EDITORIALS

Person-to-Person Spread of the MERS Coronavirus — An Evolving Picture

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Approximately 1 year ago, a novel coronavirus, the Middle East respiratory syndrome coronavirus (MERS-CoV), was first identified in the *Journal* as the causative agent of a lethal pneumonia in several patients in the Middle East.[1] As of July 10, 2013, a total of 80 cases have been identified in the Middle East (Saudi Arabia, Jordan, Qatar, and the United Arab Emirates), Europe (United Kingdom, France, Italy, and Germany), and North Africa (Tunisia), with a case fatality rate of 56%. Since this coronavirus is a close relative of the virus that caused the severe acute respiratory syndrome (SARS), a short-lived but alarming epidemic in 2002–2003 that resulted in approximately 8000 cases and 800 deaths, governmental, public health, clinical, and laboratory authorities all mobilized rapidly to respond to the new virus outbreak. Soon after the identification of MERS-CoV, information about its genomic sequence and organization, species tropism, and host-cell receptor (dipeptidyl peptidase 4) was published.[2,3] These initial studies did not identify the source of this newly identified virus, nor did they reveal whether MERS-CoV could be transmitted from human to human, a requirement for designation as an epidemic disease.

In this issue of the *Journal*, Assiri et al.[4] describe the largest outbreak of MERS-CoV infection thus far, showing that the virus is transmitted from human to human. This outbreak occurred in several hospitals in the governorate of Al-Hasa in eastern Saudi Arabia, with transmission probably occurring in dialysis units, intensive care units, and wards. Most patients had underlying diseases, with a remarkable number (17 of 23) having diabetes. In addition to showing that human-to-human transmission occurred frequently, the relatively large number of patients infected in this outbreak made it possible to define characteristics of the infection, such as the incubation time (5.2 days) and the serial interval (7.6 days). As seen in the SARS epidemic, there was variability in the numbers of patients infected by each index patient, with 1 patient transmitting virus to 7 contacts; superspreading events, in which a few patients infected large numbers of contacts, were critical factors in SARS reaching epidemic proportions. The study by Assiri et al. shows that MERS-CoV has the potential to spread widely within health care settings, infecting primarily other patients but also health care workers and family contacts, although to a lesser extent. Patients with diabetes or chronic renal failure appear to be at especially high risk for severe MERS-CoV infection, but whether these coexisting conditions represent true risk factors or whether these patients happened to be preferentially exposed to index cases is not known, given the relatively small number of infected patients. Also unclear from this study is the extent to which MERS-CoV infection is a systemic disease. Acute renal failure developed in several patients with the infection,[1,5-7] possibly reflecting a high level of dipeptidyl peptidase 4–receptor expression in the kidney. However, in the absence of tissue samples obtained at surgery or autopsy, it has been difficult to determine the extent to which kidneys or other organs are infected.

Although the report by Assiri et al., as well

as others in the *Journal* and elsewhere,[6,7] indicates that human-to-human transmission occurs, at least in the context of close contact, many additional questions related to the transmission of MERS-CoV and its ability to reach epidemic proportions are unanswered. On one hand, coronaviruses are notorious for rapid adaptation to new hosts,[8] a finding that is best illustrated by the ability of SARS-CoV to adapt to replication in the human lung. Adaptation involved changes in the surface glycoprotein, which is responsible for binding to the host-cell entry receptor, and in proteins involved in viral replication.[9] Additional adaptation of MERS-CoV to human populations, although not observed thus far, is likely to occur and would augment the possibility of widespread infection. Furthermore, the community (probably zoonotic) source for MERS-CoV remains unknown, making it difficult to know whether periodic reintroduction into human populations will occur and contribute to the potential for human adaptation. Moreover, the relative importance of aerosol transmission versus spread by large droplets or contact is unknown, but the mode of transmission will affect the likelihood of large-scale human infection.

On the other hand, an epidemic is not a certainty, since a first set of statistical analyses — performed with the use of all the available data on human-to-human transmission, including those in the study by Assiri et al. — suggests that MERS-CoV does not now have pandemic potential.[10] Thus, in the absence of further adaptation or repeated introduction from community sources, widespread infection may not develop. The prevention of future spread of the epidemic will require careful surveillance and testing of patients with pneumonia living in the Middle East or with a history of recent travel to affected regions. Current virus detection is based on polymerase-chain-reaction testing, with sensitivity depending on the viral load at the time the specimen is obtained. Some studies show that the virus is most readily isolated from specimens obtained from the lower respiratory tract,[5,6] and since the course of clinical disease is not yet well defined, diagnosis may require repeated testing. It is also essential to determine the prevalence of MERS-CoV seropositivity in human and animal populations in Saudi Arabia and elsewhere in the Middle East to establish the likelihood of an epidemic and also to prevent one from occurring. This information is critical for an effective public health response. In addition to requiring vigilance by health care workers and public health authorities, obtaining these data is dependent on the generation of a validated serologic assay, which is not currently available.

An immediate concern is that the MERS-CoV will infect pilgrims traveling to Saudi Arabia this October for the Hajj pilgrimage. Fortunately, last year's Hajj did not result in an increase of patients with MERS-CoV infection. Obtaining a favorable outcome this year will require the same good fortune and will be facilitated by careful vigilance and management of cases and contacts, as described by Assiri et al.

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

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