

MORE STUDIES SHOW THE SUPERIORITY OF HYBRID IMMUNITY

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Representational image. | Photo Credit: [Reuters](#)

Yet another study has shown that a combination of natural infection with a single dose of vaccine provides greater immunity than either natural infection without vaccination or full vaccination in infection-naïve individuals. People without prior infection but fully vaccinated with the Pfizer or AstraZeneca vaccine showed a decline in neutralising antibodies over a period of three to seven months. But the decline was much less in vaccinated people with prior infection.

Though 500 health-care workers with or without prior infection were vaccinated, those with hybrid immunity — natural immunity from an infection combined with the immunity provided by the vaccine — had a higher and more durable neutralising antibody response. The hybrid immunity offers stronger protection than just infection or full vaccination alone.

The study, posted in the preprint server *medRxiv* on October 19 (preprints are yet to be peer-reviewed), has found that in 500 health-care workers, the neutralising antibodies were twofold more in people immunised with Pfizer vaccine following natural infection compared with people immunised with Pfizer vaccine but without prior infection.

In the case of people vaccinated with AstraZeneca following natural infection, the neutralising antibodies were threefold more than in vaccinated people with no prior infection.

One of the early evidences of hybrid immunity being better than full vaccination in people without a prior infection came in end-April. The results posted in preprint server *medRxiv* found that vaccination led to increased levels of neutralizing antibodies against variants in people who had been previously infected compared with those without a prior infection.

An earlier study posted on August 25 in the preprint server *medRxiv* found that compared with vaccine-induced immunity from two doses of Pfizer vaccine, natural immunity conferred longer lasting and stronger protection against infection, symptomatic disease and hospitalisation caused by the Delta variant in Israel. But naturally infected individuals who were given a single dose of the vaccine showed additional protection against the Delta variant; the protection level conferred by hybrid immunity was even higher than the one offered by natural infection or full vaccination.

Soon after vaccines were rolled out, researchers began to notice higher levels of antibodies in people who were naturally infected prior to vaccination compared with vaccinated people without prior infection. In short, the hybrid immunity from natural infection followed by vaccination provided superior immunity than either natural infection alone or full vaccination.

However, a study published recently in the journal *Science* observed that “boosting of pre-existing immunity from prior infection with vaccination mainly resulted in a transient benefit to antibody titers with little-to-no long-term increase in cellular immune memory”.

There is a growing body of evidence that protection from natural immunity can be potent, and researchers are beginning to acknowledge this. However, scientific consensus about the exact strength or durability of the natural immunity post natural infection is not known. Also, the

strength and durability of natural immunity might not be uniform and might vary between people depending on the nature and duration of infection (asymptomatic or symptomatic) and severity of disease (mild, moderate or severe).

“Antibody levels are really variable after recovering from infections, and those at the lower end of the spectrum might be more susceptible to reinfections,” Deepta Bhattacharya, Professor of immunology at the University of Arizona told *NBC News*. “But after a single vaccine in people who have recovered from COVID-19, antibodies skyrocket up, including those that neutralize variants of concern.”

Researchers at Rockefeller University in New York City looked at how different types of immunity would protect against potential variants. They modified the coronavirus spike protein such that it contained 20 naturally occurring mutations. In the lab, the modified spike protein was tested against antibodies from people belonging to three groups — those who have been fully vaccinated without prior infection, people with prior infection but not vaccinated, and people with hybrid immunity. They found the modified spike proteins were able to evade the antibodies from the first two groups but not antibodies from people with hybrid immunity. The study is posted in the preprint server *BioRxiv*.

In August, CDC published a study in the *Morbidity and Mortality Weekly Report* (MMWR) where they showed that unvaccinated people without previous infection are twice as likely to be reinfected compared with vaccinated people with a prior infection. This study prompted the CDC Director Dr. Rochelle Walensky to urge all Americans to take a vaccine even if previously infected. “If you have had COVID-19 before, please still get vaccinated,” she appealed.

The immunological advantage from hybrid immunity arises mostly from memory B cells. While the bulk of antibodies after infection or vaccination decline after a short while, the memory B cells, which evolve in the lymph nodes, get triggered on subsequent infection or vaccination. So when people who recovered from COVID-19 are re-exposed to the spike protein, the memory B cells are capable of churning out highly potent antibodies.

“Differences between the memory B cells triggered by infection and those triggered by vaccination — as well as the antibodies they make — might also underlie the heightened responses of hybrid immunity. Infection and vaccination expose the spike protein to the immune system in vastly different ways,” Dr. Michel Nussenzweig, an immunologist at the Rockefeller University in New York City told *Nature*.

Dr. Nussenzweig’s team isolated hundreds of memory B cells from people at various time points after infection and vaccination. They found that unlike after full vaccination, antibodies produced by natural infection continued to grow in potency and their breadth against variants for a year after infection. According to *Nature*, unlike after vaccination, the memory B cells formed after natural infection are more likely to make antibodies that block immune-evading variants.

But two studies have found that memory B cells in the fully vaccinated people without prior infection are growing in number and gaining mutations up to 12 weeks after the second dose, which allows the B cells to recognise and neutralise variants.

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This decision of U.S. Nuclear Regulatory Commission was awaited by specialists

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