



# Covid-19: WHO and South Korea investigate reconfirmed cases

Elisabeth Mahase

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The World Health Organization and South Korea are investigating how several covid-19 patients who were believed to have recovered from the virus and had tested negative later tested positive.

The Korea Centers for Disease Control and Prevention (KCDC) reported on 10 April that it was “investigating the epidemiological and/or clinical characteristics of 91 cases that have re-tested positive after being discharged from isolation.”<sup>1</sup>

It said that central and local teams were “conducting joint, in-depth investigations (including virus isolation culture, blood antibody test) to confirm infectivity.”

WHO has said that it is aware of the reports. A spokesperson told *Reuters*, “We are closely liaising with our clinical experts and working hard to get more information on those individual cases. It is important to make sure that, when samples are collected for testing on suspected patients, procedures are followed properly.”<sup>2</sup>

## Re-detection and reinfection

Sung-Il Cho, professor of epidemiology at Seoul National University Graduate School of Public Health in South Korea, told *The BMJ* that this issue had “made us think harder about antibody testing. The KCDC is now trying to establish antibody testing in addition to the PCR [polymerase chain reaction] testing. We have been seeing quite a few cases of patients returning to positive . . . Whether those were re-detected or reinfected cases remains the question. Antibody testing may help distinguish between the two.”

Cho continued, “Re-detection because of clinical relapse will be indicated by not enough neutralising antibodies. Re-detection in this case is likely to be that the virus dropped to a low enough level to be negative in the test, but later increased.

“For reinfection, although unlikely, history of another exposure and positive virus culture is needed. Serologic test results may be variable, depending on the timing. Neutralising antibodies must be low for reinfection to occur, but they may rise during the reinfected period.”

He added that there was a third option: a false positive result. In that case, he explained, the “virus culture must be negative, and the neutralising antibodies would be high. However, some recovered patients may still have undetectably low levels of neutralising antibodies.”

Cho has advised that all discharged patients should “remain isolated or quarantined for a while to make sure no re-detection is observed.”

## Antibody response

As the importance of antibody testing for covid-19 becomes clearer, researchers are trying to understand the antibody response to the virus. A pre-print<sup>3</sup> of a research paper has looked at the antibody response to covid-19 in 175 recovered patients who had mild symptoms and were treated at Shanghai Public Health Clinical Center in China. It found that neutralising antibodies (NAbs) were detected in patients from day 10 to day 15 after the onset of the disease and remained throughout the two week follow-up period.

The paper, which has yet to be peer reviewed, also highlighted that elderly and middle aged patients had “significantly higher plasma NAb titers and spike-binding antibodies than young patients.”

Meanwhile, around 30% of patients failed to develop high titres of NAbs after covid-19 infection. Despite this, the researchers noted that their disease duration was similar to that of the other patients.

They wrote, “Notably, there were ten recovered patients whose NAb titers were very low, under the detectable level of this study (ID50: <40), suggesting that other immune responses, including T cells or cytokines, may contribute to the recovery of these patients.

“Whether these patients were at high risk of rebound or reinfection should be explored in further studies. On the other hand, two patients had very high titer of NAbs, which were over ID50: 15989 and 21567 respectively, but did not show any antibody-related adverse reactions.”

## Sensitivity

Paul Hunter, professor in medicine at the University of East Anglia, UK, said, “If many people only produce low levels of antibodies to SARS-CoV-2 then any community test would need to have high sensitivity. This provides further insight about why community antibody tests in the UK have not yet been authorised for use.”

Eleanor Riley, professor of immunology and infectious disease at the University of Edinburgh, added, “The results of this study are pretty much as one might expect for any respiratory virus,

suggesting that there is nothing terribly unusual about the antibody response to the covid-19 virus. This is reassuring.”

The study authors noted some limitations, including that viral load data were not available and that patients in severe and critical condition were excluded from the study because they had received passive antibody treatment before sample collection.

- 1 Korea Centers for Disease Control and Prevention. The updates on COVID-19 in Korea as of 10 April. 10 Apr 2020. <https://www.cdc.go.kr/board/board.es?mid=a30402000000&bid=0030>.
- 2 Nebehay S. WHO is investigating reports of recovered COVID patients testing positive again. *Reuters* 2020 Apr 11. <https://www.reuters.com/article/us-health-coronavirus-who/who-says-looking-into-reports-of-some-covid-patients-testing-positive-again-idUSKCN21T0F1?il=0>.
- 3 Wu F, Wang A, Liu M, et al. Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. 6 Apr 2020. <https://www.medrxiv.org/content/10.1101/2020.03.30.20047365v1>.

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