Studies find 'immune imprinting' might be making bivalent boosters less effective: What is it and how does it work?

Over the years, scientists have realised that imprinting acts as a database for the immune system, helping it put up a better response to repeat infections.

Written by **Alind Chauhan** , Edited by Explained Desk
New Delhi | Updated: January 24, 2023 01:12 IST

Scientists suggest that regardless of the type, coronavirus vaccines are crucial in staving off serious illness. But now there is a need to come up with a vaccine that can overcome imprinting and thwart the transmission of the virus. (File photo)

Listen to this article

05:31 1x 1.5x 1.8x

Since last September, countries like the UK and the US have rolled out variant-specific or bivalent boosters, in the hope that they would provide better protection against the coronavirus infection in comparison to the original vaccine. However, a slew of recent studies has shown that a phenomenon in our bodies, called immune imprinting, might be making these new boosters far less effective than expected.

Two papers, published earlier in January in the New England Journal of Medicine (NEJM), pointed out that bivalent boosters — made to counter both the Omicron strains and the original Covid-19 strain — don't generate significantly greater antibody responses than an additional dose of the **original mRNA vaccines**.

The observed ineffectiveness of the bivalent or variant-specific boosters might be due to immune imprinting, scientists of both studies concluded.

Also in Explained | Canada says 'no amount' of alcohol is healthy. Here's why

What is immune imprinting?

Immune imprinting is a tendency of the body to repeat its immune response based on the first variant it encountered — through infection or vaccination — when it comes across a newer or slightly different variant of the same pathogen.

The phenomenon was first observed in 1947, when scientists noted that "people who had previously had flu, and were then vaccinated against the current circulating strain, produced antibodies against the first strain they had encountered", according to a report published in the journal Nature. At the time, it was termed the 'original antigenic sin' but today, it's commonly known as imprinting.

Over the years, scientists have realised that imprinting acts as a database for the immune system, helping it put up a better response to repeat infections. After our body is exposed to a virus for the first time, it produces memory B cells that circulate in the bloodstream and quickly produce antibodies whenever the same strain of the virus infects again.

The problem occurs when a similar, not identical, variant of the virus is encountered by the body. In such cases, the immune system, rather than generating new B cells, activates memory B cells, which in turn produce "antibodies that bind to features found in both the old and new strains, known as cross-reactive antibodies", the Nature report said.

Although these cross-reactive antibodies do offer some protection against the new strain, they aren't as effective as the ones produced by the B cells when the body first came across the original virus.

What are the findings of the recent study?

In the first study, done by the researchers of the Columbia University Vagelos College of Physicians and Surgeons in New York, participants were 40 individuals, who had already received three shots of the original or monovalent vaccine. To carry out the experiment, 19 of them were given a booster (fourth shot) of the original vaccine while 21 received a booster of the new bivalent vaccine.

Also Read |Explained: Selecting the Covid-19 booster vaccine

It was observed that the bivalent boosters "did not elicit a discernibly superior virus-neutralising peak antibody response as compared with boosting with the original monovalent vaccines" across all coronavirus strains tested. In the second study, researchers of the Beth Israel Deaconess Medical Center in Boston evaluated immune responses in 15 participants, who had received the original monovalent boosters, and in 18 participants, who had received the bivalent boosters.

It was found that "median BA.5 (Omicron) neutralising antibody titer was similar after monovalent and bivalent mRNA boosting, with a modest trend favouring the bivalent booster by a factor of 1.3."

The findings of both studies suggested immune imprinting might be posing a hurdle in the success of the bivalent or variant-specific vaccines.

Explained |'Updated' booster shots for Omicron. Here's all you need to know

Not only this, earlier, a 2022 study done by Professor Rosemary Boyton and her team at Imperial College London observed that Omicron infection "had little or no beneficial effect of boosting any part of the immune system" among the 700 participants, who had been imprinted with older coronavirus variants, according to a Financial Times report.

One of the authors of the Columbia University research, David Ho, said in an interview, "This (the result) wasn't a total shock. There's a phenomenon known in vaccinology called immunological imprinting, which means your immune memory preferentially sees what it has seen before." However, Ho did add that even if the bivalent boosters are as effective as the original ones "that doesn't mean people shouldn't get the bivalent booster".

Even the World Health Organisation last year cautioned, "The bulk of the benefit is from the provision of a booster, irrespective of whether it is a monovalent or bivalent vaccine". Scientists suggest that regardless of the type, coronavirus vaccines are crucial in staving off serious illness. But now there is a need to come up with a vaccine that can overcome imprinting and thwart the transmission of the virus.

How to circumvent immune imprinting?

Currently, several ongoing studies are trying to find a way to deal with imprinting. Some scientists have said nasal vaccines might be better at preventing infections than injected ones. They believe the mucous membranes would create stronger protection, despite carrying some imprint of past exposure.

Researchers are also trying to find if spacing out coronavirus vaccine shots on an annual basis, could help with the problem of imprinting.

"There's also considerable effort directed toward developing what's called pan-sarbecovirus vaccines that will protect against all COVID-causing variants and maybe even protect against other SARS and related viruses. Those efforts are also rather nascent, I would say, and would take time to develop", Ho said in the interview.