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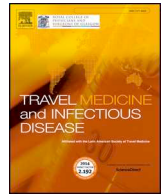
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Challenges of managing the asymptomatic carriers of SARS-CoV-2

A B S T R A C T

After an outbreak in Wuhan, China, a growing number of countries are now suffering from an epidemic by SARS-CoV-2, which causes COVID-19. Undoubtedly, reports of the skyrocketing global spread of COVID-19 has shocked people globally, from Japan to the United States. Presently, the World Health Organization indicates that the fatality rate due to COVID-19 is about 2%, inferring that many positive subjects may potentially overcome the illness with mild influenza-like symptoms and no need for hospitalization at intensive-care units. Because COVID-19 is completely new to the human immune system, many throughout the world are likely vulnerable to becoming sick after their initial exposure to SARS-CoV-2. Besides hospitalized cases, many individuals are likely asymptomatic but potentially carry the virus. While our knowledge about carriers and their virus shedding is deficient, some studies modelling the viral transmission have considered the potential contribution of the asymptomatic carriers. Protocols for managing asymptomatic cases, for example for controlling them to restrict their contact with healthy people at public places or private residences, have not been established. In-house quarantine may as well be applicable to asymptomatic cases if they could be identified and diagnosed. Presumably now, the asymptomatic subjects potentially contribute to the transmission of COVID-19 without their knowledge, intention, or being diagnosed as carriers. Thus, managing the asymptomatic subjects, who can carry and likely transmit the virus, is a major healthcare challenge while the pandemic is looming.

Dear Editor,

The cause of the novel coronavirus disease 2019 (COVID-19)—SARS-CoV-2—has been responsible for the presently growing global pandemic. While writing this letter (11 April 2020), more than 160 countries reportedly have been affected—with 1,710,148 confirmed cases [1]. The US—followed by Spain (161,852), Italy (147,577), France (124,869), Germany (122,171), and China (81,953)—presently tops the statistics with 503,177 total confirmed cases, of which 27,314 have recovered [1]. Iran and Australia respectively report 68,192 and 6,292 total cases with 35,465 and 3,265 recoveries [1].

Dry cough, fever, lymphopenia, malaise, diarrhea, and dyspnea are the predominant signs and symptoms of COVID-19. The primary symptoms may last up to 14 days after exposure, and the incubation period ranges 9–12 days. Untreated disease may result in alveolar damage and pneumonia, mostly culminating in organ failure and death. The major route of interpersonal transmission is through temporal and physical close contact with patients (by aerosols through sneezing or coughing). This was confirmed when some nurses who cared for hospitalized patients were found positive while having no history of visiting the seafood markets at Wuhan [2], the origin of the pandemic. Before strict quarantine measures were implemented in Wuhan, positive cases were rationally thought to originate after human–human transmission, instead of zoonotic transmission, in densely populated markets. However, the exact means of viral transmission is still not fully understood [3], especially in the initial cases. Indeed, investigation of the natural background of the virus as a putative zoonotic disease is important for preventing future outbreaks.

Besides hospitalized or confirmed cases, many asymptomatic individuals potentially carry the virus. Thus, diagnosing the patients and finding the asymptomatic carriers will help us understand the exact viral transmission routes. Simulation studies can mathematically model the contribution of the asymptomatic carriers to person–person viral

transmission [4], highlighting that fulminating cases are unlikely to be the only viral sources. Reportedly, the viral load in an asymptomatic carrier is akin to that in a symptomatic patient; thus, asymptomatic or minimally symptomatic patients are likely to transmit the virus as well as symptomatic patients. They could likely freely shed the virus into the environment, potentially boosting the transmission cycle as an unintentional, but dangerous, viral source. Asymptomatic carriers are thus likely to participate, more than symptomatic cases, in mass-gatherings, sporting events, shopping, and going to schools or gyms. The asymptomatic carriers may have been rapidly spreading the virus within, and to, many different countries. We postulate that the increase in the number of affected countries 10–20 days after the initial reports of the outbreak may have been partially facilitated by the asymptomatic carriers. Crowd face-masking has been suggested to prevent the transmission of the virus to healthy uninfected people, and this could also prevent the asymptomatic carriers from shedding the virus. On 2 March 2020, an expert WHO team travelled to Tehran, Iran, and aimed to investigate the viral transmission dynamics and at-risk populations. Such surveys help grow our experience on how to control COVID-19 globally. Recently, China, Bahrain, Jordan, the United States, Afghanistan, Italy, Australia, and South Korea temporarily closed their borders to decrease the viral spread. Nevertheless, cohesive guidelines on how to manage the asymptomatic carriers are lacking. Local screening and surveillance of the asymptomatic carriers by simple PCR-based assays could be effective in managing the viral transmission by the carriers. A limitation of sampling could be that oropharyngeal or nasopharyngeal swabs may fail to result in confirmatory diagnosis of an asymptomatic carrier, and deeper sampling of the respiratory tract may be necessary.

In conclusion, data on asymptomatic carriers acting as potential viral transmitters are scarce. No confirmatory or contradictory reports on the case-fatality rate or revised incubation period of COVID-19 have emerged from the involved countries, including North America, Europe, Australia, and Africa. Thus, our understanding of pathogenesis,

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transmission, carriers, virus shedding, and incubation period of COVID-19 and its complex interaction with the host immune system is mostly incomplete. We acknowledge that the highest priority by the world decision-makers is to defeat the pandemic, but concurrently, intervening with, and screening the asymptomatic carriers should be considered worldwide before a second large wave of positive cases emerges. The lessons learned from the present COVID-19 pandemic are that 1) robust research endeavors are required to change our mindset about emerging pathogens; and 2) surveillance and screening systems should be recruited for monitoring the less-known viral or bacterial pathogens.

Declaration of competing interest

No potential conflict of interest was declared.

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