Elite Learning

Podcast Transcript

No Longer Greek to You: Understanding COVID-19 Variants Episode 2 – The Omicron Game Changer

The following transcript has been lightly edited for clarity.

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Transcript

(SOUNDBITE OF MUSIC)

DR. DEBORAH MARTIN, HOST: Alpha, beta, gamma, delta, omicron — we've been making our way through the Greek alphabet of COVID-19 variants at great cost to public health and people's lives. Will it be long before we reach the last letter, omega? Or will new variants of the SARS-CoV-2 virus cause less harm than the versions we've experienced thus far?

To understand the impact of variants, particularly the highly contagious omicron variant, we turned to Dr. Daniel Griffin. An internal medicine and infectious disease specialist, Dr. Griffin's expertise in global health, tropical medicine, parasitology, and virology contributes to the weekly podcasts he co-hosts, This Week in Parasitology and This Week in Virology, and supported his co-authoring of the book Parasitic Diseases, now in its seventh edition.

Be sure to view the show notes that accompany this episode for more on Dr. Griffin's background and view helpful supporting graphics.

Let's hear from Dr. Griffin.

(SOUNDBITE OF MUSIC)

GRIFFIN: And so let's hit on Omicron. So we talked a little bit about the Wuhan ancestral, the Alpha, the Beta, the Gamma, the Delta. And now we have made it all the way to Omicron. Boy, that was pretty quick.

So let's talk a little bit about what changed in Omicron. And I don't expect everyone to memorize this. Don't worry. This is not in the 10 questions at the end, since this is more for you to start thinking about, starting to understand. So when you hear this alphabet soup, you feel like, OK, I got that.

So here are the big things that I want people to think about. So think about this as a protein that's a little over 1,000 amino acids long. Amino acids, you string them in a chain, a polypeptide, you get your protein.

And there are a couple important sections, domains, of a protein. We start with the N-terminus. And then we have our N-terminal domain. And that's really going to go from 14 to 306.

Then the next area I want people to be thinking about is sort of in the middle, sort of a little bit of a left. Visual learners, maybe you can be looking at this slide while we're talking. Receptor binding domain, this is from 331 to 528, that I talked a little bit about.

This is that area on the spike protein where it's going to bind the ACE2 receptor so that it can end up entering cells. This is a critical area where, with infection and an immune response to that infection, will produce targeting, neutralizing, antibodies. So any time you hear a number change within 331 to 528 – so let's take 417, a change at 417 – clearly associated with antibody response. So we see, when we sequence Omicron, that the genetic code is going to lead to a change at 417. We immediately start worrying about antibody escape, about this virus not being neutralized by antibodies.

We see a change at 484. Again, that's an area where our immune system often makes very effective neutralizing antibodies. The sequence has changed. The amino acid is going to be different at 484. Again, now we're worried that we're going to get immune evasion. People who've been infected before are now going to be susceptible to reinfection in a short period of time.

We see a change at 501. We're starting to get near the end of this receptor-binding domain. That change at 501, we know from other variants, can improve the ability of the spike protein to bind to that ACE2 receptor. So now we're worried. We're seeing changes that suggest that this virus can reinfect people that have been previously infected, potentially infect people at a higher rate who've been vaccinated – potentially better ACE2 binding.

Now we go a little bit farther down, and we start getting over towards the furin cleavage site. Now, when the spike is going to allow the virus to get into a cell, this big, long S protein, spike protein, is going to cleave in half. Not quite in half, but into an S1 and an S2, the famous furin cleavage site.

This is actually something we see in every different subfamily of the coronaviruses. But we see it change that is actually right there at 681.

A couple of things here. You're going to have improved furin cleavage, going to make it a little bit easier for this to cleave. It also may make it possible for this virus to evade our interferon, our innate immune system.

So just looking at the sequences started to make us quite concerned that Omicron was going to become a problem. And unfortunately, as we're going to discuss, that has actually turned out to be the case.

MARTIN: The times you don't want to be right. Correct?

(LAUGHTER)

GRIFFIN: The last two years, there have been lots of times we didn't want to be correct. But let's talk a little bit because I don't want to have this talk be a complete downer. Now we know we've got this variant of concern. It's risen to be variant of concern. It's, at this point, as we're giving this talk, it has spread quite widely.

But let's talk about the impact. How are we doing with this? So I'm going to talk a little bit about the experience with Omicron, the newest variant of concern. It's already in South Africa, in the UK, a little bit in Denmark. And we'll talk about here in the US.

So let's start talking about South Africa. So we've got this virus. It has a number of changes. I mentioned a few of them in the spike protein. But we also know there's some changes in nucleocapsid in other areas that have impacted our testing. How are we doing?

Well, say, on a positive note, the variants are not necessarily under any pressure to make us sicker. There are also, unfortunately, under any selective pressure to make us less sick.

Fortunately, what we have seen with Omicron, is that when we looked at the experience in South Africa, we actually were seeing less hospitalizations and less deaths with Omicron than we saw in the prior waves. Most recent wave, wave three, that was the big Delta wave. Over 6,000 COVID-19 patients treated, 69% of them admitted to the hospital, which is in line with the other variants – wave one, wave two, wave three. But now with the Omicron wave, we drop down to only 41% of these patients requiring admission to the hospital.

MARTIN: I actually have two questions.

GRIFFIN: Yeah, go right there.

MARTIN: One, do you think that since Omicron is less, I'm going to say intense. Does that mean the virus is starting to weaken in its ability to kill?

GRIFFIN: So I don't know, and I think that's the question, right? So many people have talked about how Omicron is less virulent, but let's talk a little bit why. Because the WHO is really cautious. They said please, everyone, stop saying it's milder. Because what we don't know – we're definitely going to get into this data – is that in people who are unvaccinated, in people who have no pre-existing immunity, looking at that same high-risk population, are they really doing better? Or are people doing better because we're looking at younger people? Because boy, in a lot of parts of the world, the highest risk, the [INAUDIBLE], the most vulnerable, they died.

MARTIN: And that was going to be my follow up question is, are we seeing what we're seeing because survival of the fittest? And the most vulnerable have already succumbed to the disease, to the virus?

GRIFFIN: Well, I think in South Africa, unfortunately, there's a lot of truth there. When we looked at the first wave, the median age – and this was true in the first, the second, the third wave – was well over 50. So these were older individuals. The majority of them had multiple comorbidities.

Couple percent in each wave died. Did not survive to the next wave. Died, did not survive to the next wave. So one of the things we are – and we refer to the immunity that a person gets after being infected as viral infection-induced survivor immunity. Because one of the things that the virus does when it affects a population, if it's a virus that can actually result in deaths, is those people are going to die, and they're going to be removed from the experience of the next wave.

So actually, interesting enough, when they looked at wave four, the average age of the people being infected was 32, as opposed to--

MARTIN: Much younger.

GRIFFIN: So much younger. Less than a quarter of them even had any co-morbidities. Younger, healthier, and people who had survived the first three waves.

The other – and I think this is really critical, which will come up again – is that a lot of individuals going into wave four, the Omicron wave, had some degree of pre-existing immunity. People think of all of Africa as just one big vaccine desert, but South Africa is a little bit different. As of December, over 40% of the adult South African population was vaccinated, and the majority of the population had previous exposure to SARS-CoV-2. So the majority of this population experiencing Omicron had some level of pre-existing immunity.

MARTIN: Interesting.

GRIFFIN: So when we see decreased hospitalizations and deaths, in certain ways we were expecting even less, if there was as much protection from vaccine and preexisting immunity as we were hoping.

MARTIN: So therefore, don't be talking about how it's less of a threat. It's actually more of a threat than what we predicted it would be, so º

(LAUGHTER)

GRIFFIN: Well, I think yeah. I think that's true. And I think it is important that we listen when the WHO says don't call it the Omi-cold. Here in the US we have days with over 2,000 deaths. We have more people in hospital than ever. We are experiencing the Omicron wave, and that is not mild.

MARTIN: No.

GRIFFIN: What about Scotland? Again, less hospitalization and deaths with Omicron. And they're actually also suggesting about a 2/3 reduction in hospitalization when compared to Delta.

But an interesting thing I want to point out here is a big role of vaccination. Scotland is a very heavily vaccinated part of the world. Seventy, 80% of the population is vaccinated.

I would have liked to see a 70% or 80% reduction in risk of COVID-19 hospitalization. We're only seeing about 60, 70%. But the booster looks like it's playing a role, not only in reduction of just ending up testing positive, but in this experience, they were actually seeing a 57% reduction in the risk of any symptomatic infection. So it looks like our vaccines are actually quite helpful at least, I'll say, in South Africa, particularly here in Scotland.

But let's move on to Denmark. What are they seeing in Denmark? And again, reassuring data, less hospitalizations, and deaths with Omicron.

But let's go through. We're seeing, as we saw in South Africa, a skew towards younger aged individuals being infected with this variant. So with Omicron, in the Danish experience, the majority of the individuals infected were under the age of 30.

MARTIN: Now when you say under the age of 30, does that also include children in that age group, or is it adults to 30?

GRIFFIN: No, this actually, so this is data from the Statens Serum Institut, and this actually goes all the way down.

MARTIN: OK.

GRIFFIN: And I do like to say – I don't want to – COVID is a risk for children, right? Here in the US, we're setting records now for the number of pediatric admissions. But the biggest risk factor for COVID-19 hospitalization and death is age. And as we move down, that risk decreases, but it doesn't go away.

We in the US are approaching about 800 deaths in our pediatric population, which maybe in a bad flu year, we have 100 deaths in a year. We're now up to almost 800, the majority of those were just in the last calendar year. So still a risk to children. Still a risk to younger individuals. But we would expect that if the majority of our infections are in under age 30 that we would end up having less hospitalizations and deaths from age alone, actually.

And what about vaccination? What percent? Denmark is an incredibly vaccinated place. They are seeing less than 10% of the Omicron infections are occurring in unvaccinated individuals.

So a couple different ways to interpret the Omicron data here. And I will quote the head of the Statens Serum Institut, Henrik Ullum. "It is primarily young and vaccinated people who are infected with Omicron. And when we adjust for this, we see no evidence that Omicron should result in milder disease."

MARTIN: Interesting.

GRIFFIN: So I think very, very sobering. We're seeing younger population. We've already lost a bunch of people in previous waves. How much of what we're seeing in reduction in hospitalizations and deaths is due to prior immunity, due to a shift in who is being impacted, versus any intrinsic change in the virus? At least in Denmark, they're not convinced that the virus itself has become any more friendly.

U.S., we're seeing, again, less hospitalizations and deaths with Omicron. Our hospitalization rate is down about 50%. I like to point out that in this cohort that they looked at most recently in the U.S., about 60% of those individuals were vaccinated.

Unfortunately, we've had a large percent of our population previously infected. So we are seeing, I will say, somewhat of a disconnect between case numbers, hospitalizations, and death. How much of that is due to immunity? How much of that is due to any change in the virus?

I think I would say, at least from what we know so far, don't go out there and take a chance with Omicron.

MARTIN: Yeah.

GRIFFIN: OK. So just a couple more things we're going to talk about. And we're going to go through, and hopefully that was enough information for our, we'll say, the thought experiment. Why is the Omicron wave different? So we're going to go through a little bit of the thoughts.

So hopefully I've shared a little bit of information to address the first idea. Is this, have something to do with the impact of viral infection survivor immunity? Hopefully, and I think the data supports this to some degree, if you recently were infected with Delta, and now you get an Omicron infection in the following months, are you more likely to have a better outcome? We think so.

Unfortunately, we're not seeing a lot of protection against infection that you got from that Delta infection relative to an exposure to Omicron.

What about vaccine induced immunity? That, I think, we have a lot of confidence, a lot of growing data, to support individuals that have been vaccinated and boosted.

We're seeing a significant reduction – well, one, in getting infected to begin with – but not quite as good for Omicron as it was for Delta. Certainly not as good as it was for Wuhan. But in the same thing, I will say, when we look at protection against severe disease, I'm not sure protection against severe disease is as negatively impacted by the variants as escape from antibodies.

And just a recent study came out showing, looking in Israel, at folks that had gotten that third dose, that boost, with the Pfizer vaccine. Didn't even matter what that primary series was. In older individuals, about a 99% reduction in hospitalization or death with the third shot.

MARTIN: And that's significant.

GRIFFIN: And that's with Omicron. So that is huge. So real disconnect. So don't lose heart here. Vaccine efficacy against infection may not be as durable as we would hope. It may be, well, I'd say it is impacted by variants. But that vaccine efficacy against severe disease, that's pretty impressive.

MARTIN: Now a question about long haul COVID, or long COVID, and severity of disease. Does that mean we may see less long COVID with Omicron than what we saw with the other variants? Or do we just not know yet?

GRIFFIN: So I think in the vaccinated population we have encouraging data on that. There was a really nice report just out of Israel. And what they did is they looked at people that had been vaccinated, and this was just two doses, and they compared those to people who were unvaccinated and got infected. And they compared that to people that had gotten no infection. And they were seeing almost complete removal of long COVID following infection in those people that have been vaccinated.

Now the authors, I think, were humble. They didn't say that we can guarantee vaccine will completely eliminate your chance of long COVID. But we're actually thinking, growing evidence, that people who end up getting infected, who've been vaccinated before that infection, are at much lower risk of long COVID.

In the unvaccinated, I don't think we have any data to suggest that Omicron is less likely to result in long COVID than Delta, than Beta, than Alpha, or even the ancestral. But it takes time. This is long COVID.

A person has to be infected. They have to survive that acute period of time. And then you have to ask after that first month. – So in that 30 to 90 days – are you still continuing to have symptoms or issues?

MARTIN: And I think it's interesting with the age that is being impacted, as it's younger and younger, that long COVID has a longer period of time to impact this person's life. At 32, if it happened – if it's ongoing for 10 years – versus the 85-year-old that had long COVID that may not live for another 10 years. So the impact on the percentage of the remainder of their lives is more impactful, really.

GRIFFIN: No, I think there's a lot of truth there. And part of it, as said for a while, is old men tend to die of COVID. Young women tend to suffer.

We're seeing younger, more female, as far as infections in a lot of these studies of Omicron. This is a higher-risk population. It's also a population with many, many years of life ahead of them.

So to have a, say, individual 32 years of age develop long COVID and then have all this period ahead of them, that's a tragedy. Someone who's reached 85, they're getting near the end of their life for instance. Shorter period of time that they could potentially suffer the post-acute sequelae of COVID.

MARTIN: Yeah.

GRIFFIN: And I do think that that's really important. So when we're talking about ALS, we've talked a lot about hospitalizations. We've talked a lot about deaths. But it's always important to include long COVID in our discussions because we are seeing really encouraging data for vaccines on death, on hospitalization, on long COVID.

And the jury's still out. What will be the percent of people that develop long COVID, post-acute sequelae of COVID, after an Omicron infection without vaccine?

MARTIN: Are you finding that people that are experiencing long COVID, that they are more prone to become vaccinated if they were unvaccinated prior to the disease?

GRIFFIN: So a lot of individuals that I take care of will actually get vaccinated after acute COVID as a therapeutic intervention. Early on we observed that people who developed long COVID after infection, if they got vaccinated, would have a significant reduction in their risk of going on to long COVID – at about a 50% reduction. But more recent data has shown the sooner you can get that vaccine after your infection, the more profound that therapeutic impact can be.

Getting that vaccination within the first 30 days after infection may reduce your chance of long COVID by four- to six-fold. You get out the next 30 to 90 days, reduces it more. Once you get past 90, you're getting about that 50% reduction.

MARTIN: OK. Good information.

GRIFFIN: Get vaccinated, preferably before you get SARS-CoV-2, before you get COVID. But if you miss the window, go ahead and get vaccinated right afterwards.

One of the other – let's talk about what else may be different in the Omicron wave. Do we have better therapeutics? Certain challenges there, actually. I don't know if we've actually really come up with much better therapies.

We have had a negative impact of Omicron on our monoclonal antibody therapies. The changes in the spike protein has really made the Omicron variant resistant to the Eli Lilly cocktail, to the Regeneron COV cocktail. It's really the – sotrovimab by Vir GSK that continues to work. But we just don't have as much of that as we would like. So I don't think I can say we're doing better in the Omicron wave because of better therapeutics.

We're starting to get oral antivirals which should work as well against Omicron as prior variants. But we really don't have enough of those out there to be explaining the difference in what we're experiencing in the Omicron wave.

Are we operating outside of surge conditions? Are we getting better at managing large numbers of COVID-19? I think it depends what part of the country you're looking at. Are we testing more?

MARTIN: I would agree. Yeah.

GRIFFIN: What was that, Dr. Martin?

MARTIN: I said I agree. I think it depends on what pocket you're at in the country. And then what is – yeah. What is happening with crowds and celebrations and all of that? And then the workforce to match the needs. And that's huge.

GRIFFIN: Yeah, no. That's been a huge challenge. I know in our area and throughout the country, staff. When you show up at the hospital, it's nice when there's people there so they can take care of you.

MARTIN: It is nice.

GRIFFIN: Not just patients. And are we testing more? Are we getting more widespread testing, so we have a larger denominator? Are we testing people we wouldn't have tested before? Maybe that's changing. So I think that's important as well.

Has the virus itself changed? I think the jury's still out there. At this point, we don't have really compelling data.

There was a hamster study everyone got really excited about. It seemed to be different in hamsters, the Delta variant versus the Omicron. I'm happy to tell everyone we have absolutely no hamsters in the hospital. The hamsters continue to do well.

But hamsters are not people. So I'm not sure that hamster study really translates, particularly when, as I point out, we have days with over 2,000 people dying of Omicron. We have more people in hospital now than we've ever had with [SARS-CoV-2]. So I'm not sure that the virus itself has substantially changed.

MARTIN: I heard that in the community that the Spanish flu strain, or this, the flu strains that we have today are actually from the original Spanish flu over 100 years ago? Is that true?

GRIFFIN: The H1N1, and that's actually how they name flus, right? We talked all about how they named COVID variants. You start off with the H and the N, so the hemagglutinin and the neuraminidase. You start with one,

and then you go to two and three. So the H1N1 is actually that originally named Spanish flu that circulated. Actually killed a lot of Griffins in New York City back in 1918.

MARTIN: Oh, dear.

GRIFFIN: Don't worry. There's a lot of us. Big Irish family, so some survived.

MARTIN: So you made it? Survivor? OK.

GRIFFIN: But yeah. Every so often, right, someone will end up with a[n] H1N1 influenza. It will circulate. That's why we include it in our vaccines now. It's still here, 100-plus years later.

MARTIN: Does that mean COVID is going to be something similar, and it'll still be around in 100 years? Or is it not that kind of virus that would continue?

GRIFFIN: No, I think most of us think SARS-CoV-2, COVID-19, is here to stay. It's in people. People can get reinfected. We certainly don't live in a world where 100% of people will get vaccinated.

But not just people. We've seen SARS-CoV-2 in felines, right? It's in our cats. It's in our tigers. It's in our lions. It's in our deer. It's in our mice. Dogs, actually, unfortunately, they can even get myocarditis. So this is a virus that can infect many mammals. So even if we do a great job, it's always waiting to spill right back over.

So I would predict the future. SARS-CoV-2 is here to stay. But we have a growing number of tools to defang this virus, to be able to go forward at some point, not living in this pandemic crisis mode.

MARTIN: And out of crisis mode would be great.

GRIFFIN: Yes. We will get there.

So we're going to wrap this up. I know people are worried about that 40-year-old schoolteacher, so let's bring it full circle, and then we'll talk about what happened with her.

So what about testing with the Omicron variant? Are those PCR tests still working, those nucleic acid amplification tests? And yes, they are still working.

But there's a little bit of a difference in the presentation we're seeing. We're not sure how much of this is pre-existing immunity, but a lot of individuals are having symptoms first, and then testing positive a day or two later. If you don't have much virus, if you don't have enough virus to pick it up on a test, you're probably not contagious.

So the dynamics are a little bit different. But we're now recommending go ahead. Use those tests. They're still working. But don't necessarily test that first day of symptoms. Test that next day.

What about those antigen tests? If you test that next day, if you're testing within the first seven days – and this is actually a person who is PCR positive and has a significant amount of virus – we're seeing great sensitivity, over 97% for those antigen tests. They continue to work very well.

They're also, as we've learned, a great measure of infectiousness. People who are antigen negative are not spreading the virus. People who are antigen positive are.

So little bit of dynamic there. The PCR still work, but they're overly sensitive. So unfortunately, you may get a positive test on an individual, and that positive test may be picking up that COVID from a month ago, which they may or not have had symptoms from.

MARTIN: Yeah.

GRIFFIN: Serology testing, it still works. But we've been encouraging people not to do so much. We're not really sure what it means. We don't have any commercially available assays out there that are true correlates of protection. So they work, but I'm not sure what they work for.

And what about our vaccines? This is really the doubling down on the boosters. To really expand that repertoire – and now evidence to not only go beyond vaccine efficacy against infection, but to really improve our vaccine efficacy against disease, hospitalization, and death – that third shot really looks like it's the way to complete. It looks like we've turned this from not just a one and done, not just a two shot, but a three shot primary series.

MARTIN: And then possibly an annual follow up? Or yet to be determined?

GRIFFIN: Well, yet to be determined, but I would not be surprised if a lot of us don't want to get a shot every October, November, every fall, to give us an enhanced vaccine efficacy against infection, to get us through the winter. But yes, the data is still not in, so we'll see where that pans out. Getting a shot every four or five months, I'm not sure that's tenable public health policy. So hopefully we'll be able to come up with a once- a-year solution.

MARTIN: Is there any way we could combine it with the flu vaccine and have one and done –

(CROSSTALK]

GRIFFIN: Yes. Yeah. Moderna is already working on that. They already have in clinical testing. You get one shot, and there's flu protection and COVID-19 protection in there. We're actually hoping that flu protection will be even a little bit better going forward, maybe using some of the newer technology.

MARTIN: That'd be great.

GRIFFIN: Therapeutics, I think I mentioned, definitely the variants impact our monoclonal antibodies; but that's something we can keep ahead of. So right now we have the sotrovimab. But the other companies are ready with their variant-specific monoclonals.

Antivirals, this is going to be a big thing going forward. So we're very excited about that. But all right, let's get back to our schoolteacher.

MARTIN: Yes, we want to know what happened with her.

GRIFFIN: How did she do? Remember, this was our 40-year-old schoolteacher without any prior medical problems seen in the telehealth visit. She'd gotten her two doses of Moderna. She got her booster. And then she tested positive, had no symptoms, on New Year's Day.

How did she do? She did well, as we expected her to do. And there was even no evidence that she transmitted this to others. This is not a vaccine failure. This is a vaccine success. This individual did well. She had minimal symptoms – none at all, really.

We expect her to be incredibly low risk of developing long COVID. And also, the great thing about the vaccine is it does look like vaccinated people are less likely to get infected with COVID, significantly less likely to transmit it to others.

MARTIN: So the bottom line is get vaccinated. Encourage your patients to get vaccinated. Do whatever you can in your community to spread the word. And be an ambassador out there as well.

Because nurses and physicians are trusted professionals, and you know it's, and pharmacists as well. What you say, your words carry impact. So get out there on social media and all those places, and get those vaccines touted.

GRIFFIN: All right.

MARTIN: Yeah. Thank you, Dr. Griffin, so much for taking the time to be with us and talk about all these different variants that are out there. I think there are five in circulation at this point, right, today, as of this recording. And who knows what the future will hold. But we know that we have science that can handle it.

And for our listeners, keep your learning about COVID variants going by exploring the references and resources for this episode in our show notes. And then listen a few moments longer to learn how you can obtain CE credit for this podcast.

This is Deborah Martin for Elite Learning.