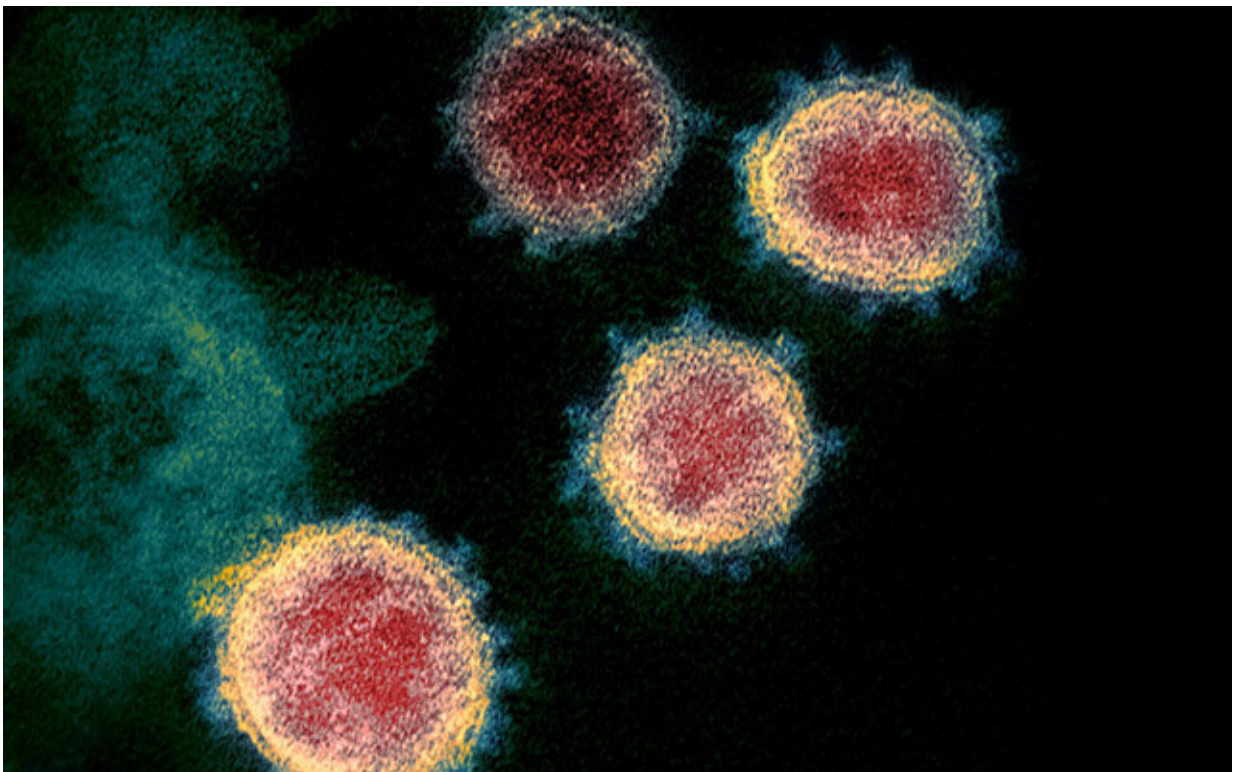


Infectiousness peaks early in COVID-19 patients, emphasising the need to rapidly isolate cases: study

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A colorized scanning electron micrograph of the SARS-CoV-2 virus. Credit: NIAID

Although SARS-CoV-2 genetic material may still be detected in respiratory or stool samples for several weeks, no live virus (that can

cause infection) was found in any type of sample collected beyond nine days of symptoms starting and people with SARS-CoV-2 are mostly likely to be highly infectious from symptom onset and the following five days, according to a systematic review and meta-analysis of three human coronaviruses published in *The Lancet Microbe* journal.

"This is the first systematic review and meta-analysis that has comprehensively examined and compared [viral load](#) and shedding for these three human coronaviruses. It provides a clear explanation for why SARS-CoV-2 spreads more efficiently than SARS-CoV and MERS-CoV and is so much more difficult to contain," says lead author Dr. Muge Cevik of the University of St Andrews, UK.

"Our findings are in line with contact tracing studies which suggest the majority of viral transmission events occur very early, and especially within the first 5 days after symptom onset, indicating the importance of self-isolation immediately after symptoms start. We also need to raise public awareness about the range of symptoms linked with the disease, including mild symptoms that may occur earlier on in the course of the infection than those that are more prominent like cough or fever."

This study specifically looked at people infected with SARS-CoV-2 and mainly those who were hospitalised, so the results are only relevant for the period of self-isolation for people with confirmed COVID-19, and do not apply to people quarantining who may or may not have been exposed after contact with someone infected. Many countries currently recommend that people with a SARS-CoV-2 infection should self-isolate for 10 days, which the authors say is in line with their findings, cautiously covering the period of infectiousness.

Understanding when patients are most likely to be infectious is of critical importance for informing effective public health measures to control the spread of SARS-CoV-2. This study looked at key factors

involved in this: viral load (how the amount of the [virus](#) in the body changes throughout infection), viral RNA shedding (the length of time someone sheds viral [genetic material](#) (RNA), which does not necessarily indicate a person is infectious, as this is not necessarily able to replicate), and isolation of the live virus (a stronger indicator of a person's infectiousness, as the live virus is isolated and tested to see if it can successfully replicate in the laboratory).

The researchers included 98 studies that had five or more participants, cohort studies and randomised controlled trials; 79 focussed on SARS-CoV-2, 73 of which included hospitalised patients only; eight on SARS-CoV; and 11 on MERS-CoV infection. From these studies, the authors calculated the average length of viral RNA shedding and examined the changes in viral load and the success of isolating the live virus from different samples collected throughout an infection.

Analysing the results from the SARS-CoV-2 studies showed that the average length of time of viral RNA shedding into the [upper respiratory tract](#), lower respiratory tract, stool and serum were 17 days, 14.6 days, 17.2 days and 16.6 days, respectively. The longest length of time that RNA shedding lasted was 83, 59, 35 and 60 days, respectively.

Of the eleven studies that attempted to isolate the live virus, all eight studies included that used respiratory samples successfully managed to culture viable virus within the first week of illness. Of the studies that also measured RNA viral load, these demonstrated a link between the success of isolating the live virus with viral load levels. No study included in this systematic review managed to successfully isolate live virus beyond day nine of symptoms in any type of sample, despite persistently high viral RNA loads. So far, only a few studies successfully isolated the live virus from [stool samples](#) despite prolonged RNA shedding, and the role of oral-faecal transmission for SARS-CoV-2 remains unclear.

"These findings suggest that in clinical practice, repeat PCR testing may not be needed to deem that a patient is no longer infectious, as this could remain positive for much longer and does not necessarily indicate they could pass on the virus to others. In patients with non-severe symptoms, their period of infectiousness could instead be counted as 10 days from [symptom](#) onset," says Dr. Cevik.

The highest viral load of SARS-CoV-2 RNA were detected early in the course of the disease—at the time symptoms begin, or before day five of symptoms. In contrast, the viral loads of MERS-CoV peaked at 10-14 days and 7-10 days after [symptom onset](#), respectively—explaining why transmission of these viruses can be effectively reduced by immediate identification, isolation and quarantine of people who show symptoms of the disease.

Only twelve studies reported on asymptomatic individuals infected with SARS-CoV-2 and of those, six also looked at how quickly people cleared the viral material out of their body.

"Although viral RNA loads appear to be largely similar between those with and without symptoms, a few studies suggest that asymptomatic individuals might clear the viral material from their bodies faster," says Dr. Cevik. "Several studies have found that individuals with asymptomatic infection may clear the virus faster, suggesting that those without symptoms may be as infectious as those with symptoms at the beginning of infection, but may be infectious for a shorter period. However, at this stage, there are limited data available on the shedding of infectious virus in asymptomatic individuals to inform any policy change on quarantine duration in the absence of testing."

This is the most comprehensive study of these three respiratory coronaviruses to date and is larger than the previous one meta-analysis on SARS-CoV-2, but the authors note some limitations. Many of the

patients across the different studies included in the [systematic review](#) and meta-analysis were hospitalised and received a range of treatments that may affect the course of their infection, the studies included different populations who were followed up and managed differently, and in the interpretation of statistics used to measure the length of viral shedding. The period of infectiousness may also not exactly align with the successful culturing of the live virus from samples, although these are likely to broadly overlap.

"The majority of studies included in our review were performed in patients who were admitted to hospital. Therefore, our findings may not apply to people with milder [infection](#) although these results suggest those with milder cases may clear the virus faster from their body. Additionally, the increasing deployment of treatments, such as dexamethasone, remdesivir as well as other antivirals and immunomodulators in clinical trials are likely to influence viral shedding in hospitalised patients. Further studies on viral shedding in this context are needed" says senior author, Dr. Antonia Ho of MRC-University of Glasgow Centre for Virus Research, UK.

More information: SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis, [DOI: 10.1016/S2666-5247\(20\)30172-5](#) , [www.thelancet.com/journals/lan ... \(20\)30172-5/fulltext](#)

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