# Can vaccinated people still spread COVID-19? How long does immunity last? Here's what science knows now

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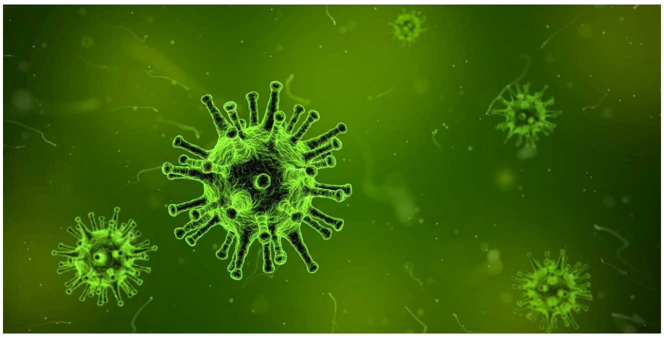

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Six times over the course of a year, some select COVID-19 vaccine recipients at the University of Pennsylvania are rolling up their sleeves for a different kind of needle: one that draws blood.

At each session, 10 vials of scarlet fluid are collected, bar-coded, and archived in laboratory freezers. Some will be tested for various kinds of antibodies, the Y-shaped proteins that the immune system makes in response to a vaccine or to a live infection. Others will be tested for antiviral defenders called T-cells, which are marked with fluorescent 'tags' and counted at high speed with a laser.

The goal: to determine how well the COVID-19 vaccines work in the real world.

The answer to this complex question has been on the minds of scientists ever since November, when the first large-scale studies suggested the vaccines could prevent up to 95% of illness.

But those promising results came from rigorous clinical trials, in which participants who met specific criteria were assigned at random to receive either the vaccine or a placebo, allowing their outcomes to be compared. All sorts of people were excluded: pregnant women, people who had previously been infected with COVID-19, and patients with certain cancers, HIV, or severe allergies.

The Penn study, led by E. John Wherry, is among many now underway to answer a variety of open questions. Can some vaccinated people become infected but have no symptoms, thereby potentially transmitting the virus without realizing it? How well do the vaccines work in people with various medical conditions? Is a previous COVID-19 infection equal in protection to a first dose of vaccine?

And for all vaccine recipients, how long does the protection last?

None of the uncertainties is reason to hesitate in getting the vaccines, which are safe and remain our best hope of curbing the pandemic. But the answers will be complicated by the emergence of new coronavirus variants, which could reduce the vaccines' effectiveness, and by the fact that the real world is inevitably messier than a clinical trial.

Said Wherry, an immunologist at Penn's Perelman School of Medicine:

"These are all things keeping all of us up at night."

When they say a vaccine prevents 95% of illness, that's an estimate. What it really means is the number of illnesses among vaccinated people is 95% lower than the number among unvaccinated people.

That certainly suggests the vaccine is preventing most cases of disease. But we can never pin down the exact number of avoided illnesses without knowing how many people in each group were exposed to the virus—that is, on how many occasions was the vaccine actually put to the test?

Large, randomized clinical trials nevertheless provide a solid estimate of disease prevention, counting on the likelihood that similar numbers of vaccinated and unvaccinated people will be exposed. But measuring a vaccine's punch in the real world, when everyone can (eventually) get it, is trickier.

And for a variety of reasons, no vaccine quite lives up to its track record in a clinical trial, said Gregory Poland, a Mayo Clinic vaccine researcher and fellow at the Infectious Diseases Society of America.

People might delay or skip the second dose. Or they may engage in more risky behavior than the health-conscious types who enrolled in a clinical trial. Or, with vaccines that require special handling, something can go amiss. The two COVID-19 vaccines to receive U.S. authorization so far, for example, consist of genetic instructions in the form of RNA, which starts to degrade after vials are removed from cold storage.

Still, an Israeli health system reported this week that the RNA vaccine made by Pfizer and BioNTech may indeed come close to the level of success demonstrated in the clinical trials. The Israeli study was not randomized, and the details have not yet been published, but it's a good sign.

Other studies, meanwhile, suggest that new variants of the coronavirus can partly "escape" the immunity that is provided by the vaccines. Yet even partial protection is much better than none. And so far, the drugs still seem to prevent severe cases of disease.

A key reason the coronavirus has posed such a challenge is that some people become infected with mild or no symptoms, meaning they can spread the virus unknowingly.

It is possible that is happening to some degree with vaccinated people, too, said Brianne Barker, a Drew University biologist who studies the immune system's response to viruses. In other words, for some people, the vaccines may prevent disease but not prevent the virus from invading and making copies of itself—the definition of infection.

But if measuring a vaccine's ability to prevent disease is a challenge, measuring its ability to prevent transmission is far harder.

"You both have to show that someone is infected, then you have to be able to document the transmission opportunity and show that it did or did not happen," she said.

That type of study is unlikely to occur, given the resources required. But various labs are at least trying to solve the first part of that equation: periodically swabbing the noses of vaccine recipients and measuring the amount of viral material therein.

People with less virus in their nasal cavities are, in theory, less able to spread disease, said Poland, the Mayo Clinic physician. And in several studies so far, various COVID-19 vaccines do seem to reduce the amount of virus in the nose.

"We have hints," he said. "We don't have definitive answers."

But some level of transmission could still be possible, if the evidence from most other vaccines is any guide. That's why experts say we need to keep up the mask-wearing for now.

Yet another way researchers plan to detect asymptomatic infection is to measure levels of a protein called an N-binding antibody. That's different from the antibodies that people make in response to being vaccinated, which bind to the "spikes" on coronavirus particles, preventing them from invading a human cell.

An N-binding antibody, on the other hand, latches onto a coronavirus protein that is not contained in the vaccines. So if that antibody is present in the blood of a vaccine recipient, it's a telltale sign that the person has been infected, even if there were no symptoms, Barker said.

Recipients of the RNA vaccines have been reporting that any side effects, such as fever and headache for a day or two, tend to occur after the second shot.

But for those previously infected with COVID-19, side effects may be more likely after the first shot. Does that suggest that a prior infection is just like getting a first dose?

That's among the questions that Wherry hopes to answer in his lab at Penn. The short answer is no, as shown by the antibodies that are present only in those who've been infected.

Yet the immune system has many agents besides antibodies. Wherry's team also is measuring various kinds of white blood cells, including "helper" T cells that can act as sentinels, marshaling support to fight an infection, and "killer" T cells that, as the name suggests, fight infection by killing cells that the virus has penetrated.

These cells are extracted from blood samples and chemically tagged with various fluorescent markers—allowing each type of cell to be counted with a laser, inside a boxy device called a flow cytometer.

So far Wherry's team has enrolled 35 vaccinated people to participate, a third of whom were previously infected. Others, including cancer patients who take immune-suppressing drugs, will be added later.

"There's this idea that previous infection may leave an imprint on your immune response," he said. "Then when you get the vaccine, how your vaccine-induced response evolves could be different than if you've never seen the virus before."

And like many others, he plans to measure how the immune response changes over time.

Plenty of unanswered questions. But on one front, the scientists who study the vaccines are united: Vaccination is the best weapon we have. Make an appointment as soon as you're eligible, and get it done.