

COVID-19 Chapter 2: Disease

Erin Updyke “Reading about it in the news, I knew it was going to be bad, but we deal with the flu every year so I was thinking: Well, it’s probably not that much worse than the flu. But seeing patients with COVID-19 completely changed my perspective, and it’s a lot more frightening.

“I have patients in their early 40s and, yeah, I was kind of shocked. I’m seeing people who look relatively healthy with a minimal health history, and they are completely wiped out, like they’ve been hit by a truck. This is knocking out what should be perfectly fit, healthy people. Patients will be on minimal support, on a little bit of oxygen, and then all of a sudden, they go into complete respiratory arrest, shut down and can’t breathe at all.

“It’s called acute respiratory distress syndrome, ARDS. That means the lungs are filled with fluid. And it’s notable for the way the X-ray looks: The entire lung is basically whited out from fluid. Patients with ARDS are extremely difficult to oxygenate. It has a really high mortality rate, about 40%. The way to manage it is to put a patient on a ventilator. The additional pressure helps the oxygen go into the bloodstream. Normally, ARDS is something that happens over time as the lungs get more and more inflamed. But with this virus, it seems like it happens overnight.

“Typically with ARDS, the lungs become inflamed. It’s like inflammation anywhere: If you have a burn on your arm, the skin around it turns red from additional blood flow. The body is sending it additional nutrients to heal. The problem is, when that happens in your lungs, fluid and extra blood starts going to the lungs. A telltale sign of ARDS in an X-ray is what’s called ‘ground glass opacity,’ like an old-fashioned ground glass privacy window in a shower. And lungs look that way because fluid is white on an X-ray, so the lung looks like white ground glass, or sometimes pure white, because the lung is filled with so much fluid, displacing where the air would normally be.

“It first struck me how different it was when I saw my first coronavirus patient go bad. I was like, Holy shit, this is not the flu. Watching this relatively young guy, gasping for air, pink frothy secretions coming out of his tube and out of his mouth. The ventilator should have been doing the work of breathing but he was still gasping for air, moving his mouth, moving his body, struggling. When you’re in that mindstate of struggling to breathe and delirious with fever, you don’t know when someone is trying to help you, so you’ll try to rip the breathing tube out because you feel it is choking you, but you are drowning.

“When someone has an infection, I’m used to seeing the normal colors you’d associate with it: greens and yellows. The coronavirus patients with ARDS have been having a lot of secretions that are actually pink because they’re filled with blood cells that are leaking into their airways. They are essentially drowning in their own blood and fluids because their lungs are so full. So we’re constantly having to suction out the secretions every time we go into their rooms.

"Before this, we were all joking. It's grim humor. If you are exposed to the virus and test positive and go on quarantine, you get paid. We were all joking: I want to get the coronavirus because then I get a paid vacation from work. And once I saw these patients with it, I was like, Holy crap, I do not want to catch this and I don't want anyone I know to catch this

"I worked a long stretch of days last week, and I watched it go from this novelty to a serious issue. We had one or two patients at our hospital, and then five to 10 patients, and then 20 patients. Every day, the intensity kept ratcheting up. More patients, and the patients themselves are starting to get sicker and sicker. When it first started, we all had tons of equipment, tons of supplies, and as we started getting more patients, we started to run out. They had to ration supplies. At first we were trying to use one mask per patient. Then it was just: You get one mask for positive patients, another mask for everyone else. And now it's just: You get one mask. "I work 12-hour shifts. Right now, we are running about four times the number of ventilators than we normally have going. We have such a large volume of patients, but it's really hard to find enough people to fill all the shifts. The caregiver-to-patient ratio has gone down, and you can't spend as much time with each patient, you can't adjust the vent settings as aggressively because you're not going into the room as often. And we're also trying to avoid going into the room as much as possible to reduce infection risk of staff and to conserve personal protective equipment.

"Even if you survive ARDS, although some damage can heal, it can also do long-lasting damage to the lungs. They can get filled up with scar tissue. ARDS can lead to cognitive decline. Some people's muscles waste away, and it takes them a long time to recover once they come off the ventilator. There is a very real possibility that we might run out of ICU beds and at that point I don't know what happens if patients get sick and need to be intubated and put on a ventilator. Is that person going to die because we don't have the equipment to keep them alive?"

[musical interlude]

Erin Welsh Oh. My. Gosh.

Erin Updyke Yeah, um, that was an account from a respiratory therapist at a hospital in Louisiana, who remained anonymous for that account. I found it on ProPublica. Uh, it was published on March 21st, and we'll put a link to the full description in our show notes and on our website, because that was just a small excerpt from the description.

Erin Welsh It's, you know, it's very eerie to read and to hear because what it does is it reminds me of a lot of the firsthand accounts from the 1918 influenza, which I know has been brought up- the comparisons have been brought up constantly- and some are inappropriate comparisons.

Erin Updyke Mmhmm.

Erin Welsh But just that description of healthy individuals being struck down, all people of all ages being struck down, and the horrible thought of not being able to breathe...

Erin Updyke Yeah.

Erin Welsh ...and drowning in your own fluids.

Erin Updyke Yeah, it's really scary. It's really scary.

Erin Welsh I mean it is scary, and um-- We should introduce ourselves before getting too much into this...

[laughter]

Erin Updyke Yeah, we should.

Erin Welsh Hi, I'm Erin Welsh.

Erin Updyke And I'm Erin Allman Updyke.

Erin Welsh And this is This Podcast Will Kill You.

Erin Updyke Welcome back, everyone, or maybe welcome for the first time ever if you jump partway into series, if you're one of those people. [chuckles] This is our not-so-mini, mini-sode series: Anatomy of a Pandemic, where we are answering all your listener-submitted questions about COVID-19, the disease caused by SARS-CoV-2. In our first chapter, we covered the virus itself, so all of the biology of SARS-CoV-2. In this episode, Chapter 2, we are going to talk about the disease that this virus causes- what it looks like, how it's spread, and how physicians and healthcare workers are dealing with this outbreak.

Erin Welsh But first! As always, it's quarantini time.

Erin Updyke It's quarantini time. [chuckles]

Erin Welsh In this episode, we're drinking the creatively named Quarantini 2.

Erin Updyke Quarantini Number 2!

[laughter]

Erin Welsh Erin, what is in Quarantini Number 2?

Erin Updyke You know Erin, it's kind of a whisky ging. It's whiskey-

Erin Welsh Yeah, I mean I would call it a Kentucky Mule-

Erin Updyke Kentucky Mule

Erin Welsh ...perhaps, if you happen to have a copper mug. I did not, [laughter] so the picture is disappointingly non-copper.

Erin Updyke That's alright, you did your best.

Erin Welsh Thank you. Yeah, so it's basically ginger ale, whiskey of whatever kind of whiskey you want, and some lime.

Erin Updyke And we'll post the full recipe for that quarintini as well as our non-alcoholic placeborita on our website and all of our social media channels, as always.

Erin Welsh As always. Okay, so as we mentioned, we've talked about the virus itself so now let's talk about the disease that this virus is causing, COVID-19. And I do think that that is a particularly important distinction because as we'll hear more about, this virus can infect you without necessarily causing severe disease. And that's super important in understanding the spread of this virus, because people who appear asymptomatic and otherwise healthy, OR just have very mild cases, could still be infected with and therefore sneezing or coughing out the virus and spreading it to other people. So we talked to Dr. Colleen Kraft, who many of you may recognize from our first coronavirus episode, and she is going to walk us through a lot of your questions about the clinical disease that this virus causes. Let's go over some of the basics first, though, shall we?

Erin Updyke Let's. We shall.

[laughter]

Erin Updyke So one big question is "What is the timeline of this illness?," and what you're going to see is that we still don't have the answers to every question when it comes to this disease, and the timeline is kind of one of those that we don't fully know. BUT we do have a better handle on it than we did in our other episode that we released back in February. So, first of all, it seems like the incubation period is on average about 5 days. An incubation period is the time from when you are first exposed to that disease to when you first start showing symptoms of that disease. Okay. So, on average this is about 5 days. It can range. Most studies it seems like the max range is about 11. So when you hear about being quarantined for 14 days, that's because we think, and we're pretty sure, that after 14 days if you haven't started to show symptoms, you're probably not going to show symptoms. So that's kind of the max range to make sure that you don't spread this disease unknowingly to someone else if you're exposed. And this number, like around 14 days, that's consistent with what we saw with SARS-1, SARS classic. Okay. Now, the other thing is that, from a retrospective study of people that had COVID, the severe disease-- this study looked at people who were hospitalized for COVID, so pretty severely ill-- the median time from when symptoms first started to discharge from the hospital was 22 days. So that's a long time for somebody to be in the hospital.

Erin Welsh Yeah.

Erin Updyke And I think that that's an important indication that for people who get seriously sick, they can be sick for quite a long time. The other thing that this study looked at was viral shedding, so at least some measure of how long somebody might potentially be infectious, and they found that the median number of days that people were shedding virus was 20 days from the onset of symptoms, which is again, a pretty long time if somebody is symptomatic.

Erin Welsh That is a long time.

Erin Updyke Yep, longer than 14 days. [laughter]

Erin Welsh Yeah, but I think the other thing that you mentioned that it's sort of, this is just looking at people who had severe disease, correct?

Erin Updyke Exactly, yes. Yeah.

Erin Welsh Okay, so I wonder, I think, I mean of course as this pandemic progresses we're gonna get more information about those people who have milder cases...

Erin Updyke Mmhmm.

Erin Welsh ...or are asymptomatic, and how much virus they're shedding at various points throughout their course of infection.

Erin Updyke Exactly, yeah. Exactly. Ok so then the question is, what are some of these symptoms?

Erin Welsh Okay, so the biggest symptoms are the ones that most people have probably heard about in the news quite a lot. So, fever, which, by the way, the definition of a fever is a temperature of over 100.4F or 38C. Then there's also cough, generally a dry cough, not a super wet or a super productive cough, and then shortness of breath. So these are the general symptoms of the disease we call COVID-19. But, we know now that SARS-CoV-2, the virus, like SARS-1 and MERS, can infect your lung tissue and cause a lower respiratory disease, not ONLY an upper respiratory infection the way most of the common coronaviruses do. Okay, so what does that mean? Well, it means the possibility of very severe disease, like we heard about in the firsthand account. And in the case of this virus it seems that about 20% of cases are severe. And, that doesn't mean that 20% of cases need ICU and ventilator care, but it does mean that potentially up to 20% of cases may need at least hospitalization and some oxygen support or some IV fluid support. Analyses from China suggest that there, at least, about 14% of cases were severe, and 5% were critical. And that means the same kind of picture that we talked about in our coronavirus episode when we talked about SARS, and the same description you heard in the firsthand account. ARDS, ground glass opacities on x-rays, potentially needing intubation-- it's serious. It's a serious, serious disease. And people can also go into shock, which we've talked about a lot on the podcast, but essentially what that means is that your organs aren't getting enough blood flow, in this case because of overwhelming infection which leads to leakage of fluids and then hypoperfusion... And then of course there is also always the risk of a secondary infection on top of this viral infection.

Erin Updyke It can be pretty gnarly. But also in this case, what we see that is different from SARS and MERS, and what in our first episode about coronaviruses was still kind of gray zone, that's a lot more clear now, is that asymptomatic or very mildly symptomatic infection is not only possible, but it's likely actually responsible for quite a lot of the spread of this disease. It's estimated that about 80% of cases are mild. Which, while that's great news for the majority of people who get infected- it means you're not necessarily going to be looking at such a severe disease. It also means that this disease is easier to spread since not everyone who is sick maybe even realizes that they're sick. And how does this disease spread, Erin?

Erin Welsh Well, respiratory droplets as we well know. But, we're not going to go into that, we're going to allow our expert, Dr. Colleen Kraft from Emory University, to explain how respiratory droplets work, as well as other characteristics of this disease, how it's spread, how we're testing for it, who we're testing for it, and finally, how we treat it.

Erin Updyke Right after this break.

[musical interlude]

Colleen Kraft My name is Colleen Kraft, and I'm the associate chief medical officer at Emory University Hospital. My training is in infectious diseases and clinical microbiology.

Erin Welsh Thank you again, so, so much for joining us. We know that you are, have just been swamped with work and so we really appreciate you taking the time to, to kind of talk about COVID-19. I mean, since our first interview with you, which has been, you know, about a month and a half ago, a lot has happened.

Colleen Kraft Yes. Like a lifetime has happened. That's how I feel.

Erin Welsh Yeah. Yeah

Erin Updyke Uh so we'll jump right in. We're talking today of course, about SARS-CoV-2, the virus that causes COVID-19. So we know that it's transmitted through respiratory droplets or direct contact with somebody's respiratory droplets like other coronaviruses. Can you tell us a little bit about what that means in contrast to viruses that are airborne, and when people talk about respiratory droplets, like what exactly does that include?

Colleen Kraft Sure. So I think it's, it was really funny to hear. I, I've been to a number of town halls around Emory and I had one of my audience members best describe it as, you know, it's your saliva. So it's sort of I view respiratory droplets as being sort of the wet aspects of our coughs and sneeze. And that's that. I thought that was very well described that way by this employee. And I didn't answer your, your airborne question. So what happens is when we cough or sneeze, it's those, it's like a wet heavy droplet and that kind of goes to the ground right sooner cause it's heavy. But when they are really small then they can aerosolize and they can actually sort of hang around in the air for longer. And so that's why every time there's a new respiratory virus we sort of, pretend like it's airborne just to make sure it's not airborne. Cause

that is sort of a different transmission route that that can hang in the air longer and it can go farther. But you know, from what everything we know this coronavirus still behaves like our droplet spread coronaviruses.

Erin Welsh Gotcha. So at this point we have a better idea of what a typical course of COVID-19 looks like. Can you walk us through what that is like, you know, day one, day two, what do you typically see?

Colleen Kraft Yeah, so we're seeing the same things as being seen and observed in other parts of the world. And so we have the vast majority of these individuals have a cold. It may be an unpleasant cold more than for others, but most people have a very mild illness, probably most similar to our common cold in general. We are seeing people though, that come in with basically a viral pneumonia type picture. Viral pneumonia should really make the hairs on the back of your neck stand up because that's probably happened in the 1918 Spanish flu. And this is again, along with the airborne aspect, this is what we're always looking for in these new viruses. Does it have a propensity to cause lower respiratory tract infection? If it does, that makes us scared. Because we can't, while we can do a lot with bacterial pneumonia, a viral pneumonia is very scary, because usually we don't, we can't treat most of the viruses that we get. And so we definitely don't want it down in the lung where it can cause scarring and difficulty breathing. And so for a subset of people that for the most part tend to be ill, ill at baseline, we have a group of people that also are getting symptomatic lower respiratory tract syndrome who are not quite as ill as the typical person we're hearing about that is succumbing to this disease. So we've had a number of individuals that, yes they have other medical problems but they don't necessarily have respiratory medical problems, and they are having you know, sort of a viral pneumonia picture. And we have had a few that have been needed to have mechanical ventilation or a breathing tube.

Erin Welsh Gotcha. About how long does, is the course of disease, you know, I know that for some people who have milder cases it may be shorter than for others, but what do we see on average or what does it look like for the people with more mild symptoms compared to the people with more severe outcomes?

Colleen Kraft I would say it's, it's that typical three day kind of feeling bad, achy and then the next day is maybe a little bit better, not great. And then the next day you're sort of back to feeling like you're among the living and then you know, then we also recommend, at least for our employees to sort of, you know, kind of self-isolate for a few more days just to make sure you're not sort of still having those secretions, coughs and sneeze, cause we don't want to keep spreading it. And so that's sort of a mild course. The more severe courses tend to be, you know, I think the damage is done within the first week and then what we're doing is trying to support the body so the body can mend after that.

Erin Welsh What does that supportive care look like? Both in terms of that, during that first week of intense symptoms and then the sort of, you know, the healing stage.

Colleen Kraft Right, so it sounds like it's your grandmother patting your hand is what supportive care sounds like, I think to most people. But in the case of some individuals that have severe disease, it may mean that they have a breathing tube, they're in an ICU and they have many other things that are helping support their body until the body can kind of get rid of the virus itself. So this is sort of how we describe things back in the Ebola days where, you know, most of the time what we were doing is just supporting, like with life support basically, to try to keep things going until, until the body can create and clear that virus. That's what happened during Ebola with coronavirus. It's sort of similar, so supportive care when you're at home, maybe NyQuil and television, which sounds really great to me right now. And when you're in the hospital though, what that is, is if we need to, to help one of your body systems function, we will do that.

Erin Updyke Okay. Do we know at this point how much things like viral load might correlate with the severity of symptoms? Are the people that have milder cases, are they as infectious to others? Are they shedding as much viral particles as these more severe cases?

Colleen Kraft Right. So I think this is a great question and I think, this is where you're going to see my laboratorian side come out quite a bit. So it's really, it's really easy when we talk about viral load in the blood or plasma or serum to sort of understand how to standardize that by copies per milliliter or something like that. When we're doing a respiratory swab, I think it's really hard to standardize. And because this test is so new, we don't have the test standardized in and of itself. So the testing results at our institution may be a little bit variable compared to another institution. And that's because we don't have a gold standard yet to compare on all of the machines. So I agree with you. However, we have seen very anecdotally that we've had people with very high viral loads that basically didn't even look like they were sick, and we questioned whether or not we should even swab them. And they had extremely high amounts in their nose. Whereas we've also had people that have had moderate amounts that are sick and on a ventilator. And so while I, I think there's an aspect that correlates, I think the way that we obtained the swab is going to make this difficult, unless there's some sort of serum or plasma or surrogate tests we can use that can be very standardized with its input.

Erin Welsh And so going, revisiting this aspect of perhaps asymptomatic individuals or people with very, very mild cases of this. Can you talk about sort of the incubation period, when people might start becoming infectious, how long they remain infectious, and then sort of how much do you think asymptomatic individuals might be contributing to the spread of disease?

Colleen Kraft So I think they probably are contributing to the spread of disease. I think that's why some of these more dramatic things that we're seeing are the social distancing and being really aware of your, even more so just your own hand hygiene, just your own persona as it relates to anybody else. And so I think that we are taking measures to have that not happen, right? Schools closing. Let's talk about where there could be a lot of asymptomatic spread of disease that would be a school.

[laughter]

Colleen Kraft So you've got a bunch of kids shedding virus everywhere in close proximity with limited hand and face and everything, hygiene, and you can tell I have children?

[laughter]

Colleen Kraft And that's just like, that's just the setup for transmission. So I do think that while asymptomatic people are shedding, we're really taking dramatic efforts unlike I've ever seen in my short lifetime, I suppose, to really to even work on stopping that. I mean, hospitals aren't allowing very many visitors, you know, public places have all but canceled everything. So we're actually really trying to break that cycle. Which I think has to me never been really done to this extreme.

Erin Updyke Yeah, yeah. And you mentioned as well that it seems at this point pretty well established that it's older people and people with other underlying health conditions or people that are otherwise immunocompromised that are more likely to experience this severe disease. But we've gotten a lot of people asking us for a bit more clarity about these groups. Like what age is it that people are considered elderly or at risk? And is it any sort of immune compromise that makes you more vulnerable or what are these preexisting health conditions that we're most concerned with in terms of the higher risk categories for this disease?

Colleen Kraft Right. So I think the way to do that and the way I've been gut checking a number of these questions that we really just don't know yet because we don't know everything about this virus, is to think about influenza and sort of start there. Right? So in, in older adults, influenza tends to be more severe because it's sort of tipping off chronic conditions that make it worse. So if you have bad heart disease, and you'd get a respiratory virus infection, sometimes people even have heart attacks from viruses, which is very rare, but we think probably happens more than we understand. But it may basically, you know, they may even be in sort of a tenuous balance, like everything's kinda holding together, but it's, it doesn't take much to push over into feeling a lot worse. And so I just think about the people that are at risk for our typical seasonal influenza are going to be the same people that are at risk. So, anybody that has lung problems, anybody whose immune system can't fight it off. I think it's hard to say to actual groups. And, you know, we're seeing that many older people are being spared and, and some younger people that are younger than we thought are getting it. So it's really, I think we're, you know, we're trying to define the syndrome as we're trying to diagnose cases as we're trying to bring up testing. And so I think, you know, we will by the end of this outbreak, have more resolution on what that looks like. But I think right now, you know, I think it's probably at this point near seasonal influenza.

Erin Welsh Gotcha. There were two groups specifically that we got a lot of emails about and questions about and one of those groups was people with diabetes type one and they were wondering, you know, people, "I, I keep seeing that people with diabetes are more at risk. Does that include me?" And then the other group that we got a lot of questions from were people who were pregnant or people with, with newborns.

Colleen Kraft Right. So the pregnancy I think is always a, we always are concerned about it very highly. I don't think that there's been any data that actually shows there's poor outcomes. I know that Dr. Denise Jamison from Emory has published a little bit about this, at least what's known from SARS and MERS. And, while early trimester is always concerning for anything, there's no evidence that anybody, again, has had any pregnancy complications from this. However, in general, we don't like to test that theory. And so we tend to be protective around pregnant women for sure. In terms of those with diabetes, I think it's, it's again, not quite known what the aspects of diabetes except that there's some level of sluggish immune response, I wouldn't say immune compromise entirely, I think it depends on how well your blood sugars are controlled, how many complications you already have from diabetes. Do you have type one diabetes, which can tend to be much more severe than type two diabetes? I think some of those questions, you know, maybe elucidated as things progress.

Erin Welsh Gotcha. So you know, on, on these, in this discussion of high risk groups and low risk groups and varying risk in general, one of the things that we've seen is that children seem to experience a milder disease than some other, some of the other age groups. Do we know why that is? Are immunocompromised kids just as vulnerable as immunocompromised people of other ages?

Colleen Kraft I should have read my pediatric textbook a little bit more, but there are definitely a number of viruses that are much worse in adults than kids. And then we sort of have the, have vice versa where kids tend to have maybe an increased predilection or maybe it's just because by the time you're an adult, you're immune to it, and when you're a kid you're sort of seeing it for the first time. So there is always this dichotomy of is it worse in kids or better in kids? This, this scenario really seems to be that the kids are these asymptomatic probably shedders, right? What we already discussed a little bit earlier. And so that this virus just for whatever reason is not that severe in children. But again, it may be that most coronaviruses aren't, we just haven't studied them because we kind of haven't cared cause they haven't been that severe in adults. And in terms of immunocompromised kids, I suppose that they are more at risk, but I suppose that they may also become increased vectors. They may just shed longer. But again, I'm not a pediatrician so I, I hesitate to sort of fully answer that one with confidence.

Erin Updyke That makes sense. So can you explain a little bit about how we are getting the numbers for things like the case fatality rate right now? Is that something that is still a moving target? Do you think that we might be able to see that number decrease as more asymptomatic or mild cases are identified since at this point it seems like testing is mostly focused on the severe cases?

Colleen Kraft Exactly. Yeah. So I think this is, you know, where again, my laboratory background and the logic of this is really interesting in a, is it interesting as anything can get right now? So what I really think is interesting is we, we really do have a decrease in throughput ability right now with our diagnostic testing. That's because we're building the car as we drive it. Right? So there's been all this contrived controversy about test kit shortage. Well we just discovered this virus and we just made a test for it. And when

we make tests that are new, we have to go back to old school methods, which are a bit slow. And so I think, I don't know what expectation we had that we had to have like a rapid test the next day. I think it was a little bit, I don't know who's setting that standard but the standard is unobtainable. And so I think that by virtue of the fact that we are going to start testing more and more people over the next month, we are going to see that that denominator is going to stretch out. So we're going to have people that are asymptomatic, barely symptomatic that are going to be positive and that will make that case fatality rate drop. I think it can look higher, again, it's exactly what you said, it's selection bias. So when you're only testing the sickest of the sick, then you're only going to find a high case fatality rate. I personally am the current gatekeeper to who gets on our daily test in house that we've developed and we only have room as of today, this probably is actually going to change tomorrow. So, you know, I have to gate keep and prioritize who gets on our in house run, which takes 24 hours versus send out to a referral lab, which may take seven days. Well, who do I prioritize? I mean, who would you guys prioritize? So we're going to do inpatients because we're also using a lot of personal protective equipment to care for these individuals. And so we want to be able to take them out of that if they don't need it. And then we can keep our supplies, you know, we need less supplies if we do it that way. And then we're also tests prioritizing our workforce. Right? so we want to make sure that the physical therapists and the respiratory therapists and the, you know, tech, and everybody can come back to work because we want to make sure we can keep taking care of these sick patients when they come in.

Erin Updyke That makes sense.

Erin Welsh Mhm. I, so I know that it's early stages yet again in this pandemic, but do, what do we know so far about longer term health consequences for people who have gotten sick? Maybe have gotten mild or severe in particular disease and are there long-term health consequences, like lung damage or other issues?

Colleen Kraft So the, the logic that I use is that anything that damages the lung can cause long-term consequences. So the lung only knows how to do one thing when it's damaged and that's to scar down. And so that's why our bodies have this lovely cough reflex so that all that stuff doesn't go into our lungs and cause scarring and damage. So when we have a virus that's infecting our lung cells, then that's going to cause this scarring to happen. And we potentially could see long-term damage. But that's the same as sort of anything that comes and damages the lung.

Erin Updyke Okay. So another question that a lot of people had, and I know we probably don't fully know the answer to this, but maybe we can sort of estimate based on what we know so far about coronaviruses in general or from, you know, the previous outbreaks, is, do we know about whether it seems possible to become re-infected with this virus if you get it and then recover from that infection?

Colleen Kraft Yeah. So I was just on another alumni call today and had this very same question. I, we probably get this question every day. And so in general, we probably don't know for sure. I think because this is a novel coronavirus introduced to the population, we will likely understand more because there's more attention to it. My understanding is

that when we have viral infections, we do become immune to them. But remember that it depends on how systemically ill we are as well. So, you know, it's a complicated immunology at this, at our nasal source, right? We talked already about how trying to say the viral load from, from the nose is not a very consistently sampled area. And so I think in the same way that immunology may be difficult to totally separate out because there may be an aspect of our mucosal immunology that plays a large role in whether or not that virus comes back to us. Right? So we may have just symptomatically gotten through it, but did we actually form true defense against it? And again, I think, you know, I would, I don't pretend to know that much about immunology except the big picture stuff. So I hope that was helpful.

Erin Welsh Yeah, absolutely. So in our first episode on coronaviruses, we ended up by asking you what about this disease concerns you and what about it makes you say, hold off on the panic or maybe has reason for optimism. Has your answer changed at all since that time?

Colleen Kraft The answer has changed. Dear Erins [chuckles] I, I think that we do see that it causes lower respiratory tract infection, much like other viruses that we know such as influenza. And so I am happy to say that it's not as severe as SARS or MERS, but it's not insignificant. And we are seeing a lot of individuals, you know, in the hospital that have this. I think my optimism is that, I'm trying to be optimistic every day. It the supply chain issues and the personal finance issues and the childcare issues to me are making this very personally difficult for a lot of people. It's, it's one thing to sort of have a bad flu season and us to have sort of sicker patients or more patients, but the personal protective equipment and you know, no visitors to the hospital, all those things really are stressing people personally. And so I, I'm just trying to be optimistic that a lot of this social isolation that we have implemented will actually make a difference. Because, you know, we're sort of, at least in Georgia we're sort of coming into the surge part of it for our location. And I think everybody's going to go through that and you know, have to just come out on the other side. But there's a lot of things that, you know, when I was bubbly three weeks ago or whenever that was, I could not have imagined the stress of like not having swabs to test or, you know, I could have understood and foreseen not having enough tests or having a low throughput on tests. That's something we deal with, with other scenarios. That's not that uncommon. But I think the, the financial, personal tolls that are occurring in the midst of trying to, of being very busy like during a respiratory season have been a lot more difficult. So I'm just hoping that our interventions while initially seeming very dramatic, will actually sort of alleviate the stress.

[musical outro]

Erin Welsh That was fantastic. Thank you so much, Dr. Kraft, for joining us and taking time out of your ridiculously busy schedule. We really appreciate it.

Erin Updyke We can't believe that you made time for us. We really, really appreciate it.

Erin Welsh Yeah. We do. Alright, so things we learned.

Erin Updyke Mmhmm.

Erin Welsh Number 1. One of the big gray areas that we didn't fully know the answer to in our first coronavirus episode back in February, was whether or not people were infectious before they were symptomatic, and whether there was asymptomatic spread or even super mild infections contributing to the transmission. So in this interview, we learned that although we don't know exactly how much virus people might be shedding throughout their infection, that there are asymptomatic or very mildly symptomatic individuals, and that they're contributing to the spread. That is super clear at this point. Dr. Kraft mentioned testing someone who seemed perfectly healthy and finding a ton of virus, in comparison to someone else who was more severely ill and had a lot less virus in their sample. And, there are some difficulties with this in terms of standardizing the test, and whether that person who had less virus *did* actually have less virus. We don't know much about the viral load changes throughout the infection, but this, I still think, personally, is alarming. Or at least is going to make transmission of this disease much more difficult to stop.

Erin Updyke Absolutely.

Erin Welsh And there was actually a nice modeling study that used data from Wuhan and fit some mathematical models to the actual infection data and it suggested that up to like 86%, 86%, of the spread of infection was likely due to unidentified cases.

Erin Updyke That's a lot.

Erin Welsh It's a lot. And it makes sense that this is possible if we know that asymptomatic or mild infections are possible and common.

Erin Updyke Absolutely. Number 2. Another big thing I think to take away from what we talked about with Dr. Kraft, and what we heard in the firsthand account, is that in people who get severely ill from this disease, these people really need to be hospitalized. And that's what's scary about this and why you hear a lot, and we'll talk more in the future, about why we're trying so hard to flatten this curve. Because if our hospitals get overrun, then more people could die simply because there aren't enough beds or there aren't enough staff, or there isn't enough equipment to actually care for them. So, for people that need to be hospitalized for supportive care like Dr. Kraft was talking about, that means that these people aren't able to breathe well enough on their own, so they either need a tube down their throat and to be on a respirator, or even if they don't need that like, maximal support, they still need supplemental oxygen or a positive pressure face mask. All of these things you can only get in the hospital. And the other thing, is that even if people don't need help breathing, they might end up needing IV fluid support as well. When you get sick when you're not eating, not drinking normally, and you're spiking high fevers, your body is working really hard to fight off an infection you can end up severely dehydrated pretty quickly. So for some people, if they get very sick, just drinking fluids isn't gonna be enough to replete that volume. So another way that we see supportive care in the hospital is support from IV fluids as well. All of these are support measures, just to help your body get through this process, not even addressing the virus itself. And we'll talk in a future episode

about what's being done on those types of treatments, but I think understanding that people who get severely ill really need the resources that are available in hospitals is an important aspect of this disease.

Erin Welsh Absolutely. Number 3. So looking at these different risk groups, I think there are a couple of important things to keep in mind. One is that we don't fully know the risks across different groups, and part of that is because this is so new we don't have a ton of data, and another part is that, because like Dr. Rasmussen said in our episode about the virus biology there is a lot of variation in host response that we can't always predict. On top of that, we have these, as we mentioned, a bunch of these asymptomatic or very mildly symptomatic individuals that are contributing to the spread of this virus. That means that we all kind of have to assume that we are potentially infectious at any point, because it's our job to help protect those around us that might be more vulnerable. And another thing I want to point out is that in the US so far, like 38% of people that are hospitalized with COVID-19 right now are under 55.

Erin Updyke That's a lot. Of young people.

Erin Welsh It's a lot. It's a lot. And I think that's not necessarily been what the messaging has suggested in terms of, "Oh, if you're not old, if you don't have underlying health conditions, then you're safe." Which, first of all, that's kind of mean to the people who are older and who do have these underlying health conditions-

Erin Updyke Exactly!

Erin Welsh -that are like, "Oh well, go ahead and die. I'm gonna be fine."

Erin Updyke Right! These are still human beings we're talking about here.

Erin Welsh Human beings, yeah. And so I think that, that messaging that everyone is susceptible, is really important. And everyone can possibly contribute to the spread of this disease.

Erin Updyke Exactly.

Erin Welsh So there was a nice retrospective analysis of this disease from patients in Wuhan, and in this analysis, the median age of people who were hospitalized with COVID was 56. So although there are some good data that suggest that older ages are especially at risk for dying from COVID-19, this is by no means a disease ONLY of older people, and it's not only older people who become SEVERELY ill from this virus.

Erin Updyke Number 4. Speaking of who gets super sick, we also talked with Dr. Kraft about the case fatality rate. So I'm gonna define that really quickly. Case fatality rate, that you're probably hearing a lot about, is the number of deaths divided by the total number of cases in a period of time. So, that denominator- the total number of cases in a period of time- is determined by the number of people that we know are infected. And as Dr. Kraft said, in this case, if we're only testing the most severely symptomatic people, then that denominator is going to be small relative to the total number of people who might actually

be infected. So then the numerator, the number on top, the number of deaths, is going to be proportionally larger. So the bottom line is we still don't know exactly how deadly this disease is. Especially here in the US where we're only testing severely ill individuals for the most part. We do have some preliminary data in the US. This is from March 16th, this data. It suggests that mortality is definitely highest in people over 85, but in this group mortality ranges from 10-27%. And in people between 65 and 84, it ranged from 3 to 11%, and it went down from there. But again, all this data is biased by the fact that we're only testing the most severe cases. And as you've probably heard in the news, the case fatality rate thus far has been different in different countries, and that's likely because of both differences in ages of the population that's ill in those countries and also differences in their testing strategies as well.

Erin Welsh Mmhmm. Yeah. Which brings us to number 5, our last point. And that is that we do not have enough resources. Period.

Erin Updyke Period.

Erin Welsh We don't have enough resources. And that is super problematic. And it's no fault of the clinicians or the laboratorians who are now faced with having to decide who they can test with their limited supplies. And the thing is, if we don't stem this infection that lack of supplies is only going to get worse. And that's what we have seen in Italy. It's illustrated this perfectly because in some areas they don't have enough ventilators and they're having to decide who they are going to intubate and ventilate. That's a decision that no physician should ever have to make. And we'll talk more in some of our future episodes about what has led to this shortage and why we are facing it, but there is no doubt that it's making it harder to get this epidemic under control and it's an enormous stressor on hospitals and healthcare workers.

Erin Updyke Yeah. It's pretty major.

[sighs]

Erin Welsh Okay, sources?

Erin Updyke Sources, Erin. We have a lot for this episode.

[chuckles]

Erin Updyke So there was an article by Lauer, et al. All of these are from 2020, okay. They're all written in the last month. There's an article from Lauer, et al. that was in *Annals of Internal Medicine*. From Bai, et al. in *JAMA*. From Zhou, et al. in *The Lancet*. We've got one from Wu and McGoogan in *JAMA*. Kong and Argawal in *Radiology: Cardiothoracic Imaging*. That one's great if you want some pictures of those ground glass opacities. Li, et al. in *Science*. And then the CDC's MMWR report from March 18th is where I got those numbers on the age stratified deaths in the US so far. So.

Erin Welsh We'll post all of those references on our website, thispodcastwillkillyou.com, so if you wanna read up a little bit more, you know where to find em.

Erin Updyke Yep. Thank you again to Dr. Colleen Kraft for taking the time out of your schedule to speak with us and to share what you have learned with our listeners. We really, really appreciate it.

Erin Welsh We really do. And thanks to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Updyke And thank you, for stickin' through Chapter 2. We'll see you next time.

[chuckles]

Erin Updyke Chapter 3.

Erin Welsh Until Chapter 3, wash your hands...

Erin Updyke You filthy animals!

[musical outro]