

Spread of Delta SARS-CoV-2 variant driven by combination of immune escape and increased infectivity

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The Delta variant of SARS-CoV-2, which has become the dominant variant in countries including India and the UK, has most likely spread through its ability to evade neutralizing antibodies and its increased infectivity, say an international team of researchers.

The findings are reported today in *Nature*.

As SARS-CoV-2 replicates, errors in its genetic makeup cause it to mutate. Some mutations make the virus more transmissible or more infectious, some help it evade the [immune response](#), potentially making vaccines less effective, while others have little effect. One such variant, labeled the B.1.617.2 Delta variant, was first observed in India in late 2020. It has since spread around the globe—in the UK, it is responsible nearly all new cases of coronavirus infection.

Professor Ravi Gupta from the Cambridge Institute of Therapeutic Immunology and Infectious Disease at the University of Cambridge, one of the study's senior authors, said: "By combining lab-based experiments and epidemiology of vaccine

breakthrough infections, we've shown that the Delta variant is better at replicating and spreading than other commonly-observed variants. There's also evidence that neutralizing antibodies produced as a result of previous infection or vaccination are less effective at stopping this variant.

"These factors are likely to have contributed to the devastating epidemic wave in India during the first quarter of 2021, where as many as half of the cases were individuals who had previously been infected with an earlier variant."

To examine how well the Delta variant was able to evade the immune response, the team extracted serum from [blood samples](#) collected as part of the COVID-19 cohort of the NIHR BioResource. The samples came from individuals who had previously been infected with the coronavirus or who had been vaccinated with either the Oxford/AstraZeneca or Pfizer vaccines. Serum contains antibodies raised in response to infection or vaccination. The team found that the Delta variant virus was 5.7-fold less sensitive to the sera from previously-infected individuals, and as much as eight-fold less sensitive to vaccine sera, compared with the Alpha variant—in other words, it takes eight times as many antibodies from a vaccinated individual to block the virus.

Consistent with this, an analysis of over 100 infected healthcare workers at three Delhi hospitals, nearly all of whom had been vaccinated against SARS-CoV-2, found the Delta variant to be transmitted between vaccinated staff to a greater extent than the alpha variant.

SARS-CoV-2 is a coronavirus, so named because spike proteins on its surface give it the appearance of a crown ('corona'). The spike proteins bind to ACE2, a protein receptor found on the surface of

cells in our body. Both the spike protein and ACE2 are then cleaved, allowing genetic material from the virus to enter the host cell. The virus manipulates the host cell's machinery to allow the virus to replicate and spread.

Using 3D airway organoids—'mini-organs' grown from cells from the airway, which mimic its behavior—the team studied what happens when the virus reaches the respiratory tract. Working under secure conditions, the team used both a live virus and a 'pseudotyped virus' – a synthetic form of the virus that mimicked key mutations on the Delta variant—and used this to infect the organoids. They found that the Delta variant was more efficient at breaking into the cells compared with other variants as it carried a larger number of cleaved spikes on its surface. Once inside the cells, the variant was also better able to replicate. Both of these factors give the virus a selection advantage compared to other variants, helping explain why it has become so dominant.

Dr. Partha Rakshit from the National Centre for Disease Control, Delhi, India, joint senior author, says that "the Delta variant has spread widely to become the dominant variants worldwide because it is faster to spread and better at infecting individuals than most other variants we've seen. It is also better at getting around existing immunity—either through previous exposure to the virus or to vaccination—though the risk of moderate to severe disease is reduced in such cases."

Professor Anurag Agrawal from the CSIR Institute of Genomics and Integrative Biology, Delhi, India, joint senior author, added that "infection of vaccinated healthcare workers with the Delta variant is a significant problem. Although they themselves may only experience mild COVID, they risk infecting individuals who have suboptimal immune responses to vaccination due to underlying health conditions—and these patients could then be at risk of severe disease. We urgently need to consider ways of boosting vaccine responses against variants among healthcare workers. It also suggests infection control measures will need to continue in the post-vaccine era."

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More information: Petra Mlcochova et al, SARS-CoV-2 B.1.617.2 Delta variant replication and immune evasion, *Nature* (2021). [DOI: 10.1038/s41586-021-03944-y](https://doi.org/10.1038/s41586-021-03944-y)

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