Episode 80: The Emergence of Omicron

Chris Dall: [00:00:00] Hi, everyone. Before we get started with this week's episode of the Osterholm update, one to let you know that CIDRAP is commemorating its 20th anniversary this year. Since its inception in 2001, our team has created what is now a globally renowned center tackling the world's toughest challenges in infectious disease and public policy, including COVID-19, Ebola virus, Zika, antibiotic resistance, universal flu vaccines, and drug supply shortages. In celebration of this milestone anniversary and to ensure we're able to continue our important work into the future, Christy Walton has pledged a $4 million challenge to complete a $10 million fundraising campaign. A $1 match will be made for every $2 donated, helping to build a solid endowment to support CIDRAP's work. Please visit cidrap.umn.edu/donate and thank you. And now to this week's episode of the Osterholm update. Hello and welcome to the Osterholm update COVID-19, a podcast on the COVID-19 pandemic with Dr. Michael Osterholm. Dr. Osterholm is an internationally recognized medical detective and director of the Center for Infectious Disease Research and Policy, or CIDRAP, at the University of Minnesota. In this podcast, Dr. Osterholm will draw on more than 45 years of experience investigating infectious disease outbreaks to provide straight talk on the COVID-19 pandemic. I'm Chris Dall, reporter for CIDRAP News, and I'm your host for these conversations. Welcome back, everyone, to another episode of the Osterholm Update podcast. Over the last 12 months of the COVID-19 pandemic, the world has veered between stretches of optimism and pessimism. Last year, at this time, we were in the midst of a terrible winter surge in COVID-19 cases, but we were also on the cusp of the authorization of the Pfizer-BioNTech vaccine, and the beginning of the end of the pandemic seemed like it may be in sight. Then in the spring, we saw the massive wave of infections and deaths in India, a reminder that the global pandemic was far from over. By June, cases began declining dramatically in the U.S. and Europe, and it seemed like the end may be near. Then Delta arrived, cases surged again, and waning protection from the vaccines began to emerge as a concern. A little more than a month ago, the delta wave in the U.S. was receding, vaccines were authorized for young children, and the booster shot campaign was underway, feeding hopes that once again, the endgame may be in sight. Then we saw cases start rising again in Europe and parts of the U.S., and now, with the arrival of Omicron, we have a new COVID-19 variant to worry about. To be clear, there's a lot we don't yet know about this new variant and a lot we need to learn before we'll know how it may impact the trajectory of this pandemic. And that's

what we're going to focus on in this week's episode of the Osterholm Update podcast. We'll also, as always, provide you with an update on virus activity around the world and in the United States, discuss why booster shots are now more important than ever, answer a COVID query, and share the latest Beautiful Place submission from one of our listeners. But first, we'll begin with Dr. Osterholm's opening comments and dedication.

Michael Osterholm: [00:03:12] Thank you, Chris, and welcome back to all of you who are regular listeners to this podcast, and we welcome anyone who may be new this time. What can I say? What a week does for us. As you know, over the course of this podcast and the kind of the history you just laid out, I have continued to raise the concern over and over again, particularly since last April, that one of the most critical aspects of knowing where this pandemic was going to go was what would happen to the variants. As some of you know, in fact, I've been teased about it the fact that I'm a 5th Dimension fan of the song, "This is the Dawning of the Age of Aquarius," because I've converted that to "this is the dawn of the age of the variants." And unfortunately, what we're seeing happen right now was exactly my worst nightmare of what might happen. Now we'll talk today about this new variant, and we'll talk about what the implications may be, and I want to be clear that we're still trying to sort that out, so that I don't want anyone to take my opening comments here to mean that all is lost, not necessarily the case at all. But I can surely tell you we're going to be challenged, we're going to be really challenged going forward. And today, I hope I can share a sense of that. And I want to start out at the very beginning because I keep hearing this message about how we can't be panicked. You know, we can't be fearful. And you know, frankly, I don't see anybody being panicked or fearful right now. Even the markets which have gone up and down are coming back this week. And so to me, I think that that's not a helpful way to look at what's happening. We should be concerned. What I worry about more than anything is are we going to find this new variant spreading in a world of indifference? The fact that just as we have seen with Delta, we have many places in the world today that seem to take this pandemic as something in history, in the rearview mirror, not done. This variant will remind us it's not, and we'll talk all about it today in terms of what we know and don't know and what we can anticipate in the future. And it's in that regard that I make a dedication today. It's one that I talked about in the past, but I think it deserves a reminder today, is the work that goes on in our clinical laboratories around the world. And in particular, I want to congratulate for lack of a better way to express my appreciation, those labs in Botswana and South Africa that first identified this new

variant and posted it so that the world could see what these mutations looked like. We now know in retrospect, as we will talk about in a moment, that this virus was actually circulating well before the November 9th time when the first variant activity was documented. But suffice to say, had it not been for these very accomplished and dedicated laboratory professionals in Botswana and South Africa, you know, we wouldn't have known about it in the time that we did. So, my hat's off to them. Thank you for your work. And I want to thank all the laboratory staff around the world right now that are working triple time to understand what's happening with Omicron in their own countries.

Chris Dall: [00:06:36] As loyal listeners of the podcast know, we usually start off each episode with an international and national update. But given that the Omicron variant is the big story right now, that's where we're going to start today's episode. So Mike, when I saw the news alert pop up on my phone on Thanksgiving about this new variant, my heart sank, and I'm sure many of our listeners had that same reaction. But as you noted, while there's a lot to be concerned about, there's also a lot we don't know yet. So what do we know at this point about the Omicron variant? What do we need to find out? And when will we have a better sense of what we're dealing with?

Michael Osterholm: [00:07:14] Well, Chris, let me start out by saying that the news of this latest variant, which was given the name Omicron by the WHO, was not at all what I was hoping for on the holiday weekend. Needless to say, it interrupted many of our weekend festivities. In a way, though, there's almost a painful level of irony that comes with its arrival being announced over our Thanksgiving. If ever there was a more prescient reminder of the tricks that this virus has up its sleeve, this is it. So what's the scoop on Omicron? Well, as you alluded to in your question, Chris, we're really in the earliest phases of better understanding this version of the virus. Of course, that understanding will improve with the accumulation of time and more data, so we'll be learning a lot more over the next few weeks. I suspect our podcast a week from now, we'll be much more informed than we are today. In the meantime, we already have several pieces of data that we can look at. And from what I've seen to date, this variant has some very concerning elements. These are the elements that I have been so concerned might in fact end up being part of our COVID-19 picture. As I have labeled it over the course of the past few days, this is the 210 mile an hour curve ball coming in straight and center. Let me back up a little bit and provide a quick overview of Omicron's

emergence into the scene. On November 11th, the sample was collected in Botswana was selected for genomic sequencing. Remember, sequencing basically gives us the genetic blueprint of the virus from the sample. Once we have the blueprint, we can see all the mutations that the virus contains and use that information as an ID, almost akin to collecting fingerprints. So prior to this sample, a lot of the sequencing being done around the world would review the usual suspect, which we know is the Delta variant, or at least a very close relative. However, with this sample from Botswana, a new fingerprint was detected. It was still SARS-CoV-2 virus. But the mutations it contained made it clear that this was a new variant, and extremely different from anything we'd seen before. On November 23rd, after the sequencing was completed, the group from Botswana uploaded the genome onto a database used worldwide, which allows researchers to compare variants and get a sense of what spreading in different areas. Later that day, a separate team of researchers from South Africa posted similar findings from a sample collected there on November 14th. Shortly after that, South Africa reported the variant to the W.H.O., which gave it the name Omicron and officially designated it as a variant of concern. So why did Omicron receive this designation so quickly? Well, as I've discussed in previous episodes, variants of concern can be placed in at least one or more of the following buckets. One, they can be inherently more transmissible. Two, they can cause more severe disease. Three, they can have a heightened ability to evade the immune protection that's offered from vaccines or prior infection. Fourth, they can be less vulnerable to existing therapeutics and treatments. And five, or they can compromise existing diagnostics so that we don't actually pick them up in a way that we would normally do with with our routine testing. With Alpha, we really saw the first variant of concern that was much more transmissible and was associated with more severe disease outcomes. As you may recall, it was with the advent of Alpha that about a thousand light bulbs went on inside my head, and I realized at that time that the variants were going to be a much bigger challenge. Some of you remember on this podcast, I said back last April that I thought some of the darkest days of the pandemic could still be ahead of us. That was not a well received or popular comment. And for a while, people said, See, look how wrong you are. I don't say that today to say that we were right or wrong, but the fact that I hope that we now finally have our arms around this virus in a way of understanding, it's not done until it's done, and the variants can make that done moment a long ways off. In addition to seeing the Alpha variant, we also saw Beta, which was first identified in South Africa, and Gamma, which emerged in and circulated in Latin America. Most of our concerns

related to their apparent ability to better evade immune protection and of course, with Delta we've clearly seen increased transmissibility and to a certain extent, some immune evasion. So in each of these instances, the virus contained mutations, or a combination of mutations that resulted in some of the abilities that I just mentioned. As I've discussed before, I believe that the one critical aspect of this virus that will make a variant become king of the virus hill is transmissibility. As we talk in a moment, what Omicron brings us is a combination of that with other very concerning factors. When it comes to Omicron, one of the most striking features is the sheer number of mutations it has. In total, the variant contains around 50 mutations, more than 30 of which are located in the gene that forms the spike protein. For the sake of comparison, the Delta variant has anywhere from 13 to 17 mutations in the spike protein. As you know, the spike protein is what the virus uses to attach to and enter human cells and thus causing infection. It's also the piece of the virus that our vaccines have primarily used to, in fact, recognize and target with antibodies and T cells. So any time there are changes in this part of the virus, there's the potential for a dampened immune response. With Omicron, there are several mutations it has that have been previously linked to immune evasion. It also contains multiple mutations that have been tied to increased transmissibility. So that's a big reason why it's been designated as a variant of concern. However, to add some additional context, I think it's worth noting that these mutations don't always work in tandem or have an additive impact. In some instances, certain combinations of these mutations can actually work against each other. This means we can't simply look at the mutations Omicron has and automatically know what we're up against. It's what makes the data so critical and the reason is why so many people are working around the clock to provide it. What does this variant mean? So while I acknowledge that the variants emergence in southern Africa is relatively recent, the growing body of epidemiologic data from that region to me has been quite striking. For example, if you look at the country of South Africa where community transmission of Omicron has been documented, you can see clear signs of a fourth wave. On November 14th, which is the same date the country collected its first sample that turned out to be this variant, average daily cases in South Africa stood at 285. One week later, the average climbed to 564. The following week, it hit 1,976. And as of this past Tuesday, the country was reporting an average of 2,750 cases a day, with health officials there warning that the number could hit 10,000 a day by the end of this week. Most of South Africa's activity is occurring in one of several provinces, particularly the Gauteng province, which is home to cities like Johannesburg and Pretoria. The same province is also thought to be the

most affected by the Omicron variant. In fact, data from the country's health minister suggests in just two and a half weeks, Omicron has already outpaced Delta in that province and appears to be the dominant variant. Finally, if you look at the latest results of ongoing wastewater surveillance in the country, you can see a clear and marked increase in detections of this virus in a number of locations, which suggests that South Africa's challenges are only going to continue to grow in the near future. Of course, the concerns of Omicron aren't just exclusive to South Africa, either. Since the news of this emergence broke last week, at least 20 countries have detected the variant. I said earlier this week that it would not surprise me that by this next weekend into early next week, 40 to 50 countries would be reporting it. So the list will continue to expand in the coming days. Even with the added obstacles of a pandemic, international travel allows this virus to move almost effortlessly. Just look at the two KLM flights from South Africa to the Netherlands this past weekend that made headlines after 61 of 635 passengers on board tested positive for COVID upon their arrival. Of these 61 cases, a total of 13 passengers have been confirmed as the Omicron variant. So despite a policy that required passengers to either be fully vaccinated or otherwise provide proof of a negative PCR test in the days leading up to the flight, you can see what happened. Regardless, although we can see that the Omicron variant has played at least some role in South Africa's latest surge and certainly hitched a ride on those planes, have we reached a point where we know that this variant has changed the game? In other words, will Omicron dethrone Delta as the dominant variant? Honestly, it's still too early to know for sure. However, I'll try to lay out what we know and don't know about Omicron. First issue, how transmissible is Omicron? At this point, we don't know. As I referenced earlier, the data out of South Africa suggests that is readily capable of out competing delta, becoming the dominant variant there in just two and a half weeks. When you consider it took a total of around three months for Alpha to become dominant and two months for Delta to become dominant, that's stunning. However, an increase in the frequency of a specific variant does not necessarily mean it's more transmissible. It's important to consider things like sampling bias and the impact that might have on the data. For example, are suspected Omicron cases being prioritized for sequencing, which artificially boost their frequency? In addition, we have to consider that the settings in which it's spreading and the population that lives there. We know only 25% of residents in South Africa are fully vaccinated. However, they've experienced three major waves of COVID, including their most recent record setting Delta Wave. So could Omicron simply be more capable of causing reinfections in populations with a fairly wide

exposure to previous variants? And if that's the case, how would it fare against Delta in a different setting? Again, as of right now, we don't know. Issue two, can Omicron evade immune protection offered by vaccines or recovery from prior infection? We're still waiting for data on this. As I mentioned in my response to the question about transmissibility, there's a possibility that Omicron is capable of causing more reinfections. With so many mutations in the spike protein, it's difficult to know what overall impact we'll see on the immune response. When it comes to the vaccines, some are predicting we'll see a pretty notable drop in their effectiveness against infections from this variant. However, even if a decline like that were to occur, there's still a general belief that the current vaccines will largely protect recipients from severe disease and death due to T cell responses, which are less influenced by variants. We actually have experience with vaccine trials that were conducted in South Africa and South America late last year and early this year, in which at that time both the beta and gamma variants were common. What did we see? Well, for these variants, vaccine effectiveness against infection declined substantially, but protection against severe infection remained relatively high. For example, a study of the Sinovac vaccine in Brazil, where the gamma variant was circulating, found low effectiveness and adjusted vaccine effectiveness of about 36% of the two dose schedule against symptomatic SARS-CoV-2 infectio during this period, 14 days or more after receiving the second dose. Similarly, another study assessed the effectiveness of Sinovac among nearly 20,000 pregnant women 18 to 49 years of age in Brazil from March to October of 2021, when Gamma was the predominant variant for most of the time. The effectiveness of one dose at preventing symptomatic disease 14 or more days after vaccination was only 5% and 41% after two doses. But the vaccine effectiveness of two doses against progression to severe disease of COVID-19, hospitalization, or death among pregnant women infected with SARS-CoV-2 was 85.4%. Finally, if we look at the J&J ENSEMBLE trial, which found that the vaccine was consistently effective against all the regions studied globally, including South Africa and Brazil, where there was the high prevalence of the rapidly emerging beta variant. Vaccine efficacy against severe critical COVID held up, and was 86% in the U.S., 88% in Brazil and 82% in South Africa. Finally, the Canadian Immunization Research Network actually looked at one dose of AstraZeneca vaccine and found it to be 50% effective against infection caused by the beta and gamma variants, but 82% effective against hospitalizations or deaths. So what this really tells us is despite the fact that the mutations that are found in the Omicron variant are the same as we saw with the beta and gamma variants, we may actually have much more

protection from our vaccines, not against getting infected but experiencing serious illness. And that by itself is a huge step forward. This is what we're going to be studying and trying to understand going forward. What does this mean? In the next week or two, I think we can anticipate some studies looking at antibodies and T cells that might help better inform our understanding of this question. Will this be useful in understanding how well our vaccines work? Remember, it's only one piece of data, and our future with this variant doesn't hinge just on these results. For example, we saw pretty substantial declines in neutralization levels from serologic studies involving both beta and gamma variants. Yet, as I've just pointed out, even though the vaccine had reduced protection against these variants from infection, it surely did reduce serious life threatening illness. And as we now know, these two variants are also in the rearview mirror and have been for quite some time. Issue three, what about severity of disease? Is it less severe? Is it more severe? When it comes to disease severity, I think it's far too early to tell. I know there were a number of anecdotal reports suggesting that Omicron causes more mild disease, but such reports aren't data. In South Africa, a lot of the early cases we saw occurred in younger individuals who at 20 to 30 years of age are known to be at less risk for severe outcomes. So any suggestion that this variant causes mild illness based on disease in this population seems premature. Also, South Africa is only several weeks into their latest surge, with case numbers really picking up dramatically over the past week. As a lagging indicator something we've talked about many times in this podcast, we have yet to get a clear picture of how many hospitalizations and/or deaths compare between Omicron and the previous variants. Unfortunately, we're going to have to see over time what this means. Issue four, will Omicron impact existing therapeutics or treatments? Again, this is yet to be determined. There are clearly some major concerns that have been expressed regarding the effect of some monoclonal antibodies, such as Regeneron, which again targets the spike protein. With so many mutations on the spike, we really have to monitor how Omicron fares against these monoclonals. The general sense is it is going to be a real challenge. On the other hand, it's believed that the COVID antiviral pills that we've all been talking about that are in the pipeline should remain effective against this variant. These antivirals target different pieces of the virus that are much less mutated, even with the Omicron variant. However, the availability of these drugs is something that will not be available worldwide for some time yet to come. Issue number five, will the current diagnostic tests we use be effective? When it comes to diagnostics, we know that the PCR test remains highly effective even with this new variant. In fact, the mutation that Omicron has, known as the S-gene dropout actually

adds some information to the PCR results, which can essentially be used as a proxy to help identify and monitor cases of the variant. So that's good news. As far as rapid tests go, they are also expected to remain effective in detecting cases of Omicron. Work to confirm their effectiveness is reportedly ongoing, but based on how they work and what they're looking for at this point, I don't anticipate any significant impact from the latest variants. So I know I've thrown a lot at you here, but I hope at least it provides some perspective on this news. We clearly have a lot of things to figure out, and I expect we'll know a lot more very soon. I know it's unsatisfying, but this is just another one of those wait and see moments. Regardless of what happens with Omicron, I think this whole situation emphasizes exactly what I've been concerned about for so many months. As long as this virus replicates, we can anticipate more variants being thrown our way. And even if we can't prevent any and all replications from occurring, we can slow it down with the best weapon we have available, the vaccines. So get vaccinated, get your booster dose. Even if you've heard reports about a variant specific vaccine, don't wait to get your booster. We know that the current vaccines have every reason to at least reduce severe illness, hospitalizations, and deaths. Yes, we would like to prevent all infections, and maybe that is what we'll see with a future vaccine, which may be for months down the road in terms of addressing, specifically the Omicron variant. In the meantime, we've got to use exactly what we have. So get vaccinated, get your booster dose. Even if you've heard reports about a variant specific vaccine, don't wait to get your booster.

Chris Dall: [00:26:31] So, Mike, as they say in the news business, we have some breaking news here. While you've been speaking, the CDC has reported that they've identified the first U.S. case of the Omicron variant. This is not a surprise, but your thoughts?

Michael Osterholm: [00:26:48] Well, yes, Chris, and I think this is one of what will be many such reports coming out in the days ahead in countries all around the world. As you noted, we do have our first case documented here in the United States. This is a joint announcement by the California and San Francisco departments of Public Health. They confirmed an Omicron case in an individual who was a traveler who returned from South Africa on November 22nd. This is an individual who is fully vaccinated. They've had mild symptoms that are improving as they're quarantining right now. So we'll follow

this case. But don't be surprised as we see many other cases like this, not only here in the United States but around the world.

Chris Dall: [00:27:34] While Omnicron is on everyone's mind right now, Delta remains the variant that is driving the COVID-19 pandemic, and it continues to hit Europe hard. Mike, what's the latest on the situation in Europe with Delta?

Michael Osterholm: [00:27:47] Well, Chris, you're exactly right. Based on the news and the reactions to Omicron and what that may or may not mean for the future of this pandemic, it almost seems like some have used it as a strange escape from the current reality we're stuck in. Now, as you've just heard, I also have my concerns about Omicron in a big way since it could ultimately dictate where we're headed. But make no mistake about it, the Delta variant still runs the variant show at this time. Let me repeat that. This is so important, but make no mistake about it, the Delta variant still runs the variant show at this time. And whatever does or does not end up happening with this latest variant, Delta has continually demonstrated just how vulnerable we are to this virus. So before I get into the latest information out of Europe, let me just quickly share where we're at globally. Last week, a total of 3.8 million cases and 47,500 deaths were reported. If you compare these totals to the previous week, you'll see that cases increased only slightly and deaths were down a bit. However, they were artificially low due to U.S. reporting delays over the holiday weekend. Without those delays, we almost certainly would have surpassed a total of 4 million cases and 50,000 deaths worldwide last week. That's far above where we should want to be. As I've mentioned, if you want the best example for what we can expect in the near future with COVID, look no further than Europe. Last week, the continent reported 275,000,000 cases, meaning that for the third week in a row, Europe has reached a new all time high for weekly cases since the start of the pandemic. Remember, before Delta, weekly cases in Europe peaked at just under two million, and that was last November. In addition, Europe reported a total of 29,300 deaths last week. Although that number is only slightly below their total from the previous week, it does break the region's streak of 10 consecutive weeks with rising death tolls. One key contributor to this overall decline has been the slow improvement in several eastern European countries. Some of these places, like Bulgaria, Latvia, Ukraine, Armenia and Romania are still reporting some of the world's highest number per capita of deaths, but those numbers are gradually getting smaller. At the same time, most of central and western Europe continues to heat up. Countries like Belgium, the

Czech Republic, Austria, the Netherlands, Ireland, Switzerland and Denmark all have some of the world's highest case rates. And remember, these are the same countries that just eight to 10 weeks ago were touting the fact that they had figured out how to live with COVID. Other places, including Germany, Finland and Norway, are experiencing their highest number of average daily cases since the start of the entire pandemic. And finally, although they haven't reached record highs, cases are growing in countries like France, Italy, Spain and Portugal countries with more than 80 to 85% of their populations vaccinated. In fact, the situation there prompted the director of the European Center for Disease Control and Prevention, Andrea Ammon, to issue a statement last week warning that the burden the surge could place on national health systems in December and January would be very high without an altered approach. She said that countries had to ramp up vaccination efforts, administer more booster doses, and reintroduce restrictions. As she put it and I quote, "all those three things have to be done now. This is not a pick and choose." So you can get a sense of what's happening there. And remember, this is Europe where the rates of vaccination are way above the global average. In fact, as of Monday, almost two out of every three EU residents were fully vaccinated. With a total population of nearly 450 million people, that means around 300 million are fully vaccinated. I can only imagine what this surge would look like if they weren't. Sitting here in the U.S., where 59 percent of the population is fully vaccinated, I look at 66% and almost feel a bit envious. While I understand that 66% is still inadequate at controlling this virus in these European countries, just think of all the pain, suffering and death that could be spared in this country with a difference of an additional seven percentage points of vaccination. Nonetheless, what has been Europe's response to that rate of 66% vaccination? Well, again, the response was made clear by ECDC Director Dr. Ammon, who said "the current rates there leave a large vaccination gap that cannot be abridged rapidly and gives ample room for this virus to spread," unquote. So as I've said time and time again, while these countries with higher vaccination rates like Germany with 69% of its population fully vaccinated, Denmark where 77% of the residents are fully vaccinated, and even Portugal which has fully vaccinated 87% of the population will be spared the level of severe disease and death that accompanied waves faced prior to vaccines. But they're not completely shielded from these upticks. As a result, the health care system, some of which have only become more fragile over the past year, are expected to deal with this horrible mess. For example, in Germany, hospitalizations are growing very quickly this week, and while they remain below levels reached during peaks this past spring and winter, numerous

hospitals are struggling to keep up. Last week, an article in Reuters reported that the German Air Force would be airlifting patients from the country's hardest hit southern region to hospitals in the north. Health officials there also haven't ruled out the possibility of another lockdown or even mandatory vaccination for all residents should the situation not improve. Again this is our current reality with Delta. I want to repeat that, this is Delta. And to pretend what's happening in Europe can't or won't play out elsewhere is unwise, to put it mildly. Comments made by the director Carissa Etienne of the Pan American Health Organization, or PAHO, during a press briefing this week, supported my position. In her opening remarks, Dr Eaton said that Europe is a window into the future for the Americas. She later added the following, "The future is unfolding before us and it must be a wake up call for our region because we are even more vulnerable." So although overall activity in places like Latin America has been steadily decreasing for months, we need to understand that it could just as easily head the other direction and quickly. In fact, most countries in South America, except for Brazil, Suriname and Venezuela, have recently reported growing activity. We're also seeing hints of upticks in other parts of the world as well. The WHO reported that cases grew in the western Pacific region last week. I have continued to emphasize my concern about what is yet to happen in India, the second most populous country in the world where only 30% of the population is vaccinated. At most, only 20 additional percent have any protection from previous infection. Think of this, the second most populous country in the world, with over half its population still susceptible to this virus. At some point, India is going to blow again. We shouldn't be surprised. And finally, there are signs of growth in Africa, which reported nearly twice as many cases last week compared to the previous week. As we've discussed, most of those cases were out of South Africa, where the fourth wave is now emerging. Of course, there's the possibility that Omicron is largely responsible for this. We'll know for sure soon enough. However, we already know how vulnerable we are with Delta. It's a bad enough virus, so the very last thing we need is an even nastier variant taking its place. Now, I don't know if it will happen. I can't say that Omicron has yet earned that label, but right now I can assure you there are deep and wide pockets of susceptible people spread throughout the United States and abroad that can still be infected. And in the virus world, this is an ideal human playground. When these places light up because it's only just a matter of time we'll be stuck facing a double whammy, on the one hand, will undoubtedly see more hospitalizations and deaths. And in addition, we're going to be giving this virus countless

opportunities to roll the genetic dice again and again, leaving the door open for more menacing variants to come in.

Chris Dall: [00:36:40] Now to the United States, where data on COVID-19 cases is a little difficult to assess because of the Thanksgiving holiday, but we do know that a lot of people traveled last week and treated this Thanksgiving as if it were pre-pandemic times. So Mike, how concerned are you about the coming weeks?

Michael Osterholm: [00:36:57] As you know, in my last week's podcast, Chris, I did my best to cover where I thought we as a country were with COVID and particularly heading into the Thanksgiving weekend. And while I tried to lay out the situation as I saw it covering the overall numbers, the various regional patterns and drawing on our experience following Thanksgiving last year, I know that listeners weren't left with a crystal clear picture of what we're going to see in the coming weeks. But I also know that would be the case before we even started recording this episode, which is why up front, I mentioned that any listener expecting absolutes or answers to all their questions from this episode would be disappointed. I have to be honest with you, I wish I knew more. Of course, I'm sure regular listeners of this podcast have almost come to expect that unsatisfaction by now and didn't need this disclaimer. But regardless, the underlying theme of this entire message about uncertainty that we're facing with COVID in the U.S. is front and center. And once again, I can tell you right now that the path forward hasn't gained much clarity since Thanksgiving. In fact, with the reporting delays that accompany the Thanksgiving Day holiday, things almost seem even more clouded. So as a quick recap, where were we last week? Well, since the start of November, up until Thanksgiving, cases in the U.S. were growing. In that time, we saw them climb from a value of around 70,000 cases a day to more than 95,000 cases a day heading into the holiday. Hospitalizations were also on the rise, growing from less than 46,000 hospitalizations a day to nearly 53,000 hospitalizations at this time last week. In several regions of the country, including the Four Corners region in the Southwest, the Upper Midwest and the Northeast, we could see a number of states dealing with either elevated activity or even clear surges. And of course, we knew we'd be seeing a lot of travel. This has been confirmed, with the TSA reporting a total of 20.9 million people traveling through airports over the course of the 10 days they consider the Thanksgiving travel period. So that was our scene heading into the holiday. As of Wednesday, we still are waiting to see the national numbers recover from that long weekend, so we don't

quite know exactly where we stand. As we saw with last year's Thanksgiving, there was a substantial delay in people being tested, people being reported, and cases actually getting counted. So I have continued to emphasize that I don't think we're going to really have a good handle on what's been happening with U.S. cases over the past week for at least another week. Right now, average daily cases sit at just under 83,000. Hospitalizations, which are a more reliable indicator of where we're at, but are also a lagging indicator, have continued to grow, with more than 50,000 patients currently admitted. And finally, the average daily death toll has dropped to around 900. When these numbers normalize a bit, we'll start to get a better sense of where we're at. And that's only starting to happen. With the single day case total for this past Tuesday, reportedly around 108,000. And of course, it'll take even more time to capture what impact Thanksgiving had on activity. And transmission that occurred over the holiday weekend would likely just be getting test results back or developing signs of severe disease. So although the activity is already baked in at this point, we have yet to see its magnitude. Finally, while I recognize that we're in somewhat of a holding pattern, I also want to add that COVID certainly didn't take the weekend off in many parts of the country. We're still seeing signals of growth or sustained activity in numerous states, particularly those located in the Upper Midwest and the Northeast. For example, this past Tuesday, the state of Vermont reported their highest number of hospitalizations due to COVID since the start of the pandemic. Let me repeat that on Tuesday, the state of Vermont reported their highest number of hospitalizations due to COVID since the start of the pandemic. And this is a state that leads the country when it comes to vaccination rates, with 73% of its residents fully vaccinated. Rhode Island, which has vaccinated an equally high proportion of its population, is also being challenged. So we need to realize what this means for the rest of the country. Even if Omicron becomes a non-issue, which I know it won't, Delta is still here in full force and we have to understand we're not done with this pandemic, despite the fact there are many people around the world and particularly here in America that are done with the pandemic. I come back and just remind everyone that in fact, until the virus is done with us, the pandemic will not be over.

Chris Dall: [00:41:51] Last Wednesday, the day before Thanksgiving, The Washington Post published an opinion piece by you and Eric Topol that argued that the CDC got it wrong on its guidance for booster shots when it said that adults between 18 and 50 may get the booster rather than should get the booster. Now, the CDC did make that change

this week in light of the news about the Omicron variant. But my question to you, Mike, is why do you think the CDC should have been urging adults all along to get a booster and why boosters are now more important than ever?

Michael Osterholm: [00:42:19] Well, let me be really clear about this, that we are dealing with what I consider inadequate data to provide a definitive answer to the role that boosters will play across all ages in the prevention of moderate or severe illness and even death. But, you know, as an epidemiologist, having spent, you know, 46 years in the trenches, I tend to look at information much like the great Wayne Gretzky used to talk about why he was such a great hockey player. Don't skate to where the puck is, skate to where it's going to be. And as you may recall, right here in this podcast, when we started seeing the breakthroughs occurring in August with people who are now approaching their fifth or six month post vaccination with either two doses of mRNA vaccine or the one dose J&J vaccine. And I noted, I thought that this was an important observation at that point, not yet declaring that I thought that it was going to be a challenge for us, but it's something we had to be mindful of and study. Well, since that time, I think the data have become increasingly clear that as you get more and more people out from that six month post full vaccination time period, that waning immunity is becoming more and more of an important issue. And there are those who initially rejected that completely, and there were those like Eric Topol and myself, including Tony Fauci, that basically thought that this was a very important finding and that this would only continue to become a more severe challenge over time. And as you think about it, also the way the vaccines were rolled out in this country was that the younger age populations didn't get vaccinated until April, May and June. And so that you would expect not to see any waning immunity situation in those individuals till much later than the people who are vaccinated in January, February and March. And so just looking at the data here, we weren't really able to understand necessarily what was going on because we had problems with the collection of data. We couldn't link up readily health records of vaccination and onset of COVID. But however, in countries like Israel, in the U.K. and even on the Arabian Peninsula had much better systems for looking at this issue. And I continue to maintain that while the severest challenge we have with breakthrough infections in terms of serious illness and deaths is in that older age population, right here in Minnesota, we have over 600 deaths now in fully vaccinated individuals. We can surely say that most of those have occurred in people who are older, people who have underlying immune compromised conditions. And that is true.

But if you look at the data, I think particularly as you look at it from Israel, the trend was there. We were going to see it reach down further and further into younger and younger age groups, causing significant morbidity and increased mortality and deaths. And I all along have always thought that this was not a booster dose. And you've heard me say this on this podcast so many times. When you look at the immunology of vaccines and you consider the design that was set up to initially evaluate these vaccines. It was all emphasizing rapid results, both in terms of safety, which were comprehensive. And I feel very good about the safety information we had, but we never basically laid out a delivery schedule for vaccines that was about getting the very most out of our immune response. It was about getting a fast response so that we could, in fact, impact quickly on this pandemic. And, you know, talking to many of the vaccine immunologists out there would have said, you know, giving a dose on day one and then either on third week or fourth week as the second dose was not an ideal approach to trying to maximize even intermediate to long term protection. But it was a very valid approach because it was about trying to get information quickly, results that we could act upon and getting vaccines out. Well, now here we sit, and I think we've come to realize that without any question, if you have, for example, a mRNA vaccine, dose one gives you a boost, dose two gives you a pretty good boost, dose three six months out gives you a hell of a boost. And that's what we're trying to accomplish. So to me, I believe that holding back on giving these booster doses to only those who are, say, over age 50, you know, may have merit based on the totality of the data we have right now. But using that Wayne Gretzky analogy, I could see that we were going to have more and more challenges with younger people with underlying health conditions that may predispose them to more severe illness or not as efficient response. And that it was going to continue to even see more and more people who would also have illnesses that, while may not be life threatening, could still lead to long COVID could in fact be a challenge. So to me, it seemed very straightforward that we would want to provide vaccines as a three prime dose or a two prime dose approach rather than a booster, because that just keeps coming off like a luxury dose. Now there are others who disagree, and some of them are colleagues I have deep respect for and are dear friends. And I think time will tell, we'll see. Because we have in this country, for example, over a hundred million people right now who were vaccinated before June of this past year, who are now past their six months time period and who have not received a booster. Those hundred million people are walking experiments right now. That's why I tell you, please get your booster and get it. Get it. Because we'll see what happens over time and we'll see what

happens in terms of number of cases, the incidents per thousand to hundred thousand. We'll see what happens with disease severity, but I don't want to see that I'd just as soon see these people get their boosters. Now the big question is going to be what's going to happen in six or eight months? Well, if you think that the waning immunity really started to accelerate it about six months post the second dose and I just mentioned that you get a good boost with the second dose, but you get that really remarkable boost with the third dose. It's very possible, if not likely, that may it be much longer time period before you'd need another boost. Now, this may all change with regard to the new variant, with Omicron on the scene, we'll have to evaluate that what it means. But so right now, I feel very comfortable and confident with the recommendation now the CDC has made for everyone 18 years of age and older, they should be boosted. And I urge people to please take this opportunity because if nothing else, it will be as I've just described earlier in the podcast, the best wall you have right now from experiencing serious, life threatening illness with Omicron, if in fact, that is what's going to happen with that variant.

Chris Dall: [00:49:33] Now to this week's COVID query, this one is from Sarah, who wrote "The raised concern about Omicron evading vaccination protection has me wondering if it is mutated enough to not be detected by PCR and rapid tests. We are planning to visit family the first time since the pandemic began following PCR and rapid testing. I want to make sure we are taking all necessary precautions before getting together."

Michael Osterholm: [00:49:56] Well, thank you, Sarah, for that very thoughtful question, and let me congratulate you on the approach that you're taking right now in terms of testing. I think it's a very smart move on your part to do whatever you can to add another layer of protection in terms of individuals getting together in groups. Let me just again reiterate what I said earlier when addressing the issue of Omicron is the good news that in fact, the current PCR test and even the rapid detection test will pick up this virus. And even more specifically, because it has what we call an S-gene dropout, meaning that one of the particular measures within the PCR test will actually turn up negative, much like we saw with the Alpha variant, but not with Delta will help us distinguish in fact, early on before sequencing is even done, whether or not this was likely Omicron variant, or in fact, is it the delta. So feel confident in the testing. Go for it.

And and this is one of the very few good news aspects of the arrival of this variant today.

Chris Dall: [00:51:05] Mike, where is our latest beautiful place submission from?

Michael Osterholm: [00:51:09] Well, Chris, I must admit that the beautiful place for this week is another one of the examples of where you don't necessarily expect to find a beautiful place you do. This is from Nadav, "Hi Osterholm crew. I'm writing to share a beautiful place as seen through the eyes of my five year old son. His assignment, one recent day was to draw a picture of his favorite place, and he chose to draw the place where I got my vaccination. Like every other parent, we have wrestled with how to help our children through the fear of the pandemic. How much should we be willing to tell our children? How can we best explain it without eroding their sense of safety? Perhaps the innocence lost among the young has been one of the greatest losses of the entire experience. When I saw Micah's drawing, I felt saddened that he had had to live through this experience, and I wish that I could have protected him better from the fear he must have felt. But I also felt touched by his ability to express this feeling and embrace the safety afforded by his vaccine. In some sense, feeling our way through is all we can do, and Micah's ability to do that here is a beautiful thing, and I agree the vaccination site is truly a beautiful place." Well, let me just say that we've included the picture that Micah actually drew. And it is a wonderful, beautiful thing. Thank you for sharing this beautiful place. Please take a look at the picture. I know that you'll enjoy it very much.

Chris Dall: [00:52:43] And a reminder to our listeners that if you found a special place of comfort or solace during this pandemic and want to share it with us, please email us at osterholmupdate@umn.edu. We love hearing about and seeing the places that have helped you get through this difficult time. So, Mike, what are your take-home messages and closing thoughts for today?

Michael Osterholm: [00:53:02] Well, since we're trying to keep this podcast under 10 hours, I won't be able to give you all my parting thoughts. I have a heavy head and an even heavier heart right now in terms of what's happening and what's before us. You know, one of the challenges I've had with this pandemic is trying to explain what it is, not just that I see through all my years of experience, but also what I feel. And I think it was hard for me in terms of the unfolding of the Omicron variant story that I saw so

many people that were surprised by that. People were taken aback by oh my, how could this happen? When to me, this was like living in the Midwestern plain states in, you know, April, May and June and expecting you'll never see a tornado. Well, it doesn't mean it's going to happen, but you have a pretty good chance of seeing a tornado when you live in Tornado Alley. This, to me, was just another tornado that we should have expected and could have expected, and we didn't. And so I hope that if nothing else, this experience wakes us up to the reality of what this pandemic is still all about and that it's not done with us. And as much as we want it to go away, as much as we don't want to live with it anymore, this is not an influenza pandemic, where at kind of two years, and you're out and it becomes a seasonal flu virus. I think it's also a commentary on people who are making all these wonderful, elaborate predictions that are based on all these models. Who modeled this variant in here, huh? Who modeled what Delta is doing right now and were at all successful? They weren't. And yet, as a society, I've seen more and more people take comfort in, well the model shows us by wintertime, cases will decrease substantially. I hope this is a wake up call to the media, to the public in general. That there are real challenges before us with the 210 mile an hour curveballs that this virus keeps throwing at us. Now the one thing that keeps coming back over and over and over again. Vaccines, vaccines, vaccines, as I've said many times over recent months, they are remarkable tools. They're not perfect, they're remarkable tools. And we're going to understand that even more with Omicron in the days ahead. But every piece of evidence we have right now is if we get more and more people vaccinated, fully vaccinated with boosters, we can even take on Omicron head on and reduce the serious morbidity and mortality that might be associated with it. So I hope that that message comes through loud and clear. My general take home messages from this podcast is what I said last April, in light of what I saw happening with the Alpha variant and the whole gamma, beta issue is emerging that some of the darkest days of the pandemic could still be ahead of us. I know that was not well received. I know that many people actually felt that I was making outrageous and irresponsible comments. You know, I can't go back and redo that, and nor can anyone else, and we don't need to. But what we have to do is today understand that we still have real challenges. And that we have to continue to deal with this pandemic, even if we think we're done with it. So understand we're in this for the long haul. We're going to have to stay tuned with Omicron. That's my second point. I don't know what's going to happen yet, but everything I see so far tells me that this is going to be a real challenge. We'll understand more. What happens with severe disease? Does it occur? We'll understand more in just

a few weeks. Will it beat out Delta? We'll understand more about how well our vaccines work or don't work, and that's what we're going to be looking at. The third point is one that I hope will hit home hard in the national update. Delta is not done with us. It's not, you know, please don't forget about it. Because that virus that you're worried about knocking on your front door and confronting you is real, but the Delta virus that's hiding in every room in your house is there. And so I think it's really important that we keep pushing forward why we have to deal with Delta and what it means. And as I just said, it's, you know, the old slogan in real estate, location, location, location, in our business, it's vaccine vaccine vaccine. And I can't say that any more clearly than that. I also want again, just to remind everyone as a matter of faith in these podcasts that today I actually have a personal experience in terms of individual to COVID. And all it takes is a couple of those to be very sobering in terms of what this pandemic is doing. And I just want to remind everybody, please, please, please, as much as we cover the numbers, never forget these are our grandfathers, our grandmothers, our brothers and our sisters, our sons and our daughters, our aunts and uncles, our friends, our colleagues. These are real people. These are not made up numbers. They're real people. And that is hard sometimes to translate these numbers into that personal moment. But when it happens, it hits you like a brick. We can't forget that. Please never forget that. So I thought long and hard about a concluding statement today or a summary, and I came up with the song that one that you might say it came a little bit later than many of my sixties tunes, but this is one that I've listened to many, many times. And I think the words never really took on the meaning before now, as they do now. This is a song by Kansas. It was in their Leftoverture 1976 LP. The song was written by Kerry Livgren. It was the band's first Top 40 single hit, reaching Number 11 on Billboard in the spring of 1977. The song is really about what I believe is also our journey right now for each of us, for myself personally. Here it is, "Carry On Wayward Son" by Kansas. Carry on my wayward son, there will be peace when you are done. Lay your weary head to rest, don't you cry no more. Once I rose above the noise and confusion just to get a glimpse beyond this illusion, I was soaring even higher. But I flew too high. Though my eyes could see I still was a blind man, though my mind could think I was still a madman. I hear the voices when I'm dreaming. I can hear them say, Carry on my wayward son. There'll be peace when you are done, lay your weary head to rest. Don't you cry no more. Masquerading as a man with the reason my charade is the event of the season. And if I claim to be a wise man, well, it surely means that I don't know. On a stormy sea of moving emotion tossed about, I'm like a ship on the ocean. I set a course for winds of fortune, but I can

hear the voices say, Carry on my wayward son. There'll be peace when you are done, lay your weary head to rest. Don't you cry no more. Carry on. You will always remember. Carry on. Nothing equals a splendored. Now your life's no longer empty. Surely heaven waits for you. Carry on my wayward son. There will be peace when you are done. Lay your weary, head to rest, don't you cry, don't you cry no more, no more." Boy, do I feel that. I hope that it gives you a sense that as confusing as things are right now, as challenging as they are, we just have to carry on and there'll be peace when we're done. That's all we can hope for today, but that's a lot. That's a gift. Thanks again for spending another podcast with us. We, as I say each week, read all of the emails, the letters, the communications you send us. Thank you so much for those. Please send us your thoughts how we can do this podcast in a way that's more meaningful and helpful to you. And just remember right now, with everything going on with COVID, the politics of the world, the issues that we have before us with the economy, trying to keep our kids in school, the uncertainty of so many things, if there was ever a time to be kind, it's now. It's hard. Sometimes it is so hard. But I know at the end of the day, kindness will get us through.

Chris Dall: [01:02:45] Thanks for listening to this week's episode of the Osterholm update. If you're enjoying the podcast, please subscribe, rate, and review, and be sure to keep up with the latest COVID-19 news by visiting our website CIDRAP.umn.edu. This podcast is supported in part by you, our listeners. If you would like to donate, please go to CIDRAP.umn.edu/donate-now. The Osterholm update is produced by Maya Peters, Cory Anderson, Angela Ulrich, Meredith Arpey, and Sydney Redepenning.