Medical News & Perspectives

As COVID-19 Cases Surge, Here's What to Know About JN.1, the Latest SARS-CoV-2 "Variant of Interest"

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Parents often bask in the glow of their children's accomplishments, so if SARS-CoV-2 variants were like people, BA.2.86 would be busting its buttons right about now.

BA.2.86's spawn, JN.1, has become the dominant SARS-CoV-2 variant in the US, status its parent variant never achieved. Fortunately, although COVID-19 cases have surged, hospitalizations and deaths from the disease are still considerably lower than they were the same time a year earlier.

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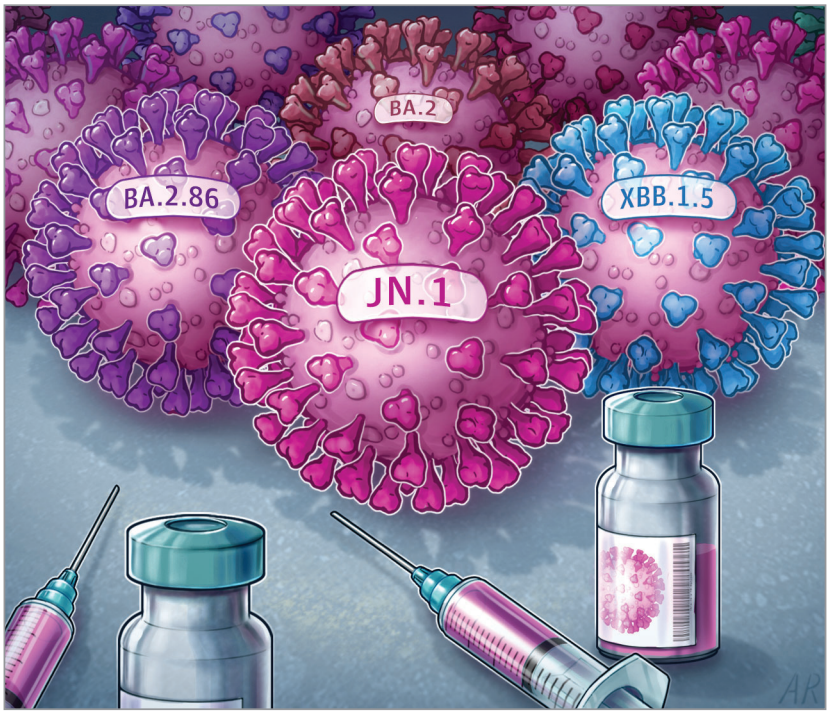
When BA.2.86 joined the SARS-CoV-2 Omicron family last summer, it grabbed pandemic trackers' attention because it was so different from its progenitor, BA.2. Compared with BA.2, BA.2.86's spike protein carries more than 30 mutations, suggesting that it might spread more easily than its predecessors.

But even armed with those new mutations, BA.2.86 failed to dominate the other subvariants. Through early January of this year, BA.2.86 never exceeded much more than a 3% share of circulating SARS-CoV-2 subvariants in the US, according to Nowcast estimates from the US Centers for Disease Control and Prevention (CDC).

Globally, BA.2.86 represented 8.9% of available SARS-CoV-2 sequences by the first week of November 2023, according to the World Health Organization (WHO), which classified BA.2.86, including its sublineages, as a variant of interest on November 20. (In a January 4 opinion piece, Eric Topol, MD, professor of molecular medicine at Scripps Research Institute, argued that BA.2.86 was so different from previous Omicron subvariants that the WHO should have designated it as a variant of concern and christened it with a different Greek letter.)

Four weeks after labeling the entire burgeoning BA.2.86 family as a variant of interest, the WHO classified JN.1 alone as one, too, due to its rapidly increasing spread. By early January, JN.1's share of circulating variants in the US had soared to an estimated 61.6%, up from 38.8% just 2 weeks prior, according to the CDC's Nowcast estimate.



What a Difference a Mutation Makes

JN.1's spike protein has just 1 more mutation than BA.2.86's spike.

That mutation, called L455S, enhances the virus' ability to bind to the angiotensin-converting enzyme 2 (ACE2) receptor, SARS-CoV-2's doorway into cells, Nicole Doria-Rose, PhD, chief of the Humoral Immunology Core at the National Institute of Allergy and Infectious Diseases' Vaccine Research Center, noted in an interview with *JAMA*.

BA.2.86 "didn't take off until it picked up this 1 mutation that made it JN.1," she said.

JN.1 appears to be highly contagious, perhaps more than any other member of the Omicron family, Vanderbilt University School of Medicine infectious disease and health policy professor William Schaffner, MD, said in an interview. "That's maybe why it's outrunning them now."

As JN.1 gained traction, indicators of SARS-CoV-2 infection levels rose. In a January 5 report, the CDC estimated that compared with the same time last year, viral activity levels in wastewater were 27% higher and the percentage of positive COVID-19 tests was 17% higher.

The news wasn't all bad, though. Despite apparently higher infection levels, indicators of COVID-19 illness requiring medical attention were lower than a year earlier, the CDC said. For example, emergency department visits for COVID-19 were down 21%. And the percentage of all US deaths that were attributed to COVID-19 was 3.6% (839 deaths) for the week ending December 30, 2023, compared with 5.2% (3658 deaths) for the week ending December 31, 2022, according to provisional CDC data.

"I think JN.1 clearly is driving transmission," epidemiologist Michael Osterholm, PhD, MPH, director of the Center for Infectious Disease Research and Policy at the University of Minnesota, told *JAMA*.

"Fortunately, there's no evidence it's producing more severe illness."

Given the high JN.1 infection rates, people with respiratory symptoms should assume they have COVID-19, even though they might test negative for the first few days, Osterholm said. "If you have any symptoms at all of respiratory illness, don't go to a public or private event, especially indoors."

Higher rates of COVID-19 and other respiratory infections have spurred hospitals in a handful of states to reinstitute mask mandates, according to news reports, at least for staff who directly interact with patients in their rooms or other clinical care areas. For example, Mass General Brigham implemented the policy on January 2 and will adhere to it until infection levels drop later in the winter or in the spring.

Latest Vaccine Is Good Enough

COVID-19 vaccine components must be determined at least a few months in advance to allow time for manufacturing and distribution, so it's not surprising they don't exactly match currently circulating variants.

The most recent COVID-19 vaccine targets XBB.1.5, an Omicron subvariant whose prevalence in the US had already shrunk to less than 3% by the time people began getting the new shots last September. In the 2-week period ending January 6, XBB.1.5—which emerged from a different branch of the Omicron family tree from BA.2.86 and JN.1—appeared to be out of circulation in the US, according to the CDC Nowcast.

Fortunately, laboratory research and rates of COVID-19 hospitalizations and deaths suggest that the XBB.1.5 vaccine still protects against severe illness in the JN.1 era.

"Our lab and others have shown that…JN.1 is about 3 to 5 times less susceptible to neutralizing antibodies than the XBB.1.5 variant that is in the updated booster," virologist David Montefiori, PhD, director of the Laboratory for HIV and COVID-19 Vaccine Research & Development at Duke University Medical Center, explained in an email. "Most scientists are not very concerned about this reduced susceptibility because the titers of neutralizing antibodies remain in a range that is thought to be effective."

BA.2.86 and JN.1 carry more than 30 mutations in their spike proteins compared with XBB, noted a research letter published January 3 by University of Tokyo virologist Kei Sato, PhD, and colleagues, who concluded that JN.1 appears to be one of the most immune-evading SARS-CoV-2 variants to date. For example, the authors wrote, "JN.1 shows robust resistance to monovalent XBB.1.5 vaccine sera compared with BA.2.86."

However, despite JN.1's rapid spread and dissimilarity from XBB.1.5, no one is calling for COVID-19 vaccines to be updated to target the new variant.

"Given the current SARS-CoV-2 evolution and the breadth in immune responses demonstrated by monovalent XBB.1.5 vaccines against circulating variants," the WHO Technical Advisory Group on COVID-19 Vaccine Composition recommended keeping the current vaccine composition in December.

Although the latest COVID-19 vaccine might not consistently prevent infections caused by JN.1 or other circulating Omicron subvariants, it still can decrease disease severity in those who do get sick, Sato wrote in an email to *JAMA*.

"The purpose of vaccination is to decrease the severity of diseases," Sato emphasized. "Many people think that the purpose of vaccination is to prevent infection, but this is wrong."

However, vaccines are effective only if people get them. As was seen with the bivalent vaccine that preceded it, uptake of the latest COVID-19 vaccine has been low. Although everyone 6 months of age or older was eligible for the bivalent vaccine, available starting in September 2022, only 17% of the US population had received it as of May 10, 2023, according to the CDC. (The federal COVID-19 Public Health Emergency declaration ended May 11, as did the CDC's routine updating of vaccination statistics.)

About 29% of US adults said they'd received the latest COVID-19 vaccine, compared with 47% who said they'd received this season's flu vaccine, according to a Gallup survey conducted the first week of December.

"The people we're seeing hospitalized today are generally people in the high-risk categories who have not taken advantage of the updated vaccine," Schaffner said.

Back to the Future

Inevitably, JN.1 will peak—if it hasn't already—as newer, cleverer SARS-CoV-2 variants replace it.

"In the next few months, many people will get infected with JN.1," Sato explained in his early January email. As they acquire anti-JN.1 immunity, he said, SARS-CoV-2 will evolve to evade it.

"At this point, most of the planet has been vaccinated or infected or both," Doria-Rose noted. "The virus is under pressure to keep mutating so it can evade immunity and infect better." As a result, she said, this fall will surely bring another updated COVID-19 vaccine.

"If this weren't so horrible, it would be absolutely fascinating," Doria-Rose said of SARS-CoV-2. "This is an animal virus that keeps evolving to adapt to its new host, which is people." ■

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Conflict of Interest Disclosures: Dr Montefiori reported that his laboratory receives funding from Moderna to measure neutralizing antibody responses in their clinical studies; he is not a paid consultant to Moderna or any other entity. Dr Sato reported receiving consulting fees from Moderna Japan Co, Ltd, and Takeda Pharmaceutical Co Ltd, and honoraria for lectures from Gilead Sciences, Inc, Moderna Japan Co, Ltd, and Shionogi & Co, Ltd. No other disclosures were reported.

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