What is the role of SARS-CoV-2 PCR testing in discontinuation of transmission-based precautions for COVID-19 patients?

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Dear Editor- The US Centers for Disease Control and Prevention, the European Centre for Disease Prevention and Control and other national bodies currently recommend that isolation of patients with Coronavirus disease 19 (COVID-19) can be stopped after resolution of fever, improvement in respiratory symptoms and two negative severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA PCRs from at least two consecutive respiratory specimens collected ≥24 hours apart [1,2]. Recently, Yuan et al reported on 25 COVID-19 patients that had significant reduction in respiratory symptoms and pulmonary radiological findings and at least two negative consecutive SARS-CoV-2 PCR tests separated by at least 24-hour interval and after treatment with ritonavir/lopinavir and an average hospital stay of 15.36 days. While in self-quarantine, these 25 patients had positive PCR (14 anal, 11 nasopharyngeal), 7.32 and 5.23 days on average since last negative PCR was taken and discharge, respectively. Within an average of 2.73 days after readmission to the hospital, all 25 patients had again negative PCR results[3]. These findings support previous report that showed that 21.4% COVID-19 patients had positive PCR test results after 2 consecutive negative PCR tests[4].

The authors concluded that additional testing should therefore be done before discontinuing transmission-based precautions for COVID-19 patients. However, different factors could explain these findings and should be carefully investigated before such data are used to guide policy mandating additional testing. First, these cases could represent false negative results of SARS-CoV-2 PCR. False negative results of SARS-CoV-2 PCRs performed on pharyngeal swabs have been reported early in the course of illness of some COVID-19 patients, which turned positive as the disease advanced[5,6]. False negative results could be caused by inappropriate sampling, sampling of anatomical sites with lower viral load, or the use of PCR tests with low sensitivity. Second, intermittent shedding of SARS-CoV-2 can result in fluctuation in the results of PCR during the course of illness, and this has been reported in COVID-19 patients[6]. Third, it remains a question whether these patients had a relapse (i.e. reactivation) of the same infecting SARS-CoV-2 strain after true virological recovery. Fourth, it remains to be investigated whether reinfection with SARS-CoV-2 with identical or slightly different strains can happen. It is also critical to know whether SARS-CoV-2 detected late in the course of illness and after patients are discharged represents viable or dead viruses.

Recently, data from 9 patients with COVID-19 showed that while SARS-CoV-2 was detected by PCR 3 weeks after illness onset, live virus was not isolated beyond 7 days even though RT-PCR detection persisted often for more than 14 – 21 days[7]. While this small study of live virus shedding in COVID-19, there have been numerous studies of other viral infections that have shown that live virus shedding is universally much shorter than PCR detection durations [8,9].

The requirement to have more than 2 negative PCR results in order to routinely remove isolation precautions for hospitalized patients requires additional data to provide rigorous justification. Implications on testing resources and personal protective equipment utilization would be significant and there is currently no evidence to suggest that these patients with very low levels of intermittent viral RNA detection are in fact infectious. Data are required on the shedding of viable SARS-CoV-2 in different populations, including those with co-morbidities, immunosuppression and different age groups, before data such as these are used to guide policy.

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