

What's the Deal with the COVID-19 Variants?

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Just as vaccines bring hope to many Americans about immobilizing the coronavirus pandemic, variants of the deadly virus—from the United Kingdom, South Africa, and Brazil—are evolving across the globe. Now the appearance of at least 147 cases of the extremely contagious U.K. variant in Florida, mostly in Miami-Dade and Broward counties, is sounding alarms for doctors and scientists working to combat COVID-19.

Four experts at the University of Miami Health System and the University of Miami Miller School of Medicine discuss how viruses evolve, the dangers of these variants, and what can be done to learn more about them. They include:

- *Associate Professor Amjad Farooq, Ph.D., a biochemist and molecular biologist who studies the interaction of proteins at the molecular level.*
- *Dushyantha Jayaweera, M.D., FACP, a professor of medicine in the Division of Infectious Diseases, who led a clinical trial for a COVID-19 vaccine—developed by Janssen, a subsidiary of Johnson & Johnson—and the convalescent plasma for COVID-19 inpatient study.*
- *Susanne Doblecki-Lewis, M.D., professor of medicine and clinical director in the Division of Infectious Diseases, who is also the medical lead on the University's vaccine task force and led a clinical trial for the Moderna vaccine.*
- *David Andrews, M.D., an associate professor in the Department of Pathology and Laboratory Medicine, who directs the molecular genetic pathology fellowship, and is vice chief of pathology for the Jackson Health System.*

How do viruses mutate?

Dr. Farooq: Viruses are inactive on their own and need a living cell to enter and reproduce or replicate. Once they find their way inside a living cell—in the case of COVID-19, a lung cell—they hijack our body’s cellular “machinery” to replicate themselves.

When viruses replicate, it’s just like anything you make in mass production, some are going to be faulty. These are called mutations. There is a proofreading function of the virus that catches and removes some mutations, but it’s not guaranteed this will catch all errors.

New strains come from these mutations. They are like typos in your manuscript. They just randomly happen, and most are not lethal. However, sometimes that mutation occurs in a key protein on the surface of the virus. For example, on the coronavirus, there are spikes on the cell sticking out like needles. Those are called S-proteins. If the mutation occurs in those, it is quite possible the new mutation—or its offspring—could have an advantage over its competitors and evade existing vaccines that are targeted to attack certain S-proteins.

What are the dangers of these evolving COVID-19 variants?

Dr. Andrews: One possibility is that if you are infected with a variant, you will actually get sicker than you would from the original form of the virus. There haven’t been any variants that have been definitively shown to do this, although some people are concerned that the U.K. variant could be a little more virulent.

Another possibility is a variant could cause increased transmissibility, and that’s the case for the U.K. variant and the Brazilian variant.

A third possibility is that a new variant would not be as responsive to vaccines or

antibody-based therapies created to fight off the virus. This means that if you got the COVID-19 vaccine and then you were exposed to a new variant, the vaccine or an antibody-based therapy like Regeneron could be less effective.

A worse scenario could be if people who have already had COVID-19, who recovered and whose bodies had a nice, robust, immune response (i.e., your body produced antibodies against the virus), are exposed to a new genetic variant that their body's immune system does not recognize. We're not in that situation now, but that is a concern about the Brazilian variant.

Can the current known COVID-19 variants evade the vaccines now being distributed?

Dr. Doblecki-Lewis: Some testing found that the Pfizer and Moderna vaccines do appear to work in laboratory tests against a variant strain that was of concern. So right now, it seems that the vaccines approved for use in the U.S. should still be effective against the variants identified. In some cases, the responses were diminished, but the immune response was still powerful enough to neutralize the variant.

However, this is something that public health and international surveillance systems will need to continually reevaluate. There's always the chance that in the future we may need to adjust our vaccines; but for the short-term, it looks like the vaccines should continue to be effective from the data we have now.

What about COVID-19 tests?

Dr. Andrews: There is a possibility that genetic changes in the virus may cause false-negative results on diagnostic tests. But fortunately, most of the PCR tests out there have redundancies, so they go after two to three targets. Therefore, it would

be very unusual, and a rare event, that you would have a mutation that affects two targets in your diagnostic test.

Why is the U.K. variant considered more contagious, and what does that mean scientifically and practically?

Dr. Farooq: It means that the virus' spike proteins are attaching easier and faster to lung cells and invading human bodies quicker. Since it can attach better, if you're standing next to someone with COVID-19, the virus will be able to move from one person to another much quicker.

The CDC recently reported that they had sequenced 51,000 of 17 million positive COVID-19 cases. Is that enough to get a handle on the variants in the U.S.?

Dr. Andrews: The U.S. needs to participate in more of a global sequencing effort. We have the highest percentage of cases in the world right now and we need to do more sequencing to discover new variants and any other clinically significant changes in the virus.

To put it in perspective, England has already done 160,000 full viral genome sequences. They have made a major national commitment to this and most of what we have learned has emerged from that effort.

But sequencing—which takes several days per sample—is also very expensive, so I think there is a need for some emergency federal funding. We have the capacity at the University of Miami, along with a lot of academic institutions, to sequence the virus. But to pivot from human genetic disease sequencing or cancer sequencing to viral sequencing requires a shift in workflow. Since we are facing a historic pandemic, the government should designate major urban centers where this effort is

critically important. And since South Florida is right at the crossroads of the Americas, we really need to be getting those resources here.

What is the University of Miami Health System doing to track the COVID-19 variants?

Dr. Andrews: We are beginning a clinical study to test the prevalence of these variants in any positive COVID-19 tests we receive from patients at UHealth as well as Jackson Health's three South Florida hospitals. All three variants have lineage specific mutations, so we can design specific PCR tests to detect them. We have already tested a few dozen samples for the U.K. variant, and we are developing tests for the South African and Brazilian variants. Once we get a few hundred samples tested, then we'll have a baseline to know where we stand for each of the major lineages of interest.

We have a parallel operation going where the positive samples are being sent to sequencing facilities at Sylvester Comprehensive Cancer Center. And hopefully, as we ramp up our operations, we will soon add the University's Hussman Institute for Human Genomics, which has a lot of sequencing firepower.

Moderna is working on a booster vaccine that may address the variants. If more variants keep evolving, how will the vaccines keep up with them?

Dr. Andrews: These are smart, powerful, and sophisticated companies. Recently, Moderna put out a paper describing the likely impact the new variants will have on their mRNA vaccine. It says that people who have been vaccinated with the Moderna vaccine are still likely to be protected; however, the immunity is diminished if you have been vaccinated and then you get the South African or Brazilian variant.

Still, it is fortunate that these new mRNA vaccines (this includes Pfizer and Moderna) are relatively easy to modify slightly to account for genetic variations. The vaccine scientists can make slight adjustments to the vaccines so that they are able to be effective against other variants pretty quickly.

What can we do to protect ourselves now?

Dr. Jayaweera: We need to continue with mask wearing and not getting together in crowds. And at this moment, the vaccines should be effective against the variants. So, when you can, get vaccinated. Even if the coronavirus keeps changing, the scientific community is in a position to tweak these vaccines and other treatment modalities to mitigate some of the bad effects.

Dr. Andrews: The more people we can get vaccinated, the more we can get out ahead of this.

Israel has been very proactive about vaccinations. And just three to four weeks after they started vaccinations, there was a 60 percent reduction in hospitalizations in individuals over 65. So, it's had an immediate impact. That's why we need to get people vaccinated in the U.S.

Is there any way to stop a virus from mutating and producing more variants?

Dr. Farooq: Not until we reach herd immunity. Eventually, we will find a way to live with COVID-19. Just like we have with the flu.

And like the flu, because the novel coronavirus will change and mutate over time, it will probably develop other strains and become an endemic disease, like the flu virus, which changes every year.

Originally written by Janette Neuwahl Tannen for News at the U. Adapted for UMiami Health News.

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