Evidence of SARS-CoV-2 Infection in Returning Travelers from Wuhan, China

TO THE EDITOR: As the number of cases of infection with the novel coronavirus (SARS-CoV-2) has continued to increase, many countries have established restrictions regarding travelers who have recently visited China.1 With lockdown measures imposed in Hubei Province, China,2 and a public health emergency of international concern declared by the World Health Organization,3 foreign nationals have sought to return to their home countries from China, and public health authorities are racing to contain the spread of Covid-19 (the disease caused by SARS-CoV-2 infection) around the world. This process is complicated by epidemiologic uncertainty regarding possible transmission of the virus by asymptptomatically or subclinically symptomatic infected persons. It is unclear whether persons who show no signs or symptoms of respiratory infection shed SARS-CoV-2.

In this context, a group of predominantly German nationals who had stayed in Hubei Province was evacuated to Frankfurt, Germany, on February 1, 2020. They were to be transferred to Germersheim, Germany, and quarantined for 14 days, since this period is thought to be the upper limit of the incubation period of SARS-CoV-2. Screening for symptoms and clinical signs of infection was performed before their departure from China. A total of 126 travelers were allowed to board an aircraft operated by the German air force (Fig. 1).

During the flight, 10 passengers were isolated. Two passengers had had contact with 1 person who had a confirmed case of SARS-CoV-2 infection, 6 had reported symptoms, were deemed to be clinically symptomatic, or both, and 2 passengers had accompanied family members who had been isolated on the flight because of suspected SARS-CoV-2 infection or because of other symptoms (i.e., symptoms related to pregnancy). These 10 passengers were transferred to University Hospital Frankfurt immediately after arrival. All 10 tested negative for SARS-CoV-2 by real-time reverse-transcription–polymerase-chain-reaction (RT-PCR) assays4 of throat swabs and sputum.

The remaining 116 passengers (5 months to 68 years of age), including 23 children, were sent to the medical assessment center at Frankfurt Airport, where each was evaluated by a medical team of physicians. Each passenger was asked to report current symptoms of fever, fatigue, sore throat, cough, runny nose, muscle aches, and diarrhea, and each one was screened for signs of infection in the nose and throat. The temperature of all passengers was taken. All were afebrile except for 1 passenger who had a temperature of 38.4°C and reported dyspnea and cough. He was transferred to University Hospital Frankfurt for evaluation. However, testing to detect SARS-CoV-2 by RT-PCR of a throat swab and sputum was negative.
In addition to the preplanned multistep process of screening for signs and symptoms of infection and observing the asymptomatic cohort in quarantine, we decided to offer a throat swab to test for SARS-CoV-2 in each of the 115 travelers who had passed triage. A total of 114 passengers consented to the test.

Two of the 114 persons (1.8%) in this cohort of travelers who had passed the symptoms-based screening tested positive for SARS-CoV-2 by RT-PCR (cycle threshold value in the two samples, 24.39 and 30.25, respectively). Testing with a second protocol consisting of two commercial sets (LightMix Modular SARS and Wuhan CoV E-gene, and LightMix Modular Wuhan CoV RdRP-gene, both produced by TIB MOLBIOL) and retesting of the positive samples at the Institute of Virology, Philipps University Marburg, in Marburg, Germany, confirmed the results. In addition, the isolation of SARS-CoV-2 from both samples in cell culture of Caco-2 cells indicated potential infectivity (see the Supplementary Appendix, available with the full text of this letter at NEJM.org).

These two persons were subsequently isolated.
from the cohort and transferred to the Infectious Disease Unit at University Hospital Frankfurt for further evaluation and observation on the following day. After a thorough evaluation in the hospital ward, a faint rash and minimal pharyngitis were observed in one patient. Both patients remained well and afebrile 7 days after admission.

In this effort to evacuate 126 people from Wuhan to Frankfurt, a symptom-based screening process was ineffective in detecting SARS-CoV-2 infection in 2 persons who later were found to have evidence of SARS-CoV-2 in a throat swab. We discovered that shedding of potentially infectious virus may occur in persons who have no fever and no signs or only minor signs of infection.

Sebastian Hoehl, M.D.
Holger Rabenau, Ph.D.
Annemarie Berger, Ph.D.
Martin Kortenbusch
Jindrich Cinatl, Ph.D.
Denisa Bojkova, M.Sc.
University Hospital Frankfurt
Frankfurt am Main, Germany

Pia Behrens, M.D.
Boris Böddinghaus, M.D.
Udo Götsch, M.D.
Frank Naujoks, M.D.
Peter Neumann, M.D.
Joscha Schork, M.D.
Petra Tiarks-Jungk, M.D.
Antoni Walczok, M.D.
Health Protection Authority, City of Frankfurt
Frankfurt am Main, Germany

Markus Eickmann, Ph.D.
Philipps University Marburg
Marburg, Germany

Maria J.G.T. Vehreschild, M.D.
Gerrit Kann, M.D.
Timo Wolf, M.D.
University Hospital Frankfurt
Frankfurt am Main, Germany

René Gottschalk, M.D., Ph.D.
Health Protection Authority, City of Frankfurt
Frankfurt am Main, Germany

Sandra Ciesek, M.D.
University Hospital Frankfurt
Frankfurt am Main, Germany

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

This letter was published on February 18, 2020, and updated on February 20, 2020, at NEJM.org.


DOI: 10.1056/NEJMc2001899

Telacebec (Q203), a New Antituberculosis Agent

TO THE EDITOR: Shortly after the discovery of streptomycin in 1943, it became clear that successful treatment of tuberculosis and prevention of drug resistance required a combination of at least three effective drugs. What followed in the 1950s was the introduction of triple therapy with streptomycin, aminosalicylic acid, and isoniazid, the so-called 100% effective regimen and a major milestone on the path to modern antimicrobial therapy.1,2

After the stepwise introduction of more potent agents and massive efforts toward tuberculosis control, the disease that once killed one in four persons became a seemingly distant threat in many countries. However, an increasing prevalence of drug resistance has made the goal of global elimination of tuberculosis a far-removed prospect once more. New drugs and regimens are needed to ensure continued progress toward this goal.

Telacebec (Q203) is a novel first-in-class antituberculosis drug that targets Mycobacterium tuber-