



Thomas A. Faulhaber

Superior COVID-19 treatment isn't working. What now?

There aren't any monoclonal antibody drugs that can treat the latest COVID-19 variants.

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There are no longer any monoclonal antibody treatments authorized for the latest variants of COVID-19

Erin Clark/Boston Globe via Getty Images

COVID-19 is once again trending upward in the United States, with new cases reaching more than 450,000 and deaths climbing up to 3,000 per week. But hospitals will have to face this year's winter surge without a valuable tool.

In late November, the Food and Drug Administration revoked its emergency use authorization for bebtelovimab, a monoclonal antibody treatment for COVID-19, because it wasn't effective against the latest variants of SARS-CoV-2, the virus that causes COVID-19. Now, there are no monoclonal antibody treatments left that work against BQ.1 and BQ.1.1., the subvariants of the omicron variant that are currently causing most new infections.

Monoclonal antibodies are synthetic versions of immune system proteins that precisely target the virus, preventing it from invading cells and flagging it for destruction by white blood cells.

They've been successfully used to treat severe COVID-19 cases throughout the country. Former President Donald Trump notably was treated with a monoclonal antibody combination developed by [Regeneron](#) when he was ill with COVID-19. But as the virus has mutated, older antibody therapies lost effectiveness, and new ones had to be developed.

Adding to the stress is that hospitals are now contending with a spike in other infections, including RSV (respiratory syncytial virus), and the [worst influenza season in two decades](#), further straining their capacity.

There are still COVID-19 therapies that remain effective, and it's still possible to prevent infections in the first place. But without monoclonals as a backstop, some of the most vulnerable people will be at greater risk of suffering and dying.

[Monoclonal antibodies have been a key part of the COVID-19 response strategy](#)

With people gathering indoors and traveling for the holidays, COVID-19 is once again finding ample opportunities to spread. Thankfully, the overall death rate from COVID-19 is far below where it was a year ago, when the [omicron variant](#) of the virus began to take root. And between vaccinations and prior infection, the vast majority of people in the US now have some degree of protection against the disease.

Yet there are still lots of people who remain vulnerable to severe illness and death from COVID-19. The highest risks fall on those who have not been vaccinated against the virus, about [20 percent of the US population](#). Among the vaccinated, older adults, people with compromised immune systems, and people who live in nursing homes and prisons also face greater rates of harm from the disease. And even among people who only experience a mild course of the illness, many end up with enduring symptoms like difficulty smelling, breathing, and concentrating, phenomenon known as [long Covid](#).

The good news is that there are [effective treatments for Covid-19](#). The most common is an antiviral pill called [Paxlovid](#), which is often the first line of defense for people at high risk of severe illness. There are other antiviral drugs available as well, like remdesivir and molnupiravir, but they are less effective against COVID-19.

Since Paxlovid is a pill, patients can pick up the drug at a pharmacy and take it at home. Monoclonal antibodies, on the other hand, are administered as injections or transfusions, making them a more involved, more expensive treatment.

The problem is that Paxlovid is most effective in the first five days of an infection, and often patients don't get tested and treated in time. Many doctors don't even know if the drug is available at any given time. Some are reluctant to give it to patients because of worries about dangerous interactions with other drugs. "Paxlovid is woefully, woefully, underprescribed," said [Amesh Adalja](#), a senior scholar at the Johns Hopkins Center for Health Security.

It is true that Paxlovid can have [harmful interactions with other medicines](#), including common blood pressure drugs, psychiatric drugs, and cancer treatments. But Adalja said that the vast majority of medicines have no bearing on Paxlovid, and of those that do, many can be managed.

Still, without monoclonal antibodies, there are people who can't take Paxlovid who now have one less option. "I do think for people for whom the drug-drug interactions are difficult, this is a setback," Adalja said.



Evusheld is a monoclonal antibody therapy used to prevent Covid-19 infection.

Jonathan Nackstrand/AFP via Getty Images

Monoclonal antibodies were also used to prevent COVID-19 in high-risk patients. For instance, the monoclonal antibody regimen [Evusheld](#) was used as a prophylactic to protect people who didn't respond strongly to vaccines or those who have depleted immune systems, like cancer patients and organ transplant recipients. But Evusheld also lost potency against omicron and its subvariants.

And for patients in later stages of severe COVID-19, like those who need ventilators, monoclonal antibodies were an important tool for bolstering their immune systems.

So while monoclonal antibodies were not always the go-to treatment, they were an important layer of protection for people facing greater chances of dangerous cases of COVID-19. Without them, vulnerable people could fare worse. “The risk is that it could potentially lead to more severe complications,” said [Bruce Y. Lee](#), a professor of health policy and management at the City University of New York.

More monoclonal antibodies are under development, but it will take time — and the target is moving

Researchers and pharmaceutical companies are already at work developing more monoclonals to target COVID-19. “There are lots of investigations already underway,” said [Aaron Glatt](#), head of infectious disease at Mount Sinai South Nassau. “I’m hopeful that there will be something that’s forthcoming.”

The challenge is that antibodies are very picky about where they will attach to the virus. Many antibodies generated by the immune system target the spike protein of SARS-CoV-2, which is what the virus uses to attach to human cells to begin the infection process. But viruses mutate all the time, and the spike protein is one of the fastest-changing parts of the pathogen. New variants can quickly become unrecognizable to older antibodies. That’s why the latest versions of SARS-CoV-2 have a higher likelihood of causing reinfections and breakthrough infections.

With monoclonals, as the name suggests, scientists pick out one specific type of high-performing antibody and clone it to administer as a treatment. That gives monoclonals a strong, targeted effect against the virus, until the target on the virus changes.

“As the virus mutates, it will be constantly changing the need for monoclonal antibodies,” Glatt said.



Monoclonal antibodies have to be transfused or injected under medical supervision.

Eve Edelheit/The Washington Post via Getty Images

Researchers have worked to speed up the development cycle for these drugs, and as with vaccines, regulators have also streamlined approvals. “We’ve been able to speed up the review process and cut down on some of the time restrictions, without compromising the quality of the studies needed to show that it’s effective and safe,” Glatt said.

But drug development is always playing catch-up to a virus that continues to confuse and frustrate our tools. Containing COVID-19 still demands a multilayered strategy that includes treatments as well as public health measures, Lee explained.

“One of the things we’ve seen during the pandemic is too much of a focus on one thing at a time,” he said. “For all this, it’s been lost that you really need to have all these things layered on top of each other.”

While COVID-19 is nowhere near as dangerous as it once was, it’s not something we can take lightly. Maintaining a tool chest of treatments for all the stages of the infection will help keep COVID-19 death rates in check. And controlling its spread with face masks, social distancing, good hygiene, and indoor ventilation remains critical for preventing infections and limiting newer variants.

[Thomas A. Faulhaber, Editor](#)

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