

First confirmed case of SARS-CoV-2 reinfection reported in Hong Kong



Enlarge / Medical staff wearing personal protective equipment (PPE) as a precautionary measure against the COVID-19 coronavirus approach Lei Muk Shue care home in Hong Kong on August 23, 2020.

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A healthy, 33-year-old man in Hong Kong is now the first person in the world confirmed to have been reinfected by the pandemic coronavirus, SARS-CoV-2—which has currently infected more than 23 million people worldwide.

The man's first infection was in late March. He reported having a cough with sputum, fever, sore throat, and a headache for three days before testing positive for the virus on March 26. Though his symptoms subsided days later, he was hospitalized on March 29 and remained in the hospital until April 14, when he tested negative for SARS-CoV-2 in two tests taken 24-hours apart.

About 4.5 months later, the man tested positive for the virus again. This time, his infection was caught during entry screening at a Hong Kong airport, as he returned from a trip to Spain, via the United Kingdom, on August 15. Though he had no symptoms, he was again hospitalized. Clinical data showed he had signs of an acute infection, but he remained asymptomatic throughout his time in the hospital.

Researchers decoded the entire genetic sequences of the SARS-CoV-2 viruses isolated from the man in both infections and found that his two infections were caused by clearly different strains of the coronavirus. The first strain looked much like SARS-CoV-2 strains collected in April and March in the United States and England. The second was closely related to strains collected in England and Switzerland in July and August. Overall, there were 24 genetic differences between the two infecting viral strains, including significant differences in the code for the infamous spike protein.

Hong Kong researchers report the case August 24 in a scientific study that was accepted, but not yet published, by the journal *Clinical Infectious Disease*. A draft version of the accepted study was released to Ars by the University of Hong Kong and a PDF is available [HERE](#). The PDF does not include the study's three figures, but the University released a phylogenetic tree (Figure 2), which you can see [HERE](#). Ars has requested the other figures and will update this text when they become available.

Don't panic

With tens of millions of cases around the globe that have accumulated over eight months, cases of reinfection are not surprising—or even necessarily concerning. Studies so far have suggested that immune responses to SARS-CoV-2 can be variable, meaning some people may develop stronger, more protective immune responses than others. There is mounting data suggesting that some immune responses can be completely protective against reinfection—at least for some period of time. From this new study, it's also rather encouraging that the man's second infection was even milder than the first—it was completely asymptomatic, in fact—hinting at helpful immune responses specifically against SARS-CoV-2.

Though there have been other, more anecdotal reports of reinfection, those have not been confirmed as this one has, with full genome sequencing and other data. And, while documenting this case is certainly important, it still leaves all of the most significant questions about SARS-CoV-2 immunity unanswered.

That is, we still don't know what levels of immune responses are necessary to prevent reinfection and/or disease. We still don't know what proportion of people develop such protective immune responses after an infection. And we don't know how long any protective immune responses last in *most* people.

Several studies have suggested that antibody responses to SARS-CoV-2 can wane after a two- to-three month period. Antibodies are the Y-shaped proteins that circulate in the body after an infection and are specifically designed to detect different bits of SARS-CoV-2. When they do, they can hail immune responses or even neutralize the virus completely, potentially thwarting another infection. Levels of antibodies naturally wane after an acute infection, but some researchers have expressed concern that anti-SARS-CoV-2 antibodies seem to

decline more quickly than expected. As such, some have speculated that protective immune responses against SARS-CoV-2 may resemble those seen from infections by other human coronaviruses, ones that cause common colds. Infections with those garden-variety coronaviruses typically only produce immunity that lasts on the scale of months rather than years or decades, and reinfections are common.

But again, all of this is still speculative. We don't know what levels of antibodies are necessary to protect against a second SARS-CoV-2 infection, let alone how long those levels last. So, we don't know if any of the declines measured are meaningful. Moreover, antibodies are not the only protective immune response to consider; there are also responses from immune cells, called B cells and T cells, that can be protective as well.

Wrinkles and limitations

It's also important to note that the case report on the confirmed reinfection has some interesting wrinkles and important limitations. For one thing, the researchers point out that the two strains of SARS-CoV-2 that infected the man had significant differences in their spike proteins.

Generally, each SARS-CoV-2 virus has many copies of spike protein jutting out from its spherical viral particle, much like the spikes of a sea mine. These protruding barbs can seize human proteins called ACE2 receptors, which stick out from the surface of some human cells. When this interaction occurs, it essentially opens the door to a SARS-CoV-2 viral infection into the ACE2-donning human cells.

Because the SARS-CoV-2 spike protein is so prominent on the viral particles, and so critical for infection, some of the most potent and neutralizing antibodies against SARS-CoV-2 target the spike protein. Some antibodies glom on to the specific bit of the spike protein used to interact with ACE2,

effectively blocking it from infecting cells.

But the researchers studying the man's reinfection found that the two SARS-CoV-2 strains that infected him have different spike proteins—there are four significant differences in the viruses' spike proteins, to be exact. These changes may have made it more difficult for anti-spike antibodies made after the first infection to recognize and neutralize the SARS-CoV-2 in the second infection. Thus, the researchers speculate, it may help explain the asymptomatic reinfection.

AWOL antibodies

But the point is perhaps undercut by an oddity in the data. The researchers looked at the reinfected man's antibody levels in blood collected 10 days after the onset of his first infection—and they didn't find antibodies. In this case, they were looking for antibodies that target the SARS-CoV-2 nucleoprotein, which is protein associated with the virus' genetic material. Antibodies against nucleoprotein usually show up in people faster than antibodies against the spike protein. However, the man didn't seem to have any 10 days after developing symptoms in his first infection.

The researchers speculate that he may not have developed any antibodies to the infection. Alternatively, he may have developed antibodies very quickly and the levels dropped equally fast, or he could have developed antibodies *after* the 10 days. After the second infection, they looked for antibodies one, three, and five days after he tested positive. They only detected antibodies on the fifth day.

Earlier studies have suggested that most people infected with SARS-CoV-2 do indeed develop antibodies against the coronavirus. So, the lack of antibody detection after the man's first infection raises questions about how common his experience of reinfection might be. That said, since the researchers only had a blood sample from the one time point—10

days—after his first infection, it's impossible to draw any firm conclusions.

Overall, the case does indicate that reinfection with SARS-CoV-2 is *possible*. But the more important questions—such as how *probable* reinfection is and how long protective immune responses *usually* last—remain unanswered.

For now, the researchers say that people who have recovered from a SARS-CoV-2 infection should continue to follow masking and distancing measures to be safe. They should also be considered for vaccination. And of course, “further studies on re-infection, which will be vital for the research and development of more effective vaccines, are warranted,” they conclude.

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