



## EDITORIALS

# Persistence of viral RNA in stool samples from patients recovering from covid-19

PCR has limitations, and isolating patients for a month or more may not be feasible isolation

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Isolation has long been regarded as the most effective safeguard against the spread of infectious diseases, and during the current covid-19 pandemic many thousands of potentially infected patients have been isolated globally. Different opinions exist about the duration of isolation, not least because data on the persistence and infectivity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in various body fluids have been scarce.

In the linked study, Zheng and colleagues (doi:10.1136/bmj.m1443) describe viral load dynamics in 96 patients with SARS-CoV-2.<sup>1</sup> Viral loads in respiratory samples, stool, serum, and urine were tested using polymerase chain reaction (PCR) techniques during four weeks of hospital admission. At the end of these four weeks more than half of the patients still tested positive for SARS-CoV-2 in respiratory samples and a third of patients in stool samples using PCR, findings with worrying implications for disease control.

In contrast, all samples in a small European case series, including those from nasopharyngeal swabs and stools, became SARS-CoV-2 negative within two weeks for all surviving patients.<sup>2</sup> It is not clear whether these differences reflect different clinical courses or differences in PCR test characteristics.

PCR was first used more than 30 years ago in a paper describing a novel enzymatic amplification of nucleic acid.<sup>3</sup> Since then technical improvements have made PCR the tool of choice for specific enzymatic amplification of nucleic acid in vitro.<sup>4</sup> An important limitation of PCR testing, however, is the inability to differentiate between actual viral replication and the detection of non-viable, and therefore non-infectious, viral material. This has been a key challenge in previous epidemics when assessing the infectiveness of recovering patients and determining the clinical relevance of detecting viral RNA in stools is particularly difficult. In Ebola virus disease, viral RNA has been found in stool samples after clearance of viraemia in blood in recovering patients, yet attempts to recover virus from cell cultures have so far failed.<sup>5,6</sup> Similarly, in patients with Middle East respiratory

syndrome (MERS) coronavirus infection, RNA was usually detected from faeces, but viral isolation trials had negative outcomes.<sup>7</sup>

During the 2002-03 SARS-CoV-1 pandemic, reports of positive PCR results in stool were also reported. These data, combined with observations of indirect transmission through contaminated surfaces and fomites, led to the suggestion of faecal-oral transmission of SARS-CoV-1.<sup>8,9</sup>

So what can we conclude from the linked study? Is it better to be safe than sorry and should patients be kept in isolation as long as they show signs of viral RNA shedding? In terms of containment of the disease this could be advocated. However, the impact on health care systems, virology laboratories, and, most importantly, patients kept in isolation for at least a month, would be enormous. However, meticulous hand and toilet hygiene could be warranted and should reduce considerably the clinical relevance of viral shedding from stool.<sup>10</sup>

It remains necessary to accept some uncertainties in these challenging times and to rely on clinical improvement from covid-19 to inform strategies for ending isolation. Such uncertainty is reflected in proposals from institutions such as the US Centers for Disease Control and Prevention, the National Health Service, and European Centre for Disease Prevention and Control, all of which advocate combinations of testing and other public health measures to reduce the risk of transmission.<sup>11-13</sup>

More epidemiological data, testing, and mathematical modelling will be needed to fully understand the clinical relevance of viral shedding from various body fluids in patients recovering from covid-19. Meanwhile, policy makers, healthcare workers, and patients should continue to cooperate to make the best use of available scientific and clinical knowledge to limit the spread of the virus, without putting too much strain on healthcare systems that are already stretched to their limits.

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