Omicron, Now 2 Years Old, Is Not Done With Us Yet

The dominant variant of the coronavirus has proved to be not only staggeringly infectious, but an evolutionary marvel.





 $Covid\ testing\ in\ Washington,\ D.C.,\ in\ December\ 2021\ as\ Omicron\ surged\ across\ the\ United\ States.\ Kenny\ Holston\ for\ The\ New\ York\ Times$



By November 2021, nearly two years after the coronavirus emerged in Wuhan and spread across the world, the surprises seemed to be over. More than four billion people had been vaccinated against the virus, and five million had died. Two new variants, known as Alpha and Delta, had surged and then ebbed. As <u>Thanksgiving approached</u>, many Americans were planning to resume traveling for the holiday.

And then, the day after turkey, the pandemic delivered a big new surprise. Researchers in Botswana and South Africa <u>alerted the world</u> that a highly mutated version of the virus had emerged and was spreading fast. Omicron, as the World Health Organization called the variant, swiftly overtook other forms of the virus. It remains dominant now, on its second anniversary.

In the two years since its emergence, Omicron has proved to be not only staggeringly infectious, but an evolutionary marvel, challenging many assumptions virologists had before the pandemic. It has given rise to an impressive number of descendants, which have become far more adept at evading immunity and finding new victims.

"It was almost like there was another pandemic," said Adam Lauring, a virologist at the University of Michigan.

Dr. Lauring and other Omicron watchers are now trying to make sense of the past two years in order to prepare for the future. It's possible that Omicron will become a permanent part of life, steadily mutating like seasonal influenza. But researchers warn that the virus still has the capacity to surprise us, especially if we stop paying close attention.

When Omicron first came to light, the United States and other countries wrongly believed they could stop its spread by banning travel from South Africa. In reality, it had already spread far and wide. In a matter of days, Britain, Italy and Germany discovered Omicron in positive Covid tests. Image



Travelers at O.R. Tambo International Airport in Johannesburg on Nov. 27, 2021, as travel bans were imposed on people coming from South Africa because of Omicron. Credit...João Silva/The New York Times

Omicron's gift for spreading fast was the result of dozens of mutations. They altered the virus's surface, so that antibodies produced by vaccines or previous infections could not stick tightly to it and prevent the virus from invading cells.

"It was the first virus to figure out in a major way how to escape immunity," said Dr. Jacob Lemieux, an infectious disease specialist at Massachusetts General Hospital.

Dr. Lemieux and many other Omicron experts suspect that the variant gained its new mutations while infecting a single person with a weak immune system. Immunocompromised people can only fight off some of the coronaviruses in their bodies during an infection, allowing the ones that remain to acquire mutations that can thwart the immune system.

More on Covid-19

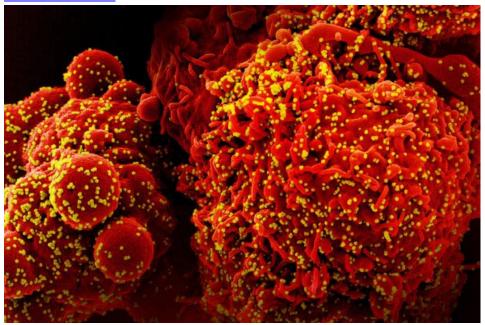
- **Long Covid:** As more young Americans report serious cognitive problems, scientists <u>suggest that the increase captures the effects of long Covid</u>, most likely in addition to other effects of the pandemic, including psychological distress.
- **Stroke Risk:** The Covid vaccines made by Pfizer-BioNTech and Moderna may be linked to a slight increase in the risk of stroke when administered along with a high-dose flu vaccine that is usually given to older people, according to a new analysis by the F.D.A.
- **Vaccine Side Effects:** A new study has found that the chills, fatigue, headache and malaise that can follow a Covid shot may be <u>signs of a vigorous immune</u> <u>response</u>.
- **Nasal Sprays:** Some people are turning to <u>over-the-counter nasal sprays that claim to protect against several respiratory infections</u>, including Covid. But their formulas are not F.D.A. approved.

"It becomes like a laboratory for virus evolution," said Peter Markov, a virologist at the London School of Hygiene and Tropical Medicine.

As epidemiologists tracked the Omicron wave in late 2021, they saw a crucial difference from earlier surges. Compared with previous variants, Omicron put a smaller fraction of infected people in the hospital. One reason for that shift was that so many people had immunity to earlier forms of the coronavirus. Our immune defenses include not just antibodies, but special immune cells that can recognize and kill infected cells. This second line of defense held-up-even against Omicron, preventing many of the new infections from becoming severe.

Still, Omicron caused so many new infections — the initial wave infected almost half of all Americans, according to <u>one recent estimate</u> — that it still unleashed a devastating wave of hospitalizations.

The Omicron surge hit the United States and most other countries in early 2022. China managed to hold back the waves with its "zero Covid" policy, but protests against its brutality grew so intense that President Xi Jinping dropped it abruptly in November 2022. The floodgates opened: Within a few weeks, more than a billion Chinese people contracted Omicron, resulting in over a million deaths.



A colorized scanning electron micrograph of a cell (red) infected with Omicron virus particles, yellow. Credit...NIAID

As Omicron moved from person to person, its descendants gained more mutations. Sometimes two Omicron viruses would wind up in the same cell, which would produce new hybrid viruses with a mix of their genes. One of these so-called recombinations hit the jackpot by mixing together two sets of evasive mutations. The result was a new hybrid called XBB.

XBB easily infected people, even those who had already been infected with Alpha, Delta or earlier forms of Omicron. As a result, XBB became dominant in the United States in early 2023.

Vaccine makers tried to keep up with Omicron's rapid evolution. In August 2022, the Food and Drug Administration authorized <u>booster shots</u> that targeted the BA.5 Omicron variant, which was then dominant. In September

2023, the agency authorized an <u>XBB shot</u>. But XBB is now ebbing as a menagerie of even more evasive variants has evolved.

"Right now we're in a period of chaos," said Marc Johnson, a virologist at the University of Missouri.

Several Omicron experts said the chaos might soon end. In August, a variant called BA.2.86 emerged with a host of new mutations — likely the result, once again, of evolution taking place in an immunocompromised person.

At first, BA.2.86 did not seem to live up to its genetic potential, failing to spread fast. "If genetics was all that mattered, it would have gotten its own Greek letter," said Thomas Peacock, a virologist at the Pirbright Institute in Woking, England. "But BA.2.86 was a bit of a damp squib."

Over the past few months, however, the BA.2.86 lineage seems to have kicked into high gear, gaining a mutation that allows it to evade even more antibodies. JN.1, as this mutated form is known, has become the most resistant version of the coronavirus. It appears to be growing quickly in France, and may soon spread to other countries.

Image



Vaccination in Phoenix at the end of 2021. As Omicron continues to evolve, epidemiologists still see a benefit to vaccinations, possibly saving up to 49,000 lives a year. Credit...Adriana Zehbrauskas for The New York Times

It is hard to predict the future path of a new variant like JN.1. Its success will depend on what kind of immune defenses it encounters while spreading from

host to host. At the outset of the pandemic, things were simpler because no one had developed immunity to the coronavirus.

"At the beginning, we were one big kindergarten," said Michael Lässig, an evolutionary biologist at the University of Cologne.

Today, in contrast, most people on Earth have immunity of one form or another, whether from a natural infection, vaccination or both. "The virus sees a much more complex ecosystem," Dr. Lässig said.

This worldwide immunity means that a smaller fraction of people will die than did at the start of the pandemic. Still, Omicron's toll remains heavy. The U.S. Centers for Disease Control and Prevention <u>found</u> that between October 2022 and September 2023, more than 80,000 people died of Covid, more than eight times as many as those who died of influenza.

As Omicron continues to evolve, epidemiologists still see a benefit to vaccinations. Justin Lessler, a researcher at the University of North Carolina, and his colleagues recently ran a projection of future Covid infections and <u>concluded</u> that annual vaccination campaigns could save up to 49,000 lives a year.

Those vaccines will be more effective if they're updated to keep up with the evolving virus. But Katrina Lythgoe, a biologist at Oxford University, worries that their development will slow down as governments stop paying for genetic sequencing of new variants.

"If we don't sequence things, then we won't see them," she said.

<u>Carl Zimmer</u> covers news about science for The Times and writes the <u>Origins column</u>. <u>More about Carl Zimmer</u>

Anyone who thinks we "over-reacted" throughout the first extended wave of the pandemic has a conveniently poor memory and/or a stubborn bias towards stupidity. Remember Milan in Italy, and how the virus hit New York? We had good reason to fear a similar toll as it flooded across the Continent.

To call the public response to COVID-19 "imperfect" is to grossly overlook a medley of mistakes and opportunistic profiteering. But this does not mean the public health measures instituted were wrong and unnecessary. And when a public health system has been sidelined, ignored, gutted and crippled, is it any wonder if it struggles and regularly fails to follow through masterfully on its obligations? When a true pandemic finally lands on us?