

Re-Testing Patients for COVID-19 after Symptomatic Recovery: a Work in Progress

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INTRODUCTION

As the coronavirus disease 2019 (COVID-19) pandemic slowly begins to resolve, preparations are being made to re-open businesses and schools across the USA, and individuals who have recovered from COVID-19 will need to return to work with appropriate modifications. Patients and clinicians are currently faced with conflicting information and recommendations about when it is safe for patients who have had COVID-19 to terminate their quarantine and return to work. This article presents the case of a patient trying to return to work after having COVID-19, and then discusses the challenges posed by current clinical guidelines.

CASE PRESENTATION

JA is a 59-year-old male with diet-controlled hyperlipidemia and no other medical history who works in maintenance at a skilled nursing and assisted living facility in Massachusetts. In early April, he developed fatigue, myalgia, and decreased appetite over the course of 3–4 days. Several residents and other employees at his workplace had tested positive for SARS-CoV-2. On April 10, he developed chills, headache, and pressure behind his eyes, prompting him to call the COVID-19 hotline at his primary care physician's office (Fig. 1). The patient had a nasal swab at the facility's drive-through testing center on April 11 and received a positive result on April 12. He self-quarantined at home with care from his wife, who is a registered nurse. His symptoms remained mild with no cough or shortness of breath. On April 15, he had an episode of convulsive syncope in the setting of fever of 101.7 °F, for which he was treated briefly at the emergency department and followed up with telemedicine visits with his PCP and a neurologist. Within the next week, the patient's symptoms largely resolved and he felt ready to return to work. His last fever of 99.5 °F was on April 22. Because JA works in

a high-risk environment for transmission of COVID-19, his primary care physician ordered a repeat nasal swab test on April 28, which was positive for SARS-CoV-2 RNA. Two additional nasal swabs were positive on May 7 and May 18. Finally, on May 29, a fourth test resulted negative and JA was able to return to work. JA's case highlights several important clinical and public health issues currently facing physicians and patients dealing with COVID-19.

DISCUSSION

Current Guidelines

The Centers for Disease Control and Prevention (CDC) currently offers two strategies for determining when it is safe for a patient who has had symptomatic COVID-19 to terminate quarantine: a symptom-based strategy and a test-based strategy.¹ Both strategies require the patient to be afebrile and have an improvement in respiratory symptoms (Table 1). Recommendations from the Massachusetts Department of Health are consistent with the CDC's guidance.²

As of April 25, patient JA met criteria to terminate his quarantine by the symptom-based strategy (3 days since last fever, > 10 days since symptom onset, and never had respiratory symptoms). However, because his work brings him into contact with a high-risk elderly population, his primary care physician wanted to be sure that JA was not infectious before returning to work. With multiple positive repeat nasal swab tests, JA did not meet criteria for termination of quarantine according to the CDC's test-based strategy until May 29.

The Trouble with Qualitative Test Results

Like most patients across the USA, JA's nasal specimen was tested with reverse transcriptase polymerase chain reaction (RT-PCR), which detects the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral RNA and is reported to the clinician as "detected" or "not detected." When considering if it is safe for a patient to return to work, clinicians need to know whether a positive RT-PCR test result means that the patient is actually *infectious*, that is, the patient risks infecting others in the workplace. In our patient's case, his positive test result was accompanied in the electronic medical record by a message from the reference laboratory,

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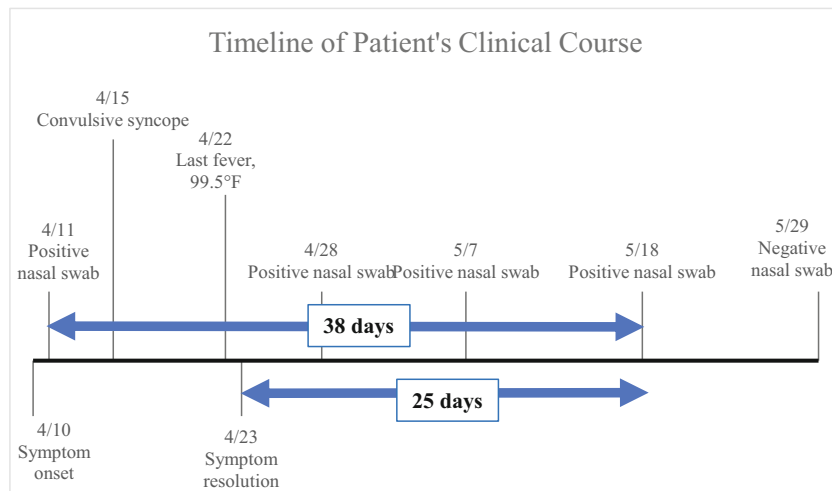


Figure 1 Timeline of patient’s clinical course.

reading, “A Detected result indicates that RNA from SARS-CoV-2 was detected, and the patient is infected with the virus and presumed to be contagious.” On the other hand, the CDC cautions clinicians that “detecting viral RNA via PCR does not necessarily mean that infectious virus is present.”¹ Indeed, a recent study from France found that viral cultures could not be grown from nasopharyngeal samples with quantitative PCR (qPCR) Ct values of greater than or equal to 33 or 34.³ In other words, qPCR testing can be used to determine whether or not a patient’s nasopharyngeal sample contains enough viral RNA to be infectious. In contrast, the results of RT-PCR currently being reported for most patients in the USA are qualitative, simply reporting whether or not viral RNA was detected but providing no insight into the quantity of RNA present.

Prolonged Viral Shedding and Termination of Quarantine

Growing evidence suggests that some patients may continue to have positive nasal swab tests for many weeks after the resolution of symptoms. Retrospective cohort studies among hospitalized patients in China have found median durations of viral shedding ranging from 17 days (IQR 13–22 days)⁴ to 20 days (IQR 17–24 days),⁵ and maximum duration up to 37 days.⁵ A 71-year-old woman in France was found to be shedding viral RNA for 36 days after symptom resolution and

a total of 60 days from symptom onset.⁶ Additionally, a case series from China found positive RT-PCR tests in several patients 7 days after they had already achieved full symptomatic recovery *and* had two consecutive negative RT-PCR tests.⁷ Our patient JA had repeated positive test results for 38 days after symptom onset and 25 days after full symptomatic recovery.

As the economy reopens in the USA, there may be thousands of patients who continue to have positive RT-PCR tests despite full symptomatic recovery: how should clinicians and public health officials regard these positive test results when the link with infectiousness is unclear? In the case of JA, his work in maintenance at a skilled nursing facility is considered essential, so it was important for him to return as soon as possible; however, the residents at his workplace are a high-risk population for contracting COVID-19 so it was imperative that he not be contagious when he returned to work. This case illustrates the questionable utility of RT-PCR for re-testing individuals who have achieved full symptomatic recovery from COVID-19.

One hospital in France is using q-PCR to identify patients whose viral loads are low enough to be considered non-contagious and, therefore, safe to be released from the hospital or home quarantine.³ Hospitals, health systems, and laboratories in the USA should focus efforts on deploying q-PCR tests for patients who need to return to work in high-risk environments (e.g., healthcare settings, or working with the elderly). For patients with lower-risk occupations whose symptoms have resolved, repeat RT-PCR testing should be used cautiously so as not to waste resources or unnecessarily delay return-to-work. Under the current guidelines, the CDC’s symptom-based strategy may be more effective and efficient than the test-based strategy for helping patients with low-risk occupations return to work both quickly and safely.

Table 1 Recommendations for Termination of Quarantine for Patients with Symptomatic COVID-19 as of May 10, 2020

| Symptom-based strategy | Test-based strategy |
|---|---|
| <ul style="list-style-type: none"> At least 3 days (72 h) have passed <i>since recovery</i> defined as resolution of fever without the use of fever-reducing medications <i>and</i> Improvement in respiratory symptoms (e.g., cough, shortness of breath); <i>and</i>, At least 10 days have passed <i>since symptoms first appeared</i>. | <ul style="list-style-type: none"> Resolution of fever <i>without</i> the use of fever-reducing medications <i>and</i> Improvement in respiratory symptoms (e.g., cough, shortness of breath), <i>and</i> Negative results of two consecutive respiratory specimens collected ≥ 24 h apart |

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Compliance with Ethical Standards:

Conflict of Interest: The authors declare that they do not have a conflict of interest.

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