

## COVID-19 Recovery: Duration of Isolation and Precautions for Adults and Potential Treatment for Post-Intensive Care Syndrome

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Several previous studies demonstrated that after onset of symptoms, concentrations of SARS-CoV-2 (COVID-19) ribonucleic acid (RNA) in upper respiratory tract specimens decline [1-5, unpublished CDC's data-2020]. Replication-competent virus has not been found in COVID-19 patients with mild to moderate symptoms after 10 days following initial onset of symptoms [2,6-9, unpublished CDC's data-2020]. Recovery of replication-component virus after 10 days and 20 days following initial onset of symptoms was demonstrated approximately, 88% and 95% of the severe COVID-19 patients' specimens [5]. A previous study conducted by Chen., et al. demonstrated that if their SARS-CoV-2 (COVID-19) exposure to a case SARS-CoV-2 (COVID-19) patient began at least 6 days after the initial symptom onset of a case patient, the high-risk household and hospital contacts did not get infection [10]. SARS-CoV-2 (COVID-19) RNA can be continuously detected in upper respiratory samples of the recovered COVID-19 patients for 12 weeks or more although replication-competent virus was not isolated 3 weeks after symptom onset [8,11,12].

A previous study revealed that there was no secondary infections among 790 contacts who contact with 285 persistently positive SARS-CoV-2 (COVID-19)-RNA tested individuals, including 126 individuals with recurrent symptoms [8]. Recovered patients with subsequent development of new symptoms and their specimens retested positive by reverse-transcriptase polymerase-chain reaction (RT-PCR) had no replication-competent virus detected [8,9]. Based on limited evidence from another betacoronavirus (HCoV-OC43), the genus to which SARS-CoV-2 belongs, the risk of reinfection with SARS-CoV-2 (COVID-19) may be lower in the first three months after initial infection [13].

The current reinfection reports have been infrequent is expected to increased with time after recovery from infection due to possibly genetic drift and immunity waning. A recent study demonstrated that one of 48 SARS-CoV-2 (COVID-19)-infected skilled nursing facility workers had weakly positive-nasopharyngeal swab more than 20 days after the first diagnosis of COVID-19 [14]. Nevertheless, the specimen of this patient was not subjected to serial passage to reveal the presence of replication-competent virus [14]. The robustness and duration of immunity to SARS-CoV-2 (COVID-19) remains under investigation [15]. Individuals with mild to moderate COVID-19 and individuals with more severe to critical illness or severe immunocompromise likely remain infectious no longer than 10 days and 20 days, respectively [15]. Several previous studies have not demonstrated evidence that clinically recovered individuals with persistent SARS-CoV-2 (COVID-19) detection have transmitted SARS-CoV-2 (COVID-19) to others [15]. Relying on a symptom-based, rather than test-based strategy for ending isolation justification according to this strengthening findings should be followed [15]. Hence, individuals with current evidence of no longer SARS-CoV-2 (COVID-19) infection are not kept unnecessarily isolated and excluded from responsibilities [15]. Currently, SARS-CoV-2 (COVID-19) reinfection is likely to be infrequent during the first 90 days after initial onset of symptoms [15]. A positive RT-PCR without new symptoms among individuals recovered from SARS-CoV-2 (COVID-19) infection during the 90 days after initial onset of symptoms is prone to be persistent viral RNA shedding [15]. Currently, equivalent data from children and infants are not available. Most of the current available data are derived from adults [15].

If COVID-19 critical illness is prolonged, the patients will develop chronic inflammation, fibrosis, and thrombosis. Evidence of low-grade inflammation in patients with major cardiac events, anemia, and lung cancer were reduced when treated for secondary prevention with interleukin-1 $\beta$  (IL-1 $\beta$ ) monoclonal antibody canakinumab, suggested in the CANTOS trial [16]. Interestingly, the COLCOT trial demonstrated that reducing IL-1 $\beta$ -related inflammation increased risk of infection, a significant consideration in the functionally immunosuppressive post-intensive-care-syndrome population [17].

In conclusion, presently, there are some questions urgently needed to be answered whether recovered individuals are definitely immune to SARS-CoV-2 (COVID-19) reinfection due to uncorrelated biomarkers of immunity with human-infection protection. Nevertheless, most recovered persons would have a level of immunity for 3 months or more after the first diagnosis. The intensive care unit (ICU) community should conduct large internationally multicentric trials for ICU survivors to investigate the efficacy of these drugs for COVID-19-ICU survivors, including investigation on immune biomarker profiles based on disease prognosis.

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