Peter Hotez, MD, PhD, on the omicron variant and Delta winter surge

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AMA CXO Todd Unger discusses the new omicron variant and what it means for the months ahead with good friend of the show, Dr. Peter Hotez, dean of the National School of Tropical Medicine at Baylor College of Medicine and co-director of the Texas Children’s Hospital Center for Vaccine Development in Houston.

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Speaker

- Peter Hotez, MD, PhD, dean, National School of Tropical Medicine, Baylor College of Medicine

Transcript

**Unger:** Hello, this is the American Medical Association's COVID-19 Update video and podcast. Today we welcome back Dr. Peter Hotez, dean of the National School of Tropical Medicine at Baylor College of Medicine and co-director of the Texas Children’s Hospital for Vaccine Development in Houston, for discussion about, what else? Omicron variant and what it means for the months ahead. I'm Todd Unger, AMA's chief experience officer in Chicago. Dr. Hotez, thanks. Welcome back. I think there was one other thing we needed to add to your bio, which is grand marshall of Houston's Thanksgiving Day parade since we last met, how was that?

**Dr. Hotez:** That was very exciting, except there was lightning as it was about to begin and so we had to shut it all down. But at least the beginning part was a lot of fun and very meaningful to be recognized by my city. So that was, and the mayor was terrific, so that was great.
Unger: Well, maybe that lightning was portended of something coming, which we're now in the middle of. And I know that you're on this.

Dr. Hotez: I think there's, it just the anti-vaxxers for figured out how to generate that lightning, so bad about it. I'm—

Unger: I know you're—

Dr. Hotez: I'm certain of it.

Unger: ... you're bouncing from interview to interview. This is a topic being discussed around the world on Omicron. I actually read already this morning in an interview you'd done in the Houston Chronicle and I was really struck by, something I've learned from you and that you hit on in this article, which is about the predictability of a new variant. Why don't you just start there?

Dr. Hotez: Well, for instance, a lot is being made to the fact that now the Omicron variant is in multiple European countries, in Hong Kong and Australia and Canada, and it's likely in the United States and to which I say, "Well, that's been true of just about every variant we've had. By the time we identify it, it's already gone global." And that happened since the beginning with the original variant that came out of central China. By the time we realized it was in the United States and enacted travel bans from China, the virus had entered into New York City from Southern Europe to ignite the terrible epidemic in New York. And so this is the way this virus operates.

So I think the first point to make is the fact that it's in multiple countries at this point to me is not necessarily meaningful. It could be but it's pretty much every variant we've ever had has done this. And then, so I think it's worth keeping a few things in perspective, I think. And the other piece to this is the fact that we're hearing different things about severity of illness, some claiming it's mild illness, some claiming it's ... you're seeing patients in the hospital with it, to which I say, pretty much all the variants have more or less presented with a similar clinical spectrum of illness. We haven't seen big game changing differences in severity of illness between variants. It's not to say this couldn't be the first but so when I hear anecdotes about that, I don't hold too much stock in them.

I think the two things that we have to look at a little more closely is its transmissibility. Is this something that can outcompete the Delta variant? The question one and question two, is this going to have immune escape properties just because of all the mutations in the spike protein and the receptor binding domain from existing vaccines. So, for the first part, well, let me stop there and see if you think that's the good way to go.

Unger: Yeah, I think that's actually ... that's what's on people's minds right now. I think what I read this morning was what you've told me before, which is we have large portions of unvaccinated people
around the globe, we're going to see new variants like this. And the question on everybody's mind is, if there's so much we don't know at this point that is anecdotal. So why don't you go into those two topics that you talk, what do we know?

Dr. Hotez: Sure. Well, in terms of transmissibility, what I say is, the idea that you can have a variant that's so transmissible that it'll outcompete the Delta variant. That's a pretty high bar. I mean, the Delta variant is by far the most transmissible we've seen. It's not to say it's not possible but when I do look at the sequences of the areas that many of us hypothesized was responsible for the transmissibility of both the Alpha and Delta variant, meaning a couple of mutations outside the receptor binding domain in the spike protein at the 681 position, which is the site of the furin cleavage site. And also in the nucleocapsid area encoding the nucleocapsid.

To me it looks more like the Alpha mutations. So on that basis alone, I would not expect it to outcompete Delta. So I think we're still going to have Delta in this country in the foreseeable future. But what could happen is the immune escape properties because of the spike protein. So if you're incompletely immunized, such as if you've been infected and recovered, you might be particularly susceptible to Omicron. So one possible scenario, and again, it's awfully soon to speculate but one possible scenario is that you could have the Delta variant in the United States, for instance, continuing to accelerate among the unvaccinated population. But in parallel, you might have Omicron among those who've been infected and recovered but who've chose not to get vaccinated on top of that because they live in complete immunity. So they'll be susceptible to reinfection with the COVID-19 but the Omicron variant.

So two syndemic coexisting variants but affecting, disproportionately affecting, different populations—Delta among the unvaccinated, Omicron among the partially immune because of infection and recovery or because they got a single dose of vaccine. That's a hypothetical scenario. We'll see how it unfolds. But I think that's a possibility. I think the bigger, the other question that's on everyone's mind of course is, "Hey doc, I got three doses. I've got a 30-fold increase, 30 to 40-fold increase in my virus neutralizing antibodies. After getting my third dose, I have enough virus neutralizing antibodies to defeat the Taliban. What happens now when I get Omicron?"

And the answer is, we don't know. I, hoping, and that there'll be enough virus neutralizing antibodies to cross neutralize the Omicron variant in people who've got triply immunized. And all of us are looking at that now, right? So on our lab for our vaccine, we're looking at the virus neutralizing antibodies to our vaccine, seeing if it crosses over, as Tony Fauci says, "Spills over." Pfizer's doing the same. Moderna is doing the same. And the way you do those experiments is you take blood from either experimental animals who have been injected with a particular vaccine or people who have gotten immunized with a particular vaccine. You look at the virus neutralizing antibodies against the original variant to confirm it's still there.

And if, assuming it is, then you compare it with other variants and see if it starts to go down. That's
how we saw diminished, predicted diminished efficacy against the initial South African variant back in last year, which we called the B.1.351, the Beta that we think came out of South Africa. Or the Lambda variant that was found in South America. There was some diminution in or decrease in the amount of virus neutralizing antibodies when you looked at pseudo viruses encoding that spike protein. We'll see if that happens with this Omicron variant and almost certainly will be a decrease. The question is, how much? Will it look more like Beta or Lambda or something worse than that?

Unger: How long do you think it's going to take to figure out some of these questions in the meantime? Like we've got, you've got the CEO of Moderna saying, "This doesn't look good. You've got a lot of conjecture." When do you think the facts roll in?

Dr. Hotez: Well, there's going to be two types of studies. Those laboratory investigations that I have just talked about to look at virus neutralizing antibodies in the laboratory. And we'll look at some vaccine effectiveness studies as well in places where Omicron is already around. So Israel has always been ahead of the game in terms of doing vaccine effectiveness studies. The Israeli ministry of health came out, I think last night with an optimistic statement that they thought it could be 90% protective. I'll have to look at the data that they based that on. And I'm assuming that's based on triply immunized individuals. I'm hearing less good numbers coming out of South Africa but is that because they only got two doses and waning immunity or is it because they got a different vaccine? So there's going to be a lot of back and forth going on and the key is to be able to assess the claims and the statements.

And then, the other, so the hope is that people who are triply immunized will get vaccinate, will have at least some degree of protection and I have some optimism about that. But then I say, "Look, whether or not you're worried about the impending Delta wave that's supposed to start this winter or the Omicron variant, your strategy really isn't too much different. I mean, if you haven't gotten your booster shot yet, your third immunization, whether or not you're worried about Delta or the Omicron, it's the same, get your booster, right? Because that'll give you the 30 to 40-fold bump in virus neutralizing antibodies and prolong your immune response. So you got to do that anyway.

Second, if you've been infected and recovered, we already have data for Delta showing you're less susceptible to reinflection if you get vaccinated on top that. And almost certainly that's going to be more true of the Omicron variant and vaccinate your kids. So, no matter what you're concerned about, your course of action to me looks roughly about the same, which is get vaccinated, get vaccinated and get vaccinated.

Unger: There we go.

Dr. Hotez: And then, will we need an Omicron-specific booster coming out of Moderna? Maybe, but we have to be careful about that too because it's not necessarily certain that that's going to work. Because if you've been primed with antigens from the original variant, it's not clear by giving a booster...
with some new sequence that you necessarily just develop antibodies to that new sequence. So there's not a guarantee that if there is even a new Omicron booster that it's going to work because, and the reason I bring that up is I'm getting emails and texts and things on Twitter saying, "Hey doc, should I wait for that new Omicron booster instead of getting my current booster?" And the answer is, absolutely not. Don't wait, get your booster now. And if you need, if it turns out you do need a fourth immunization later on, then we can worry about that at that time.

Unger: I mean, that would be months and months away.

Dr. Hotez: Could be, could be.

Unger: What we're seeing, now you mentioned the issue about surges. It's kind of a strange situation. We've got 25 states where we're seeing that numbers headed in the wrong direction. Some of the states where we were seeing surges before, like Texas, where you are, Florida seemed to be declining a bit. Is this just going to kind of keep rolling through the unvaccinated population in these kind of intermittent two to three month type surges until it kind of left, so to speak?

Dr. Hotez: I think so, it's everyone's wringing their hands about Omicron. I say, Omicron right now is not my number one worry. My number one worry is this next big Delta wave that's about to engulf our country and whether it does it in more drips and drabs and then in the dramatic fashion from last year, I can't say. But I'm more, right now if you ask me what my number one worry is for the country, I'd say overwhelmingly it's Delta among the unvaccinated and under vaccinated by far. And if Omicron comes up and creates a twin epidemic or syndemic, it could play out as I've outlined before. But right now, worry about what's in hand, which is Delta.

Unger: So we'll of course wait and see what information rolls in. But you know, what you're saying is, the playbook remains the same, which is to get vaccinated right now. Is there anything that we in the meantime, we've got travel bans in discussion, all this kind of stuff. Is that going to be effective given our experience from the original?

Dr. Hotez: Yeah, since from our original experience when we, where all eyes were towards across the Pacific to China and the virus then just said, "Hello, here I am," coming from Southern Europe. I said, that's just a sign that travel bans are not going to be effective. We have no way of predicting the course of this virus. And history, the two year history, this tells us that travel bans, with a couple of exceptions, maybe New Zealand, Australia, island nations had had some impact but for North America and Europe, South America, it's really had no impact. And I don't think that's the way to go. I think if you're really concerned, we've got to vaccinate the world. And that also troubles me that there is no plan to vaccinate, to help Africa get itself vaccinated, or to fully vaccinate South America or Southeast Asia. The Southern Hemisphere remains as vulnerable as ever.

Unger: I mean, the numbers are pretty stunning there. I read that in Africa we're talking about an 8%
vaccination rate. Do I have that right?

Dr. Hotez: Yeah, it basically runs off to zero, right? I mean, the African continent, except for Morocco, which has done okay. But it's pretty much unvaccinated and that's tragic. And as I say, Latin America, it's a little better but a lot of that is with the Chinese whole inactivated virus vaccines that have uncertain efficacy against some of these emerging variants. So even though the numbers look better in South America, in fact, I think it's still highly vulnerable, Southeast Asia is highly variable, very low, and the Middle East, parts of the Middle East are low. So, we still have long ways to go.

Unger: I watched the press conference yesterday. The thing that was discussed, we have shipped 250 million doses abroad more than all the other countries combined but we're talking about billions of people—

Dr. Hotez: Yeah. I think I was, I forget if I was on CNN or MSNBC right after that. But I threw some shade at that. And I was angry actually because it just shows the lack of situational awareness the White House has about what's needed to vaccinate the Southern Hemisphere. We've got more than, and we've talked about this before, Todd, we've got a billion people in Sub-Saharan Africa, almost a billion in South America and lower, smaller income, lower income countries, Southeast Asia is three billion people, that's nine billion doses of vaccine, and the president is saying, "We have 275 million doses, 110 countries." I mean, that's a drop in the bucket. And the fact that he would boast about that says to me that the White House has no plan, that the U.S. government has no plan to vaccinate the world.

And then I got even more upset when he said, "And we need the other countries to step up." And there wasn't that kind of, I don't know what the word is, situational awareness or what that says, "Wait a minute, President Biden, this is your job to lead. I mean, who's going to lead? I mean, is it, are you going to ask Putin to do it or Xi, or some nameless bureaucrat at the European Commission?" I mean, no, it's got to be the president of the United States and the U.S. government has to lead. And you might say, "Well, that's not fair to always make it to United States." But that's life in the big city. This is the way it's always been. If you want to do big things, you need the U.S. leadership. And that's where we've, and I've ... By the way, what I've said to you is I'm not talking out of school. I've said this to multiple members of the White House, either on phone or by Zoom. And so it's not like they're hearing this from me for the first time.

Unger: Well, just in closing, what advice can you offer physicians out there who are going to get a lot of panicky calls from their patients regarding Omicron?

Dr. Hotez: Well, the hope is they're getting panicky calls from their patients. I'm more concerned about the calls they're not getting from their patients who are refusing to get vaccinated. That's the bigger problem. And how do you reach those individuals? I would say, for the panicky ones, get everybody fully vaccinated to the max. And I think there's a high likelihood that you will get partial
protection at least, and maybe better than that, if it holds up what they're saying out of Israel, which I don't know. And be mindful and be aware. And if you have travel plans for the holidays, be mindful of that as well. And don't do reckless things and don't go to parts of the world necessarily where things are really accelerating more than in the United States.

**Unger:** Well, thank you so much, Dr. Hotez. Please keep us updated as you learn more. That's it for today's COVID-19 Update. For resources on COVID-19, visit ama-assn.org/COVID-19. Thanks for joining us. Please take care.

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