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Immunity against Omicron from breakthrough infection could be a matter of timing

Laboratory studies hint that a longer interval between vaccination and infection is better than a shorter one.

Saima May Sidik

 People sitting in an aisle of mechanical arcade games are given vaccinations.

A medical worker administers a COVID-19 vaccine in a gaming arcade in Osaka, Japan. Credit: Jiji Press/AFP/Getty

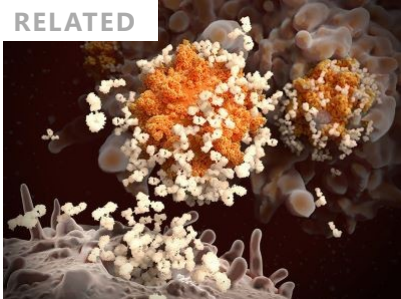
Good timing is a key to success – even for riding out the [Omicron wave](#). Research from Japan suggests that COVID-19 vaccination followed months later by a breakthrough SARS-CoV-2 infection offers greater protection against the Omicron variant than do closely spaced vaccination and infection¹.

The finding implies that countries that saw large numbers of non-Omicron infections in late 2021 have an advantage as 2022 rolls in with the new variant. The study has not yet been peer reviewed.

Many countries' populations have gained immunity through a combination of vaccination and infection with an array of variants. But Japan's population is protected mainly by vaccination with [mRNA vaccines](#). Study co-author Takeshi Arashiro, an infectious disease researcher at Japan's National Institute of Infectious Diseases in Tokyo, and his colleagues wanted to understand whether the country's

mostly single-source immunity would leave the population especially susceptible to Omicron. So far, the country has had few breakthrough cases, but “we are afraid that once the Omicron variant is in high transmission in Japan, we might see a whole different picture”, Arashiro says.

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The team collected antibodies from people in Japan who had received two doses of the Pfizer–BioNTech COVID-19 vaccine and later been infected with either the Alpha or Delta variant. The researchers tested these antibodies' ability to protect cultured cells from SARS-CoV-2 infection, and found that the length of time between a person's vaccination and the breakthrough infection was strongly correlated with how well the individual's antibodies protected cells

against infection – particularly [with Omicron](#).

“It's an interesting study,” says immunologist Jenna Guthmiller at the University of Chicago in Illinois. She cautions that the results are solely correlative, but adds that they are in line with immunologists' general understanding of how antibody responses mature over time.

Guthmiller explains that vaccination leads to an emergency blast of antibody production, as a natural infection would. If a person gets infected soon after vaccination, these antibodies are probably still circulating in the blood, where they'll bind to the virus and quickly eliminate it.

But when a person becomes infected months after vaccination, the antibodies that respond come from a new and improved batch made by [long-lived cells that carry a memory of the pathogen](#). When the body encounters the pathogen again, these memory cells are called back to duty and have a chance to refine the antibodies, providing better protection against subsequent infections.

Boosters versus breakthroughs

Guthmiller says she would like to see similar data focused on vaccine **boosters** instead of breakthrough infections. “Does the amount of time between your first two doses, and then your booster, impact how many cross-reactive antibodies you have?” she asks.

Arashiro and his colleagues have not investigated that, but he thinks boosters are still Japan’s best bet for combating the Omicron wave. “We’re trying to push for booster doses as soon as possible – especially among vulnerable populations – because we are only protected by vaccines, not by natural infections,” he says.

doi: <https://doi.org/10.1038/d41586-022-00004-x>

References

1. Miyamoto, S. *et al.* Preprint at medRxiv <https://doi.org/10.1101/2021.12.28.21268481> (2022).
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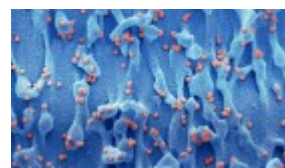
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