



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



## Letter to the Editor

## Patients with COVID-19: are current isolation guidelines effective enough?



As the coronavirus disease 2019 (COVID-19) pandemic continues to evolve, the number of cases and the death toll continue to rise, posing a substantial threat to global public health. As of April 23, 2020, the United States (US) has the highest number of COVID-19 cases (31.5%) and deaths (22.8%) in the world.<sup>1</sup> Both clinicians and hospitalized patients are facing complications including limited resources, workforce, and information, thus making infection control an even higher priority. The median basic reproduction number ( $R_0$ ) of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is estimated to be 5.7 (95% confidence interval, 3.8–8.9);<sup>2</sup> this value holds great significance as, theoretically, an infection will continue to spread as long as  $R_0 > 1$ . With growing concern, the focus needs to shift toward strategies to mitigate the spread of infection in both hospital and community settings alike. We believe the current isolation guidelines need to be revisited and clinicians should counsel patients with COVID-19 to practice contact precautions for longer duration, given the new evidence suggesting the possibility of a fecal-oral route of transmission.

According to current Centers for Disease Control and Prevention (CDC) recommendations, discontinuation of transmission-based precautions as per the test-based strategy in patients with COVID-19 is warranted after all of the following: (1) resolution of fever without the use of fever-reducing medications; (2) improvement in respiratory symptoms; and (3) two consecutive negative reverse transcriptase polymerase chain reaction (rRT-PCR) results of nasopharyngeal swabs obtained at least 24 h apart.<sup>3</sup> For asymptomatic individuals, contact precautions can be discontinued seven days after diagnosis; should they remain asymptomatic three days after the discontinuation, individuals should still practice social distancing and nasal/oral barrier protection.<sup>3</sup>

To date, COVID-19 has been thought to be transmitted via respiratory droplets, with most patients commonly presenting with fever, cough, or dyspnea. However, studies have also reported gastrointestinal manifestations including diarrhea, nausea, vomiting, and abdominal discomfort in addition to respiratory symptoms.<sup>4</sup> When selectively tested, 28 of 42 patients were positive for SARS-CoV-2 viral RNA on rRT-PCR in both nasopharyngeal and fecal specimens.<sup>5</sup> Detecting extrapulmonary viral RNA does not necessarily confirm the presence of infectious virions; however, active infection cannot be excluded. Studies have found that viral shedding of SARS-CoV-2 RNA in feces occurred even after testing negative in nasopharyngeal swabs, having lasted for approximately seven days.<sup>4,5</sup> In a study from China, 41 of 74 patients had both fecal and respiratory samples tested positive for SARS-CoV-2 RNA, with stool samples showing positive results for longer periods than respiratory samples (days after onset of first symptom,  $27.9 \pm 10.7$

versus  $16.7 \pm 6.7$ ).<sup>6</sup> In a case series conducted examining the first 12 patients with COVID-19 in the US, SARS-CoV-2 RNA was detected in the stool sample of 7 of 10 patients.<sup>7</sup> Furthermore, a recent case reported an asymptomatic patient with COVID-19 who retested positive for SARS-CoV-2 despite being discharged after two negative consecutive respiratory nucleic acid tests at least 24 h apart, raising concern for inadequate discharge protocol. Notably, he was found to have a weakly positive stool sample test during his observation. Should these patients remain contagious and prematurely discontinue self-isolation, they may disrupt current infection control.<sup>8</sup> Moreover, to date, one study has successfully cultured live SARS-CoV-2 from a fecal specimen, with implications that stool samples may contaminate hands, food, water, and so on.<sup>9</sup>

The resilience of SARS-CoV-2 plays a role in its virulence and pathogenesis. Owing to its hard outer shell, the virus can remain active for extended periods of time and may be more resistant to antimicrobial and digestive enzymes in body fluids.<sup>10</sup> In addition, as per nucleocapsid and membrane protein analysis, SARS-CoV-2 has been classified as category B, which means it has intermediate grades of both respiratory and fecal-oral transmission potentials.<sup>10</sup> A study suggested that the half-life of the aerosolized form of SARS-CoV-2 is approximated to be 1.1–1.2 h. However, it was found to remain viable on wooden and metal surfaces for up to 72 h, supporting a concern for indirect transmission beyond respiratory particles.<sup>11</sup>

Given the possibility of fecal-oral transmission, evidence noting the occurrence of viral RNA shedding in feces for up to a month, and the current state of the pandemic, we believe it is reasonable to extend the duration of contact isolation precautions as currently outlined by the CDC for patients with COVID-19 in efforts to strengthen infection control. If patients with COVID-19 were discharged home or to a nursing home facility based solely on two negative respiratory samples, it could put families, close contacts, and/or healthcare providers at risk because of the yet unknown full transmission potential of COVID-19. Healthcare providers should also exercise additional precautions when transferring patients with COVID-19 within the hospital or de-escalating levels of care. However, with current limitations in the supply of personal protective equipment, prolonged self-isolation may prove beneficial for adequate infection control while conserving resources. The consideration of testing for viral RNA by PCR in fecal samples, in addition to respiratory samples, to confirm recovery of active COVID-19, may offer clinicians guidance as to the duration of isolation precautions for patients on discharge.

What recommendations should clinicians provide patients amid the COVID-19 pandemic? Those exhibiting gastrointestinal

symptoms with high probability of COVID-19 infection should practice extended periods of contact precautions for at least 4 weeks, given the data that suggest that viral RNA sheds in feces beyond a month. They should also be educated on contact precautions and preventive measures to minimize fecal-oral transmission until further definitive evidence arises confirming or disproving such a route. Clinicians should emphasize education as a non-invasive means of infection control. Patients should be advised that close contacts are at high risk and that they may be at risk of reinfection themselves. The World Health Organization recommends effective preventive measures in the community including frequent hand hygiene using an alcohol-based solution or soap and water; avoiding touching the eyes, nose, and mouth; practicing respiratory hygiene; and maintaining social distance.<sup>12</sup>

Currently, time and resources are limited, but our efforts should not be. The COVID-19 pandemic is a public health emergency, and clinicians need to act accordingly. With consideration of its high virulence, high infectivity, and the concern for a fecal-oral route of transmission, we suggest modifying guidelines to extend isolation and/or contact precautions in the best interest of patients, healthcare workers, and the global community as a whole.

### Conflicts of interest

The authors declare no conflicts of interests.

### References

- World Health Organization. *Coronavirus disease 2019 (COVID-19) situation report – 94* [Internet]. World Health Organization; 2020 Nov. Available from: [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200423-sitrep-94-covid-19.pdf?sfvrsn=b8304bf0\\_4](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200423-sitrep-94-covid-19.pdf?sfvrsn=b8304bf0_4).
- Sanche S, Lin YT, Xu C, et al. High contagiousness and rapid spread of Severe acute respiratory syndrome coronavirus 2. *Emerg Infect Dis* 2020;**26**(7).
- Disposition of non-hospitalized patients with COVID-19* [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2020. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html>.
- Gu J, Han B, Wang J. COVID-19: gastrointestinal manifestations and potential fecal–oral transmission. *Gastroenterology* 2020;**158**(6):1518–9.
- Chen Y, Chen L, Deng Q, et al. The presence of SARS-CoV-2 RNA in feces of COVID-19 patients. *J Med Virol* 2020 Mar.
- Wu Y, Guo C, Tang L, et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. *Lancet Gastroenterol Hepatol* 2020;**5**(5):434–5.
- Kujawski S, et al. *First 12 patients with coronavirus disease 2019 (COVID-19) in the United States*. Preprint at, <https://www.medrxiv.org/content/10.1101/2020.03.09.20032896v1>; 2020.
- Zhang J-F, Yan K, Ye H-H, et al. SARS-CoV-2 turned positive in a discharged patient with COVID-19 arouses concern regarding the present standard for discharge. *Int J Infect Dis* 2020.
- Zhang Y, Chen C, Zhu S, et al. Isolation of 2019-nCoV from a stool specimen of a laboratory-confirmed case of the coronavirus disease 2019 (COVID-19). *China CDC Weekly* 2020;**2**(8):123–4 (in Chinese).
- Goh GK-M, Dunker AK, Foster JA, et al. Shell disorder analysis predicts greater resilience of the SARS-CoV-2 (COVID-19) outside the body and in body fluids. *Microb Pathog* 2020;**144**:104177.
- Doremalen NV, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med* 2020;**382**(16):1564–7.
- Rational use of personal protective equipment for coronavirus disease (COVID-19) and considerations during severe shortages: interim guidance, 6 April 2020* [Internet]. World Health Organization; 2020. Available from: <https://extranet.who.int/iris/restricted/handle/10665/331695>.

K.P. Patel\*

Department of Internal Medicine, University of Nebraska Medical Center College of Medicine, Omaha, NE, USA

P.A. Patel

Nova Southeastern University Kiran C. Patel College of Osteopathic Medicine, Fort Lauderdale, FL, USA

S.R. Vunnam

Department of Internal Medicine, University of Nebraska Medical Center College of Medicine, Omaha, NE, USA

R. Jain, R.R. Vunnam

Division of Hospital Medicine, Penn State Health Milton S. Hershey Medical Center, College of Medicine, Hershey, PA, USA

\* Corresponding author. Department of Internal Medicine, University of Nebraska College of Medicine, 985520 Nebraska Medical Center, Omaha, NE, 68198, USA.

E-mail address: [kishanp.patel@unmc.edu](mailto:kishanp.patel@unmc.edu) (K.P. Patel).

24 April 2020

Available online 11 May 2020