

# First U.S. SARS-CoV-2 Patient

*[Announcer] This program is presented by the Centers for Disease Control and Prevention.*

[Sarah Gregory] Hi, I'm Sarah Gregory, and today I'm talking with Dr. Natalie Thornburg, a research microbiologist at CDC. We'll be discussing better ways to understand, prevent, and control SARS-CoV-2.

Welcome, Dr. Thornburg.

[Natalie Thornburg] Hi, Sarah. It's really great to be here. Thanks for inviting me to talk.

[Sarah Gregory] What does SARS-CoV-2 stand for?

[Natalie Thornburg] SARS-CoV-2 stands for severe acute respiratory syndrome coronavirus—CoV stands for coronavirus—and the 2 is because it's the second virus in its...in its species to be identified...the first one being SARS...the original SARS.

[Sarah Gregory] Back in 2002–3, right?

[Natalie Thornburg] Exactly—2002–2003, yes.

[Sarah Gregory] What's the difference between SARS-CoV-2 and COVID-19?

[Natalie Thornburg] Well, the...the naming conventions were chosen, I think, back in February of this year. And the groups who named the virus decided to do something like “HIV” and “AIDS.” They have named the virus separately from...from the, the disease. So, COVID-19 is the syndrome, the disease, the infection that you have; it is coronavirus disease, “19” refers to 2019, because that's whenever they identified it. And then SARS-CoV is the virus that causes COVID-19.

[Sarah Gregory] Okay, so, all this talk where mostly people are talking about COVID-19, they're actually really naming SARS-CoV-2?

[Natalie Thornburg] Exactly. If you're talking about the spread of, of...the spread, it is SARS-2. If you're talking about you have a friend with something, it's COVID-19. “My friend has COVID-19. They got a SARS-CoV infection and now they have COVID-19.”

[Sarah Gregory] I think there's probably a lot of confusion about that, right now, up there. So, thank you for explaining it.

So, there was a patient in Washington state with pneumonia. At the time, January of 2020, it was believed that the SARS-CoV-2 was not spread from human to human and was not particularly virulent. Why did you even test the patient for it?

[Natalie Thornburg] Well, you know, there were...there were some reports being...percolating through the media. You know, there, there...I began hearing rumors of a pneumonia in China, through the media. The first I had heard about this pneumonia outbreak was on New Year's Eve. I was at home and I was putting dishes away, and my husband was in the next room and was reading something in the news. And he asked me “Have you heard about this pneumonia

outbreak?” And people are saying maybe it’s a coronavirus. And I put the dish down and said “Oh my goodness, no I haven’t—that’s concerning!”

So, you know, we had some discussions within my branch for the next several days, and then the sequence was released to the public on January 10th. So, that confirmed it was a coronavirus. So, any time you have a coronavirus causing a pneumonia, it is concerning. Even if it’s not spread easily from person to person, it’s concerning. Like MERS coronavirus doesn’t spread efficiently person to person, but in certain circumstances, like in healthcare settings, with a lot of close contact, you can still get some person-to-person spread. And it can cause major issues, because some coronavirus have very high mortality rates, even if it’s not very efficient person-to-person spread.

So, we were concerned, and we began to act, as soon as the sequence was released on January 10<sup>th</sup>, preparing by designing detection assays, figuring out who would need to do what if we got what we thought was going to be an imported case, who should we test to look for imported cases. So, that’s the context of identifying that first case. We thought it was possible that we could be getting imported cases and that it could be pretty severe. You know, we were hearing fatality rates around 4 percent, 2 percent; and those fatality rates have...they’ve held, at least with we know so far.

So, that’s the context of that time. You know, sequence was released on January 10th—the identity of the virus—and of course, we had our first case identified on January 20<sup>th</sup>. So, in that 10-day span, CDC had to design a lot of different ways to detect the virus, they had to make plans for how are we...how are we going to find travellers. You know, it was right after our holidays; Chinese New Year was coming up; there’s a lot of travel during that time. So, we had to figure out where might people come into the country who could have this infection. So, I think there was a lot of information spread quickly, which is...which was good, about the potential of being exposed to this virus. And this first case was aware that they could have been exposed to it, just because of where their travel history was. And when they became sick, they were very astute and alerted their healthcare provider and said “I’m sick and this should be a consideration because I was in an area where there was a lot of COVID-19.” Of course, it wasn’t COVID-19 then; at that time, it was NCoV, I think. So, that is...January 20<sup>th</sup> is the day that that person’s specimen was tested in our diagnostics group, and that is the specimen we used to generate our first virus.

[Sarah Gregory] So, how did you go about this testing?

[Natalie Thornburg] Well, it’s a...it’s a...it’s a step-by-step thing. So, we have different labs with different skills. So, our diagnostics lab are...is the lab that designs...designs tests to detect the genetic material of viruses in different specimens. So, it’s a respiratory virus infection, one should probably test respiratory secretions—so nose swabs, oropharyngeal swabs. So, they design tests where they look at the sequence of the virus and then they design short...short pieces of DNA to find only that virus. And then, if the virus is present, it’s amplified; and if the virus is not present, it’s not amplified. And they can do this for lots of different viruses. So, the diagnostics lab is the group that actually does the detection and says “Yes, this person is infected,” or “No, this person is not infected.” And if they are, they will hand the specimen to us, so, the nasal swabs. They’ll give us the nasal swabs and then we will take those navel...nasal swabs and grow viruses from them.

[Sarah Gregory] Okay. So, you tested and you found that there was some kind of match, um, yeah?

[Natalie Thornburg] Yes, so that person was...that person was infected. And then we take the nasal material, the nasal swab material, and then we put it into cells that we grow; we call it enculture. So, we have cells from different kind of animals, from different kind of organs, and we just grow it on plastic with, like, liquid food. And so we're able to take cells and mix it with that patient specimen, and...and then we watch the cells. And so, we have cells that are not infected and we watch what they look like. They look healthy, they're sitting down on the plastic, they're growing. And then we watch the cells that we mixed with the nasal specimen, and see how they look. Now, if they start showing what we call cytopathic effect, which is basically cell...cell death, you know, we'll start seeing patches of the cells kind of like squishing together, rounding up, just looking very unhappy. So that...looking at the cells, and when they look like that, we...we can presume that maybe there's a virus growing in there.

So, once we see enough of that cytopathic effect in a...in the cells, we can take those cells out and do the same diagnostic test that was done on the nose swabs and see if it's the virus we think it is. And so, in this case, yes, the diagnostic test said, yes, it is the same virus, and not only is it the same virus, but there's more virus now that it's gone through cells than there was in the nose. So, that always gives us an indication that the virus is growing in cells. The test results look the same, plus there's even more of it once it goes through the cells, meaning the cells are amplifying the virus.

[Sarah Gregory] Okay, so did you have samples from the Wuhan outbreak? I mean, how did you match the results?

[Natalie Thornburg] No, we didn't have any samples from the Wuhan outbreak. So, once we have the virus culture, then we can take the virus that we've grown through cells and we can send it to our lab next door to us that can sequence the virus. And they can generate the sequence from the entire virus genome. So we can compare that to other viruses that have been sequenced from Wuhan. But also, the person who was our first patient in the United States...they had traveled in Wuhan, so they had a travel history. Back in the beginning of the outbreak, before we knew about person-to-person transmission, we were primarily looking at imported cases because that has been the precedence with coronavirus outbreaks is, most cases are import and person-to-person transmission is not efficient. Of course, we know differently now, but this was the context of January 20<sup>th</sup> before we ever knew about person-to-person transmission. Those reports didn't start coming out until right around the same time, we started hearing some rumblings...there was one household that same week, where there was reported to maybe be some person-to-person transmission in Wuhan. But that was happening simultaneously. So, our patients had been traveling in Wuhan, our virus that we isolated from that patient had a sequence similar to what was being sequenced in Wuhan.

[Sarah Gregory] Okay, so how did this person get the virus? They got it from...it was actually transmitted person-to-person to them in China, and then they came back with it? Is that right?

[Natalie Thornburg] We don't know. We don't know what that person's exposure was. So, they reported not having gone to the seafood market that was the original...supposedly the original source of the outbreak. So they had reported not going that seafood market. And they had reported not having any contact to...with anyone who was known to be sick. So we don't know

what that person's exposure was. Now, we know now that there might be some presymptomatic transmission. So, it's possible they were exposed to somebody who wasn't yet sick, and then after they...they returned to the United States, that person became sick. So, we don't know what that person's exposure was.

[Sarah Gregory] These samples...clearly, your initial samples are very important to the ongoing situation. Where are they now, the samples?

[Natalie Thornburg] So, the original specimens, the patient specimens, are held here. Part of diagnostic rules are that, if you diagnose someone, you have to hold them in the lab that did the diagnostics. So, the original patient specimens are held here in the diagnostic lab.

[Sarah Gregory] Here being CDC?

[Natalie Thornburg] Oh, yes. So, here being CDC, correct. And then the virus that we generated, we still have that here, but we have also tried to get that out to other labs as widely as we could, so that they can do as much research as possible on the virus. So, the virus that we made, we put it in two repositories. One is called BEI Resources. The other place we put it is in UTMB World Reference Center for Emerging Viruses and Arboviruses. Both of those repositories are publicly funded, and they can provide viruses and other reagents to research labs, to public health labs, to whomever might need the viruses who have the expertise and the appropriate facilities to handle the virus. And by making these viruses available, laboratories can get the virus and test their antivirals against them, test their vaccines, see how the virus gets transmitted, how it grows in cells, how it might work in animals. So we're really trying to proliferate research to accelerate development of anything that might help in this outbreak and slow it down or stop it, whether that be a drug or a vaccine, or through understanding how it's transmitted between people so that we can stop behaviors to slow it down. So we put it in those two repositories, and then we also sent it to a couple of labs who we've worked with for many years...we sent it to Rocky Mountain Labs at NIH in Montana; we shared it with UNC-Chapel Hill, the Baric group has been working on coronaviruses for, I think, 30 years; we shared it with Vanderbilt University, who does antiviral testing under Mark Denison, who's been working on coronaviruses for 20 years; we've shared it with Dr. Matt Frieman at University of Maryland, who's doing quite a bit of antiviral testing. So, we really tried to get it into as many scientists' hands as we possibly could to get research moving as quickly as we possibly can.

[Sarah Gregory] And just one little bit of clarification...UTMB is what?

[Natalie Thornburg] Ah—it is University of Texas—Medical Branch. It is part of the University of Texas system, and it is in Galveston, Texas, and they have a lot of containment labs there in Galveston. So this is...this is a virus that needs to be handled under what we call “containment.” You need to have special engineering control to keep the lab staff safe from the virus and you have to wear a lot of what we call “PPE,” personal protective equipment. So, you need to wear a hood with a...you know, it looks like space suits like you think about in movies. You need to wear a lot of equipment to protect yourself from the virus and make sure you're not spreading it outside the lab. So, UTMB has a lot of containment labs and a lot of expertise there about handling dangerous viruses.

[Sarah Gregory] Okay. You already kind of touched on this a little bit, but why is it important to have these original specimens, and what impact do they have on public health?

[Natalie Thornburg] You know, as scientists, we're really trained very narrowly and deeply. We know our subject very, very well. We know it deep. But we don't train broadly, like I don't know everything about every virus. I know my viruses very, very well. And that's true for everyone, and every scientist has sort of like a unique set of skills and a unique set of knowledge. And it's really important right now to play to our skills and our knowledge, and to make sure—I said earlier that we proliferate our research—but if someone is very good at antiviral testing, I want them doing that. I don't want to have to learn that new skill. We are very good at isolating viruses. So, we're going to do that and hand it to the people who can do antiviral testing. There are people who are very good with animal tests, so I want them to do their part. And it's kind of this idea of “the sum is better than each of the parts.” So that, if everyone is doing their job, everything speeds up that much more because they're doing what they're best at. So it was really important for me to get the material to the people who can do all of these different things better than we can do that, so that they can do what they're good at and try just every different way we can to stop this pandemic or at least slow it down in some sort of way.

[Sarah Gregory] So many people have died already, just in the United States there's been over 10,000 people. Do we know the status of...do we know the status of this particular patient?

[Natalie Thornburg] This particular patient recovered. You know, the severity of illness varies pretty widely. We've heard several people having very mild illness, and then of course a proportion of people go on to die. So this patient did recover, and I have heard that this patient continues to give sera to investigators at University of Washington to try to help with research and contribute in any way that they feel possible. So they're being very generous after having been through this pretty, I can imagine, traumatic experience.

[Sarah Gregory] I was just wondering this week, does it make a difference how you catch it? I mean, if you catch it from another person, or a surface, or you know, walking through somewhere somebody was two hours ago...I mean, does it have any impact on the severity?

[Natalie Thornburg] You know, that's a really good question. I don't think we have enough information to really answer that with certainty yet. What I can say is that, you know, healthcare workers can get more severe disease than non-healthcare workers, even if they're young and healthy. So, to me that indicates that the mechanism of transmission might matter, in that if a healthcare worker is exposed in that setting, there is something about that exposure setting that makes them more prone to severe disease. So, I believe that might be true, but we don't have enough data to say with certainty yet.

[Sarah Gregory] Alright. Also along those same lines, I know myself ...I've been isolated for three weeks now, over three weeks, but I do have groceries delivered. And I'm fairly paranoid about those groceries. I take them in the garage, I spray them down with disinfectant, I let them sit for days....and then I'm still scared! Am I being neurotic or is this a reasonable...?

[Natalie Thornburg] You are not the only person I've heard that from. I'm hearing that from my non-corona scientist friends that they're doing the same thing. Full disclosure, I am not doing that. But I don't know whether it's the busyness of my life right now, or some understanding that coronaviruses really are transmitted most efficiently person-to-person. So, the biggest danger you're going to have is close contact with a person who is either presymptomatic or is actively ill. That is, by far, going to be the highest risk. Now, I was a coauthor on the paper that has sort of created all this buzz about surfaces. So, in that paper—it was published in the *New England*

*Journal of Medicine*—in that paper, the investigators at the Rocky Mountain Lab, with whom we shared our virus, they detected the ability for the virus to live on different surfaces, so on plastic and metal and copper, and found that it lives on different surfaces for different amounts of time, up to even days. Now, there's a difference between living on the surface and, like, a large amount living on the surface. So, the half-life, which means that's the time it takes for half the virus to go away, is actually only hours, not days, on most surfaces. So, someone sneezes on a plastic key-thing at the grocery store...in three hours, half that virus is gone, and then three more hours, half still. So, now you're at a quarter. And then three hours later, you're at one-eighth, and so on and so forth. So, the decay is in the context of hours, not days. And the dose matters. So there is some sort of infectious dose. So if you get exposed to a huge amount of virus, you're more likely to become infected than a low amount of virus.

So, I am concerned about surfaces, so I'm being very careful about washing my hands and not touching too many high-touch surfaces. But, your groceries...yes, they could have something on them, but then they come into your house and after they are there for a few hours, there's really not going to be much on it. There's been no data suggesting foodborne transmission of SARS-CoV-2. So, I don't think by eating something you're going to expose yourself. And then they sit in your refrigerator—we don't know what refrigeration does—or you microwave something. So, you know, what I'm doing with my groceries, I'm not going to say to someone “don't surface disinfect your groceries” because especially if you're nervous about it, it's not going to hurt. But what I am doing is I'm bringing them inside, I'm washing my hands, I'm putting them away, and then I'm washing my hands again. And then right before I eat, I wash my hands. So, I'm just trying to wash my hands anytime I'm touching food, which is a good idea anyway.

[Sarah Gregory] Not on the subject of this particular outbreak, but I was again thinking just today that I'm hoping this creates a new culture of more hand washing throughout the world. And, maybe we'll have less disease spread? You're laughing...

[Natalie Thornburg] Oh, I would hope you're right! But memories are very short. [laughing] And I can tell you that my nine year-old is still having to be reminded to wash his hands. I can't believe I'm saying to him so many times a day, “Wash your hands, we're in the middle of a pandemic! We're in the middle of a pandemic, please wash your hands!” So, the children...I'm not sure it's going to sink in. And, yeah...

[Sarah Gregory] Ah, oh well! Tell us about your work at CDC. What do you mainly focus on? Tell us what you're focusing on now, and also what you focus on when we're not in the middle of a pandemic.

[Natalie Thornburg] So, my lab is both the virus culture lab and we are what we call “the immunology lab.” So we are studying both the ability to grow viruses, and we study antibody responses to the viruses. So the ability to grown viruses—in the beginning of the outbreak, it was important for us to make viruses so people could do their research. And then once we got those out, we started trying to figure out what patient specimens can we culture virus from, how long after symptom onset can we culture virus, and might we be able to culture virus from, like, asymptomatic people or presymptomatic people. So, we're trying to use virus culture to inform understanding about how the virus might be transmitted, or when it might be transmitted. And then for our antibody studies, we're trying to learn from patients who have had confirmed COVID-19. Do they mount antibody responses? How quickly do they mount antibody responses? And might those antibody responses what we call “neutralize” the virus, which means

bind the virus and stop it from entering cells? And we can hope that if they make neutralizing responses, that maybe in the future those would be protective. Although, we don't have that data yet and won't have that data for...until the virus, you know, continues...if it continues to circulate. We won't really know if a person that is infected, can be reinfected, until they either are or aren't. So, we're really spending a lot of effort on doing antibody studies from patients and now we're really starting to do a lot of—we're calling it “serosurveillance”—so, collecting serum from healthy people, from people who had contact with patients, to figure out what percent of the population has made antibodies against the virus, in areas where there's been a lot of infection, like New York City, and areas where there hasn't been a lot of infection. So, we're just starting to get a picture of what immunity to the virus might look like over the next year.

So, that's what we're doing, focusing on right now. And when we're not in a response, we are the non-flu respiratory virus group. So, we're responsible for any respiratory virus that's not flu. So we've done a lot of work with another coronavirus called “MERS,” Middle East Respiratory Syndrome virus, that is a...also a severe coronavirus, but it doesn't transmit easily between person-to-person. It goes from camel to people pretty easily, and then person-to-person in only limited ways. So we work on that virus and its immune response. And then we have a big program studying respiratory syncytial virus, which is a common respiratory virus that is...causes a lot of hospitalization in infants. So it can be pretty devastating to young children and potentially older adults, so we do a lot of research with respiratory syncytial virus, as well.

[Sarah Gregory] Can you say the name of that virus again?

[Natalie Thornburg] It is called respiratory syncytial virus, or RSV for short.

[Sarah Gregory] Okay, so what's next for you?

[Natalie Thornburg] So, I think we're going to be really...my lab is going to be working on this virus quite a lot over the next six months to a year. So, we need to figure out...I think our most important work is going to be looking at antibody responses in people who've been exposed in the general population and trying to figure out if the antibodies that they're making might be protective, because we really need to start understanding if healthcare workers have made antibody responses. Is it safe for them go back to work? Is there no protection from their antibody responses? Getting to the bottom of these questions is very important to sort of resuming normal life. So, I think our big push is going to be antibody responses against this virus.

[Sarah Gregory] Thank you so much for taking the time out of what is clearly a very busy world right now, and such interesting and useful information. I really appreciate it.

[Natalie Thornburg] You're welcome, and thanks for inviting me! I'm happy to share our work anytime.

[Sarah Gregory] Listeners can read the June 2020 article, Severe Acute Respiratory Syndrome Coronavirus 2 from Patient with 2019 Novel Coronavirus Disease, United States, online at [cdc.gov/eid](https://www.cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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