

VIEWPOINT

Middle East Respiratory Syndrome A Global Health Challenge

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In May 2013, World Health Organization (WHO) Director-General Margaret Chan warned that a novel coronavirus, Middle East respiratory syndrome coronavirus (MERS-CoV), posed “a threat to the entire world.”¹ Her warning was prescient. As of June 12, 2015, WHO had been notified of 1289 individuals with laboratory-confirmed infections in 25 countries, of whom at least 455 individuals (37%) had died.² More than 85% of cases have been diagnosed in the Kingdom of Saudi Arabia.

Unlike the distantly related, more contagious, but less fatal severe acute respiratory syndrome coronavirus (SARS-CoV), MERS-CoV had not been publicly linked to a “super-spreading” event (1 patient linked to ≥ 10 infections) until May 2015 in the Republic of Korea. When the index case, a man aged 68 years from the Republic of Korea, returned to Incheon International Airport (located 30 miles west of Seoul) on May 4, he was asymptomatic. He reportedly had traveled to Bahrain, United Arab Emirates, the Kingdom of Saudi Arabia, and Qatar, but initially declared travel only to outbreak-free Bahrain. He became symptomatic on May 11 and sought care in 2 outpatient clinics and 2 hospitals. He was eventually admitted to Pyeongtaek St Mary's hospital, Gyeonggi province, but MERS-CoV was unconfirmed until May 20, reportedly initiating chains of transmission that increased to involve 126 cases with 11 deaths as of June 10. The index patient was still hospitalized as of June 12.

China reported a MERS-CoV case on May 29, 2015—a man aged 44 years from the Republic of Korea who flew to Hong Kong on May 26, subsequently traveling to Huizhou, Guangdong province, where he was placed in isolation. Genetic sequencing showed no MERS-CoV mutations.

Origins, Epidemiology, and Clinical Features

MERS is a viral respiratory illness novel to humans. First reported in Jeddah, the Kingdom of Saudi Arabia, in June 2012, the earliest outbreak occurred in March or April of 2012 in Zarqa, Jordan, with 9 laboratory-confirmed cases. The outbreak was retrospectively linked to MERS-CoV using frozen specimens.^{3,4}

MERS is a zoonotic disease, with dromedary camels the likely animal reservoir. Transmission risk factors include respiratory exposure to camel secretions, drinking raw camel milk, or eating undercooked camel meat. Studies report increased risk in individuals with occupational contact with camels.⁵

MERS-CoV is transmissible person-to-person, but sustained community transmission has not been observed. Like SARS-CoV, health care settings pose the highest risk. Yet MERS-CoV is less contagious than SARS-CoV and has higher fatality rates. Hospital-related outbreaks have occurred in multiple countries, including substantial nosocomial transmissions across the Kingdom of Saudi Arabia.

MERS typically presents as a nonspecific febrile respiratory tract infection, but can progress rapidly to respiratory failure, or it may never become severe. Thus far, children have rarely contracted or died from MERS-CoV. Risk factors for disease progression include comorbidity with lung disease, kidney disease, diabetes, and immunodeficiency.

A Global Health Emergency?

The WHO director-general has convened 8 Emergency Committee meetings on MERS under the International Health Regulations, declining to declare a Public Health Emergency of International Concern (PHEIC). Given the ongoing outbreak, the director-general convened the ninth meeting on June 16, with 2 major events in mind: the month of Ramadan, which begins June 17 with a surge in travelers and pilgrims performing the Umrah pilgrimage in the Kingdom of Saudi Arabia, and the Hajj pilgrimage, the largest gathering in the world, which occurs September 20 through 25.

WHO was sharply criticized for delays in declaring Ebola a PHEIC, but that should not provoke an overreaction to MERS-CoV. WHO should amend the International Health Regulations to grant the director-general flexibility to designate graduated alert levels, from heightened vigilance, rising to a PHEIC only when justified. On June 13, WHO and the Republic of Korea presented the results of a joint mission to understand the virus and its transmission patterns.

Public Health Strategies

Public health measures—infection prevention and control, isolation, contact tracing, and quarantine—historically have controlled MERS-CoV and were also widely employed during SARS and Ebola outbreaks.

Transparency and Trust

Public fear and mistrust in government can impede epidemic response. The MERS-CoV outbreak in the Republic of Korea occurred in the aftermath of the Sewol ferry disaster in April 2014, which resulted in the deaths of 304 students. The government of the Republic of Korea was criticized for what some perceived to be an uncoordinated response and government obfuscation. In the case of MERS-CoV, health authorities initially withheld the names of hospitals handling cases. Transparency builds public trust; given inevitable scientific uncertainty, health authorities should fully disclose what is and is not known about the MERS-CoV outbreak.

Community and Health Care Settings

MERS-CoV, like other coronaviruses, spreads through respiratory tract secretions, with hand hygiene recom-

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mended. The Republic of Korea has seen a surge in hand sanitizers, as well as face masks.⁶ WHO recommends health worker precautions (eg, contact and droplet protective equipment), as well as airborne precautions for aerosol-generating procedures. Crowded hospitals and comingling of health workers, patients, and family members likely contribute to transmission in health care settings.⁷ Early identification can prevent transmission and requires careful travel histories for differential diagnosis. Health worker training on infection prevention and control, as well as diagnostic testing of certain travelers, remains critical for an effective response.

Isolation and Quarantine

Isolation of patients with a known infection is recommended, but optimal implementation of quarantine for exposed individuals is more controversial (home-based, medical facility, or special housing). For example, the cordon sanitaire (a guarded line preventing residents from leaving) to control Ebola provoked violence in Monrovia, Liberia. During the SARS outbreak of 2003, China and Singapore employed mass quarantines in apartment complexes or other structures, monitored by armed guards or ankle bracelets. The Republic of Korea placed more than 3000 individuals exposed to MERS-CoV in quarantine, mostly at home, but some in state-designated facilities. Authorities were tracking cell phone signals to monitor patient compliance. To gain public trust, quarantines should be limited to well-documented exposures using the least restrictive means possible.

Travel Restrictions

The Republic of Korea restricted the travel of quarantined MERS-CoV contacts following a security breach allowing a quarantined patient to fly to Hong Kong. The traveler denied MERS-CoV exposure, even though he was febrile on arrival. He was then allowed to proceed by bus to Guangdong province where he tested positive for MERS-CoV. Hong Kong issued a “red alert” advising against unnecessary travel to the Republic of Korea—a decision likely to be followed by other countries. This contravenes WHO guidance, which finds travel restrictions ineffective due to lack of community transmission.

School Closures

More than 2400 kindergartens, schools, and universities were closed in the Republic of Korea, despite Ministry of Health guidance that it

was “medically wrong,” too drastic a precaution given disruptions in child education.⁶ WHO has urged the reopening of schools, and the Republic of Korea has begun doing so. School closures may have a role with novel influenzas, but are unproven for MERS-CoV given the lack of community transmission.

Who Owns MERS-CoV?

In June 2012, a microbiologist in Jeddah sent blood samples from a patient with unexplained pneumonia to Erasmus Medical Center, the Netherlands, which identified a novel coronavirus later confirmed as MERS-CoV. Erasmus then shared samples with multiple laboratories under material transfer agreements, contracts for transferring pathogens. Erasmus filed for patents on the use of the MERS-CoV gene sequence. The Kingdom of Saudi Arabia warned that the microbiologist violated national rules and that Erasmus acted unethically.⁸

Following Indonesia’s refusal to share influenza A(H5N1), WHO adopted the Pandemic Influenza Preparedness Framework in May 2011, governing virus sharing. This framework, however, fails to cover noninfluenza pathogens. Impediments to virus sharing, restrictive material transfer agreements, and patents can impede research on novel pathogens. In May 2013, Dr Chan stated, “No [intellectual property] should stand in the way of you, the countries of the world, to protect your people.”⁸ Yet there remain substantial holes in international rules needed to facilitate critical research.

Strengthening Health Systems

A critical lesson from SARS, Ebola, and now MERS is that health settings can amplify transmission risks. Historically, health settings have exposed patients and visitors due to close contact that facilitates spread of respiratory tract secretions and infected body fluids, as well as health workers who have not employed personal protective equipment. However, a well-trained and well-prepared health workforce—both health care and public health—usually can rapidly bring outbreaks under control. The International Health Regulations require all states to build core capacities, including diagnosis, treatment, laboratories, contact tracing, isolation, and humane forms of quarantine. Fully funding and implementing that international obligation offers the best assurance of global health security. The ongoing outbreak in the Republic of Korea is an important reminder that MERS requires constant vigilance and can be brought under control with effective public health strategies.

ARTICLE INFORMATION

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