- Virus / Vaccination

IS HYBRID IMMUNITY REAL?

Covid survivors who get vaccinated likely to get up to 100 times more protection

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Vaccination of previouslyinfected persons is now a reality. What's the effect, or benefit? It turns out when people who recovered from Covid-19 get a jab against SARS-CoV-2, people pile up a high wall against reinfection — better known as "hybrid immunity".

Today, thanks to teams of researchers who have done independent clinical work, the underlying process behind this is now better understood. Scientists have bridged the knowledge gap on how much vaccinations among previously infected persons affect their response to a possible reinfection, with reports published in Cell and Clinical and Experimental Immunology.

What's hybrid immunity?

It happens when previously infected individuals are vaccinated with just one dose, specifically when using an mRNA vaccine. Researchers found that when natural immunity to SARS-CoV-2 is combined with vaccine-generated immunity, a larger-than-expected immune response arises. One data set that investigated this phenomenon shows up to 100 times antibody response in those with "hybrid immunity".

How does it work?

Clinical researchers showed Covid-19 patients who had recovered and then got vaccinated had the highest antibody count in their blood samples.

A breakthrough study led by Prof. Alessandro Sette and Prof. Shane Crotty published in Cell describes how CD4+ T cells, CD8+ T cells and neutralising antibodies all contribute to control of SARSCoV-2 in both non-hospitalised and hospitalised cases of Covid-19.

"Overall, the strength and breadth of the antibody responses after vaccination of previously SARS-CoV-2 — infected persons was unanticipated," wrote Crotty of the Centre for Infectious

Disease and Vaccine Research at the University of California, San Diego.

They found that antibodies do protect against SARS-CoV-2 reinfection, but only to a limited extent. There are other mechanism at work: more importantly, they found T cell responses against SARS-CoV-2 in natural infection are quite broad. As scientists investigate the relationships between immune responses and SARS-CoV-2 infection, one picture has emerged: CD4+ T cells, CD8+ T cells, and neutralising antibodies all contribute to control of viral infection.

Do vaccinations enhance immunity of previously-infected individual against reinfection?

Yes, according to the several peerreviewed studies. Research published in Clinical and Experimental Immunology in June 2021 further bolsters this conclusion. It examined data on real-time assessments of adaptive immune responses (which include CD4+ /CD8+ T cells, "natural killer" T cells, memory B cells and T follicular cells) specifically against Covid-19 peptides in infected and normal individuals.

Stan C. Jordan of the Cedars-Sinai Medical Centre, Los Angeles, led a research team that published results of a study showing innate and adaptive immune responses to SARS-CoV-2 in humans, its relevance to acquired immunity and vaccine responses.

Another study came out of a cohort of UK health care workers given the Pfizer/ BioNTech vaccine in which half of the participants had experienced natural virus infections early in the pandemic.

On August 30, 2021, Emily R. Egbert published in the journal JAMA another example of hybrid immunity benefit with respect to durability of antibody levels to 10 months in health care workers.

Still another study posted August 31, 2021 on the medRxiv biology preprint server confirmed hybrid immunity, i.e. single-dose Covid-19 vaccines in healthy individuals with past Covid-19 infections "seem to provide better immunity than double doses in Covid19-unexposed individuals".

What's the driver behind hybrid vigour immunity?

Researchers have shown what happens to the immune system: when a natural Covid infection occurs, the body's own innate and adaptive defences kick in.

So it's widely known that, in case of a natural infection, the body's "adaptive immune" immediately springs into action. But there's a problem with this: adaptive immune response takes time to develop.

Why is it a problem?

The researchers seem to agree on one thing: early adaptive immune responses are beneficial; adaptive immune responses are just too late. As adaptive immune response takes time to develop, it leads to a fundamental and undesirable result — many cells are already infected by the time an antibody response develops.

In this case, the virus gets a huge advantage: unfettered replication in the upper respiratory tract (URT) and lungs. It only gets worse: it also fails to "prime" an adaptive immune response for a long time, resulting in conditions that lead to severe-enough lung disease, that leads to hospitalisation.

This also happens when a pathogen (virus, new variant) is particularly efficient in evading immune response, a person has defective innate immunity — or a delicate combination of both.

One study conducted by Moderbacher C Rydyznski (published September 16, 2020 in Cell), shows why the elderly have less ability to mount a T cell response quick enough to recognise the new virus. The reason: elderly individuals have a smaller T cell pool — which then hampers

neutralising antibody responses, because neutralising antibody responses are generally T cell-dependent.

That's why they are prioritised in vaccination schedules. So antibodies, by themselves, cannot clear an ongoing infection. They also need other components (helpers) of the immune-response mechanism to act up: Specifically, B cell and T cells. These are the body's own fighters that are now seen behind the hybrid immunity boost.

What's the evidence of this immune mechanism?

One evidence: single-dose vaccination adds immune protection for people with prior Covid, with 25-100 times higher antibody response, along with B cell and T cell response, as explained by the Crotty-led study.

Most clinical researchers have noted the absence of a correlation between neutralising antibodies and recovery from Covid-19. On the other hand, SARS-CoV-2-specific CD4+ T cells and CD8+ T cells strongly correlated with reduced disease severity. Researchers conclude that B cells and T cells are the key actors in fighting primary SARS-CoV-2 infection.

What's the significance of the findings

Overall, the strength and breadth of the antibody responses after vaccination of previously SARS-CoV-2 — infected persons was unanticipated."

The researchers found that after vaccination of individuals previously infected with non-B. 1.351 SARS-CoV-2, neutralising antibodies against B. 1.351 were about 100 times higher than after infection alone and 25 times higher than after vaccination alone — even though neither the vaccine nor infection involved the B. 1.351 spike.

This is significant: it shows enhanced "neutralising breadth", first reported by scientists like Leonidas Stamatatos and then confirmed by other research groups. The other research team, based in the UK and led by Catherine Reynolds, of the Department of Infectious Diseases, Imperial College London, reported their findings in Science on June 25, 2021. It showed a significant antibody boost from a previous infection, followed by a vaccine — specifically, Pfizer's mRNA shot.

Reynolds' team found that antibody and memory responses in individuals vaccinated after infection were substantially boosted "to the extent that a single vaccine dose is likely to protect against the more aggressive B.1.1.7" (Alpha variant, first reported in the UK).

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Prof. Shane Crotty | Centre for Infectious Disease and Vaccine Research at the University of California, San Diego