

Middle East Respiratory Syndrome-Coronavirus (MERS-CoV): CDC Update for Clinicians

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Key Points:

Cases of Middle East Respiratory Syndrome-Coronavirus (MERS-CoV), including travel-associated cases, continue to be reported. The risk of exportation of cases to the US mandates that clinicians need to be vigilant to identify cases and implement infection control measures expeditiously.

Abstract

Although much recent focus has been on the recognition of Ebola virus disease among travelers from West Africa, cases of Middle East Respiratory Syndrome-Coronavirus (MERS-CoV), including travel-associated cases, continue to be reported. US clinicians need to be familiar with recommendations regarding when to suspect MERS-CoV, how to make a diagnosis, and what infection control measures need to be instituted when a case is suspected. Infection control is especially critical, given that most cases have been health care-associated. Two cases of MERS-CoV were identified in the United States in May of 2014; because these cases were detected promptly and appropriate control measures were put in place quickly, no secondary cases occurred. This paper summarizes information that US clinicians need to know to prevent secondary cases of MERS-CoV from occurring in the US.

Although much recent focus has been appropriately placed on the recognition of Ebola virus disease in travelers returning from West Africa, the continued reports of cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infections (including travel-associated cases) are also of concern.[1, 2] MERS-CoV is a novel virus first reported in Saudi Arabia in 2012. As of January 30, 2015, a total of 956 laboratory-confirmed cases of MERS-CoV infection, including at least 351 deaths (36.7%), have been confirmed by the World Health Organization (WHO) (Figure 1).[2] Between August 1, 2014 and January 30, 2015, there have been 102 cases (and 44 deaths) confirmed by WHO with an additional 14 cases including 3 deaths (and 5 additional deaths from previous cases) pending WHO confirmation. All cases reported thus far have had a direct or indirect link through travel or residence to 9 countries in or near the Arabian Peninsula (Saudi Arabia, United Arab Emirates, Qatar, Oman, Jordan, Kuwait, Iran, Lebanon, and Yemen); at least 17 countries (including the United States) have had travel-associated cases (Figure 1). Most MERS-CoV patients have had fever, cough and shortness of breath, often leading to severe respiratory complications (e.g., pneumonia or acute respiratory distress syndrome);[3, 4] some cases with mild or no symptoms (often tested as part of a contact investigation) have also been reported.[5, 6] Other reported symptoms include chills/rigors, headache, cough, dyspnea, myalgia, sore throat, coryza, dizziness, nausea/vomiting, diarrhea, and abdominal pain. Laboratory findings seen in some patients include leukopenia, lymphopenia, thrombocytopenia, thrombocytosis, and elevated levels of lactate dehydrogenase, alanine aminotransferase, and aspartate aminotransferase.[3, 4] In some MERS-CoV patients, co-infection with other respiratory pathogens has been reported;[7, 8] thus, identification of an alternative respiratory diagnosis should not rule out the possibility of MERS-CoV. The median age of persons with laboratory-confirmed MERS-CoV infection is 49 years, ~63% have been males, and ~18% have been health-care workers.[2] Early on in the outbreak, a predominance of male patients and those with comorbidities was noted, and most cases had severe illness. However, as additional data are collected, the full spectrum of illness is becoming more clear, with a decrease in the

percentage of severe cases and increase in asymptomatic cases, as well as a decline in the male-to-female ratio, median age, and case-fatality rate.[9]

MERS-CoV transmission is not fully understood; however, many cases have had exposures to health-care settings during the 14 days before symptom onset (the median incubation period is approximately 5 days, with a range of 2-13 days). Recent data highlight the likely role of camels as a source of human infection in some cases (e.g., MERS-CoV has been found in camels in the region; MERS-CoV gene sequences in camels are similar to those in humans; camels have had antibodies to MERS-CoV or a MERS-CoV like virus, suggesting previous MERS-CoV infection, and full gene sequencing has linked MERS-CoV identified in a camel to a patient who died of MERS-CoV). [10-15] On May 1 and May 11, 2014, two cases of MERS-CoV infection were identified in Indiana and Florida, respectively.[16, 17] Both US cases were healthcare workers in Saudi Arabia and presented to hospitals in the US with mild to moderate, non-specific findings, where they were identified as having MERS-CoV by astute clinicians sensitized to the need to identify and test returning travelers with respiratory illnesses. Both patients were appropriately isolated and no secondary cases were identified despite extensive follow-up. These cases emphasize the importance of US clinicians becoming familiar with the clinical and epidemiologic features and actions needed to detect and manage MERS-CoV patients. The number of MERS cases has continued to increase; therefore, the risk of exportation of cases to the US mandates that clinicians need to continue to be vigilant.

CDC recommends evaluation for MERS-CoV infection for the following: [18]

1. Patients with fever and clinical or radiographic evidence of pneumonia or acute respiratory distress syndrome and either a history of travel from countries in or near the Arabian Peninsula (Bahrain; Iraq; Iran; Israel, the West Bank and Gaza; Jordan; Kuwait; Lebanon; Oman; Qatar; Saudi Arabia; Syria; the United Arab Emirates; and Yemen) within 14 days

- before symptom onset, or close contact with a symptomatic traveler who developed fever and acute respiratory illness within 14 days after traveling from countries in the region.
2. Patients who are a member of a cluster of patients with severe acute respiratory illness (e.g., fever and pneumonia requiring hospitalization) of unknown etiology in which MERS-CoV is being evaluated, in consultation with state and local health departments.
 3. Patients with fever and symptoms of respiratory illness (e.g., cough, shortness of breath) who have a history of being in a healthcare facility (as a patient, worker, or visitor) within 14 days before symptom onset in a country or territory in or near the Arabian Peninsula in which recent healthcare-associated cases of MERS-CoV have been identified.

Laboratory testing for suspected MERS-CoV cases in the US can be performed using CDC's real-time reverse transcription–PCR (rRT-PCR) assay.[19] Testing of multiple specimens from different sites (i.e., nasopharyngeal swab, oropharyngeal swab, sputum, serum and stool/rectal swab) at different times after symptom onset is recommended to maximize the probability of MERS-CoV detection. Lower respiratory tract specimens (e.g., sputum or bronchoalveolar lavage) and serum should be tested when possible because MERS-CoV infection has sometimes been detected in lower respiratory specimens or serum when upper respiratory specimens had tested negative, including in the two US cases.[16, 17] Most state health department laboratories in the US are approved for MERS-CoV testing; clinicians should contact their state or local health department when evaluating a patient for MERS-CoV infection. If testing is not available through coordination with state and local health departments, samples can be sent to CDC for testing.[18] Serologic testing, which is useful for making a retrospective diagnosis, is only available in the US at the CDC.

Health care-associated infections have played a major role in the transmission of MERS-CoV.[4, 9, 20-23] Based on the experience with SARS-CoV patients and early data from MERS-CoV, strict infection control practices prevent spread of infection.[24] Thus, CDC recommends implementation of

screening and triage procedures for early recognition of potentially infected patients and prompt institution of infection-control measures, including standard, contact, and airborne precautions (airborne precautions include care in an airborne infection isolation room, eye protection with goggles or face shield, and respiratory protection at least as protective as a fit-tested N95 filtering facepiece respirator that has been NIOSH-certified), to prevent secondary cases in health-care workers or other patients.[18] Health care workers exposed to aerosol-generating procedures (e.g., sputum induction, intubation and airway suctioning) appear to be at particularly high risk.[23] A high degree of respiratory protection (i.e., including airborne precautions) is currently recommended by CDC because data on MERS-CoV transmission are limited; these guidelines are similar to what was recommended during the SARS response and will be updated as additional information becomes available.

No specific vaccine or treatment is currently available for MERS-CoV. Many hospitalized patients become severely ill, with respiratory failure followed by multi-organ failure.[8] Clinical management focuses on supportive care.[8, 16, 18] In a small retrospective cohort study, 20 severely ill patients with MERS-CoV were treated with a combination of ribavirin and interferon alfa-2a, compared to 24 patients in a comparison group. Improved survival in treated patients was noted at 14 days, but the results at 28 days were not statistically significant. A randomized controlled trial will be needed to determine if this treatment is of benefit. [25]

No restrictions on travel to or from the Arabian Peninsula are recommended.[26] However, CDC recommends that travelers protect themselves from MERS-CoV exposures by washing their hands frequently and avoiding close contact with ill persons. Given the emerging data on camels as a reservoir, the World Health Organization and CDC recommend general hygiene measures (including regular handwashing before and after touching animals and avoiding contact with sick animals) for persons visiting farms, markets, or other places where animal contact is possible.[26] Consumption of raw or undercooked animal products, including camel milk, should also be avoided. Additional precautions that

are recommended for persons at high risk for severe MERS (people with diabetes, kidney failure, chronic lung disease or weakened immune systems) include avoiding contact with camels as well as consumption of raw camel milk and urine. In addition, people who are traveling to the region to provide health care services should review CDC's infection control guidelines for MERS.[26] Travelers from the region with onset of fever or respiratory symptoms during their trip or within 14 days of leaving the region should seek medical care. Before presenting for care, patients should inform the health care facility of their recent travel so appropriate isolation measures can be implemented.

To prevent further introduction of cases of MERS-CoV into the US, CDC has developed guidance for US travelers to countries in or near the Arabian Peninsula about MERS-CoV, including information aimed at those attending mass gatherings, such as the Hajj and Umrah,[26] and public health messages about MERS have been posted at US airports. CDC has also conducted MERS outreach with community-based organizations, travel agencies, institutes of higher learning, and businesses for travelers to the Arabian Peninsula. CDC has also shared guidance to rapidly identify MERS-CoV cases among travelers to the US with airlines, Customs and Border Protection, and the Transportation Security Administration.

CDC is working with international partners to conduct studies aimed at better understanding MERS-CoV transmission and risk factors for illness in community and hospital settings. As new information becomes available, CDC will update its recommendations.[18] MERS-CoV and Ebola virus disease remind us all of the interconnectedness of the US to the rest of the world. With the increase in global travel, we must remain alert for emerging infectious diseases to protect Americans and the world from these public health threats.

Disclaimer:

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Figure Legend

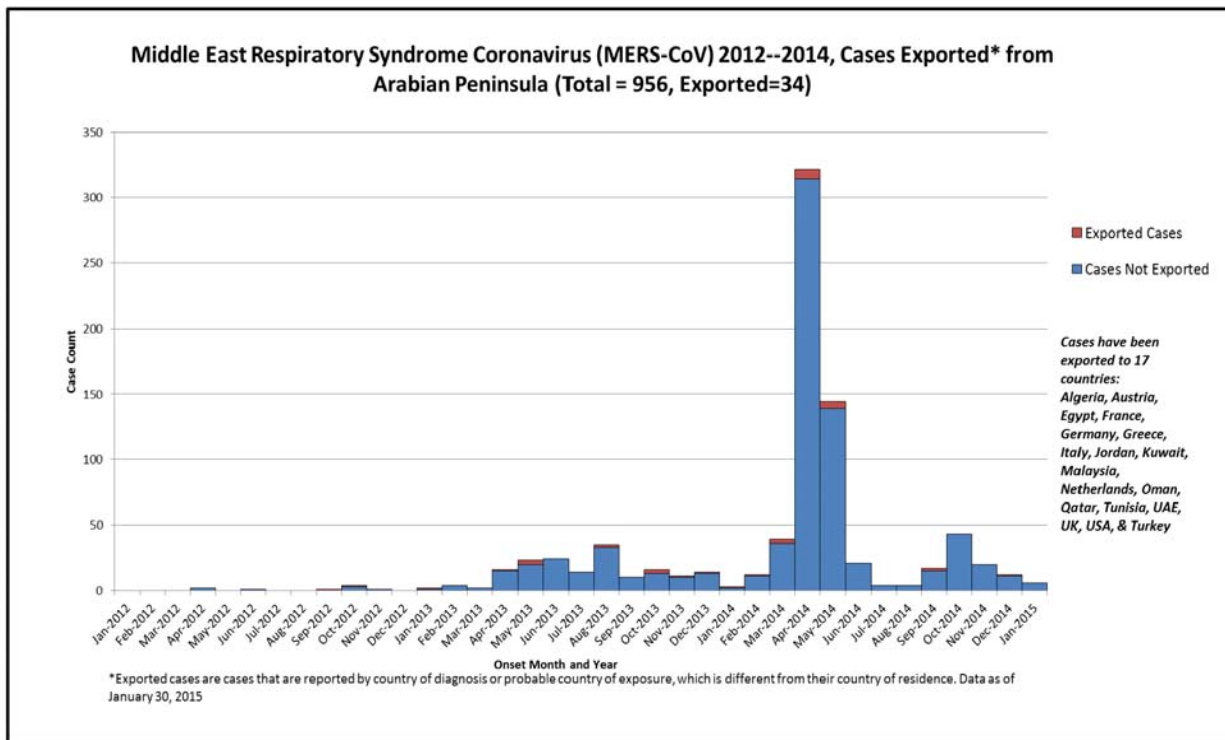
FIGURE. Number of confirmed cases of Middle East Respiratory Syndrome-Coronavirus (MERS-CoV) infection (including those that were travel-associated) reported by the World Health Organization (WHO) as of January 27, 2015, by month and year of illness onset — worldwide, 2012–2015.[2]

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