

# EXHIBIT 13

**Why is Delta more infectious and deadly? New research holds answers. Studies show that Delta replicates more quickly and generates more virus particles than other variants, but vaccines still protect against serious infections.**

BYSANJAY MISHRA  
PUBLISHED AUGUST 6, 2021  
• 13 MIN READ

As the United States battles a fourth surge of COVID-19, scientists are learning much about the Delta variant that wasn't known when it was first reported in India in March: it is one of the most infectious respiratory viruses known, it causes more severe COVID-19 than other variants, and it is more likely to evade antibodies.

Evidence of all these traits is clear. The Delta variant has caused a sharp rise in COVID-19 cases, hospitalizations, and deaths across the U.S. and the rest of the world. Driven by relaxed social distancing and mask guidelines, poor vaccine uptake in parts of the U.S., and lack of availability elsewhere, Delta has rapidly become the dominant variant in the U.S., causing more than 93 percent of new infections, according to the Centers for Disease Control and Prevention. It has also spread to more than 135 countries, according to the World Health Organization.

**The secret to Delta's success is the ease with which it spreads. The CDC estimates that Delta can be as infectious as chicken pox and is only slightly less contagious than measles, which is considered one of the most transmissible viruses.** Now the Delta variant is spreading like wildfire through the South, particularly in Louisiana, which has one of the lowest vaccination rates in the country; only 37 percent of the population is fully vaccinated compared to 50 percent nationally. In the U.S., daily cases are now averaging 100,000, a nine-fold jump from mid-June.

**"It's surprising the extent of how infectious this particular variant is, and how well it can then replicate in the upper respiratory tract.** Just the increased infectivity of this Delta variant has sort of increased our concern relative to what was there for the Alpha variant, which was increased relative to the original virus," says Mehul Suthar, a virologist at Emory University.

**Because the Delta variant is so much more contagious than previous variants, CDC issued new guidelines on July 27, 2021, which recommend that even after vaccination, people should "wear a mask indoors in public if you are in an area of substantial or high transmission."**

### **A vastly more transmissible virus**

To track how easily an infectious disease such as COVID-19 spreads, epidemiologists use a metric called the basic reproductive number or R0 (pronounced "R naught"). R0 is the

average number of susceptible people that each infected person is expected to infect. It is difficult to be certain about the R0 for ancient pandemics, but for the 1918 influenza pandemic, the average infected person is thought to have passed the disease to between two and three people, giving it an R0 of between 2.0 and 3.0. The first SARS coronavirus epidemic of 2002, has an R0 of three; for the second coronavirus epidemic—Middle East Respiratory Syndrome (MERS) first identified in 2012—R0 was between 0.69 to 1.3.

Now the CDC estimates that people infected with Delta pass the virus to between five and 9.5 people. This is higher than the original virus identified in Wuhan, China, which had an R0 between 2.3 and 2.7, and the Alpha variant which had an R0 between four and five. Delta can be as infectious as chicken pox, which has an R0 between 9 and 10.

If R0 is larger than one, the number of infected people will keep growing exponentially until all susceptible people have either died or recovered and herd immunity is reached. If R0 is less than one the outbreak will likely fizzle out on its own.

For the original SARS-CoV-2, herd immunity could be reached when around 67 percent of the population was immune—either through natural infection or vaccination. “For Delta, those thresholds we estimate being well over 80 percent, maybe approaching 90 percent,” Ricardo Franco, an assistant professor of medicine at the University of Alabama at Birmingham said at a press briefing organized by the Infectious Diseases Society of America.

### **A higher viral load**

Delta is not only more transmissible than previous SARS-CoV-2 variants, it can also cause more severe disease. People infected with the Delta variant harbor about 1,000 times the number of viral particles (which experts call the “viral load”) in their nasal swab compared to those infected with another strain, “which is an enormous increase,” says Eric Topol, the founder and director of the Scripps Research Translational Institute, who was not involved in this study.

One reason for this is that the Delta variant replicates more quickly in the nose. A study, not yet peer reviewed has shown that the Delta variant took an average of four days to reach detectable levels after exposure to a sick person, compared to about six days for the original Wuhan virus.

Even after vaccination, Delta infections produced a 10-fold higher viral load than non-Delta infections. In fact several recent studies, none peer reviewed yet, show that vaccinated people carry the same viral load as the unvaccinated. “We are seeing infections and seeing the large number of people being infected by a single case, which is quite worrying. It means that the virus is highly transmissible and is able to avoid ... vaccine-induced immunity,” said Ravindra Gupta, a clinical microbiologist at the University of Cambridge, who led the study that is not yet peer reviewed.

Delta is also better at destroying cells because of a mutation at position 681 of its spike protein, which is fast becoming common in other variants around the globe and is thought to be an **evolutionary game changer**. This P681R mutation makes it easier for Delta and the related Kappa variants to invade the host cell by fusing infected cells into structures called syncytium, which is a way of accelerating infection. Syncytia are also formed by other viruses such as HIV. “We found in cell culture experiments that Delta variant shows bigger syncytia when compared to SARS-CoV-2,” explained Kei Sato, a virologist at The University of Tokyo, Japan.

The Delta variant has also undergone multiple mutations in its spike protein that seem to improve the virus’s ability to bind to the ACE2 receptor and evade the immune response.

### **Breakthrough infections and boosters**

The good news is that a complete dose of the currently authorized COVID-19 vaccines remains effective. “All the vaccines work pretty well,” said Jeff Kwong, an infectious diseases epidemiologist at the University of Toronto. “And the vaccines were more protective against the severe outcomes compared to symptomatic infection,” Kwong has shown in a study, not yet peer reviewed, the effectiveness of Pfizer, Moderna, and AstraZeneca vaccines against symptomatic infection, hospitalization, or death between December 2020 and May 2021.

**Many studies have shown that Moderna and Pfizer vaccines still protect against Delta, though not as well as against previous variants.** Unvaccinated people make up more than 90 percent of confirmed new cases among the states that track case data along with vaccination status.

“[Vaccines] do reduce the risk of serious outcome such as hospitalization quite substantively,” says Aziz Sheikh, a primary care specialist at The University of Edinburgh, Scotland, UK who showed that Delta caused twice as many hospitalizations than the Alpha variant, which caused more severe illness than the original SARS-CoV-2. “Overall, they are working.”

**The CDC estimates that COVID-19 vaccination reduces the risk of SARS-CoV-2 infection by eight-fold and the risk of getting ill, being hospitalized, or dying by 25-fold.**

**But inadequate testing nationwide makes it impossible to know the true extent of the spread of Delta and other variants. When there is high transmission of Delta in the community, even fully vaccinated people are vulnerable to so-called “vaccine breakthrough infections,” which the CDC defines as when genetic material or protein from SARS-CoV-2 is detectable in the nasal swab more than 14 days after a person has received the recommended dose of an FDA-authorized COVID-19 vaccine.**

Two doses of the AstraZeneca and Pfizer vaccines are estimated to be 60 and 88 percent effective, respectively, against symptomatic disease caused by Delta. The majority of vaccines administered in the U. S. (Moderna and Pfizer) require two shots for maximum protection. These

vaccines are much less effective against Delta after just a single jab, says Olivier Schwartz, head of the Virus and Immunity Unit at Institut Pasteur, Paris, who led a study that showed that a single dose of either AstraZeneca and Pfizer vaccines or previous infection barely inhibit Delta variant.

Prompted by the data on the reduced efficacy against new variants such as Delta, Pfizer is seeking authorization of a booster dose of its vaccine. Moderna is also testing an updated mRNA vaccine booster dose. The U.S. Food and Drug Administration (FDA) is expected to finalize a COVID-19 vaccine booster plan soon.

The single shot J&J vaccine has been shown to be effective against the Delta variant. But a study, not yet peer reviewed, has shown that although all vaccines triggered the development of antibodies that were somewhat less effective against Delta, the reduction was much steeper for J&J than for mRNA vaccines. This study is consistent with similar ones in monkeys and people where two doses of the J&J vaccine show greater efficacy compared with one dose.

To compensate for the lower efficacy of the J&J shot against Delta, people in San Francisco who received this vaccine can now request a “supplemental dose” of an mRNA vaccine. Germany will begin offering mRNA vaccine booster shots in September to a range of people considered vulnerable. **However, the demand for boosters is magnifying the inequities in COVID-19 vaccine availability between rich and poor countries. “WHO is calling for a moratorium on boosters until at least the end of September to enable at least 10 percent of the population of every country to be vaccinated,”** said Tedros Adhanom Ghebreyesus, Director-General of WHO in a press briefing.

Some preliminary data from Israel suggests that **efficacy of the Pfizer vaccine might decline within six months. But this is not surprising since vaccine designers knew that making the antibody response long-lasting was going to be a challenge. Antibodies against the first SARS and MERS viruses declined after one to two years. For coronaviruses that cause the common cold, protection ranges from three to six months, and almost always less than a year.**

A study in the U.S. has shown that, following the second dose of the Moderna vaccine, neutralizing antibodies remain high in the blood for six months. “Those antibodies that are there, for the most part, neutralize many of these variants [including Delta]. However, these antibody responses do wane over time,” explains Emory's Suthar, who led the U.S. study.

## Vaccines have prevented millions of infections

Vaccination may have saved approximately 279,000 lives in the U.S. and, by the end of June 2021, prevented up to 1.25 million hospitalizations, according to The Commonwealth Fund’s computer models. Similarly in England the vaccines may have prevented about 30,300 deaths,

46,300 hospitalizations, and 8.15 million infections. The aggressive vaccination campaign in Israel is estimated to have caused a 77 percent drop in cases and a 68 percent decline in hospitalizations from the peak of the pandemic in January, 2021.

**Although COVID-19 vaccines in the U.S. are free and effective, only 49.9 percent of the population—just over 165 million people—are fully vaccinated as of August 4, 2021.**

Vaccination rates vary widely nationwide, and many counties in southern states, including Louisiana, Florida, Arkansas, Mississippi, and Alabama, have low vaccination rates that are now fueling raging outbreaks of the Delta variant.

While more than 347 million COVID-19 shots have been administered in the U.S. since distribution began on December 14, 2020, there are still about 93 million Americans age 12 and older who are eligible for a shot but have not yet received one. There are also 48 million children under the age of 12 who are unvaccinated because they are still not eligible. That makes it difficult to predict how long this current surge will last.

### **No vaccine is 100 percent effective**

**With more than half the population incompletely vaccinated, the Delta variant can continue to infect and evolve, leading to more vaccine breakthrough infections than expected and possibly yielding new infectious variants.**

**Evidence is emerging that breakthrough Delta cases may be as transmissible as Delta infection in unvaccinated individuals.** “The vaccines are protective, but obviously a lot of vaccinated people are also getting exposed, some from the unvaccinated and [some] from each other. And so, it's testing the vaccine capabilities,” says Topol.

**But most breakthrough cases, which occur in less than one percent of fully vaccinated people, cause mild or no symptoms. Of the more than 164 million people fully vaccinated nationwide there were only 7,525 patients with COVID-19 vaccine breakthrough infections who were either hospitalized or died in the U.S. through August 2, 2021.**

**Breakthrough infections are more likely among health care workers who are in frequent contact with infected patients, older age vaccinated people, and those with weakened immunity**, such as people with cancer and prior organ transplant. Breakthrough infections are also more likely to occur in situations of close contact, such as in large public gatherings, restaurants, cramped working spaces, and outdoor or indoor parties.

While vaccines can effectively slow down the contagious pandemic by increasing the herd immunity, preventive measures such as social distancing and masking are proven strategies along with vaccination in curbing the spread of the virus. “Even if people have been vaccinated, they can still get infected and can still spread the virus in the population. So that means variants have the chance to get more mutations or to evolve. It is important for people to stop giving the virus [that] chance,” says Sato. (**Emphasis added**).



Nurses attend to 20 COVID-19 patients inside Little Company of Mary Medical Center Friday, July 30, 2021 in Torrance, CA. The majority of these patients are unvaccinated.  
PHOTOGRAPH BY FRANCINE ORR, LOS ANGELES TIMES VIA GETTY

SCIENCE · CORONAVIRUS COVERAGE

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BY SANJAY MISHRA



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The secret to Delta's success is the ease with which it spreads. The CDC estimates that Delta can be as infectious as chicken pox and is only slightly less contagious than measles, which is considered one of the most transmissible viruses. Now the Delta variant is spreading like wildfire through the South, particularly in Louisiana, which has one of the lowest vaccination rates in the country; only 37 percent of the population is fully vaccinated compared to 50 percent nationally. In the U.S., daily cases are now averaging 100,000, a nine-fold jump from mid-June.

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