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COVID-19 cases, hospitalizations and deaths are declining in the U.S., but it's still important to remain cautious as the spread of new variants and changing social behaviors could cause another spike, especially among under vaccinated communities.

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Welcome, everyone to Mayo Clinic Q&A. I'm your host, Dr. Halena Gazelka. We're recording this podcast on Monday, March the 14th, 2022. And we have passed a big milestone. Last week we passed the two-year milestone of the World Health Organization declaring COVID-19 to be a
pandemic, can you believe it? While infection rates and hospitalizations in the United States continue to decline, globally there are some areas of concern. Here to give us our COVID-19 updates and share more about this is Dr. Greg Poland from the Mayo Clinic. He is our virology and vaccine expert. Thanks for being here, Greg.

Dr. Gregory Poland 01:28
Good morning, Halena. Good to see you.

Dr. Halena Gazelka 01:30
Oh, wonderful to see you, too. I just realized, Greg that we are probably going to be releasing this perhaps on St. Patrick’s Day. So, we probably should have been wearing our green today.

Dr. Gregory Poland 01:45
Good point. Well, you know, COVID has quieted down enough that we're doing these podcasts a little less frequently. But we might do an extra one if something happens. But you're very right, when you opened, you know, you look at new cases per day in the U.S., it's down to 34,000. Now, you know, with any other infectious disease we'd be saying what's going on that we're having that many cases. We've kind of become normalized to this sort of thing, and about 1,300 deaths each day are still occurring. One thing that's really important, when you mentioned other areas of concern, you know, masks are starting to come off worldwide, essentially. And there are two areas that we really need to be concerned about. China, Hong Kong, Ireland, the UK, and Denmark are seeing surges back up again as soon as they took those masks off. So, this is, you know, when you and I last talked we urged go slow here. We're on the, you know, if we think of it as a four-lap race, we were at three laps, and we could see what we hoped would be something of the finish line. But you don't stop running and walk. You take your, you know, you do the right thing in terms of getting to that finish line. I think the other thing when we think about why, one potential would be this BA.2 variant that's occurred. You know, I just looked back at some of the data in the U.S. January 29, only 1% of all of our COVID sequences were BA.2. By February 6th, it was 3.6%. Today it's 12%. In New York and New Jersey, it's 17%.

Dr. Halena Gazelka 03:43
What should we expect to see from that, Greg?

Dr. Gregory Poland 03:46
Well, you know, it looks to be about 30 to 60% more transmissible. It does not look to be more severe. I think most of these cases are very mild cases occurring in people who haven't been boosted, and here's where the risk is, unvaccinated individuals. So, we're just simply not going to be rid of this until we get higher levels of vaccination and probably some level of regular boosters.
Kind of consistent with what we've seen through all the variants.

As we have consistently seen, and as you and I have repeatedly pointed out based on these data. You know, there's another really interesting indicator. I'll take just a minute to explain this. But in about 650 municipalities, that's not an easy word to say, across the U.S., the CDC and local health departments are doing, to use a kind word, wastewater surveillance. Okay, so they actually take these and then test them for the presence of COVID virus and sequence them, much more cost-effective than trying to do every individual that lives in that municipal area. So, 650 areas, in 28 of those areas, the amount of virus has surged more than 1,000%.

And that is a very sensitive indicator where we see that about seven to 14 days before we start seeing an uptick in cases again. So, that has me concerned. We've talked a little bit about this before. But some of those wastewater testings in New York City, for example, are showing some very unusual, the technical name for it is cryptic sequences, but very unusual SARS-CoV-2 sequences we have not seen before. We don't know are these from animals, are these from humans, but you put all that together, you put together infection with deer, so another animal reservoir of disease, and I would again, just urge caution with people. I think it's too early to be taking masks off in indoor areas. I think we still have to do the non-pharmaceutical interventions and getting vaccinated or boosted if you haven't, to remain safe and to try to dampen this down as much as possible. I mean, 1,300 deaths a day, and we think, Well, okay, the pandemic is over. Imagine if you know, what is a 747 full? Let's call it 400 people or so. If three to maybe four 747s crashed out of the sky every day in the U.S., would we say oh, yeah things are better? We'd be beside ourselves demanding explanation. So, you know, we're getting there. But let's go slowly toward this idea that we can abandon all of these precautions and that the pandemic is over. It's not.

Sage advice, Greg. Now you were just mentioning vaccines earlier, as we often do. Tell me what about new vaccines. What's going on in that arena?

We have some good news there, Halena. We not only have, you know, the vaccines that are fully authorized now in the U.S., but over the next month or two, about then I expect two, if not three new vaccines that will come before the FDA. One made by Medicago in Canada. One made by Novavax here in the U.S., and a third made by a partnership between Sanofi and GSK. All three of those are recombinant protein vaccines. And I think this may be attractive to some people who have been hesitant about the adenovirus or mRNA virus vaccines, because these are protein, a very well-known platform. Commonly we get protein-based vaccines, and people accept those very well. And at least in the data that I've seen for two of these, the
reactogenicity, the side-effect profile is very, very mild. So, I think this may be a very important factor in kind of getting us to the finish line of people getting immunized and getting boosted to prevent infection.

Dr. Halena Gazelka 08:38
Speaking of vaccines, Greg, I have a very personal interest in two and three-year-olds being able to get vaccinated, my grandsons. What's the latest on kids and vaccines?

Dr. Gregory Poland 08:49
Yeah, this is a point that needs to be thought of and maybe even a bit nuanced carefully. I think the headlines do a bit of a disservice here. So, let's divide those up into several different groups. So, under the age of five-years-old, the vaccine did not work well in preventing the outcomes of interest. This is very unlikely to be due to the extremely low dose they used. So, they were trying to balance in the first study reactogenicity, you don't want to have high fevers in young kids. That's a much more concerning situation than in older kids where you can do an exam and rule out things like meningitis and pneumonia. It's much harder in young toddlers and infants. And so, I think the issue there is that the dose is just a little too low. So, they're redoing the study by adding a third dose to see if that will give them the efficacy that we would like to see happen. Yeah, I know I've got a grandson too. I want to see that happen. In the five to 11-year-olds and the 12 to 17-year-olds, we're seeing almost a bit of an accelerated phenomenon of what we've seen in adults. And that is for these vaccines against this pathogen, immunity that prevents infection, different than disease, that prevents infection, wanes and wanes moderately quickly compared to other vaccines that we're used to. So that by, let's just look at the five to 11-year-olds. After their second dose, and same with 12 to 17-year-olds, after their second dose, if you look out 90 to 150 days, that vaccine efficacy against asymptomatic and symptomatic disease starts waning down to 30 to 60%, not the 80 or 90% that it was soon after the second dose. So, you know, there's some more work and thinking to be done about whether even in that age group a booster may be needed, or as we get to the second generation and third generation vaccines, will we be able to do it in two or three doses and done? Or is this going to be something where we get a booster every six to 12 months? We're still early in understanding that.

Dr. Halena Gazelka 11:30
Greg, a little earlier, you were talking about COVID related mortality and the incredible numbers of deaths in the United States and around the world since this pandemic began. I had read something about the excess or indirect deaths related to COVID, and that we may be under estimating deaths from Covid by almost three times. What do you think about that?

Dr. Gregory Poland 11:56
No. Yeah, I think that study that you're referring to is a truly massive global effort. And in that regard, kudos to those researchers. And I think that number is likely to vary in different regions. We have a hospital and public health system that is more likely to pick those up than, say,
lower income countries that may not have the same infrastructure. But even in the U.S. Halena, the estimate is that the number of COVID related deaths is probably underestimated by as many as 300,000, meaning that we haven't had a million. We've probably had more like 1.3 million deaths due to COVID. And this can happen for our listeners who may not understand why would that be. It's one thing if a patient comes into us with pneumonia, with COVID, and end up dying. That's a pretty clear case. But, what if they come in with a stroke and die from that stroke, and we find that they have COVID pneumonia? Well, we now know, this is different than what we knew two years ago, or even a year ago. We now know that COVID induces a hypercoagulable state. You're more likely to have kidney damage, a stroke, a heart attack as a result of COVID. So, it's underestimating that because we don't have a standardized way of saying, did you have COVID in the last 30, 60, or 90 days, and then saying, okay, the clinical symptoms that you came in with and the disease that you have, is it related? That's a hard thing to do, and hence those estimates.

Dr. Halena Gazelka 13:53
Greg, I also wondered about the incredible toll that this has taken on the mental health of individuals. Would those be counted in a study like this?

Dr. Gregory Poland 14:03
No, they really wouldn't, Halena. And you raise a very good point. Thank you for bringing it up. I hadn't thought to mention it. But, both in mental health, cardiovascular, neurological, we are seeing follow-on effects. In fact, it's funny because my daughter is a mental health specialist, once said this. She said, Dad, mark my words. After this pandemic, you're going to see a pandemic of mental health issues. And we really have. More severe in those who got hospitalized, but even those that were not hospitalized new diagnoses, mental health hospitalizations. Because it's your area of specialty Halena, you'll be interested, I think it's a 34-36, somewhere about that percent increase in opioid use disorders. And, all of this related to the, if you will, the ripple effect of what this pandemic has done.

Dr. Halena Gazelka 14:04
Changing lanes just a little bit. Greg, what do we know about the neurologic side-effects of the vaccine versus the neurological effects of a COVID-19 diagnosis?

Dr. Gregory Poland 15:14
Yeah, that's a really good question, and some nice papers have come out about this. And, you know, anything that causes a neurologic side-effect is of concern. Let's not whitewash this. And you and I have pressed into transparency as best anybody knows the data. There are neurologic side-effects that have been associated. We don't always know whether they're caused by, so I'm using a bit of a scientific nuance here, but associated with these vaccines, more so in this particular study, with the Johnson & Johnson vaccine about 0.15% of people that got that vaccine reported some kind of neurologic side-effect. For the mRNA vaccines, it was terribly low, 0.03%. What kind of side-effects are we talking about? Well, the cerebral venous
thrombosis was one, Guillain-Barré. One that came out from this study is new seizures, so very, very low, but you don't want to see any if possible. But then you have to say, well, if I don't get the vaccine, because I want to avoid that risk, what is the risk that those would happen if I got COVID? And here's where, you know, we've talked about this over and over about wisdom residing in that balance. The risk of those same neurologic side-effects occurring, if you get COVID and have not been vaccinated, depending on which disease we look at are 132 to 617 times more likely in the unvaccinated. And this is of concern. In addition, we're starting to see papers come out, demonstrating that people who have had COVID, even mild COVID, which is concerning, they're seeing evidence of brain tissue shrinkage, and of degenerative changes. Now, this interests us as investigators, because after the 1918 influenza pandemic, that was an unusual strain, not of COVID, but of influenza, there were neurologic side-effects that developed in people who got infected, some of which were not detected for years afterwards. And I'm very concerned that as these papers come out demonstrating the long-term effect of COVID on brain, nerve, cardiovascular, reproductive health, etc., that we're going to see, what to call it a pandemic of complications that will come out over these next few years in people who didn't get vaccinated and who are getting COVID. And we can ameliorate that, if not prevent that, by the simple use of these vaccines. So, they are not risk free. Let me be very clear and honest. No vaccine, and I'm a vaccinologist, is completely risk free. But, you have to balance that against the risk of getting that disease and the complications that result. And the simple headline in the case of neurologic issues is, if you choose not to get vaccinated and you get infected, which will happen with these kinds of highly transmissible variants, your risk of those same neurologic side-effects is over 600 times more likely.

Dr. Halena Gazelka 18:57
You got another plug in there for vaccines, Greg. Good for you.

Dr. Gregory Poland 19:02
I want people to be aware, because it's heartbreaking when we see these problems, and we know that this could be prevented.

Dr. Halena Gazelka 19:10
All right, Greg, I have to have you put your thinking cap on now.

Dr. Gregory Poland 19:14
Okay.

Dr. Halena Gazelka 19:14
Because we're gonna do listener questions, and you know how our listeners make you think. They challenge you. I love this first question, because I hadn't thought to ask you, but it's a great question. How does a virus become seasonal? And when a new variant or strain of flu
pops up in the southern hemisphere, why don't we see it until October? Will COVID continue like it is currently. or will it become seasonal?

**Dr. Gregory Poland  19:41**
Those are good questions. Are there others? Those are really good questions. And, you know, again a gold star to our listeners. I'll try to remember that there were about three questions involved in there. So, why does it take a while for flu to get here? No one really knows the exact answer to that. We have theories that revolve primarily around the fact that when winter time comes, you have a variety of respiratory illnesses, including flu, related to being indoors, crowded together, lower humidity levels, lower levels of ambient UV light, etc. Those probably account for that. And yet, this is fascinating because it has never been seen in human history before. A year ago, when most of us and the vast majority of us were wearing masks, in part because we had to put in place mask mandates, there was a essentially for the first time in human history, zero influenza in the U.S. I mean, remarkable. So, what makes a virus go from pandemic or epidemic to endemic? The truth is we do not fully understand, if you will, the virologic or immunologic rules that govern that. All endemic means is that there has been enough immunity that you have suppressed it to a constant baseline level. Endemic is not normal. It just means we always have a pool of susceptible people that allows continuing lower level transmission of the virus. We are not at endemnicity now. I know a lot of people want to declare a victory and say we are, we're not, 1300 deaths a day should not be considered normal, nor endemic. And I'm hoping we'll continue to see that drop as people get vaccinated and realize these things. But I don't want to be the bearer of bad news, but I think it's very likely that this summer or fall, we're going to see this surge again, because we have enough people unvaccinated and currently enough people who are too young to get vaccinated, that if we continue to see these highly transmissible variants arise, we will see surges again.

**Dr. Halena Gazelka  22:23**
So Greg, in answer to the question of how does it become seasonal? Was that the fact that we're inside more in the fall?

**Dr. Gregory Poland  22:32**
Right. Right.

**Dr. Halena Gazelka  22:34**
I had always understood kids go back to school, people go back to college, they're living in close quarters.

**Dr. Gregory Poland  22:39**
Yeah. So, you're indoors, you know, you materially change the dynamics of movement of people, and you're changing the ambient environmental conditions. And we think it's those combination of factors that co-increase respiratory viral diseases.
combination of factors that so increase respiratory viral diseases.

Dr. Halena Gazelka 23:02
Alright, our next question. This is from a gentleman who is 68-years-old. Actually, I don't know it's a gentleman. So, my apologies, an individual who is 68-years-old, and in reasonably good health, retired as a high school principal, and since vaccine availability has been filling various substitute administrator positions. This individual is a little concerned about working on campus. When masks were mandatory, and that changed, and they're not requiring masks anymore. Is this individual being overly cautious at their age? And they'd appreciate your opinion on that.

Dr. Gregory Poland 23:46
If I had to put a label on this, I would say this individual is a wise and discerning individual. And I mean that. He or she, by virtue of age, is at increased risk of complications from COVID infection. In addition, they are working in a higher risk environment. Most all schools I know of now have eliminated mask mandates, I think prematurely. And when you look at that age group, whether we're talking about grade school, middle school, high school or college age students, unlike people my age, 65 and older where the immunization rates are 90 plus percent. In those age groups, you're talking about substantially lower rates of immunization. So, it is a ripe set of conditions for the continued transmission of the virus, and you know, maybe a 12-year-old might have moderate to mild disease, may or may not have a complication. A 68-year-old is much more likely to have those side-effects. So, for that individual, I would say be sure you've gotten your full immunization series, get your booster, and right on. Continue wearing your mask on campus.

Dr. Halena Gazelka 25:08
All right, thank you, Greg. Those are the questions that I have in the mailbag today. Do you have any last thoughts for us?

Dr. Gregory Poland 25:13
Um, you know, I think just the admonition that we are seeing a surge again of cases in geographic locations and countries that many of us believe prematurely dropped mask wearing and non-pharmaceutical interventions, and really have sort of stopped pushing and encouraging people to get vaccinated. I think that's a mistake. I think it's a mistake that's likely to come back to haunt us as individuals, as communities, and as nations. So, what can you say but what we have said all along, hands, space, face, and vaccines. It works.

Dr. Halena Gazelka 26:00
Thank you, Greg, for being here today.
Dr. Gregory Poland 26:02
My pleasure.

Dr. Halena Gazelka 26:03
Our thanks to Dr. Greg Poland, virologist and vaccinologist at Mayo Clinic, for being here to give us our COVID-19 updates. I hope that you learned something. I know that I did. And we wish each of you a wonderful day.

Narrator 26:18
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