

TPWKY

This is Exactly Right.

Vince

My name is Vince, 36 years old from New York and I work in the veterinary field and this is my COVID experience. Last April I had become ill, I thought that I had like a sinus infection or something. I tried to wait it out up until I just started coughing up blood constantly. I went to the hospital and sure enough I was COVID positive and I also had pneumonia that I'd gotten through COVID. So I was admitted and I was in that hospital for a month and I really didn't improve. But at the end of that month, that hospital, they were becoming overcrowded with COVID patients, they kind of rushed me out even though I told them that I didn't feel like I was any better or ready to go, but they discharged me. And two days after they discharged me, not only was I still coughing up blood but when I moved around I felt like I was going to black out, I would just lose all my energy, I was just exhausted.

So I went back to the hospital and I was only there for about a day and they transferred me to a larger, far more competent hospital. And two things were found out at that hospital. The first being that I had an abnormal blood clot in one of my lungs that effectively killed off 1/3 of my lung. The other being that since I was fighting COVID, pneumonia, and I was compromised from the damage to my lung, me who was at the time 35 year old athlete was in clinical heart failure. The virus had attacked my heart aggressively and I was in heart failure, that's what was going on. I was taken to ICU and a number of things were done. There was a tube placed in my back that was constantly pumping out all sorts of gunk from my lungs, I had neck congas placed in both sides of my neck, I had some sort of port put in my chest. I was barely conscious a lot, I was hallucinating as well. Things got really bad and they had to install a balloon pump in my leg to keep my heart beating.

The only solution was that I needed a heart transplant. They found a donor and that's what happened. I had to have a heart transplant. I was in the hospital for over three months, just shy of four months actually. And I've had to go back several times since just because my immune system is compromised now due to the transplant. When I was healthy enough after the transplant to be weighed, I went from going into the hospital as a 210 lb combat athlete to being 153 lbs. life's been hard since, I can honestly say it's ruined my life. People tell me, 'Oh you're so lucky you survived.' But you know what? I don't feel lucky. I don't feel lucky at all.

Anonymous

I work as a case investigator on the COVID response in Georgia. My role includes calling people who have tested positive to gather data about their symptoms and medical history, collect their close contacts for contact tracing, give guidance for isolation, and connect the cases to resources. I've spoken to hundreds of people who have had COVID, most of whom who have had mild to moderate cases and many of whom have had severe cases, some later died. The emotional toll can be a lot to bear and the work never stops. In the current surge, we cannot even begin to reach everyone who is sick and the most we can do is hope that they are okay.

The story I want to share happened shortly before Christmas. My team was focusing on school-aged children in an effort to control transmission in schools before they return from break. I spoke to a mother whose two children had tested positive and she was quite sick herself. She was very helpful in giving me information about her children and very attentive to the guidance I gave her. Towards the end of the call, she revealed her husband had tested positive first and was now in the hospital on a ventilator. I offered my condolences and told her I would connect her to available resources to help pay his medical bills. She replied, "Thank you for your help, I just hope he doesn't die on Christmas. I don't want our kids to associate his death with Christmas." I have dealt with death and grieving loved ones for months now. It was all a part of the training and the mortality rates have become background noise to my daily life. But this woman's story hit me in the pit of my stomach. I took a few minutes to gather my thoughts and then moved on to the next case.

I found out a week later that this father passed away the day after Christmas. I knew the hospital he was in was using tablets on tripods to allow people to say goodbye to their loved ones. The image in my mind of this woman and her children saying goodbye for the last time on a screen turns my stomach. I am angry, I am heartbroken, and I am so tired. The only hope that I have is that the vaccine will be able to win the war that those of us working in public health have been fighting for almost a year.

John

Hello, my name is John and I am a paramedic in northeast Texas. I have worked for 8 years in a small community approximately an hour and a half east of Dallas. I staff a dual-medical and ICU on 12 hour rotating shifts. Many of the patients in our community are older, they reside in rural farming areas, we also have a large Latin American population in our community due to a sizable manufacturing industry. We began to see an influx of cases in late March at one of the industrial plants in town. Due to many cultural as well as socioeconomic reasons the virus spread like wildfire, faster than we expected and faster than we were prepared for. By mid May, our town of less than 30,000 had more than 850 cases and made regional as well as national headlines. We have no more ICU beds or ventilators, our dispatch was completely unprepared and we had no system in place to properly warn crews of probable cases.

In April my partner and I were sent to a house for a simple anxiety attack, that's all the information that we had. Upon entering the home, the patient was found sitting on the floor gasping for breath and a tinged hue of blue around her lips let us know she was in severe respiratory distress. She began to plead in one word sentences for help. The patient was using a nebulized breathing treatment which we know to be contraindicative in COVID patients. The haze of the expired vapor of that breathing treatment surrounded my partner and I. Blindsided by these severe symptoms, my partner and I were caught with our metaphorical pants around our ankles. We were wearing none of the appropriate PPE. We had gloves and surgical masks, that's it. The patient's oxygen saturation was 50%. The decision was made to intubate her despite our lack of PPE. That same patient died in our ICU two days later due to complications of the novel coronavirus.

Three days after the incident I began running a fever. I had body aches, a cough, I was more tired than I'd been in my entire life. Ostensibly I contracted that very disease that was ravaging our community, however I'm 30 years old, I'm physically fit, and I have no preexisting conditions. Due to the lack of testing nationally I was denied a test. Needless to say, I recovered, I've been back on the front lines since returning 14 days after my initial symptoms. I believe EMTs and paramedics have a unique perspective as well as a unique challenge during this pandemic. Hospitals, clinics, and other healthcare facilities have some amount of control over their environments. Entering into patients' homes and interacting with these patients in public many times without full knowledge of what the circumstances are, we are many times at the mercy of our environment.

We have had to adapt and overcome the ever-changing variables as they occur during this pandemic. I have been lucky to work alongside many wonderful employees and I have exceptional leadership where I work, including the chief who has been an immense help through it all. He's helped us with all the challenges that we face, giving us the resources that we need, as well as helping us with the physical and mental toll this has taken on us. Obviously my story is not unique, nearly half a million EMS personnel in this country have endured the same hardships for months. Some have even lost their lives doing so. Now with the rates increasing again and the hospitals working at the cusp of full capacity, we continue to work and continue to adapt day after day to this pandemic.

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh	Thank you so much to everyone who provided their firsthand account for this episode and thanks to everyone who has sent in a firsthand account or filled out the form, we really appreciate it.
Erin Allmann Updyke	Yeah, thank you so much for sharing your stories with us.
Erin Welsh	Hi, I'm Erin Welsh.
Erin Allmann Updyke	And I'm Erin Allmann Updyke.
Erin Welsh	And this This Podcast Will Kill You.
Erin Allmann Updyke	Yeah, welcome to a long-awaited, another update episode in our Anatomy of a Pandemic series where we cover all things COVID-19.
Erin Welsh	Yeah. Erin, this is our 15th episode.
Erin Allmann Updyke	I honestly can't believe that we've made this many episodes, that's so many episodes.
Erin Welsh	I know. It's a lot. It's a lot.
Erin Allmann Updyke	But there's so much to cover when it comes to this pandemic and so we just feel like we really have to cover it all.
Erin Welsh	(laughs) Yeah I mean we've learned so much in terms of virology or epidemiology but we've also learned as this pandemic has gone on just how much we still don't know or how much our knowledge about this virus or about this pandemic or about the disease that the virus causes, how much all of these things have changed from our earlier understandings.
Erin Allmann Updyke	Exactly. Which brings us to the focus of this particular episode. This week we're addressing all of the new things that we've learned about the disease caused by the SARS-CoV-2 virus, that is COVID-19. We'll touch on things like what is long COVID? Or how long does immunity actually last? Or what is the impact of infection on pregnant people?
Erin Welsh	But before we get to that and so many other questions about COVID-19, we have some very important business to take care of.
Erin Allmann Updyke	Yeah we do.
Erin Welsh	Erin, it is quarantini time.
Erin Allmann Updyke	It's quarantini time!
Erin Welsh	(laughs) What are we drinking this week?
Erin Allmann Updyke	We're of course drinking Quarantini 15! So creatively named.

Erin Welsh	Quarantini 15 has vodka, it has grapefruit juice, it has some maraschino liqueur and a little splash of grenadine. And we will post the full recipe for this quarantini as well as the nonalcoholic placeborita on our website thispodcastwillkillyou.com as well as on all of our social media channels.
Erin Allmann Updyke	Any other business, Erin, that we have to discuss?
Erin Welsh	There's the usual. You know we have a bookshop.org affiliate account, we have a Goodreads list. You can find those things on our website where you can also find transcripts, alcohol-free episodes, and...
Erin Allmann Updyke	Merch!
Erin Welsh	Oh merch, yeah! (laughs) And we also are still soliciting firsthand accounts for this COVID-19 series and so if you would like to submit yours, please head to our website where you can find a link at the top of the page as well.
Erin Allmann Updyke	All right. Let's get to the meat of this episode, shall we?
Erin Welsh	Yes, let's do it.
Erin Allmann Updyke	We were fortunate enough to chat with not just one but two awesome people today who answered our many, very long list of questions about all the things that we've learned about COVID-19 in this past year.
Erin Welsh	We were joined by Dr. Krutika Kuppalli, infectious diseases physician and assistant professor at the Medical University of South Carolina and whom you may have heard on a previous episode in this series, as well as Dr. Jason Kindrachuk, assistant professor and Canada research chair in molecular pathogenesis and emerging viruses at the University of Manitoba.
Erin Allmann Updyke	We recorded this interview on March 16th so keep that in mind if you hear any numbers, things may have changed. And we'll let them introduce themselves right after this break.
TPWKY	(transition theme)
Jason Kindrachuk	I'm Jason Kindrachuk, I'm a PhD, I'm an assistant professor and Canada research chair in molecular pathogenesis and emerging viruses at the University of Manitoba in the department of medical microbiology. Most of my work focuses on both the pathogenesis as well as the transmission and circulation of emerging viruses including Ebola and coronaviruses.
Krutika Kuppalli	And I'm Krutika Kuppalli, I'm an infectious diseases physician and assistant professor in the division of infectious diseases at the Medical University of South Carolina and my area of research and interest is in emerging infections and biosecurity. I am interested in looking at the clinical care and pathogenesis of emerging infections and understanding how we can better prepare for outbreaks and pandemics. And I was doing that before coronavirus hit.
Erin Welsh	Awesome. Thank you so very much for taking the time to chat with us today, we're very excited to hear what you have to say about all of our many questions, so let's dive in. So in our virology update episode which we released a few months ago, we talked about how this virus is transmitted. But how much does the infectious dose or the amount of virus that a person is exposed to, how much does that play a role in whether they will get the disease or how severe the disease might be?

Jason Kindrachuk

Yeah, so this is such a good question right? And I think really we're maybe getting a better glimpse into what this looks like. In particular, we think about this idea of infectious dose. So certainly I think we're still at somewhat of an infancy in understanding what is the specific amount of virus that you need to be exposed to to get infected. There's been some modeling studies that suggested it's a bit higher than SARS but a little lower than MERS, so somewhere in kind of the hundred particle range. But a lot of that is somewhat subjective, right? So we're saying okay, that is the number you need. But there's also this aspect of exposure time and I think that's become maybe a little bit more prominent the past few months, we've talked about these superspreader events, we've talked about things like people being in close settings, that it's not just a function of the amount of virus that somebody is exposed to at one moment in time or that static moment in time as much as it may be about the accumulation over a specific period of time.

And I think that's really important, I think we're getting a better understanding of the fact that, listen, if you have people that are in enclosed settings and they are subject to poor ventilation and you have somebody that is releasing virus, even if they're releasing virus at a low rate, you probably are gonna have people that are continually exposed and you have that overall accumulation. So I think that that is starting to be this indication of the fact that we have to think about this not as just a static number but also a function of the situation as well as again, the person themselves and whether or not there are biological consequences that allow them to basically take up more virus or are more vulnerable or susceptible to virus than others.

Erin Allmann Updyke

That makes sense. So speaking a bit more about viral shedding by infected people, how soon after being exposed does someone become infectious? And how does that infectivity change over the course of a person's infection?

Jason Kindrachuk

Yeah this has been kind of a longstanding question, right. Is when somebody's exposed, how long does it take for them to start shedding virus? And I think again we're getting a much better picture. Dr. Muge Cevik has done some really great work I think in providing good contextual data, looking at overall infectiousness and periods of infectiousness for COVID-19 and for shedding SARS-CoV-2. And I think again we look back at this idea that the majority of people within 5-6 days post-contact or post-infection are likely going to start to have symptoms in some cases that may trail out a little bit longer, 2-12 days.

But if we look at that or we take that average, say that 5-6 days when people will usually start showing symptoms, well we know that now it looks like that infectious period when you can actually recover infectious virus from that person tends to be about two days prior to symptom onset. So we're in the neighborhood of up to about 10 days post-symptom onset. So that starts to give us a picture that even within the span of day 3 or day 4 post-exposure, that you would potentially have somebody that is starting to be able to release virus. And then I think again when we look at all the clinical data that's kind of been accrued over time, what we're getting a good perspective of is the fact that people are likely most infectious and that kind of one day to two days just prior to symptom onset to about 5 days post-symptom onset.

Erin Welsh

Okay, gotcha. And so because we know that the amount of virus shed changes throughout clinical disease, how much does it change looking at a different sort of snapshot? How does it change across different severity of disease? So are people who are severely infected, are they shedding more virus, are they more contagious than people who are asymptomatic?

Jason Kindrachuk

Yeah, again I think we're starting to get a better picture of this looks like, right. And I think in particular when we think about this idea of asymptomatic patients vs those that are presymptomatic vs those that are symptomatic, certainly some of the household contact data suggested that people that are asymptotically infected seem to have a much lower secondary attack rate than what people that are symptomatic or presymptomatic do. So that starts to suggest that people that have basically mild or asymptomatic infections likely are going to lead to lower numbers of infections based on the amount of virus that they release as compared to people that have more moderate or more severe symptoms. But there's also kind of a converse to that. When we think about this idea that people that are severely ill, we certainly know that people that are severely ill may have a longer period at which they're able to release infectious virus.

But the likelihood is also that those severe disease cases are probably also going to be hospitalized or receiving care. So the likelihood is that those people that are severely ill, even though they're releasing a lot of virus, are probably not going to be in a position where they're going to be exposing a lot of additional people in public. So again, I think we get back to this phase of saying that it's somewhere kind of inbetween people that are mild to moderately ill and kind of looking at the viral loads from the data that we have in that kind of primary infectious period, it probably still follows that somewhere again in that 0-5 day range that people that are moderately ill or mildly ill probably are going to have the greatest ability to release virus during that period.

Erin Allmann Updyke

That makes sense. So overall we're now like a full year into this or even longer and we've got a much better picture of the spectrum of disease that SARS-CoV-2 can actually cause, like you mentioned already from asymptomatic infections to very severe or even fatal outcomes. So could you walk us through a little bit this spectrum of disease in terms of symptoms or clinical observations? First talking about how many people really are asymptomatic and then what mild infection looks like and what moderate or severe cases are like. Like what proportion of cases are we talking about that are very severe vs mild vs completely asymptomatic?

Krutika Kuppalli

Sure. So as you mentioned, we have a much greater understanding of the clinical syndrome that we see now and I think that there are various definitions out there for patients who are infected and some of these criteria may overlap or vary across the different guidelines that we see. But for the most part when we talk about patients are asymptomatic or presymptomatic, these are people who test positive for SARS-CoV-2 via the nucleic acid amplification tester antigen test but they have no symptoms consistent with COVID-19. And then the next step up that we would consider a patient to have mild disease and these are people who have various signs and symptoms of COVID-19. So these are very nonspecific symptoms, so patients who could have fever, cough, headaches, muscle aches, nausea, vomiting, diarrhea, and then loss of taste or smell which has become one of the characteristics that we see with this viral disease. But typically these people don't have any shortness of breath, they don't have any abnormal chest imaging.

And then the next stage of disease that we tend to see are people of moderate disease and these are people who have some lower respiratory disease on their clinical assessments or imaging and they may have a little bit of hypoxia or low oxygen saturation on room air. The next severity of disease would be what we call severe illness and these are people who have an oxygen saturation less than 94% on room air and they might be breathing pretty fast, so they're breathing greater than 30 breaths per minute and they have pretty significant lung infiltrates.

And then the most severe illness is gonna be what we call critical illness and these are people who have respiratory failure, these are the people who are intubated and have multiple organs involved with their SARS-CoV-2. And I think we're still getting an idea of the number of people that are asymptomatic/presymptomatic vs those who go on to develop critical illness. You know, last projections estimate that about 30% of people have asymptomatic/presymptomatic infection, however we are still learning more about this disease and what percentage of people have asymptomatic disease vs go on to develop moderate to severe and critical illness.

Erin Welsh

Mm-hmm, yeah. So the symptoms, like you mentioned, there's this huge spectrum of disease. And how much do these symptoms or the general course of disease, how much does that vary from person to person? Like how predictable is this virus?

Krutika Kuppalli

Well there's lots of things that go into determining how a person is going to respond to getting this disease, right. So we know that underlying comorbidities play a huge role, people who have things like cardiovascular disease, chronic lung disease, diabetes, if they're obese, they have chronic kidney disease, those types of things are going to put them at higher risk to having a more severe disease. Additionally we know that if you're older that's going to put you at higher risk. So some of the data CDC showed that if you're 85 years or older compared to someone that's 5-17 years old, you have an 80x higher risk of being hospitalized and over 7000x more likely to die. So it's significantly higher given your age compared to someone who's younger. So there's so many different modifying factors that you have to look at when you're looking at how a person's going to react compared to another person.

Erin Allmann Updyke

So kind of along those lines, while a lot of people who become infected will have their symptoms resolve within a relatively short period of time, it seems that others are experiencing much longer-term issues with lung performance or even kind of a fogginess. Can you talk about some of these lingering effects of infection and how frequently they seem to occur?

Krutika Kuppalli

Yeah, that's a really great question and it's another aspect of COVID-19 that we're still learning about. It's what we call long COVID now and it's really not known why some people's recovery is prolonged, you know it's not sure if it's related to persistent viremia due to weak or absent antibody response, if it's related to some other inflammatory or immune reaction. So we're still learning about it but a lot of what we're seeing are long-term respiratory, musculoskeletal, and neuropsychiatric sequelae in some of these patients and it's occurring in about 10% of people who've had COVID-19. And many of these patients recover spontaneously but it takes a long period of time with holistic support, rest, symptomatic treatment, and gradual increase in activity.

And these patients will require some focused assessment, so if they're having prolonged shortness of breath, really trying to do some focused assessment on their respiratory function. So looking at things like pulmonary function testing, more focused imaging, possibly pulmonary rehab, if they're having neurological symptoms maybe doing some further brain imaging, neuropsychiatric testing, and again like I said, holistic support. A lot of focus is now going into trying to understand why these things are happening and how we can better support these patients.

Erin Welsh

Mm-hmm. Gotcha, yeah. So how much has our estimate of the case fatality rate changed over the course of this pandemic and how much of that is due to better testing ability? Or is it also being able to actually treat some of these cases or provide supportive care? So can you talk a little bit about sort of this case fatality rate and what goes into it?

Krutika Kuppalli

Sure. So I think this is something that we're also beginning to get a better understanding of, I think it's really important to understand the difference between the infection-fatality ratio which estimates the proportion of deaths among all infected individuals and the case fatality ratio which estimates the proportion of deaths amongst identified, confirmed cases. So to measure an infection-fatality ratio accurately we need to know the complete picture or the number of infections and deaths caused by a disease and so in the early stages of a pandemic, most estimates of fatality ratios are based only on the cases detected and so it can be underestimated. And so I think as we've gone along we're identifying more and more cases and through better testing and better surveillance methods. However I still think we have to continue to do more testing because there may be asymptomatic cases out there that we haven't been detecting and testing for. We still have some work to do to further identify them. So I think we're doing a better job but I think we still have some work to do for that.

Erin Allmann Updyke

And so you kind of talked a little bit already about how we know that there are some people who are at higher risk than others even though we know that no one is entirely safe from this virus. Can you talk a little bit more about some of those risk factors that seem to be associated with severe infections? And I've heard things like is there any link between blood type and risk of infection? Things like that.

Jason Kindrachuk

Yeah, you know, from my standpoint I think Dr. Kuppalli kind of touched on some of these but from a uniquely Canadian aspect, I mean one of the things that we certainly have been very awakened to throughout COVID-19 was just how much age has played into severe and fatal disease. Certainly when you look at our fatality rates we have a massive overrepresentation of people that are seniors and people that are above the age of 65, in particular those that are in long-term care facilities and personal care homes. So certainly I think we're getting quite the perspective on the role of age but then of course we look across different groups and we certainly see that much like with other emerging infectious diseases that there's a disproportion effect certainly in minority groups, in people that are in lower socioeconomic status, people that are in underserved communities.

So I think it certainly is opened our eyes to the fact of the differences in how infectious diseases really affect different segments of our population. And then of course we look at the underlying medical complications that are related to this, whether we look at somebody that has cardiovascular disease or we look at people that have a high BMI or who are obese or those that have diabetes, those that are immunocompromised or in positions such as those that have cancer. I think we certainly realize more and more that there is a broad spectrum of people that are susceptible to severe disease and yes, we have an overrepresentation of people that are seniors but we cannot discount the people that are overrepresented across other groups as well. And I think that's gonna continue to expand, I think certainly as we start to go through the data more and more from across different countries, I think we'll get a better perspective of how that looks. And again in particular within minority groups, what the particular risk factors may have also been within there.

Then we think about this idea of blood groups. I mean certainly there was quite a bit of discussion and there was this discussion that type O was related to less severe disease. Well there's been some additional data that's come out fairly recently that has said, you know what, there isn't actually, there doesn't appear to be a link between this. So I think we're still trying to figure out what all the data says. Certainly there are standouts that we know are related to more severe disease and worse outcomes but I think it's these kind of more finite symptoms and finite biological factors that we still have to spend some time trying to understand a little bit more deeply.

Erin Welsh

Mm-hmm, yeah. And so what do we know, even though there might be a lot more to uncover as the pandemic goes on and as the data are analyzed and so on, but at this point what do we know about pregnancy and infection with COVID-19? Are there risks and do the risks vary depending on when during pregnancy somebody may be exposed or infected?

Krutika Kuppalli

So that's a really wonderful question. The full impact of infection with SARS-CoV-2 in pregnancy is still being learned and being understood. We know that pregnant women with coronavirus disease are at increased risk for severe illness and they may be at risk for preterm birth. There are definitely some surveillance systems out there, one of them is the CDC has the Surveillance for Emerging Threats to Mothers and Babies Network that has been collecting data, looking at pregnant women who have COVID-19 to see what happens to women who are infected and their babies. One of the things that have been discussed is that if women who are pregnant or hospitalized for COVID-19, they should be definitely monitored closely and be at a facility where they can have the highest level of care.

We know that they should be given a multi-specialty approach to care with maternal-fetal medicine, IV, pulmonary critical care. Also the most recent NIH guidelines also recommend that any of the therapies that we would use in non-pregnant women should be also given to pregnant women to help treat them appropriately. So in terms of any of the other data, you know, that data is still being collected and being looked at. But other than the pregnancy data that shows that they might be at risk for full preterm birth, we're still learning about it.

Erin Allmann Updyke

So we know that, or it appears that people who recover from COVID-19 do have some immunity to the virus that lasts for at least a few months. Do we know any more about the duration or kind of the nature of immunity and the risk of reinfection especially in light of the new variants that we're seeing?

Jason Kindrachuk

Yeah, I think we're starting to get some perspective on that, right. And certainly Dr. Florian Krammer and others have really led the charge in trying to take a look at what this looks like. But first of all we have to maintain this perspective that we're 14 months, roughly 15 months I guess now, post-SARS-CoV-2 emergence. So our understanding of long-term immunity is pretty limited when we think about even those first cases from China that ended up in the hospital and then recovered. You know, the data is longer term but I wouldn't necessarily call it long-term. So I think we're still certainly at an infancy in understanding that but right now it looks like the majority cases that we see, there's at least good memory within the immune system out to around 8 months post-infection. So certainly in regards to antibodies directed against the virus, it looks like those are maintained for longer periods of time, it looks as well like T cell responses, that other aspect of our immune system, our longer term immune system and our immune memory also is maintained for upwards of 6 months or longer.

So I think it gives us a picture that yes, there certainly is some aspect of immunity that appears to be carried long-term. The difficulty in this is trying to understand how that relates to susceptibility to subsequent infection and whether or not we see any sort of immune waning and of course how that looks across the population. Is it the same in seniors as it is in somebody that is in a middle age group vs somebody that is 19 or younger? And I think we're trying to see what that looks like and that's been one of the drives to try and promote vaccination because at the very least, we understand that people that are getting exposed to vaccine, that are getting exposed to a constant amount of viral antigen or constant amount of the particular gene that we're using, that they will get a robust response that's maintained.

Certainly with the variants it's added a new variable for us, right. When we look at data coming out of Brazil, in particular the data that came out of Manaus, Brazil, there has been a lot of question about what was the potential for reinfection with the P1 variant that was first identified there or with SARS-CoV-2 in general. And does some of the kind of high burden we've seen of disease in subsequent waves within that area, does that suggest that there is immune waning after a certain period of time and that's why we have seen such high amounts of infection even though there seem to be a high seroprevalence within a population that would suggest that a lot of people have been infected early.

And I think we don't specifically know yet and that's what makes it difficult, certainly I think we're probably looking at reinfections that again are more the exception, not the norm at this point regarding the data that we've seen but we're also at a point of saying we don't really wanna test that hypothesis. So if we can try and cut transmission and we get people vaccinated, the likelihood is that we're probably gonna see lower numbers of new variants that are gonna emerge because there will be no ability for the variants to emerge if transmission is cut and we suddenly reduce any concerns about that question.

Erin Welsh

Mm-hmm, yeah. Fingers crossed that the immunity will-

Jason Kindrachuk

Exactly.

Erin Welsh

Yeah (laughs). So throughout this pandemic, how has treatment for people with COVID-19 changed? Are we any better at treating people with severe cases now than we were a year ago or 8 months ago even, 6 months ago?

Krutika Kuppalli

Yeah so I think that that's another really interesting question. So I think a couple of things have happened. One, I think we are better at treating patients and I think we have a couple of therapeutics that help. So let me tackle the first part of that question first. So I think that in terms of how to support patients who have critical disease, we've gotten better at managing them. When we first started seeing these patients who had significant disease that were intubated, we had a difficult time managing them and I think throughout the course of this pandemic our really wonderful critical care doctors have really gotten used to being able to manage them, right. So we have intubation protocols, we have mechanical ventilation protocols, we have protocols for proning these patients which I think has really helped in how we manage them. And the supportive care in managing these patients have really become protocolized which has helped in terms of improving the care for these patients. Concomitantly we definitely have information for how to treat these patients.

So we have a couple of therapeutics that may help, right. So we have remdesivir that has been the only therapeutic that has been approved by the FDA for the treatment of COVID-19 that is recommended to be used in hospitalization of a patient. We have dexamethasone which was found to improve survival in hospitalized patients requiring oxygen and having the greatest effect on patients who are ventilated. So those two therapeutics are pretty much routinely given out to patients who are hospitalized. So I think it is a combination of things. On top of that we have when patients are hospitalized with severe COVID, it's not uncommon that we find them to have superimposed bacterial infections, so making sure we appropriately manage those infections as well. So I do think it is a combination of things that have happened over a period of time. But that being said, these patients still become critically ill and can be very difficult to manage and they have numerous complications throughout the course of their hospitalization and so we still have a long way to go in trying to figure out how to more effectively treat this disease.

Erin Allmann Updyke

Yeah, that makes total sense. So a lot of the very positive news that everyone's talking about with COVID-19 has really focused on these new vaccines that we have. So speaking of these vaccines, what do we know at this point about these different vaccine candidates in terms of their effectiveness against new variants that have emerged? And what does it really mean if these vaccines are in fact slightly less effective against some variants than they are against others?

Jason Kindrachuk

Yeah, such a great question, right. So we're in this period of I think kind of intense optimism because the vaccines, not only have we had a single vaccine that has worked amazingly well, we've had multiple vaccines developed within a span of 12 months or just around 12 months that all seem highly efficacious and that certainly has renewed a sense of optimism. But we have this new variable with variants that have emerged and ones that will potentially subsequently emerge. Our understanding of how the vaccines behave in regards to the variants is still kind of growing. So we have some inference at least from looking at antibodies from those that have been vaccinated that would suggest that most of the vaccines seem to have decent neutralizing activities, so the antibodies that they generate still seem to be able to neutralize the different variants.

The B.1.351 variant that was first identified in South Africa certainly has created some issues, it has been the one I think that everybody has been quite focused on in regards to this idea of antibody escape. But I think we have to also look at what we're seeing in terms of real world data right now. So Oxford-Astrazeneca, their data at least with B.1.1.7 looks quite promising, they still have I think it was about 75% efficacy rate. And as well we're seeing real world data coming out of the U.K. where administration of Oxford's vaccine has really made a massive reduction in or led to mass reduction in transmission in cases. So I think you could make the argument that even in an area where B.1.1.7 is circulating, we're actually seeing a great benefit at the population level of the Oxford vaccine. Same thing for Pfizer that gained real world data from the U.K. also would suggest that we're seeing really good effectiveness within the population.

Moderna, I think there's some data certainly to suggest that in regards to antibodies, that there still is neutralizing antibody that is there but we don't know the efficacy yet in the population. And Novavax and Johnson & Johnson, certainly when we look at the 1.351, they have had lower reported efficacies against that variant. But again, I think we have to kind of move ourselves back a step and say okay, when we think about the variants what have we seen in regards to transmission in the community? Certainly B.1.1.7 has been a concern because the increased transmissibility has led to a broad destruction overtaking circulating strains. B.1.351, we haven't necessarily seen that. Certainly in South Africa it has been an issue, an ongoing issue. Here in Canada we've had cases but we certainly haven't seen the explosiveness that we've seen with B.1.1.7. So I think again with the vaccines, the more that we can get these vaccines out, all of which seem to at least so far have some capacity to reduce transmission to some extent, that will help us with control of these variants. And I think that's the important factor is if we wanna try and push back case variants, if we get people vaccinated we're gonna reduce transmission and that really to me at least is one of the most critical factors at this point.

Erin Welsh

Mm-hmm, yeah. So one of the early concerns about the vaccines was that they may not prevent asymptomatic infections. So maybe if you were veen still fully vaccinated, you may not get the disease but you could still spread the virus to other people. But you know it's a few months now since these vaccines have been implemented widely, what do the latest studies show about that?

Jason Kindrachuk

Yeah the data I think is suggesting that certainly for Oxford as well as I believe for Pfizer that they have been able to show that there's been at least some evidence for reduced transmission just looking at the amount of virus within the nasal passage within people that have been vaccinated and subsequently had been exposed. So I think it's kind of a good news story. But also at the same time it should not maybe come as that much of a surprise that if we have vaccines that ultimately are able to protect against severe and fatal disease. So they take that severe disease down to something that is more moderate or even in some cases down to a very, very mild disease. That period of infectiousness is probably going to be fairly limited.

And I think that that also probably plays at least some component into this. And so I think that it's important for us to understand that the vaccines, while initially I think we were all hopeful that they would at the very least cover severe disease and protect us from that, now we're getting more data to suggest that in fact they likely reduce transmission and hopefully that that will impact and lower rates of asymptomatic transmission. And I think in the real world settings where the larger vaccination campaigns occurred, we're seeing that play out. Certainly we're seeing transmission rates and cases dropping substantially very, very quickly and I think that's very reassuring.

Erin Welsh

Mm-hmm, absolutely.

Erin Allmann Updyke

That's what I wanted to hear.

Erin Welsh

Yeah (laughs). So as the light at the end of the tunnel gets closer and closer even though it sometimes doesn't feel that way, what is something that you hope we take away from this pandemic either at a personal level or as a society?

Krutika Kuppalli

I think on a personal level, one of the things I will take away has been my appreciation for the amazing collaborations and friendships I've made across the country and across the world because of this pandemic. I've made friends with people that I probably never would have made friends or collaborations with because of this disease and I think that that has really been an amazing opportunity for me. So I think that's something that I will cherish and I think also really speaks to the power of science. When things get really bad, you know, seeing how the world comes together. And I find that to be very humbling and very special. From a societal perspective I really, really hope that people will take away the importance of investing in preparedness, investing in the global health security agenda. We have a very short attention span and when things happen, we get up in arms and say we're gonna do something but then as soon as it's done, we forget.

And I really think that if this pandemic has shown us anything it's that we do need to invest in preparedness, we do need to invest in strengthening healthcare systems, we need to invest in surveillance. And this can't be a one-time thing, it's something we need to do longitudinally and I really hope that as a society we can put our differences aside and recognize the importance of doing that so that when the next infectious diseases outbreak comes along, and it will, that we will be prepared and we will be ready and that we recognize that this is a global threat, not a threat that affects certain people, certain races or certain ethnicities, that this is something that affects all of us.

Jason Kindrachuk

Yeah and I think I would compliment a lot of what Dr. Kuppalli said, certainly from a personal standpoint I, much like herself, was involved in the Ebola epidemic in West Africa. There's an aspect of it that I think for both of us and all of those that I know that were involved in that outbreak as well as other outbreaks, certainly it changes you, it changes your perception and your viewpoint on infectious diseases. But it doesn't necessarily impact your family and the people around you. And that certainly is something very different. I mean for me with a family, with a 2.5 year old at home, this was one of those kind of first instances where there was the question of what is going to happen? What is the world tomorrow gonna look like as we go through the pandemic? But Dr. Kuppalli said it very well that there was this immediate response with people across the globe, that certainly I would've never been in contact with had it not been for COVID.

And I think it really energized all of us and certainly made us feel as if there is a global community that is working together at a moment's notice to try and come up with novel answers and novel techniques and diagnostics and vaccines and therapeutics to fight back against infectious diseases. So there's that aspect that I think from a personal standpoint has changed me. From a broader perspective, as much as I'm an optimist, there's a pessimistic side because I look at COVID-19 and I think is this going to be the thing that finally changes global perspectives on how we deal with emerging infectious diseases? Or is this going to be the same as post-SARS and post-2009 pandemic flu and post-Ebola where yes, our attention span is opened for a few months or a couple of years but then the interest drops off outside of the research community and more so within governments and funding communities? And that's a concern for me.

I think we have to appreciate that when we look at emerging infectious diseases, these diseases disproportionately affect low and middle income regions of the world and emerge in those regions. Our preparedness and our ability to deal with these as a global community is gonna be reliant on ensuring that we have basically the safety nets and the early warning systems, not only in our own countries but more so within those regions where we know these diseases are gonna emerge from to increase our preparedness. And we have to be prepared to work with locals within those areas. So I hope that this will change things, I hope that there are enough younger voices in the generations around me and the generations below me that have been invigorated by this and want to instill change so that there is actual change post-COVID.

TPWKY

(transition theme)

Erin Allmann Updyke

Thank you so much Dr. Kuppalli and Dr. Kindrachuk for taking the time out of your schedule to talk with us. That was an amazing conversation.

Erin Welsh

Oh my gosh, so much information, it was incredible. We covered so much ground.

Erin Allmann Updyke

Yeah, we really did. So let's as always go over the five most important take-home points that we learned, shall we?

Erin Welsh

Let's do it.

Erin Allmann Updyke

All right. Number one. While there are still some unanswered questions as per usual about what the infectious dose of virus might be in this case, one thing that has become clear is that exposure time is a really important indicator of risk. So not just how close you might be standing to somebody but also how long are you in contact with people and in what context. Like are you indoors vs outdoors, do you have good air circulation vs very poor circulation? All those sorts of things. We also know that the majority of people will start to show symptoms about 5-6 days after infection but they're contagious to others starting about 2 days before symptoms appear. And this infectious period lasts for at least 10 days. So that means that as early as 3-4 days after exposure is when somebody could begin shedding virus even before knowing that they're sick. And I think that really highlights why and how masks, which we know are so important, have become such a big component of risk mitigation in this pandemic since they're what's preventing us from exposing others even early during infection when we don't know that we're sick.

And while some data suggests that people who are asymptomatic or in that kind of presymptomatic phase might be less contagious than someone who is symptomatic or severely ill, if behaviorally those people are walking around interacting with more people, then they might be actively infecting more people than people who are severely ill even though those are the ones shedding more virus because they end up hospitalized with their infection.

Erin Welsh

Mm-hmm, yeah. And number two, speaking of asymptomatic vs presymptomatic, this is a conversation that has gone on throughout the course of this pandemic and truthfully we still don't have a perfect handle on what proportion of cases are truly asymptomatic vs those who test positive without symptoms but then go on to develop symptoms a few days later, which is what we would call presymptomatic. Overall about 30% of people that test positive fit somewhere in this category. So they are testing positive for SARS-CoV-2 without having any active symptoms. We just don't know how many of those go on to develop symptoms. And speaking of symptoms, we know a lot more now about what exactly they look like and there is a huge range of symptoms from pretty mild and nonspecific, aside from a loss of taste and smell which is one of the few kinds of hallmark symptoms of COVID, to critical disease involving multi-organ failure. And while age is a major risk factor for disease severity, it certainly isn't the only one and we've seen even young and otherwise healthy people become severely ill and die from COVID.

Erin Allmann Updyke

Yeah. Number three: long COVID. So this is a phenomenon that we've recognized now that this pandemic has been going on for over a year and it's causing persistent, in some cases pretty debilitating symptoms long after someone was initially infected with the SARS-CoV-2 virus. And in some cases symptoms are reappearing even after someone seems to have recovered completely. It seems like about 10% of people, and I have actually heard even higher estimates on some other news sources, are experiencing things like neurologic problems which can range from brain fog to severe psychiatric changes or muscle weakness or persistent lung and breathing problems, really long-term effects. And this is a lot more common than I realized, Erin.

Erin Welsh

Mm-hmm. Yeah, for sure.

Erin Allmann Updyke

Yeah. And people who are experiencing this can take a very long time and need quite a lot of support and symptomatic treatment to actually get to a point of full recovery. At this point today, we still don't know exactly what the cause of this is, whether it represents like a persistent viremia, so someone still has virus infecting them, or whether it's some kind of immune inflammatory reaction. We're still trying to understand why and exactly how this is happening.

Erin Welsh

Yeah. Number four. There is kind of good news though in that immunity does seem to last for some time at least. But just due to the nature of this being a brand new virus emerging for the first time, like just over a year ago, we still don't have long-term data on this. And when it comes to new variants and their ability to evade our immune responses and reinfect those who have already had COVID, while this is definitely something that's concerning, we do have ways to prevent it. So cutting down and slowing transmission as much as possible is going to ensure we don't test the limits of immunity. And this will also help prevent new variants from emerging since less transmission means less opportunity for viral mutation.

Erin Allmann Updyke

Number five. Finally the best news of all is that we have multiple highly effective vaccines, which is truly incredible.

Erin Welsh

It really is.

Erin Allmann Updyke

Yeah. In the U.S. as of today which is March 25th, three vaccines are already licensed and being distributed, several more are being used across the globe. And while some of these vaccines do seem to be slightly less effective against some of these newly emerging variants, it also seems as though these vaccines not only prevent against disease but also have the capacity to reduce transmission, which is thrilling. This is still an ongoing area of research but the data are really promising. It seems as though some of these vaccines might be helping to reduce infection, not just disease from infection. And even in the cases where they might be a little less effective at preventing infection, the role that these vaccine splay in reducing disease severity and shortening a course of illness likely plays at least some role in reducing the likelihood of transmission since we know that infectiousness seems to vary with like the course and severity of disease.

This is really, really great news because like we've mentioned several times throughout this series, reducing transmission and spread of the virus reduces the likelihood of new variants emerging, not to mention less people getting sick and dying. It has been a very, very long year full of so much heartbreak and unbelievably depressing news and we have spent a lot of time in many of these COVID episodes kind of really focused on all the bad news. So it's really nice to be able to end this episode with some real, actual light that seems visible in this dark tunnel that we're all in.

Erin Welsh

I know. The light at the end of the tunnel does still seem far away but yeah.

Erin Allmann Updyke

It does. I feel like it's getting closer though.

Erin Welsh

I hope so. Maybe it's just that good news takes longer to sink in than the bad news.

Erin Allmann Updyke

Yeah.

Erin Welsh

Well this was such a great interview, thank you again so much to Dr. Kuppalli and Dr. Kindrachuk for taking time out of their schedules to chat with us.

Erin Allmann Updyke

Yeah, thank you so much. And thank you again to the providers of our firsthand accounts and to everyone who has sent in your stories, we really appreciate it.

Erin Welsh

Yes. And thank you to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Allmann Updyke

And thank you to the Exactly Right network of whom we're very proud to be a part.

Erin Welsh

And finally thank you to you, listeners, for listening.

Erin Allmann Updyke

Yeah.

Erin Welsh

We really appreciate it, you allow us to keep doing this thing that we love to do and so we are forever eternally grateful.

Erin Allmann Updyke

Yeah, yeah. We would never be able to make even our regular series let alone this COVID-19 bonus series if it wasn't for you all listening, so thank you.

Erin Welsh

Yeah. Well, until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.