Pfizer-BioNTech vaccine recipients have lower antibody levels targeting the Delta variant

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Levels of antibodies in the blood of vaccinated people that are able to recognise and fight the new SARS-CoV-2 Delta variant first discovered in India (B.1.617.2) are on average lower than those against previously circulating variants in the UK, according to new laboratory data from the Francis Crick Institute and the National Institute for Health Research (NIHR) UCLH Biomedical Research Centre, published today (Thursday) as a Research letter in *The Lancet*.

The results also show that levels of these antibodies are lower with increasing age and that levels decline over time, providing additional evidence in support of plans to deliver a vaccination boost to vulnerable people in the Autumn.

And, the researchers support current plans to reduce the dose gap between vaccines since they found that after just one dose of the Pfizer-BioNTech vaccine, people are less likely to develop antibody levels against the B.1.617.2 (Delta) variant as high as those seen against the previously dominant B.1.1.7 (Alpha) variant, first found in Kent.

Although laboratory results such as these are needed to provide a guide as to how the virus might be evolving to escape the first generation of vaccines, levels of antibodies alone do not predict vaccine effectiveness and prospective population studies are also needed. Lower neutralising antibody levels may still be associated with protection against COVID-19.

This is the largest study published to date investigating vaccine-induced antibody neutralising capacity against the newest variants of concern in healthy adults. Researchers have submitted their findings to the Genotype-to-Phenotype National Virology Consortium (G2P-UK), the New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) and the Joint Committee on Vaccination and Immunisation (JCVI), as evidence of the level of protection people might receive against the new variants after one dose and both doses of the Pfizer COVID-19 vaccine.

As part of the SARS-CoV-2 Legacy study, led by the Crick and partners at UCL and University College London Hospitals NHS Foundation Trust (UCLH), healthcare workers and staff from the institutions have been donating regular blood and swab samples so that researchers can track changing risk of infection and response to vaccination.

Thanks to samples of the latest variants of concern being provided by NHS labs to the G2P-UK consortium, researchers have been able to quickly assess the potential risks they might pose.

Within just a few days of having enough of each variant to study, they were able to analyse antibodies in the blood of 250 healthy people who received either one or two doses of the Pfizer-BioNTech COVID-19 vaccine, up to three months after their first dose. Using a new highly accurate high throughput viral neutralisation assay developed at the Crick, they tested the ability of antibodies to block entry of the virus into cells, so called 'neutralising antibodies', against five different variants of SARS-CoV-2:

- The original strain first discovered in Wuhan, China
- The dominant strain in Europe during the first wave in April 2020 (D614G)
- B.1.1.7, the variant first discovered in Kent, UK (Alpha)
- B.1.351, the variant first discovered in South Africa (Beta)
- B.1.617.2, the newest variant of concern, first discovered in India (Delta)

They then compared concentrations of these neutralising antibodies between all variants. Data from previous clinical studies suggests that higher antibody titres (the greatest dilution level that still blocks 50% of virus infection in the lab) is a good predictor of vaccine efficacy and greater protection against COVID-19.

They found that in people who had been fully vaccinated with two doses of the Pfizer-BioNTech vaccine, levels of neutralising antibodies were more than five times lower against the B.1.617.2 variant when compared to the original strain, upon which current vaccines are based.

Importantly, this antibody response was even lower in people who had only received one dose. After a single dose of Pfizer-BioNTech, 79% of people had a quantifiable neutralising antibody response against the original strain, but this fell to 50% for B.1.1.7, 32% for B.1.617.2 and 25% for B.1.351.

While antibody levels decreased with age against all variants, no correlation was observed for sex or BMI.

The study participants analysed here had all been vaccinated with the Pfizer-BioNTech vaccine. More work is underway to test neutralising antibodies against these same variants in people who have been vaccinated with the Oxford/AstraZeneca vaccine.

Emma Wall, UCLH Infectious Diseases consultant and Senior Clinical Research Fellow for the Legacy study, said: "This virus will likely be around for some time to come, so we need to remain agile and vigilant. Our study is designed to be responsive to shifts in the pandemic so that we can quickly provide evidence on changing risk and protection.

"The most important thing is to ensure that vaccine protection remains high enough to keep as many people out of hospital as possible. And our results suggest that the best way to do this is to quickly deliver second doses and provide boosters to those whose immunity may not be high enough against these new variants."

David LV Bauer, group leader of the Crick's RNA Virus Replication Laboratory and member of the G2P-UK National Virology Consortium, said: "New variants occur naturally and those that have an advantage will spread. We now have the ability to quickly adapt our vaccination strategies to maximise protection where we know people are most vulnerable.

"Keeping track of these evolutionary changes is essential for us to retain control over the pandemic and return to normality. This work is a powerful example of effective collaborations between NHS and academic colleagues, that can help us to navigate changes in this new phase of the pandemic."

More information: Wall, E. C., Wu M. et al. Neutralising antibody activity against SARS-CoV-2 VOCs B.1.617.2 and B.1.351 by BNT162b2 vaccination. *The Lancet*. 2021. www.thelancet.com/journals/lan … (21)01290-3/fulltext

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