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CORRESPONDENCE

Duration of Culturable SARS-CoV-2 in Hospitalized Patients with Covid-19

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TO THE EDITOR:

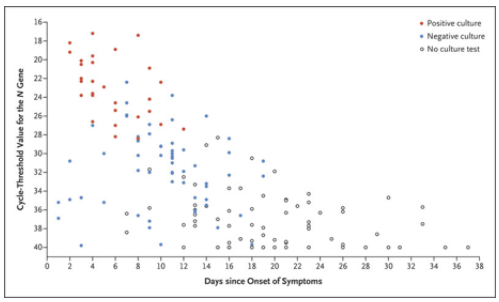
The duration of transmissibility of coronavirus disease 2019 (Covid-19) and the associated level of contagion have been uncertain. We cultured severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in serial respiratory samples obtained from hospitalized patients with Covid-19 to assess the duration of shedding of viable virus.

The data reported here represent all the patients with Covid-19, as confirmed by positive real-time reverse transcriptase–polymerase chain reaction (RT-PCR) testing, who were hospitalized at Chung-Ang University Hospital in Seoul, South Korea, between February and June 2020. The Allplex 2019-nCoV Assay (Seegene) for nasopharyngeal and oropharyngeal samples was used for real-time RT-PCR testing.[1] Patients were isolated until two consecutive negative or inconclusive results on real-time RT-PCR were documented, at least 24 hours apart.[2,3] We endeavored to obtain samples at approximately 2-day intervals, but this was not always possible. Viral RNA was quantitated with the use of the cycle-threshold value for the N gene of SARS-CoV-2.[4] Viral cultures were conducted by means of a plaque assay until at least two consecutive cultures showed no growth.

We compared the time from the onset of illness to viral clearance in culture with the time to clearance in real-time RT-PCR tests.[5] Detailed methods and sensitivities of the culture and real-time RT-PCR assay and the definition and estimation of the time to viral clearance are described in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

A total of 21 patients with Covid-19 were enrolled. Their clinical characteristics are shown in Table S1 in the Supplementary Appendix. The median age of the patients was 62 years, and 76% of the patients were men. A total of 71% of the patients had pneumonia, and 38% were receiving supplemental oxygen therapy. The median Sequential Organ Failure Assessment (SOFA) score was 0 (scores range from 0 to 24, with higher scores indicating more severe organ dysfunction and a higher risk of death), and the median Acute Physiology and Chronic Health Evaluation (APACHE) II score was 5 (scores range from 0 to 71, with higher scores indicating more severe disease and a higher risk of death); these scores indicated mild-to-moderate illness. A total of 165 samples were tested by means of real-time RT-PCR at intervals of 1 to 5 days (median, 2). Of these 165 samples, 89 were cultured for SARS-CoV-2. The timing of the tests, the kinetics of the viral loads, and the clinical course in each patient are shown in Table S2.

Figure 1.



Timing of Presence or Absence of Viable SARS-CoV-2 on Viral Culture and Cycle-Threshold Values for 165 Serial Samples Obtained from 21 Consecutive Patients Hospitalized with Covid-19.

SARS-CoV-2 was cultured in 29 of the 89 samples (33%) (Figure 1). The median time from symptom onset to viral clearance in culture was 7 days (95% confidence interval [CI], 5 to 10), and the median time from symptom onset to viral clearance on real-time RT-PCR was 34 days (lower boundary of the 95% CI, 24 days) (Fig. S1 and Table S4). The latest positive viral culture was 12 days after symptom onset (in Patient 6). Viable virus was identified until 3 days after the resolution in fever (in Patient 14). Viral culture was positive only in samples with a cycle-threshold value of 28.4 or less. The incidence of culture positivity decreased with an increasing time from symptom onset and with an increasing cycle-threshold value (Table S3).

Our findings may be useful in guiding isolation periods for patients with Covid-19 and in estimating

the risk of secondary transmission among close contacts in contract tracing. Given the small sample size, inconsistent timing of sampling, and relatively mild illness of the enrolled patients, our results should be verified in larger and more diverse groups of patients.

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Dr. Kim, Mr. Cui, and Drs. Park and Chung contributed equally to this letter.

5 References

Supplementary Material

Supplementary Appendix	PDF	800KB
Disclosure Forms	PDF	243KB

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