Emerging Human Coronaviruses — Disease Potential and Preparedness

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It is likely that novel zoonotic virus infections causing serious disease and death in humans will increasingly test our ability to respond appropriately. Changes in commercial and social practices, the environment, and travel will continually provide new opportunities for zoonotic pathogens to infect humans. In addition, ever more sophisticated tools to detect novel pathogens will increase the chance that we will identify sporadic infections that do not cause widespread disease.

Zaki et al.[1] now describe in the *Journal* the detection of a novel betacoronavirus (called HCoV-EMC) in a patient from Saudi Arabia who died of pneumonia and renal failure in June 2012. A similar virus was detected in a second patient with severe pneumonia in Qatar.[2] Astute clinicians recognized that these illnesses were unusual, with a severe progressive pneumonia in an otherwise healthy person. Pathogen-discovery tools for pan-coronaviruses, polymerase-chain-reaction assay and sequence studies, detected the novel virus in both infections. In previous studies, similar betacoronaviruses have been detected only in bats. In addition, serologic studies reported by Zaki et al. suggest that the virus had not circulated to a substantial degree in the affected community in Saudi Arabia.

The 2003 outbreak of the severe acute respiratory syndrome (SARS) illustrates the epidemic potential of a novel coronavirus to threaten global health.[3] That outbreak was also caused by a novel betacoronavirus (lineage B, as compared with the Saudi lineage C virus), which probably originated from bats and rapidly spread globally, causing approximately 8000 cases and nearly 800 deaths over 4 months.[4]

The global community has learned much from responding to past outbreaks. Four past responses illustrate some of these lessons. The Nipah virus outbreak in Malaysia in 1998 and 1999 showed the importance of an intermediate host — in that case, swine herds that amplified infection and facilitated transmission to humans, resulting in a large outbreak. Epidemic control was mediated by eliminating spread from swine.[5] However, there have been continued infections when humans contacted infectious secretions from the bat reservoir species in contaminated date-palm sap.[6] Since human-to-human transmission of Nipah virus is inefficient, it has not yet presented a global health threat.

The SARS outbreak of 2003 and the pandemic A (H1N1) 2009 influenza virus illustrate the potential for rapid global spread when a zoonotic virus acquires the ability to efficiently transmit from human to human. These outbreaks also show the speed and efficiency with which a global response can be mobilized to protect the

public's health. For both viruses, circulation in intermediate hosts — multiple species in wild-animal markets for the SARS virus and swine for the pandemic A (H1N1) virus — and in humans allowed the viruses to adapt to human infection and gain efficient human-to-human transmission.[7-9] The rarity of mild illness and lack of transmission early in the illness allowed public health control measures to stop the spread of SARS. Interestingly, since early 2004, SARS betacoronaviruses have not been reported in humans, possibly because control measures stopped transmission in wild-animal markets. In contrast, the frequency of mild infection and greater efficiency of human-to-human transmission precluded the control of the pandemic A (H1N1) virus, and it is now one of the endemic influenza viruses.

In 1999, an astute clinician and public health officials noted an unusual cluster of cases of encephalitis, and the subsequent investigation resulted in the detection of West Nile virus shortly after it was introduced into the United States.[10] The virus had been endemic in Europe, Asia, and Africa but had not been previously detected in North America. With the mosquito vector in place and a previously unexposed bird population, the virus quickly spread across North and Central America and is now one of the principal causes of viral encephalitis in the United States.[11]

In all four of these zoonotic infections, the initial clinical and epidemiologic investigations correctly guided the approach to response efforts, but ongoing surveillance and epidemiologic and laboratory investigations were needed to revise and fine-tune response efforts and develop therapeutic and preventive approaches. Since there has been no evidence of human-to-human transmission or virus transmission to health care workers, HCoV-EMC is not currently a public health risk.

The detection of HCoV-EMC, as described by Zaki et al., probably forecasts an increasingly common theme in which new pathogens are identified before they may develop the potential for efficient human-to-human transmission. From past experience, an astute clinician, public health official, or laboratory worker will recognize an unusual event and contact the appropriate health officials, who will investigate the event. Good communication between the clinic, laboratory, and public health community is important for rapid and effective assessment of the health risks.

Experience has shown that local investigation, if performed carefully and thoroughly, will correctly guide future response strategies. The dissemination of data on the clinical features of the illness allows for rapid case identification and contact tracing. Assessing the risk of human-to-human transmission indicates the broader health risk from the pathogen. Cooperation with the veterinary health community is essential in identifying the animal reservoirs and in establishing methods to prevent future introductions of the virus. Laboratory studies provide the tools to detect the pathogen and develop diagnostic assays to confirm acute infections and detect previous ones. The global community, represented by the World Health Organization (WHO), should be informed about cases in a timely fashion. The WHO can then lead the risk assessment and coordinate response efforts.[12,13]

The global community was apparently not aware of the first case of HCoV-EMC infection until it was reported on ProMED, a website for monitoring emerging diseases, on September 20, 2012, approximately 3 months after the patient died. Luckily, there have been no new reports of cases since September 22, 2012, but local surveillance should continue. With no evidence of human-to-human transmission, the WHO currently recommends no heightened global surveillance for this virus but continued "routine surveillance for early detection and rapid response to all potential public health threats." However, such cases provide an opportunity to reconsider response strategies.

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

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