CORRESPONDENCE



SARS-CoV-2 Infection among Travelers Returning from Wuhan, China

TO THE EDITOR: As severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections (causing coronavirus disease 2019 [Covid-19]) spread globally, uncertainty surrounds estimates of the true number of infected persons, which is crucial to determining the severity of infection and the incidence of mild or asymptomatic cases and their possible transmission.1 Modeling estimates suggest that in Wuhan, China, the city with the most Covid-19 cases, there are substantially more cases than were officially reported, because milder cases may not have been captured in hospital-based surveillance.2,3 Data on travelers returning from areas with cases of Covid-19 could be useful in estimating its incidence.4

We followed up on 94 persons who boarded an evacuation flight from Wuhan to Singapore on January 30, 2020. Screening for body temperature was conducted at check-in and before boarding, and 3 febrile persons were prevented from boarding (Fig. 1); no additional information regarding the status of these 3 febrile persons was available. Surgical masks were provided to passengers on board the plane. On arrival in Singapore, the passengers underwent repeat

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screening for body temperature (fever was defined as a body temperature ≥38°C), and 2 persons (a woman 48 years of age [Patient 1] and a woman 47 years of age [Patient 2]) had a fever. The 2 febrile women were transferred immediately to a hospital, and they tested positive for SARS-CoV-2 (their clinical course is described in the Supplementary Appendix, available with the full text of this letter at NEJM.org).

The remaining 92 afebrile passengers (age range, 2 to 82 years) were quarantined for 14 days at a government quarantine facility, where they were checked for symptoms and fever three times daily. Six persons reported symptoms (4 on quarantine day 2 and 2 on quarantine day 3) and were placed in isolation in a hospital and underwent polymerase-chain-reaction (PCR) testing; all 6 persons tested negative for SARS-CoV-2. On quarantine day 3, samples from 76 of the 86 asymptomatic persons (75 nasopharyngeal swab samples and 1 nasal swab sample) were obtained and tested by means of PCR assay. A 17-year-old boy (the son of Patient 1) tested positive for Covid-19 and continued to have PCR-positive status for 2 weeks, and a 41-year-old man had an inconclusive result (positive for N gene and negative for ORF1ab gene). On quarantine day 6, samples from all 87 quarantined asymptomatic persons (85 nasopharyngeal swab samples and 2 nasal swab samples [3 of the 6 persons who had been transferred to the hospital before February 2 had returned to the government quarantine facility]) were obtained and tested; all tested negative. All persons who were not isolated in the hospital were released from quarantine on day 14, and all remained uninfected with Covid-19. Understanding the implications of transmission of SARS-CoV-2 infection from persons with

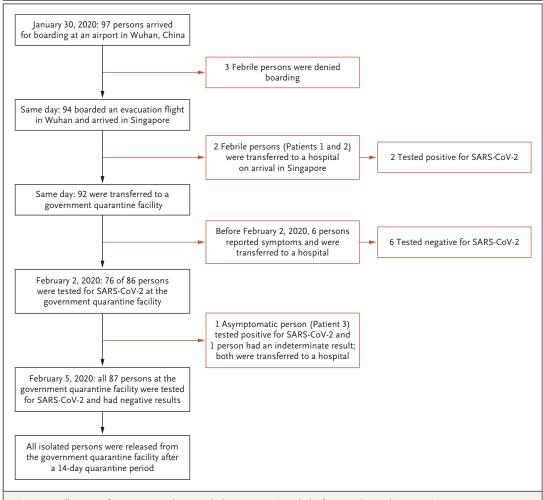


Figure 1. Follow-up of 94 Persons who Boarded an Evacuation Flight from Wuhan, China, to Singapore on January 30, 2020.

Of the 6 persons who had been transferred to a hospital before February 2, 2020, 3 returned to the government quarantine facility and are included with the 87 persons who underwent testing at the facility on quarantine day 6 (February 5, 2020). SARS-CoV-2 denotes severe acute respiratory syndrome coronavirus 2.

asymptomatic or very mild symptomatic cases of Covid-19 is vital for the formulation of containment strategies.

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- 1. World Health Organization. Novel coronavirus (2019-nCoV): situation report - 12. February 2020 (https://www.who.int/docs/ default-source/coronaviruse/situation-reports/20200201-sitrep -12-ncov.pdf?sfvrsn=273c5d35_2).
- 2. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. Lancet 2020;395:689-97.
- 3. Imai N, Dorigatti I, Cori A, Riley S, Ferguson NM. Estimating the potential total number of novel Coronavirus cases in Wuhan City, China. London: Imperial College London, January 17, 2020 (https://www.imperial.ac.uk/media/imperial-college/ medicine/sph/ide/gida-fellowships/2019-nCoV-outbreak-report-17 -01-2020.pdf).
- 4. Hoehl S, Rabenau H, Berger A, et al. Evidence of SARS-CoV-2 infection in returning travelers from Wuhan, China. N Engl J Med 2020;382:1278-80.

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Consequences of Abrupt Cessation of Alpha,-**Antitrypsin Replacement Therapy**

TO THE EDITOR: Genetic deficiency of alpha,antitrypsin (AAT), a serine protease inhibitor¹ and potent antiinflammatory and immunomodulatory protein,² is an inherited cause of emphysema. In February 2017, Irish health care policymakers opted against reimbursement for intravenous augmentation therapy with plasma-purified AAT for people with AAT deficiency-associated emphysema, the only approved disease-specific treatment available for the condition,3 citing a lack of evidence of clinical benefit. A cohort of patients with AAT deficiency who had participated in the RAPID and RAPID-OLE trials of AAT replacement^{4,5} continued to receive treatment with Respreeza (CSL Behring) as part of an extension agreement brokered by physicians with the manufacturer.

After the February 2017 decision, the manu-

facturer and Irish health care authorities entered negotiations aimed at securing public funding for treatment of these patients, but the talks concluded in September 2017 without resolution. As a result, 19 patients with severe AAT deficiency had their therapy discontinued immediately in late September.

We conducted a study involving these 19 patients, a natural experiment that would not have been ethically possible to perform under usual circumstances. At the time of withdrawal. patients had been receiving intravenous AAT administered at a dose of 60 mg per kilogram of body weight per week for a mean (±SD) of 9.2±1.2 years and had severe emphysema, with a mean forced expiratory volume in 1 second of 40.6±11.7% of the predicted value and a mean diffusing capacity for carbon monoxide