit about one of the particular cases, sort of skirting things so that we protect patient identity, but we're now seeing in the New York area evidence that we've had local community spread since mid-February.

VG: Yeah, so Times has reported tonight that um, we have a couple of cases in upstate New York not too far from the city, and one of them they reported was brought into Columbia to the hospital and I assume that's why the camera crews were waiting although the person's probably in the ICU, not in the Emergency Room, I would guess.

DG: Yeah, they're at the wrong place. (laughs).

VR: So those are the first confirmed infections in New York state? Is that correct?

DG: So, the first confirmed case was the woman who came over from Iran who was in Manhattan and was actually kept quarantined and then there was a delay in testing which I think we'll talk about - people are probably aware of this. What had happened was in the United States, to do testing you need to use something that has been approved by the FDA, so an FDA-approved test, and there's a whole process. So what had happened is getting up to this point, the CDC was working on having their test - a test that they felt would be validated, sensitive, specific. And then there was some breakdowns in the process. Kits were distributed, but those kits had a reagent that did not work, and we basically were reduced for the last bit of time to - you had to reach out to the CDC, you had to meet a stringent number of criteria, including that known exposure, known travel from endemic area. Then, the CDC would send you a kit. The sample would be procured. The sample would be sent back. It was really a matter of days from the time you became curious to getting any result, and we were maxed out at the ability to do very few tests. As of last Friday (five days ago), we'd only been able to perform 500 tests in the entire United States. So you can imagine with so few tests, you will definitely be seeing less than 500 cases. And then fortunately, I think a lot of people just said, "We've really got to bend the rules here. This is not a standard situation." And Saturday morning, New York State was given permission to use their own test, and you know, if you think about it, and I think a lot of the TWiV listeners, creating a PCR assay to detect a virus is not rocket science. It's virology science. (laughs). We have a lot of bright people that can come up and do those - so the CDC said to a lot of states, "Okay you can go ahead and use your tests, if you've confirmed them internally. We will jump on, you know, later, to you know, basically confirm as well that this is reliable." So that was the first diagnosis we saw - the test was sent on Saturday with a one-day turnaround. Sunday, we had our first confirmed case. Actually, while I was giving one of these informational webinars, so that was the woman who had been to Iran. And then we had another infection that presented Thursday, and this was actually one of our ProHealth patients, and I have to applaud the heightened radar of the ProHealth clinician who said, "You know what? This just doesn't make sense. This is a young individual. This individual who's now at Columbia, who really shouldn't be this sick and actually went ahead, they ended up in the hospital. They ended up in the ICU, and it wasn't until more recently that the testing could be done and it was confirmed that this gentleman had actually been sick since the 22nd of February and had actually ended up in the ICU with CoVID-19.

VR: And we know this individual was sick since then because it was self-reported. He or she said, "I've been sick since this date", right?

DG: Yeah, this individual started to feel poorly on the 22nd of February. We've gotten sort of an incubation that we think is on average about five or six days, so we're saying this person was probably exposed in mid-February, right?

VR: Yeah…

DG: And this person who is commuting in and out of the city on trains, and then we've already seen this little cluster grow to his family and five other people, so I think it's like ten people is what is publicly reported at the moment.

VR: Wow.

DG: Yeah, so very quickly… for us, the challenge as clinicians, we now know that there's active transmission in the community but yet the symptoms look for all the world like the flu, like RSV, like a lot of other common winter viral infections… so, who do you test?

VR: And you can't test everyone because it would be a logistical nightmare, I guess, right?

DG: Well, we're still, even with our ramped up - in a best case scenario, we can test at maximum 200 people a day in New York state, which is still just - this is still best case scenario, and that's still with the 24 hour turnaround with two labs and the state doing the testing.

VR: So tell us, how are you going to get past the cough and fever and decide who to test?

DG: So that is the challenge. I think at the end of the day, it's going to be just about everyone, but no, we've created a bunch of different - I'll say, algorithms, for approaching this. And the first one is, I think, to be reassured and to realize fortunately that the vast majority of people who come in contact and are exposed and infected with SARS-CoV-2 will not get seriously ill. And this is reassuring to me, as we have not seen a single death in a child under 9 years of age, so children seem to be a special protected population so there's some justice in the world, I think. (laughs)

VR: Wonderful. (laughing)

DG: At least we have that. But then the next thing is that we've started saying is that you can't - this isn't a joke, this is a line that I say. You can't acquire this infection over the telephone, so we've been trying to minimize the point of contact between providers and patients and actually between patients who might be infected and other patients who might get infected. By doing a little bit of a change in how we practice medicine in the United States, is trying to get doctors on the phone with patients and doctors are a little resistant ,right? You're not getting paid for this.

You're basically telling a patient, "Don't come to my office. Don't let me do what I do for a living. I'm basically going to be turning patients away, and giving you free medical advice over the phone. And saying, "Alright. How are you feeling?" And if the person says, "You know, I'm young. I don't have anything else going on. I don't feel so great, but I have a fever and I have a cough and some other symptoms" and I think the large majority of patients are going to be told, "you know, you sound like you're okay. YOu sound like you're going to be okay. This might be the flu. It might be this new virus. But you sound like you're in the group that is going to be just fine, so if your symptoms get worse, just call me back. Otherwise, I want you to stay home. We don't want you going to work because at the moment we can't test for this." That's gonna be hopefully the large majority. At the other end of the spectrum, is going to be someone calls and says, "You know, I'm 83 years old. I'm feeling really bad. I feel like I might have to go to the hospital. I've got a history of heart disease, diabetes." That is also sort of straightforward. You say, "You know what? You're going to need to go to the hospital to be assessed. You sound like a high risk individual, whether it's flu or RSV or the new virus." And then we're coordinating with which hospitals they should go to and actually calling ahead and letting them know so this person can be assessed without creating an exposure. The middle zone, this is our challenge, the grey zone, where the patient or the doctor just says, "You know what? Not sick enough to go to the hospital but I need to be seen. I'm not feeling well." And this is our challenge at the moment because the current recommendation is for airborne precautions when we're seeing patients, which I think on TWiV, you guys have been pretty good at\bout saying, "If anything, airborne is probably quite an exceptional situation with regard to spread of this virus. You know, someone's gotta cough on you. They've got to create droplets. Ballistic travel… so if you're six feet back and you're not on a cruise ship where there's not AC sucking these things around the ship and blowing it on someone else, which is a wonderful design, or you don't have some modified toilet system, in general, if you wear a gown, you have gloves, you protect your face, you put a surgical mask on the patient so that when they cough that's catching the droplets - in general, you can protect yourself quite well but if you're going to be in a closed room with the patient, they're recommending you actually wear a N95 respirator. And we have a national and local shortage. We also have a national and local shortage of people trained and fit-tested to adequately use those safely. So we're creating, at least ProHealth is creating a triage system, where I'm actually going to be on site at one of the urgent cares tomorrow with the head of the ProHealth urgent care, basically a limited number of personnel will be trained and going in the rooms and doing sort of, the grey level assessment. People who need to be seen so that they can be better triaged either back to the home or need to be in the hospital or maybe are given an alternative diagnosis such as flu, RSV etc.

VR: So if you have a patient who should be tested and they're positive for SARS-CoV-2, would you admit them just so that you can isolate them?

DG: No, no… and actually the majority of patients, we do not want to have in the hospital. The majority, and I think this is reassuring, the majority of people can go home. You know, 90% of people are going to get better with no hospitalization, with no specific care, really just with taking it easy, drinking some tea, staying hydrated. It's going to be a minority that actually are sick enough that there's a benefit to being in the hospital. We don't want to just cohort them there. We really are going to need to - from a resource point of view - basically, keep people in their homes, not spreading it, not sneaking out to a company party or something, which seems to be happening (laughs).

VR: So for the people who are seriously ill, have you know, acute respiratory distress, pneumonia, who clearly have to be hospitalized, at this point, we don't have antivirals, so what do you do for them?

DG: So that's true. We don't have any antivirals that have demonstrated efficacy in this. So, um, the biggest supportive care that is being utilized is a lot of people will have such severe lung inflammation, so we call it an ARDS, or basically, can say, SARS - (acute reactive lung disease) - where they actually can no longer breathe on their own. And they may for a period of time require the assistance of a ventilator, of a breathing machine.

VR: So speaking of antivirals, let's say we did have some amazing antivirals that have been developed in a time between SARS and now. Maybe we should have been doing that. And they were broadly acting against coronaviruses. How would you use those if you have now a patient who has tested positive?

DG: Now, I feel like that was a plug for you virus researchers, or us virus researchers, wanting funding so that we would be in this situation because that would be quite the godsend, right?

VR: Well I think as you would probably agree, we should have been doing this after SARS 1.0 went away. There has been a little bit of research, but we should have had broadly anti-coronaviral antivirals and I don't think that's too much to ask because the RNA polymerases are all conserved among all of them.

DG: You know, that's an excellent point. There's the RNA polymerase. There's also, and I think this is something that people talk about, the protease - there was some work done on targeting the protease because there's a protease in the coronaviruses. If there were medicines then again, you've got to make a decision about - we do this thing with influenza where I think everybody gets Tamiflu. Now, it works and you get it whether you need it or not. I think sometimes. You know, and part of it is that it is nice to be able to do something. But clearly, if someone is sick enough that they require hospitalization, particularly if they're pregnant, particularly if they're sick enough to be in ICU, there is a significant impact on outcomes by using Tamiflu. And it

would be ideal in situations like this, it almost would create a dilemma, right? Because if you tell someone to go home and self-quarantine, you somehow have got to get them that medicine as well, right? Because they don't want to be home without treatment. And then it also creates more of a need to actually confirm the diagnosis so we're not just giving everyone these medicines and then potentially creating resistance and losing a medicine that might be an important part of our arsenal.

VR: Yeah, and also of course if you had an approved antiviral, you would know when in the clinical course of disease it's too late to use it, right?

DG: And that's critical too, like for instance, we know in influenza, actually in several situations, the first 48 hours tends to be the critical time to get a medicine started. Once past that window, you're not making as big a difference.

VR: Yeah. So let's talk a little bit about the clinical course and I want your view on this because we've bandied this around on TWiV. So you're infected. There's an incubation period. Do we have good evidence that people are transmitting during the incubation period to others?

DG: Um, I think it's sort of how strict you use the word incubation, so yes. We have a sense of this incubation period, and you know, it could be as short as 1 or 2 days. It could be as far out as we say 14 days, and we're catching probably hopefully 99% of the people by then. Once you start to get symptoms, I think the thought is that you're starting to get viral replication right before the symptoms and there is a little bit of evidence concerning that there may be some spread before you have I'll say significant symptoms because when you look back, "oh I think that person said that their back was…" My back is always bothering me. What I would say is that there is some concern, I think, and I think some evidence that before you have symptoms that you would be concerned enough about, you may be shedding virus. You may be able to spread it. And that, for us, is presenting a problem. This pre-clinical transmission.

VR: And of course, as we said earlier, people have very mild disease and they don't think twice because it's flu season and cold season, and they're walking around, and they're probably transmitting infection.

DG: Yeah, yeah. And the people even - someone I was interacting with who was like, "Oh my allergies are just acting up horribly the past few days" in the middle of what, February/March, I'm like "okay I'm not sure what's in bloom" (laughs) I'm not sure it's your allergies.

VR: There's cherry blossoms. That's for sure.

DG: Exactly. And I think this is a big difference between SARS, shall we call it CoV-1? Or basically SARS?

VR: SARS, yeah.

DG: Yeah, SARS. I guess there was no - World War was World War and then it became WWI after the fact.

VR: Yeah, that's right. (laughs)

DG: But SARS had a characteristic where the transmission clearly peaked and was really centered around the height of symptoms, which again made it easier to quarantine. This was when they were in the hospital. The doors were shut. We had our infection control practices in full swing, but here what we're concerned about is the shedding and spreading prior to significant symptoms, and we're also concerned that there may be a tail to this. That you know, people may be feeling better, um, and then you know, going out and about and there may be some transmission at the tail end as well.

VR: Is that unusual for a respiratory viral infection?

DG: You know, it isn't. I listened to some of the TWiV's where you guys were talking about this. So for instance, I'll use influenza as a model. So influenza, we have these infection control practices where someone comes in and let's say they end up on Tamiflu and they finish their five days, which is twice a day, five-day course of Tamiflu for influenza. And now we say, alright, you're done, this is great, you can head out in the world. We can take you off precautions. By day five, 20% of patients are still actually shedding viable virus that can be transmitted, so it's.... I think Ebola we heard a little bit about too, a lot of viruses even when you feel better there can be a tail with this continued but reduced transmission.

VR: The few cases that have been mentioned in the literature that get a lot of attention and people freak out and say, you know, "Oh my gosh. We're never going to be free of this virus." And so people are saying, "Is it going to become persistent?" But i think this is typical. Right? It's nothing unusual.

DG: And that is reassuring, I mean, this is a virus - it's a coronavirus. We have growing experience with this. This is not something from another planet - it's something that is a little different and uh, yeah, it's something that I feel we are going into what will be a difficult time but we're going into this with knowledge, with techniques, with tools, and if anything we're getting more tools, you know, not as quickly as we would like, but the tools are coming and the

big tools, I think, are you know, better ability to test and determine where it is, and then what's going to take a bit longer is therapeutics and even quite a bit longer, is you know, vaccines.

VR: So I heard the Surgeon General say the other day the one thing you can do is stop buying face masks. You know, I'm seeing more and more people walk around. My students are asking me, "Should I wear a face mask?" So let me hear it from you. Should people wear face masks walking around on the street?

DG: So the science is pretty clear that face masks do not protect you. If you have an active infection, it will catch the droplets and protect others, so I guess if you have COViD-19 or influenza, and you're just a wonderful citizen worried about others (laughs), but nah, I think people are trying to wear them for personal protection and unfortunately, there's no evidence in that setting that it works. Now, a healthcare professional uses them in a certain way, but I watch people and they do this all the time. They pull the mask down to talk to me. "So, what are you doing?" (laughs)

VR: Did you hear on the last TWiV, Rich Condit, got on a plane and a lady next to him offered him a facemask and he declined, and she put hers on and then he said that when the peanuts came, she moved it up to feed herself peanuts. (laughs)

DG: Exactly (laughs). I view it - it's like the seatbelts. If everyone else in the car wears seat belts so they don't fly around and potentially bump into me and then I drive without. And the problem, actually, is because everyone is buying them we are having shortages, and that's going to be a problem. Well, it already is a problem for physicians, clinicians trying to take care of patients. And that cycles back - if there aren't clinicians out there to evaluate and care for this what looks like it's going to be a growing number of infected patients in the US, who's going to do that?

VR: You know, the one thing I think is okay is if you wear a face mask and you leave it on, it may stop you from touching your nose and mouth so frequently, and maybe not contaminating yourself.

DG: You know, my dad wore a face mask on the train for a few months and he did it because he always got like, the two seats to himself because no one would sit next to him. It's like "Okay, that's clever."

VR: That's very good. I like that. Alright, one more thing - my class tonight at Columbia. I have about 120 students in the class so it's quite large. They said they're hearing that Columbia is going to suspend classes, especially big ones, because there are a lot of people sitting together in

a room and I don't know anything about it but I can imagine that if the number of cases gets to a certain point and it looks like it's increasing uncontrollably, that could happen, right?

DG: No, it definitely could. And it's going to be interesting to watch and see and learn from how the United States responds to this, how the many different countries respond to this relative to how China responded. The first thing that we're a little delayed in is, I'd say, we're basically asking how many cases are present in the United States right now but we're asking with the door shut and the lights are turned off and it's anyone's guess until we can actually do the testing. Um, once we do the testing, we're going to have numbers and then we're going to very quickly how we respond to those numbers. Do we do what China did, where we say "Okay we've gotta come up with ways of schooling and educating people without having them come to a central area which is potentially an area for transmission? Are certain workers able to do their jobs from home? And not everyone can do that. And you know, we already have a couple of school closures, and we'll have to see going forward based on the numbers what the American culture and people and politicians are willing to tolerate.

VR: I have a feeling we're not going to tolerate what China did, having people stay in their apartments, leaving once or twice a week, getting a fever check when you leave, right? I don't think that's gonna happen here…

DG: It's gonna be a challenge. Like, the threshold for that trigger in the United States, I feel, is quite different, than the trigger for that in China.

VR: I spoke to someone in Switzerland today and she said that, well you know this probably, but Italy closed schools until March 15th.

DG: Yes, they did.

VR: So, I record my lectures so I could keep going and I could give my tests online and they could complete the entire course without having to come in, so I hope the university gives us that option. I think they probably will because Daniel, I have to say, for my virology course to be cancelled by a virus would really be something.

DG: That would be something.

VR: That would be ironic. And, the way I look at this, Daniel, I see this tiny virus bringing humanity to its knees. It's just remarkable.

DG: It is amazing but hopefully while we're down on our knees, we rise up with a little wisdom so that when we face the next challenge like this, we have a little better preparedness and a little

better experience, so hopefully there will not be a SARS-CoV-3 that sweeps around without us having the ability to respond a little quicker, having the testing capacities and hopefully have therapeutics.

VR: Well Daniel I really appreciate your taking the time. I know you're really busy. Why don't you come back in a couple weeks and as this thing evolves, back on TWiV and we'll do this again?

DG: Sounds great! It's a pleasure always.

VR: So you can find Daniel on TWiP (This Week in Parasitism). I think we have one next week, right?

DG: We do, on Thursday.

VR: OK. That'll be fun. Maybe we'll speak briefly about this beforehand anyway. And you can find him there. That's on microbe.tv/TWiP. He's also at Parasiteswithoutborders.com. And as he told you earlier he's at Columbia University Irving Medical Center. Daniel, thanks very much. I appreciate it.

DG: Thank you.

VR: My guest on TWiV is from the University of Geneva in the laboratory of Molecular Virology - Valeria Cagno. Welcome to TWiV.

VC: Thanks.

VR: Did I say your name right?

VC: Um, more or less. It's Valeria Cagno.

VR: Valeria Conyo. Are you of Italian origin? You were born in Italy?

VC: Yes, I am. I live in Switzerland since 4 years.

VR: And you're a virologist, right?

VC: Yes, I work in antiviral research and yeah, I always did that since my undergraduate studies and then I moved to Switzerland and I kept working in the antiviral field.

VR: And we met some time ago, right?

VC: Yep, at the European Conference of Virology in Rotterdam in May.

VR: Yeah, not too long ago, that's right. And you contacted me because you've started a couple of podcasts and one of them you said is a daily podcast on the current coronavirus, right?

VC: Yes, exactly. That is correct, and the name is Paziente Zero,, and you can find it on Spotify and all the major Podcast platforms.

VR: And it's in Italian, right?

VC: Yeah, exactly. Also, the other one that is - it's not a new podcast but it's a major scientific podcast in Italy. It's called Scientificast. Both are in Italian. The Scientificast is about general science - it's also about physics, etc. While the other one, Paziente Zero,, is only about coronavirus.

VR: So the other podcast, the bigger one, you do with other people, is that correct?

VC: Yes, we are like, 20? So we have both a blog and a podcast, and we have different expertise, so there are... I am the virologist but there are physics and mathematicians and there are chemists. I mean, a bit of everything.

VR: And the other one, Paziente Zero, do you do alone?

VC: No, I am with Lorenzo Paletti. He is an expert in podcasting and he studies physics, so he's still a scientist but he's really a podcaster.

VR: And this coronavirus podcast, you started recently, right?

VC: Yeah, we started two weeks ago. It was Monday, not of this week but the one before. It was basically the first case in Italy was on Friday and there was a lot of interest trying to understand what was going on. We received a lot of questions on Scientificast and so we felt like there was the need for clear information and not too many information, and so that's why we decided to start this. It's 10 minutes per day and key points of the virus. Like the transmission, or are there vaccines? Antivirals? We try to answer different questions on different days.

VR: So tell us, what's the current situation in Italy with respect to SARS-CoV-2?

VC: So, the decision of today is to close the schools as of the 15th of March - both schools and universities. There is still this red zone in Lombardy where initial cases were found. The number of cases is still increasing, so today we are around 3,000 cases in total but there are also some that don't have any more of the virus, so they are not in the hospital. They are fine. So the number of positive is 2,706 according to what I can read on the website of the authority, and there are 107 deaths.

VR: Wow. That's very different than the Johns Hopkins website that I always look at.

VC: Maybe it's because they have different validation. The Italian website only has cases that were confirmed by the Institute - the reference center, let's say - so the cases are increasing and they are expected to. I think they will increase more in the next days. And the point is that now there are a lot of imported cases in the neighboring countries. I'm in Switzerland and I was talking today to with the doctors of the Hospital of Geneva which is actually the reference center for Switzerland for testing for the coronavirus, and they were saying that the 60% of Swiss cases at least updated to yesterday - they are from the virus in Italy, let's say, and the 40% remaining is people that had direct contact with these people so there is no community spread in Switzerland. We can still trace where the virus is coming from, but the major source is Italy.

VR: So presumably, that will change in Switzerland. There should be at some point community spread, right?

VC: Right now, the definition of a case is if you have respiratory symptoms and you have traveled in Italy, Iran, Korea, Japan, or China. The point is that this was also the definition of a case without all of the other states, but it was like that in Italy and then they just found out randomly that this first patient had the coronavirus because he didn't have any relation with China and then from there, they understood that the virus was there since some weeks.

VR: So, do we know what brought the initial viruses into Italy?

VC: Uh, no, we just - I mean, from the sequences that are now accessible in NextGen website, it's still related to China so it doesn't seem to come from another imported case from another country. But, it's still unknown exactly when and who brought the virus but according to the spread that we have, it seems that something happened in January, maybe before the restriction of travel from Wuhan. I mean, we need time to find it out.

VR: So, in Italy you have extensive community transmission, right?

VC: Yes, now there are some… the point is that the mortality seems to be high because there are a lot of old people so like, one of the first people that died was actually an aged person that

apparently was infected playing cards at the local bar in the small village and the other thing is that it's weird that the place where there are the majority of cases are small villages, some in Veneto and some in Lombardy that are really like, there is not a density of population that is in China, for example. So it would be interesting if possible to understand how the virus arrived there.

VR: And are most of the deaths in elderly people?

VC: Yes. Absolutely yes. And I talked today with a friend that is living in the red zone, in this area that is completely quarantined. They cannot go out. There is an army checking the border, let's say, and they were saying that all the people that died in the neighboring villages are all people above 60 years old. It's as expected.

VR: You said there are over 3,000 confirmed cases, which I assume is RT-PCR, right?

VC: Yes.

VR: And of those, are most of the infections mild or are some of those serious as well?

VC: The majority of infections are mild. There are some - so the point is that in some areas where there are the majority - the hot spots, including the red zone and other provinces of Lombardy that is the region that is interested - there are some problems in the hospitals because they're filling up all their ICU places, so they start to have some problems. That's why they decided to close the school and to try to control as much as possible the spread in order to get the hospital ready to face this type of patient.

VR: So what are the diagnostic criteria? Who's gonna get tested? Do you have to be in the hospital? Or can you get sick and go to your doctor and get tested there?

VC: The procedure is to call the doctor and then to have a swab. it's not absolutely to go to the hospital. This is what's absolutely not said. In Switzerland, it's the same. You call your family doctor and then in case they consider you might be, you are included in the criteria, you can do the swab and have the qPCR done. In Geneva, they are doing qPCR on two different genes of the… so it's like, the RNA-dependent RNA Polymerase and the E gene. So it's like two different types and the recommendation of the WHO.

VR: So you said if you meet the case criteria, what would that be to get tested?

VC: So in Switzerland, for example, is to have a proven contact with someone that has been diagnosed with SARS-CoV-2, or having respiratory symptoms or fever and have a recent history

of traveling in Italy, China, Japan, Korea, or Iran. In Italy, in the beginning, they started doing tests to everyone. I mean in the hot zones, and then they decided also because there were some shortage of swabs and other logistical problems, they are now doing the tests only on symptomatic persons.

VR: Interesting. Yeah, it makes sense, because at this time of year you're going to have a lot of respiratory viral infections. Flu, rhinovirus, parainfluenza, etc. So you can't test everyone, otherwise as you said, you have logistic problems.

VC: Yeah, exactly.

VR: Same thing is going on here. Here, we have fewer cases, but I'm sure we have more in the coming weeks, and the diagnostic criteria are just being sorted out. It's a real problem, I think. But you can't test everyone for sure. Now you mentioned that schools, all schools in Italy, are closed now until the 15th of March.

VC: Exactly. So this is the decision of today, so today is the 4th of March and they just decided to close all the schools.

VR: What about other things? Are stores and businesses and everything else still open?

VC: Yes, the other businesses are still open. The only decision was to football - they will keep playing but without audience in the stadium.

VR: (laughs)

VC: And that's also happening in Switzerland as well, we have only 93 cases as of today, so if you have more than 1,000 people you cannot do an event, so for example the hockey matches here are without audience and they canceled some big events, so like Geneva has the motor show that is, I would say, the most famous in Europe, and this year is canceled because they want to avoid any announcement of the spread of the virus.

VR: I'm wondering if they're going to cancel Europic in Finland this year.

VC: We'll see. I hope to be there and to meet you again there, but I will understand in case they will make this decision.

VR: Yeah, I mean, it's in June so we'll probably have a little time to make a decision, but they should really tell us sooner because everyone has plans and if we have to change them, you know.

VC: Yeah, many countries have also restricted flights - for example, there are canceled flights from Italy to a lot of other countries such as Israel or Jordan. For Israel, the news today is that people from Switzerland, France, Austria, and Spain, I guess, they are quarantined if they want to go there, they say they have to stay in quarantine for 14 days and then they can have access to the country.

VR: What kinds of questions are you getting on your podcast? What are people worried about?

VC: At the very beginning, they were like "Is there anyone that survives?" I mean it was really panicking and not understanding exactly the extent of the illness. Then, there is a lot of interest in hand sanitizers, so how do I have to disinfect my hands or my phone or, I mean, yeah… and there was also a lot of videos on YouTube, like how to make your own hand sanitizer according to WHO guidelines. Then, there were questions about why the vaccine, if we have it, why we don't have it. Now we have a question because one of the ten points that the Health Minister said in Italy was, "Do not worry about your pet. You cannot spread the spread virus." So it's like, "How can you be sure that your dog your cat doesn't have the virus?" Then the other questions are obviously "What are the symptoms?" and "Why do old people get sicker?" and "What can I do to make my immune system work well in order to not get the virus?" and yeah, so a bit of everything.

VR: Do people ask about wearing face masks?

VC: Yes, they asked so this is very clear from the guidelines of the WHO, so we always say it's for people that work at the hospital and only the sick people to not contaminate the others, but in any case, there is a shortage of masks everywhere. In the red zone, in Italy, for example, you can go to the super markets. There are super markets inside the red zone are open but the big super markets, there is a queue so not too many people can be inside at the same time, and you need to wear a mask to enter. But then at the same time, if you don't have it and you go to the pharmacy and you want to buy it, there are no masks, so it's a bit complicated.

VR: No one's doing fever checks yet, right?

VC: No, this is only at the airports.

VR: Oh, okay. So if you want to travel at the airport, you get fever checks in Italy, is that right?

VC: Yes.

VR: And no matter where you're flying, within the country or out of the country, right?

VC: Yes, as far as I know, in all the airports there is the fever check.

VR: So what's happening in the rest of Europe? Do you have a sense for that?

VC: So I think at the beginning, there is this like, the relation with the Italian people was a bit like with the Chinese people at the beginning, like a big scare but now it's clear that without borders closed, it is normal that there are imported cases everywhere. In Italy at the same time, they say that we have a lot of cases in Italy because we started looking for them while still the definition of why you do a test in France or in Germany or in other countries is if you have a connection with Italy, so it's still a bit of this weird relation between Italy and the rest of Europe, but it's true that for example all the cases in Switzerland are related to Italy, but it's because the criteria to do the test is defined like that.

VR: So what is your sense for how long this is going to continue? It went on for a good two months in China and they still have cases every day. Do you think it will be similar in the rest of the world?

VC: I think, I mean, now - also if WHO doesn't say so, I really see it difficult to block the spread. We can just delay it, in my opinion. I mean, we know that other respiratory viruses tend to be more frequent in the winter season, so we hope that with the warm weather it will get a bit better. At the same time, I don't think we are seeing all the cases so if it's spreading that fast and that well, it means that there would be also more people immunized, probably. I mean, it's a mitigation, let's say, period, and I hope it will be, yeah… but I don't think it will end super soon, but at the same time, I hope summer will bring good news.

VR: I think that will happen. I mean, with the original SARS, it went from February until like the summer or less, and I think you're probably right but then again, there are cases in very hot countries, right, ongoing now, so who knows?

VC: Yes, but these are mild and imported…

VR: Yeah, they're imported. Exactly, right, yeah. The other thing I wonder is that in China they limited movement so they didn't build up herd immunity so then I'm afraid that when they release everyone to move around again that they'll have another wave of infection.

VC: Yeah, I read the WHO report from China and they say the Wuhan measures limited or at least delayed the spread of the virus, I mean, they say that it's highly possible that we will see a rebound.

VR: I was very surprised that it was so long in China without really substantial movement elsewhere in the world.

VC: Yeah, I mean we need more data to really understand what's going on and then with the cases in the other countries, we will figure it out, I guess.

VR: So, it's too bad we don't have a broadly acting antiviral, right?

VC: I'm working on that, but it's still early, but yeah, we are trying to target the.. So, what I work on is antivirals targeting the interior of the virus, in particular the attachment receptor, because many different viruses use heparin sulfate or sialic acid to attach and then they look for a more specific receptor that triggers the entry, so we have successfully made some nanoparticles and some cyclodextrins that are mimicking sialic acid and heparin sulfates and so the one against heparin sulfates are actually working against ten different viruses, and today we got the news that actually because in Bern, they are working with SARS-CoV-2 and it seems to work, but this is really a secret, so it's the news as of like, half an hour ago, so we have to verify everything but we are working on some coronaviruses.

VR: Well, maybe for the next spillover, because there will be a next one, your drugs will be ready.

VC: Yeah, let's see. I mean, for the next coronavirus, at least, or for the next emerging virus, because I mean for example we know it's working against Zika as well and yeah, we will see. We will keep working on that.

VR: I do think, though, that the coronavirus RNA polymerase is highly conserved and we could have a broadly acting antiviral that targets that and it's kind of a shame that we don't because once there's no SARS, the original SARS went away, the urgency also went away, but maybe people will learn a lesson now and fund that kind of work more substantially. What do you think?

VC: Yes. So, there are some European calls for funding and also some Swiss calls so there are a lot of money now is dedicated to this emergency but for sure, I think that we will look for a more broad, at least pan-coronavirus, inhibitors, and let's hope also that Remdesvir (I always have problems pronouncing it)- the drug that was developed against Ebola, it's showing good results in clinical trials, because this could already help.

VR: Yeah, I do think that would be interesting… apparently it's being tested in China, so we should know soon what's going on with that - Remdesvir, right?

VC: Okay, thank you (laughs).

VR: Well, this has been great. You know, you should come on regularly during this outbreak and give us a report on TWiV if you could do that every couple weeks.

VC: I would be happy to do it. Thank you.

VR: Because this has been really informative, because here in the US we don't know much about what's happening elsewhere, especially in Europe, so I appreciate that. And I just found the website. It's www.pazientezero.net - right? So if you're speaking Italian and you wanna hear about what's going on, check it out. And where can people find the other podcast as well?

VC: The other one is www.scientificast.it - I think. Now I have doubts.

VR: How do you spell the scientificast?

VC: S-C-I-E-N-T-I-F-I-C-A-S-T.

VR: Oh, -cast! I get it. Valeria, thank you so much for joining us.

VC: Thanks to you!

VR: And good luck with your research and with your podcast and I hope we can talk again soon.

VC: Thanks to you for inviting me, and it was a great pleasure.

VR: That's a special episode of TWiV all about SARS-CoV-2 and CoVID-19 here in the tri-state area of the US and over in Italy and Switzerland with our two guests, Daniel Griffin and Valeria Cagno, and if you like what we do, you can hear more - microbe.tv/twiv or you can subscribe to the podcast on any podcast player. In fact, this Sunday, that's March 8th, we'll be releasing our next episode. This is a special one. Our next regular episode where we answer most of your questions and also bring you up to speed on the science and the virology and if you do have a question about the disease and the virus, hand it over to TWiV at microbe.tv. We'll be doing weekly updates on coronavirus for the foreseeable future.

I'm Vincent Racaniello. You can find me at virology.blog. I want to thank ASV and ASM for their support of TWiV and Ronald Jenkees for the music. This episode of TWiV was recorded, edited, and posted by me - Vincent Racaniello.

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