

COVID-19 Chapter 1: Virology

Tiziano

My name is Tiziano. I am from the northeast of Italy. I live in a small town in the northeast. I am a schoolteacher. I teach English in secondary school here. So, the thing is, the schools stopped, but the rest of the country went on, but things started moving fast. So we are now under this lockdown, which means that we cannot leave our homes, unless it's for either work reasons or basic needs. Kind of a soft lockdown, because we can actually move but we have to provide some sort of declaration, a written statement for the reason why we are out of our homes. Until the government came out with the lockdown, I think people didn't really appreciate what that meant. And so it was just a few days before that that there were still parties going on and restaurants open and so on.

For the, let's say, for the lockdown we are under now, um, so if I was to go out tomorrow without a good reason. The police is going to stop you and check your statement, so if it's for work reasons, they are going to call your workplace and that, so there is a fine or you could face charges, you could go to jail, but that's only for extreme cases. After the last, um, regulation, so this past week, I think that people are taking the thing more seriously, and from what I see from my immediate vicinity and from people I, I know, we are starting to embrace the social distancing and so we are moving to Skype calls with friends, and uh, you know, the indoors life, as much as we can [chuckles].

As a schoolteacher, I maybe have a slightly different perspective than most other people because we started from the very beginning to find ways to still keep doing school in some form. But, um, there wasn't really a plan for that, so a lot of it was left to our own, you know, creativity and good will to do things. There are still issues with that. The first one is that it's very hard to keep in touch with all our students because, of course, not everybody is available, not everybody has the same resources, and it's hard, and it's impacting families, especially families where the parents are still working. And so they need to take care of the children. Traditionally, here, families are very close-knit, and this was something that often grandparents did, but grandparents are, of course, one of the most impacted categories for the virus, so that has raised some issues.

We have one of those flash mobs on the balconies every day, basically. You know, I'm in a small town, so there's not a lot of houses around here. Every day there is someone either playing songs or the other day they were clapping for the people in the medical professions, which are doing a great job and taking double shifts to cover everything, so that's good. There's this other thing that's going on now, which is the kids are making these rainbow paintings and with a hashtag that's basically, "everything is going to be fine" in Italian. And they are, you know, sharing those pictures on the social media. This is bringing out a lot of, you know, good things. I see that people care. People care about their neighbors, people care about what's going on. That's a big thing.

[musical interlude]

Erin Welsh You just heard from Tiziano, who was kind enough to spare us a few minutes to chat about his experiences while under lockdown in Italy. Thanks so much for chatting with us.

Erin Updyke Yeah, we really appreciate it.

Erin Welsh Hi, I'm Erin Welsh.

Erin Updyke And I'm Erin Allmann Updyke.

Erin Welsh And you're listening to This Podcast Will Kill You.

Erin Updyke Oh yes, you are. [laughter]

Erin Welsh You are. Yes, welcome to our first ever mini-isode series, which we're calling Anatomy of a Pandemic.

Erin Updyke Mmhmm.

Erin Welsh Which is shaping up to be less of mini-isodes and more like full length ones, so.

Erin Updyke Yeah. It's maxi-isodes.

Erin Welsh So, sorry not sorry? I don't know.

Erin Updyke It's long. Strap in. [laughter]

Erin Welsh There's a lot of information out there, and there's a lot of ground to be covered, so you know, we're going to do the best we can. And this is, this is the first episode of six that we're dropping all at once, but throughout this pandemic, as it progresses, we're gonna keep revisiting different topics or visiting new topics to get you all the information that you could ever want about COVID-19.

Erin Updyke Yep.

Erin Welsh So, we asked everyone out there for questions, and hundreds of you submitted your questions, so thank you so very much, because that really helped us to figure out what you wanted to know and how to organize these episodes. And so we are so excited to bring you not one, but six of these episodes where we ask the experts to answer your questions.

Erin Updyke So today, we're starting with Chapter 1, the virus itself. Uh, and that's what we're gonna cover in this episode. But, before we get started, we have to report, of course, that if ever it was quarantini time, right now is most definitely quarantini time.

[laughter]

Erin Welsh Most definitely.

Erin Updyke Uh, quarantinis have been making the rounds in social media and, first of all, we appreciate everyone shouting us out, um, in that.

Erin Welsh Yeah. We do.

Erin Updyke So what are we drinking today, Erin?

Erin Welsh We are drinking what we're just calling Quarantini 1 because, you know, let's keep it simple.

Erin Updyke We'll keep it simple. Uh, disclaimer. If you're gonna listen to all six of these episodes in one sitting, you don't need to make all six quarantinis.

Erin Welsh Yeah.

Erin Updyke That's probably a bad idea.

Erin Welsh I personally, so I am recording this, it's 8 my time and I'm drinking coffee.

Erin Updyke It's 10 am my time. I'm drinking water, but I did drink a quarantini last night while researching.

Erin Welsh I drank a couple while taking the pictures of them all.

[laughter]

Erin Welsh It's important, you gotta taste test!

Erin Updyke So what is Quarantini number 1, Erin?

Erin Welsh Quarantini number 1 has rum, it has coconut cream, it has lime juice, and, you know, we wanted to make these so that hopefully they're things that you might have lying around the house, more simple ingredients and so on. But I will suggest, if you happen to have apricot liqueur, pop some of that in there as well.

Erin Updyke If your bar cart is as well stocked as Erin Welsh's.

[laughter]

Erin Welsh Apricot liqueur is really good in tiki drinks!

Erin Updyke Yeah, yeah.

Erin Welsh That's all I'm gonna say.

Erin Updyke Mmhmm. I believe you.

Erin Welsh We will post the recipe for that quarantini, Quarantini 1, as well as the non-alcoholic placeborita, on all of our social media pages as well as our website.

Erin Updyke Excellent.

Erin Welsh Okay.

Erin Updyke Alright, so.

Erin Welsh So way back in February, which feels, honestly, like an entire lifetime ago, we did a whole episode about coronaviruses in general. And so we wanted to give you a really quick recap on that. Alright, so coronaviruses are not brand-new, alien viruses. They are a large family of viruses that infect a number of different animals. SARS-CoV-2, which stands for Severe Acute Respiratory Syndrome Coronavirus number 2, which is a little bit of a mouthful, this is the official name for the virus that causes the disease COVID-19. You can break that down to see where that comes from. It's COronaVirus Disease 19. COVID-19. And so this is a virus that is new to humans, and it emerged, as it turns out, or as it likely turns out, in November 2019. Obviously, this is now a pandemic. And so we are going to talk, in this episode, about the biology of this virus and some of the characteristics that have allowed it or facilitated it to reach pandemic proportions.

Erin Updyke Exactly. So let's do a quick primer about viruses in general, especially for any new listeners that haven't heard any of my virus spiels, many times over. So viruses are essentially just packets of genetic material. They're made of either DNA or RNA along with protein. Viruses can't replicate on their own, so unlike most bacteria, for example, which can multiply just by replicating their DNA and dividing into two, viruses have to infect a cell of some kind, a host cell, and use that host's cellular machinery to actually replicate their genetic material. So in the case of SARS-CoV-2, this is an RNA virus. It's a positive-strand RNA virus. That means that once it gets into your cells, that viral RNA is released into our human cells. And then our cells do two things with this RNA. Number 1, they start copying it directly, as if it was our own RNA. And number 2, what RNA does in normal cells is it codes for protein. So our cells start to use this viral RNA to make the proteins that that viral RNA codes for. And then the replicated RNA, plus those proteins, get assembled into new little virus packets. Okay? And those new viruses can then burst forth from the cell and go on to infect another cell, either in your body or in another host. So that's how RNA viruses work. DNA viruses do essentially the same thing, except that, in order to make protein from DNA, your cells have to first translate into that RNA. So RNA viruses sort of skip that step. And, as you'll hear our expert talk more about, they also tend to make more mistakes in that process of replication. But either way, viruses are using your host machinery to do this. They can't replicate outside of host cells. Cool?

Erin Welsh Cool. So, in this episode, we talked to a virologist, Dr. Angela Rasmussen from Columbia University, to answer your questions about the biology of this virus, how it works, how it infects your cells, and what markers it uses to get into our cells, and

then we also chat about its mutation rate and what that means for disease severity to its longevity on surfaces and whether the existence of multiple strains is a concern.

Erin Updyke Mmhmm. So she'll introduce herself to you right after this break.

[musical interlude]

Angela Rasmussen I'm Dr. Angela Rasmussen. I'm on the faculty at the Center for Infection and Immunity at the Columbia Mailman School of Public Health. I'm a virologist who studies, I specialize in studying the host response to infection. So when you get infected with a virus, your body responds to that. There is an immune response, an inflammatory response, sometimes there can be metabolic responses. And I study those. And sometimes those responses, depending on what they are, can mean the difference between getting rid of an infection and having, you know, a mild short illness, versus having a chronic illness or a more severe disease. So the viruses that I've been studying lately are ebolavirus, MERS, coronavirus, influenza virus other hemorrhagic fever viruses. And, of course now, like many of my colleagues, I'm also studying SARS-coronavirus-2 or COVID-19.

Erin Welsh That is the reason that we brought you on today. So thank you so much. First of all, for agreeing to be on the podcast. And yeah, so jumping right into the SARS-CoV-2, what are the origins of this virus? Where did it come from?

Angela Rasmussen So, we don't know for sure and I suspect that that's going to be my answer to almost every single one of your questions today. [laughter] But we do know that there was a very, very similar virus found in a bat in a cave in China in 2017. And this virus is a member of the same genus as SARS-coronavirus or SARS classic and SARS-coronavirus-2, this novel coronavirus that we're all dealing with now. There are a number of these viruses that have been discovered. They're called bat-SARS-like-coronaviruses, very clever original name, [laughter] because they are very much genetically like SARS-coronavirus and now SARS-coronavirus-2. We do know that this virus probably, based on our analysis of the genome, evolved from one of these bat-SARS-like-coronaviruses. We don't know if there was another animal involved in the spread of this virus from its wildlife reservoir, the animal that had it in the wild, to humans. What we do know is that this spillover, which is the transmission of a virus from its wildlife reservoir into humans was probably a single event. Meaning that there weren't multiple instances of animals infecting people after the first patient or patients were infected with this from whatever animal it came from. It's been transmitted human to human ever since. The reason why it's important to understand eventually if this came directly from a bat or if it came from a different animal, is that both SARS classic and MERS coronaviruses were amplified in an intermediate species. So both SARS and MERS are thought to have also originated in bats. However SARS classic was transmitted into humans, most likely from an animal called a Civit. And MERS coronavirus is known to be transmitted primarily from dromedary camels to humans. So we don't know if there was another animal in between the bat and the human that also was involved in the spillover from its wildlife reservoir.

Erin Welsh To follow up on that, so you mentioned that likely came from one spillover event, so from one infected animal, whether it was a bat or a different intermediate host into a human, how can we tell whether it's one spillover event or multiple?

Angela Rasmussen Yeah, so you can tell that by looking at the genome. And one thing that's been really incredible, and also really hard to keep up with, about this particular epidemic, is that this is really the first time that we've had sequence data from the virus genome really, really soon after the first patients were reported. So, the first viral sequences were uploaded and shared with the international scientific community in early January. So we've been able to analyze the genome of this virus since before we actually were able to even isolate the virus. So we can look at the genome of this virus and we can look at the specific individual changes in one isolate of the virus versus another. And by looking at those changes, we can deduce how many different viruses came out of the bats versus came versus went from person to person. There are specific genetic signatures that are associated in many cases with bat coronaviruses and coronaviruses that are transmitted within bats, including some sequences that are a part of the envelope glycoprotein, which is called spike. And that molecule is on the surface of the virus and it allows the virus to enter a cell that it's going to infect. That protein spike has changes sometimes that are specific to bats versus specific to humans. And we can look at that as well to determine how recently the virus emerged from a bat versus emerged from a human.

Erin Welsh Awesome, thank you.

Angela Rasmussen Does that make sense? Okay.

Erin Welsh Yes, absolutely.

Angela Rasmussen Okay, good.

Erin Updyke So kind of along those of the proteins on the surface, are those related to how the virus gets in and actually causes disease? What do we know about the mechanism of how this virus causes disease in humans?

Angela Rasmussen So that's a very excellent question because it gets into what I study, the host response. So there are two things to any virus infection to keep in mind. The virus can infect cells, and that determines whether it can establish an infection, get inside, versus the viruses' what we call pathogenicity, or ability to cause disease. Not all viruses cause severe disease. Some viruses, most viruses that can cause disease, which we call pathogens, those pathogens in some people will cause very mild disease and in some will cause very severe disease. And we're seeing that in terms of the fairly broad range of disease presentations of COVID-19. So the ability to get into the cell is just one part. And of course, in order to cause disease, a virus has to be able to infect the cell. So those proteins on the surface of the cell, or on

the surface of the virus particle called spike, spike binds the host cellular receptor, which is, in humans, the molecule we know about anyways, is called ACE-2. And ACE-2 is on a variety of different tissues, but there's a lot of it in your lungs, which is why this causes a pulmonary disease. So certainly in that sense, the virus spike protein is involved in determining that this is going to be a pulmonary disease. Similarly, we know that ACE-2 is expressed in the gastrointestinal tract and there have been reports that infectious virus has been found in stool of some patients. Also, people have reported diarrhea, which may again suggest that the ability to infect the intestine because of that receptor binding, the spike protein on the surface of the virus particle allows this virus to cause a gastrointestinal disease. But when you're talking about what is the difference between a virus in two different people causing a mild cold like illness in one person versus causing severe pneumonia in another, that difference is often related to the host response. And that can be determined by a lot of different things. It can be determined by genetics, it can be determined by the health state of that individual, which we, again, already know as a risk factor because people with preexisting medical conditions are more susceptible to severe disease. So really, a lot of the disease is likely caused by a sort of out of control inflammatory response in infected tissues. And that largely depends on the person who's infected, as well as their overall health condition, and sometimes the circumstances in which they're infected.

Erin Updyke That was so, beautiful.

Erin Welsh It was such a great answer. Yeah.

Angela Rasmussen Thank you. I get passionate about the host response [laughter]

Erin Welsh So recently there was a paper that was published that found that there were two strains of the virus and they named these strains "L" and "S". And these strains, according to this paper, seemed to differ in their virulence, one being more aggressive than the other. And this finding has seemed to be a little bit controversial. So, can you talk about why it is controversial, and whether the possibility of multiple strains is a real concern, and maybe whether this finding is actually valid. Are there multiple strains of SARS-CoV-2?

Angela Rasmussen Right. So this, this definitely gets down into an inherent property of RNA viruses like coronaviruses, and that is that every time the virus copies its own genome in order to replicate or make more viruses, the virus makes mistakes. The enzyme that copies the genome does not have proofreading capability the way that the analogous enzymes that we have that copy our DNA genomes do. So that means that the virus makes mistakes. We call these mutations. Many of these mutations are silent. They don't have any effect on the way the virus works. Many more of them will have a negative effect on the way the virus works and make it so that the virus can't work essentially. And some of them will confer an advantage. These mutations occur randomly. So there has to be a selection pressure to maintain mutations from generation to generation. And some of these advantages can be an enhanced ability to replicate in various host cells. It can be the ability to evade the

host immune response. It can be something that would make the virus more capable of infecting cells, or capable of inducing a response that would lead to more severe disease. So right now, we don't know what a lot of those theoretical mutations would be that could make the virus more virulent, capable of infecting more cells, or more pathogenic, capable of causing more intense disease. The paper that you mentioned is controversial because, essentially it's grouping these two viruses into what they're calling strains. But what are normal groupings of RNA viruses that have replicated in multiple hosts? What makes a virus a different strain often depends a lot on which virus you're talking about. In this case, if we're talking about two different genotypes, or virus genomes that encode virus genes that result in differential disease, or more severe disease in one person versus less than another, whether that's a strain or not is sort of up for debate. What I think is controversial about this paper is that essentially they were just grouping a variety of different clinical isolates of the virus and then going back to the clinical data that had been recorded about those patients and making assumptions that these genetic changes that distinguish these two groups were responsible for any differences they found in the patient's conditions. That is, it's really hard to say. First of all, the group, the viruses and the "L" group versus I think, what is it, the "S" group?

Erin Welsh Mmhm. Yeah.

Angela Rasmussen The differences between those viruses, they're not all, it's not just two viruses. They're groups of viruses that cluster together when you look at their genomes and compare them. So it's really difficult to say that any one of the specific genomic changes that are characteristic of either group are directly responsible for causing increased or decreased disease severity.

Erin Welsh Gotcha. So it's possible or likely that there might be multiple quote unquote strains of this virus. But whether or not that translates into any, manifestations in terms of disease severity is not yet clear and we probably won't know it for a while?

Angela Rasmussen Yeah, that's fair to say. And this is really also a question that needs to be addressed in terms of doing experiments to understand what are features of the virus that make it more pathogenic, or able to cause disease. So, the only way to really look at that is either through human volunteers or patients who at least could be identified very early after infection and then followed over time, what we call longitudinal observations, or by looking in animal models to try to understand the various mechanisms of pathogenesis. My personal suspicion, and again, this plays to my bias for the host response, but, when you're looking at humans who are genetically diverse, you will see the same virus, the same identical strain of a virus cause two different types of disease in two different individual people. So even when you're looking at a fairly large patient population and you're just making correlations between certain clinical features that were recorded by their doctors during clinical care as well as the genomic sequence of their disease, you're not really able to look at any of those mechanisms that might distinguish a host from one from another. So you can look at the differences in the virus, but you're never going to know what's different from one person to the next, so it's really difficult to conclude even

on a dataset of hundreds or thousands of patients, that genetically different strain of a virus is the only thing that is causing one person's disease to be more severe than another's.

Erin Welsh Right. Right.

Erin Updyke That makes sense. Yeah.

Erin Welsh SARS, being a much deadlier coronavirus, I think a lot of people that wrote to us expressed their concern about whether this virus, SARS-CoV-2, might mutate into something more deadly, such as SARS classic. You mentioned, or you talked a bit about the mutation rate of this virus and mRNA viruses. Can you say anything to our listeners about whether there's a risk of this virus mutating into something more deadly, especially maybe also in the context of control measures or how behavior might influence viral evolution?

Angela Rasmussen Right. So this is a concern and I think one of the reasons is that mutation is a very scary sounding word. And it has not been helpful I think that a lot of movies are always like, "Oh my God, it's mutated and it's now airborne" or something. [laughter] And the, the thing is, coronaviruses are RNA viruses. RNA viruses, mutation is an inherent property that they all have because the enzyme that replicates the genome is prone to making these mistakes. Every RNA virus will have the, the normal mutation rate for an RNA virus is about one in every thousand units of the genome that gets copied is a mistake, or a mutation. Coronaviruses actually have an enzyme that does some limited proofreading, so their mutation rate is lower than many other RNA viruses, but it's still higher than for enzymes that replicate DNA. So, it still has a relatively high mutation rate, and there will be mutations every single time the genome is copied. In terms of mutating to become more virulent, or more lethal, it's really, really difficult to predict that. Because mutations don't stick around unless there's some sort of selection pressure. It's hard to imagine what the selection pressure would be to make the virus more lethal. If anything, viruses are selected to become less lethal, only because viruses can't replicate without a host, and if you kill your host before they can transmit the virus to another host that pretty much cuts off that virus's evolutionary chain. So, I think that it's likely, certainly, that the virus could mutate, or has mutated, and there will be mutations every time the virus copies itself within a single person, much less is transmitted to another person. But, it's very difficult to say that the virus would be evolving, on its own, the capacity to be more lethal. Now, however, if there is an antiviral drug developed, for example, and that targets a specific part of a viral protein, then it's possible that that would be a selection pressure for the virus to evolve resistance. That's one example of how viruses can become more lethal by evading countermeasures. If there's a vaccine, it's possible that the parts of the virus the vaccine recognizes could be a pressure for those parts to mutate. The way that your immune system works for most vaccines is by making antibodies and those antibodies recognize a shape on the surface of the virus. So, if you think of a virus as a three-dimensional sort of ball that's covered with spikes, antibodies would recognize the shape of those particular spikes. It's possible that a virus could evolve a slightly different shape spike that those antibodies from a prior infection or

from a vaccine would then not be able to recognize. So that is another way in which a virus could potentially evolve to become more lethal in the sense that it would be able to, again, evade a counter measure that we had developed for it. Will that happen? I don't know. A lot of that depends on the types of antivirals that we find are able to work against this virus as well as the vaccine strategies that are being tested right now, how well they work and how well they are able to induce immunity.

We do know from some other viruses, though, that certainly antiviral drug resistance is something that happens. We know that from influenza evolving to be resistant to oseltamivir or Tamiflu. We know that influenza, normally its surface antigen, so the proteins that are recognized by vaccines change all the time. So that's how we have to get a flu shot every year. So there are certainly examples in the wild world of virology that that viruses can do this, but on its own, I don't think that there's any particular pressure that I've seen anyways that would cause SARS-coronavirus to spontaneously evolve greater lethality or virulence.

Erin Welsh Gotcha.

Erin Updyke So, speaking of antivirals, remdesivir is going around the new, there's potentially trials happening, it seems to be maybe promising for looking at treatment for SARS-CoV or for COVID-19, the disease. Could you tell us a little bit about what this drug is and how it works?

Angela Rasmussen Certainly. So, remdesivir is a nucleoside analog. That means that it is shaped a lot like the A, T, C's and G's that make up a given virus genome or human genome for that matter. When viruses are replicating, the enzymes that that copy the genetic material is reading the existing genome so it knows where to put which A,T,C or G. Remdesivir Works by fooling that enzyme into thinking that it is an A,T,C or G and gets inserted into the genome, and then when enough of that happens, the genome doesn't work. It's also thought that some of these so-called nucleoside analog drugs can also activate components of your innate antiviral immune system, making yourselves more capable of responding to and resisting viral infection. So, that's thought to be the mechanism of action for remdesivir as far as I know. So, these nucleoside analogs don't always work for some RNA viruses, but there is data in nonhuman primates suggesting that remdesivir is effective at treating MERS coronavirus. And now some people have showed, I think in vitro, at least, that it's capable of reducing virus titers of SARS-coronavirus-2. So, we do know that these nucleoside analogs can be effective against certain RNA virus infections. We just won't know if it's effective in people until the clinical trials have been completed.

Erin Welsh Gotcha. Our sign off for this podcast is "wash your hands, you filthy animals." We've been saying it for years. [chuckles]

Erin Updyke Yeah, we started it. Just kidding. [chuckles]

Erin Welsh So, can you tell us why hand-washing is a great way to reduce the risk of getting a respiratory infection?

Angela Rasmussen

Yeah, that's, that's a great one. And this is, so both for enveloped viruses, which coronaviruses are, the envelope that I'm talking about is a membrane that is derived from your cells on the surface of the virus particle. The spike protein that I talked about that's needed to bind the receptor and for the virus to enter the cell, is embedded in this envelope, in the membrane. That's why spike is called an envelope glycoprotein, cause it's part of the envelope. So, either alcohol-based hand sanitizers or soap will disrupt that membrane. If you disrupt that membrane, wash it away, there's no more spike, the virus can't get into your cell, the virus is inactivated. Soap, soapy water is more effective than hand sanitizer because that also has the added effect of physically washing things off of your hands. So in addition to disrupting the membrane and making any viruses or some bacteria or other microorganisms that have a membrane that can be disrupted by soap or hand sanitizer, that's great. But in general, there may be other things. There may be non-envelope viruses on your hands. Soap and water washes them away physically so that they're no longer on your hands at all, whether it disrupts the envelope or not. For that reason, washing your hands is by far the best thing you can do to reduce your own risk, besides practicing of course social distancing. Hand-washing is better than hand sanitizer, although it is important to know that for this particular virus, hand sanitizer, as long as it's 60% alcohol or more will work in between hand washes.

Erin Welsh

So one of the other questions that we've gotten a lot, and I'm also curious to know and have been sort of keeping a good amount of skepticism with whatever I read, is just how long this virus can survive on different kinds of surfaces. So hard surfaces, soft surfaces, and maybe how does this compare with some of the other common respiratory viruses?

Angela Rasmussen

Yeah, so a great pre-print just came out. I like to pitch my collaborators at Rocky Mountain Labs, this is Neeltje van Doremalen who is with Vincent Munster at NIAI Rocky Mountain Labs have just released a preprint with some of their colleagues, I believe at Princeton, showing that SARS-coronavirus-2 and SARS classic have some different properties as well as some similar properties for remaining infectious on various surfaces. So they looked at experimentally generated aerosols, which for SARS-coronaviruses is only an issue for the most part in hospital settings where there are aerosol generating procedures, but they showed that for both of these, the aerosol half-life is only about three hours. So that's good news in that you know, if somebody that you love or care about is working in a hospital or an ICU or is getting treated there, these aerosols are not going to persist for days at a time in the environment. They also looked at survival of the virus on copper, stainless steel, plastic and cardboard, and the virus lasts the longest on stainless steel and plastic. So it lasts 48 to 72 hours, and it can potentially be there for longer than that, but what's important to note is that there was a three-log reduction, so a thousand times less virus that was infectious after 72 hours. So, even though you can detect infectious virus on surfaces, plastic or stainless steel surfaces after three days, it's a greatly reduced amount of virus. Compared to SARS classic, SARS-coronavirus-2 lasted longer on cardboard, however it didn't last longer than 24 hours. So before everybody gets worried about getting packages in the mail or opening letters or

calling, ordering stuff from Amazon it, it also was essentially undetectable after 24 hours. So cardboard is probably not a surface that's going to retain the virus for, for days and days at a time. What we don't know is the effect that temperature and humidity and other environmental conditions would have on this because they didn't look at that in this paper. However, the same group had previously done work with MERS coronavirus and that showed that temperature and humidity were also really, really important factors in terms of the virus being able to persist and remain infectious on various surfaces. So my take home from this is that I assume that the virus under ideal conditions can last for a couple of days on surfaces. So I just try to, again, wash my hands and where I can disinfect shared communal surfaces like tables. Take precautions to avoid being exposed to virus that may be on shared surfaces, but it's probably not going to persist in the environment for more than a couple of days.

Erin Updyke Awesome. And you mentioned that this is a virus that's spread by respiratory droplets. What do we know so far about the minimum infective dose of this virus?

Angela Rasmussen Well, that's a great question and I, that is definitely a question for which I will say, I don't know.

Erin Updyke Okay [chuckles]

Angela Rasmussen And this has been discussed a lot in the context of that reduction I was talking about on surfaces after seven, you know, 48 to 72 hours depending on the material. If you have a thousand times less virus after a couple of days, is that enough virus to establish an infection? It's really hard to say and probably a lot of that also depends on the route of infection too. So if you are touching your hands to your nose you know, the inside of your nose, your nostrils, is a mucous membrane. It's a mucosal surface. Mucus itself acts as a barrier that prevents virus particles from coming into contact with the cells that are in your nose to infect them. That's going to be different than in your mouth and in your eyes. And all of these different mucosal surfaces that could potentially be infected, there are inherent mechanisms, barrier mechanisms that protect those surfaces from being infected. So it's not enough to necessarily have one infectious virus particle. You may have to have a certain number of those infectious virus particles to overcome these other obstacles to infection that your body has. We don't really know what that is. I don't think that anybody has looked at that. And because the animal model work is still in development, we can't really look at that in the context of a controlled experiment where we would be able to look at different amounts of virus on different surfaces and see which animals got infected and then how sick they got.

Erin Welsh Gotcha. So in our first episode on coronavirus, we ended our interviews by asking our interviewees what about this disease concerns you and what about the response or how the epidemic has been progressing reassures you?

Angela Rasmussen Oh boy. The second part of the question, nothing. [laughter]

Erin Updyke Oh, gosh. [laughter]

Angela Rasmussen No, I, I've been, what scares me the most by far about this is the, the federal response here in the US. It has been unacceptable for a variety of reasons, and I suspect that largely because the response has been heavily politicized and influenced by considerations that should not be a factor in public health responses. Worrying about case numbers from, you know, an electability point of view is a really, really terrible way to approach an effective public health response. That concerns me greatly because initially I felt, you know, I was concerned about this, but I felt that if we were on top of it in terms of surveillance and testing, then we could really limit and contain spread. In January when there were a few patients coming into the United States with travel history who are identified and rapidly sequestered, and there didn't seem to be a ton of secondary transmission, I felt pretty calm that we were responding to this correctly identifying and isolating patients, which is what you should do. And doing contact tracing back when it was manageable to do that. Then it turns out through genomic analysis that it looks like here in Seattle anyways, we've had community transmission since that first patient arrived, and potentially transmission from other patients who may not have even been identified. And some of this has been the absolutely unacceptable slow rollout of effective testing and the continued failure to adequately increase testing capacity and throughput. I think that that has really, really harmed our ability to contain this outbreak. And while, where we can, we should still make efforts to contain it by doing contact tracing and isolation and quarantine, these, you know, tried and true public health methods, part of our focus now has to be mitigation. And that has to be the so-called flattening the curve. Trying to limit and reduce spread or the speed of spread to avoid overwhelming hospitals. Trying to make sure that there is a safety net in place for people who can't afford to work from home, who don't have sick leave, who may not have adequate insurance. We need to make sure that all of those things are addressed so that we can at least mitigate the effects that this is going to have on our healthcare systems and on our public health as a country and really as a species on this planet. We really need to have all hands on deck including full engagement from the public. And I'm concerned that with the amount of misinformation that our federal leadership has provided, the constant still downplaying of the seriousness of this situation, I'm very concerned that some of these measures won't even work. And I'm not so much concerned for myself. I'm not in a high risk category. I do have asthma, but I, I still, you know, I don't think that I would be personally likely to die from this. But, of course, I'm concerned about all those other people who do have preexisting health conditions, who are immunosuppressed, who are older, who have underlying medical conditions that would cause them to have a bad outcome, or other people who may not even have coronavirus but are unable to access medical treatment that they need for other things because our hospital systems are overwhelmed. So my concerns, really my concerns about the virus are the least of my concerns with regard to this public health crisis.

[musical interlude]

Erin Welsh Awesome. Thank you again so much, Dr. Rasmussen, for joining us. We really appreciate you taking the time out of your busy schedule.

Erin Updyke And it was really lovely chatting with you. Thank you.

Erin Welsh It really was. Alright, so we wanted to wrap up each of these episodes with a “what did we learn” section, and we wanted to take the top five things, or the five key things, that we learned from our conversation with these experts. So we’ll go through each of these five things. We’ve already talked about this. This is, this is different than our normal episodes.

Erin Updyke Yeah.

Erin Welsh None of what we’re saying to each other is a surprise, so.

[laughter]

Erin Updyke But.

Erin Welsh I don’t know. It’s how we had to do it.

Erin Updyke It’s how, I think it’s important because, like, you know, we go over, we went over a lot in this episode, we’re gonna go over a lot in every episode, and I think that kind of trying to wrap up what are the most important points is gonna be, um. It was helpful for me, even, to go through. So.

Erin Welsh Absolutely. It’s very easy to get lost in the details of this, and so let’s big picture this situation.

Erin Updyke Let’s. Alright. So one of the biggest things that we learned is that this particular virus, SARS-CoV-2, because of the specific receptors that it uses to get into our cells, that ACE2, this virus can and does infect the lower respiratory tract. So that’s why we are seeing as severe of disease in some cases as we’re seeing. And that is something that sets this virus apart from a lot of other coronaviruses, the more common ones that circulate and cause the common cold. But this is a similarity that SARS-CoV-2 shares with its closest relative, if viruses have relatives, and that is SARS classic, SARS 1.

Erin Welsh Number 2. We also learned that this novel virus can definitely survive on surfaces for at least some time, and we’re gonna provide a link to that paper that Dr. Rasmussen mentioned on our website and in the show notes, but what we still don’t have a great handle on is what exactly that means for transmission because we don’t know exactly how many viral particles it takes to actually make you sick. Or how different environmental conditions like temperature and humidity, how these might affect the longevity of the virus. But what we’ll touch on in another episode in more detail is that we don’t even know how much virus people are even shedding. So, really the best thing you can do is just kind of assume that your saliva and the saliva of everyone around you is infectious, so wipe down surfaces, wash

your hands before you touch your face. These are basic steps that will protect you not only from getting this virus but also from spreading it to others, and it'll also do those things for so many other viruses too.

Erin Updyke Yeah, absolutely. Number three. We also learned that, I like this one, that viruses aren't evil creatures intentionally setting out to kill you.

Erin Welsh There's no malice.

Erin Updyke There's no malice there. They're just-

Erin Welsh As far as we're aware.

[laughter]

Erin Updyke Guess we haven't asked the viruses, but still. And the thing about this is 'mutation' doesn't have to be a scary word. So yes, because this, SARS-CoV-2, is an RNA virus, it does have a higher mutation rate than a DNA virus might, or than a bacterial disease might, and certainly it has a mutation rate than our cells have. But, that doesn't necessarily mean it's going to mutate to become more virulent, or make you more sick, and it's probably uncommon that it would mutate in really drastic ways. There's been a lot of talk about "this is going to mutate to be airborne" and we'll talk in more detail in a future episode about what respiratory droplet vs airborne transmission really means, but in general, it's very uncommon for viruses to mutate in that drastic of a fashion, to change their mode of transmission. Okay?

Erin Welsh Number 4. So the other thing that Dr. Rasmussen helped clarify is that we don't know for sure yet if there are different strains of this virus. But, even if there are different strains, we don't know if that actually will result in different virulence or infectivity between those strains. Because so much of what goes into disease severity is related directly to our individual host response, it's hard to tease apart the individual effects of certain virus strains and how much a particular virus strain is going to affect us or cause disease or be more infectious than another. And so that's something that's really important to remember as this talk of strains comes into the news, that this is also something that's going to probably take a bit to figure out, whether there are any differences in the infectivity or virulence among any of the strains that we might detect.

Erin Updyke Yeah absolutely. And finally, the fifth and, I don't know, maybe most important thing that we learned from this episode is something that all of our listeners already knew. And that is wash your hands. Because washing your hands is really effective at reducing the spread and the chance that you're going to get infected or spread an infection to somebody else. Washing your hands really works!

Erin Welsh And alcohol-based hand sanitizers also work as well, if you don't have the availability to wash your hands at a certain time, but we do wanna note that hand washing is better because it actually washes those little viruses and bacteria off of

your hands, while the hand sanitizer just kind of leaves, uh, a sea of dead bodies on your hands.

Erin Updyke [laughter] A sea of dead bodies.

[laughter]

Erin Welsh Dead cells and viral particles.

Erin Updyke Exactly. Erin, do we have any references that we'd like to shout out for this episode?

Erin Welsh We do. So we've got a couple of papers. One is by Van Doremalen et al. from, obviously, 2020, because we're talking about SARS-CoV-2, and we also have, and that's titled "Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1". And so this is the one that Dr. Rasmussen mentioned that looked at how well the virus survives on different surfaces. And then the other paper that we mentioned in our interview that referred to the L and S strains of SARS-CoV-2 is by Tang et al., and that's also from 2020, and it is titled "On the origin and continuing evolution of SARS-CoV-2".

Erin Updyke And as always, we'll post the links to all of our sources for this episode and every single episode on our website. We're also working on a specific COVID-19 section of our website where you can get answers to frequently asked questions to share with friends and family.

Erin Welsh Mhmm. And thanks again to Dr. Rasmussen for droppin some knowledge on us and all of you out there listening.

Erin Updyke Absolutely. I will say, too, if you want lots and lots of detail on the virology of this virus, there is a whole podcast series called This Week in Virology that has been doing a lot of updates about COVID-19 and SARS-CoV-2, and they have a lot of details. It's hosted by a bunch of virologists. Ologies also had a great virology episode that interviewed another expert about this virus, and there's a whole bunch of other podcasts out there too if you just can't get enough!

[laughter]

Erin Welsh Thanks to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Updyke And thank you for listening. We'll see ya soon for chapter 2.

Erin Welsh Until next time, wash your hands...

Erin Updyke you filthy animals!