COVID-19 Real-Time RT-PCR: Does Positivity on Follow-up RT-PCR Always Imply Infectivity?

To the Editor:

We read with interest the study by Chang and colleagues, wherein they have addressed the important question relating the duration of coronavirus disease (COVID-19) symptoms with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral positivity on real-time PCR. Among 16 patients with predominantly mild disease, they found that the median duration of symptoms was 8 days. They found that eight patients remained positive by real-time PCR beyond symptom resolution for a median of 2.5 days after clinical recovery (1). These findings are in congruence with the work of Young and colleagues, who reported that SARS-CoV-2 remained detectable by PCR in nasopharyngeal swabs for a median duration of 12.5 days after symptom onset. Furthermore, viral positivity by PCR outlived symptoms in half of their patients as well (2).

We noted that in the present study, Chang and colleagues have erroneously pointed to an instance of disease transmission from a patient after symptom resolution. However, on perusal of the cited report, contact between the index case and secondary cases occurred before the onset of symptoms in the index case. The discovery of the contagion occurred subsequent to the recovery of the index case who remained PCR positive on nasopharyngeal swab and sputum at this time (3). High communicability of COVID-19 in the presymptomatic and early symptomatic phase has been pointed out in epidemiologic modeling studies also (4).

The natural question that emerges is where does this leave us in terms of contagiousness of patients who have symptomatically recovered? Though there is no definitive answer to this, many organizations have promulgated a test-based discharge strategy. This implies that patients may be discharged from the hospital only after they have two negative PCR test results 24 hours apart on their nasopharyngeal swabs to prevent disease transmission. However, there is already a shortage of testing to detect new cases in most countries around the world, thus placing immense strain on a stretched public health response.

In this regard, it must be stressed that positivity on PCR does not necessarily translate to infectivity in respiratory viral illnesses. Inagaki and colleagues have demonstrated in a ferret model that transmission of influenza occurred until only 5 days after the experimental infection of donor ferrets. This period correlated with culture positivity and antigen detectability. In contrast, PCR positivity continued for 11–13 days after inoculation of the donor ferrets (5).

Interestingly, Wölfel and colleagues examined nine patients with mild COVID-19 infection for the correlation between PCR and viral culture results. They found that despite symptomatic recovery, the patients continued to have detectable SARS-CoV-2 RNA by PCR on nasopharyngeal swab for around 2 weeks. On the contrary, peak viral shedding occurred early in the course of illness; all viral cultures beyond Day 8 were negative despite positive PCR. Furthermore, SARS-CoV-2 genomic replication was not observed beyond 1 week on respiratory samples (6). This coincides with the findings of He and colleagues that patients are unlikely to be infectious beyond 1 week despite positive PCR (4). Therefore, we need to find newer tools to judge infectivity beyond symptom resolution and revise the hospital discharge (or ending isolation) criteria, especially in mild cases who have recovered clinically. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Author Contributions: All authors contributed equally to the manuscript.

Originally Published in Press as DOI: 10.1164/rccm.202004-1287LE on May 13, 2020