Like all viruses, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been mutating as it spreads from person to person throughout the world during the coronavirus disease 2019 (COVID-19) pandemic. Some variants that have emerged recently are raising concerns about the possibility of increased transmissibility, along with questions about whether they will lead to more severe disease, whether current vaccines will provide protection against them, and how they might affect public health efforts.

During a recent webinar titled “Emerging SARS-CoV-2 Variants: What You Need to Know,” the MJH Life Sciences™ COVID-19 Coalition discussed emerging variants of SARS-CoV-2 that have appeared across the globe during the pandemic and what they mean for immunity and public health. The coalition is a partnership with top health care thought leaders across a variety of medical disciplines.

“Genetic mutations are anticipated, especially for RNA viruses as they multiply,” said Carlos Del Rio, MD, distinguished professor of medicine at Emory University School of Medicine. “But at what point should clinicians and the scientific community become concerned?”

Del Rio, who also is executive associate dean of the Emory School of Medicine & Grady Health System, moderated the event, which was part of the coalition’s biweekly series of webinars.
Speakers at the event were:

**Angela Rasmussen, PhD**, an associate research scientist with Columbia University’s Mailman School of Public Health;

**Adam S. Lauring, MD, PhD**, associate professor, infectious disease physician, and virologist at the University of Michigan; and

**Saskia v. Popescu, PhD, MPH, MA, CIC**, assistant professor at George Mason University in the biodefense program, an infectious disease epidemiologist and infection preventionist.

What follows are 8 key takeaways from the event related to the variants, immunity, and public health.

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**Variants**

1. **Mutation is normal in viruses, and many new SARS-CoV-2 variants have emerged since the beginning of the pandemic.**

Coronaviruses, including SARS-CoV-2, are RNA viruses with smaller genomes that evolve quickly.1 Mutations occur after a virus infects a cell that is replicating.

> “While it’s replicating, the enzyme that copies the genome will make mistakes,” Rasmussen said. “These are called mutations. Sometimes these mutations have no impact whatsoever. They’re just there like a fingerprint, effectively, of that mutation, that mistake, happening. Sometimes they can happen in a place that’s actually detrimental to the virus. This would be a mutant virus that has a defective genome. Sometimes we call this a defective interfering particle. And sometimes, randomly, mutation will occur in a site of the genome that confers some type of advantage to the virus.”

After several subsequent rounds of replication, a population of viruses will emerge that carry a mutation that conferred a benefit to the virus, outcompeting other variants in a population through positive evolutionary selection.

Genome sequencing data have tracked variants since the beginning of the pandemic.2

> “The reason why these variants that we’re talking about today are of such concern is because they really go beyond variant to being distinct strains, in that they have distinct properties compared to the other variants,” Rasmussen said. “Specifically, they appear to be more transmissible between people.”

Mutations can occur anywhere in the genome with differing effects. A mutation on a structural protein, such as the spike protein, can change how the immune system recognizes the virus and how the viral protein functions, for example, by altering its efficiency at infecting cells.

2. **Three variants of concern have emerged that have drawn widespread attention.**

Three variants of note are B.1.1.7 (501Y.V1), which was first detected in the UK; B.1.351 (501Y.V2), which originated in South Africa; and P.1 (501Y.V3), which originated in Brazil.
These 3 variants, which arose independently, have some mutations in common as well as some unique mutations.

“One of these mutations alone is not necessarily going to create a dramatic increase in transmissibility,” Rasmussen said. “It may be a combination of these different mutations working together synergistically. Usually viruses, especially ones with relatively large genomes like coronaviruses, are going to need more than one mutation to cause a massive functional difference that’s going to be apparent globally in a very diverse population like the human population.”

A robust genomic surveillance system in the UK revealed evidence of increased transmissibility by observing that the B.1.1.7 variant became dominant in the population over a short period of time.4, 5

3. A new strain was a harbinger of increased transmissibility.

D614G, a mutation first reported in May6, had a mutation at position 614 in the spike protein, which had become prominent, suggesting it was more transmissible.7

“This was very unclear at the time whether this was true or whether this was due to something called founder effects, which is effectively if you have enough of that variant imported into a population, it will appear to become dominant and have some sort of competitive advantage. But really it was just that there was more of it there to begin with,” Rasmussen said. “So this was a matter of debate for a while.”

Experiments in cell culture suggested the mutation conferred a fitness advantage that allowed it to replicate at higher titers. Studies in animal models8 found more infectious virus being shed in the upper respiratory tract. Another study found that the strain spread more rapidly in hamsters.9

D614G didn’t take over the way that B.1.1.7 did, suggesting that other changes may have combined to make the variants even more transmissible.

“So right now we know [that these variants are] more transmissible, but we don’t know why,” Rasmussen said.

Some possibilities include that the variants could have increased fitness, increased viral shedding, a longer interval of contagiousness, changes to receptor binding affinity, or a type of stabilizing mutation that allows them to be infectious for a longer period of time.

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Immunity

As variants of SARS-CoV-2 proliferated, questions emerged about whether current vaccines could provide protection against them.10

4. Mutations can affect both the virus and the immune response to it.

Investigators have focused on changes to the spike protein.

“The spike is the protein that sticks out on the top of the virus, and its main function is to bind the receptor and help the virus get into cells,” Lauring said. “And so, a mutation in spike that makes it bind a receptor better is going to be an advantage for the virus in many cases.”11

The spike protein also is a main target of the immune system, particularly antibodies, and mutations can change how the virus is recognized by the immune system.

“That just underscores how these mutations can have multiple roles in terms of what they’re doing for the virus [and] also what [they mean] for [the] ability of our immune system to control them,” Lauring said.

5. Serological responses are complicated.

Recent preprints of studies12, 13 have shown reductions in how well sera from people who had recovered from COVID-19 were able to recognize and block the virus.

“That indicates that these mutations are affecting how the virus looks to our immune system,” Lauring said, adding that it’s too soon to draw conclusions about the vaccines. These early studies are too small to generalize to the population. Antibodies from different individuals may target the virus in different ways,14 and people’s immune responses also vary over time.

“We also know that the responses to vaccines are different from the responses to infection,” Lauring said. “That’s because when you’re infected, the virus messes around with you in many ways, and that affects your ability to respond with antibodies.”

6. The only way to know for sure whether current vaccines will protect against variants is to wait and see.

Serological responses are easy to measure, but they don’t give the whole picture. T-cell responses and other immune system responses are harder to measure.

“The only way to know if a vaccine is going work or not is to see if it works or not,” Lauring said.

He pointed to a 2016 study of vaccines against the influenza A virus that found that the vaccine worked to a different degree depending on the different variants involved.16
“But of course, we don’t want to wait for that data, so the best thing to do is to find these correlates of protection,” Lauring said, pointing to a study done in macaque monkeys that showed that relatively low titers of antibodies were sufficient to protect against infection with SARS-CoV-2.¹⁷

Recent studies¹⁸, ¹⁹, ²⁰ that have taken blood samples from people who have received COVID-19 vaccines and tested them against the SARS-CoV-2 variants also have offered hope, demonstrating an ability of the sera to neutralize the mutated virus.

“I feel a little bit like a virological pundit, where you have a little bit of data and you’re trying to see the future and make predictions, as these CNN pundits appear to be doing, perhaps, on election night,” Lauring said. “I currently think that the vaccines are going to be just fine. But we’re just going to have to wait and see.”

Public Health

The emergence of concerning new variants has raised questions about public health and infection prevention efforts.

7. Conversations are evolving about the implications of new variants on public health.

Health officials are exploring whether the new variants will affect the transmission dynamics and secondary attack rates, routes of transmission, severity of disease, and testing or vaccine efficacy.

“We have to be prepared to answer these questions and also prioritize these questions because some of them have a bigger impact potentially on the health care environment [and] also the public,” Popescu said.

Questions concerning infection protection include: Will potential changes in viral shedding impact things like duration of isolation? Will there be an increase in asymptomatic cases and a possible increase in testing and screening to identify them? Will current disinfection strategies still work?

With the risk of increased transmissibility and secondary attack rates, health care professionals must be mindful of infection protection measures not just in the health care environment and during patient interactions, but also in the break room and at home.

8. Adhering to infection prevention and control recommendations remains important.

Any possible changes to infection prevention and control measures will emerge as more is learned about the disease. In the meantime, Popescu recommended that health care workers stick with current recommendations.

“You don’t suddenly have to change everything you’ve been doing for the past 13 months against COVID, but you have to do it,” Popescu said. “It’s that Swiss cheese model. Risk reduction is additive. It’s not just the masking, but it’s the distancing and all of those pieces together, the washing your hands, the cleaning and disinfection.” It’s also important to guard against fatigue as the pandemic wears on.

Popescu emphasized the importance of communicating openly with health care workers as the pandemic evolves and new developments emerge.

“There are these periods of unknown where we identify something and we’re trying to understand the complexity, the problem, and there [are] multiple questions that we’re working to understand,” Popescu said. “I think that unknown is really, really hard on health care workers, on everybody. But from
an infection prevention standpoint, going to a frontline worker and saying, ‘We’re still figuring that out’ is hard. It feels a little bit like a letdown.”

She said it’s also important to discuss issues surrounding variants in a way that doesn’t induce unnecessary stress.

Health care workers are encouraged to think critically and remain flexible.

“We’re literally building the bridge in some ways as we walk across it,” Popescu said. “We want people to be able to evolve with that guidance and to not feel so overwhelmed when it changes.”

References

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For over 20 years, MJH Life Sciences™ has established a reputation for embracing agility and offering relevant, practical information that meets the needs of our diverse audience.

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