Introduction

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) was first identified in Saudi Arabia as a novel coronavirus in 2012 causing severe respiratory illness in persons in the Arabian Peninsula in the Middle East. MERS-CoV is highly virulent, and about one-third of known infected individuals die from the infection. The virus appears to be most aggressive in people with underlying medical conditions. Most people confirmed to have MERS-CoV infection have developed lower respiratory infections manifesting as fever, cough, and shortness of breath. However, other symptoms including sore throat, coryza, nausea and vomiting, dizziness, diarrhea, and abdominal pain have been reported. MERS-CoV specific antibodies and MERS-CoV infection have been detected in dromedaries (Arabian camels) in several countries in the Middle East, Africa and South Asia. These animals have been suggested to be major reservoir hosts for and an animal source of MERS infection in humans. However, phylogenetic analysis of the evolutionary origins suggests bats are the original source of the virus. The route of transmission from animals to humans is not fully understood. Currently, there is no evidence that the virus spreads easily from person to person. Most cases of person-to-person spread have occurred in healthcare personnel and other close contacts such as family members and caregivers of patients with MERS-CoV infection.

As of October 2021, 2,578 laboratory-confirmed cases of infection with MERS-CoV have officially been reported to the World Health Organization, including 888 deaths. The vast majority (>80-90%) of cases and deaths were reported from Saudi Arabia. All cases have an epidemiologic link to the Middle East (Arabian Peninsula; see Figure 1). The largest known outbreak of MERS, involving 186 patients and 38 deaths, occurred in Korea in 2015 and was associated with a traveler returning from the Middle East. The risk that MERS-CoV poses to the U.S. public remains low. To date, only two cases of MERS have been reported in the United States, both of which were diagnosed in May 2014. Both patients were healthcare personnel who had traveled from Saudi Arabia, where many cases of the virus have since been confirmed. Both patients were hospitalized and recovered. The Centers for Disease Control and Prevention (CDC) continues to closely monitor the situation and offers testing at their laboratory and through public health laboratories throughout the country.
Who to Test

The CDC recommends testing for individuals who meet the criteria for a Person Under Investigation (PUI). These include any travelers from the impacted regions within or neighboring the Arabian Peninsula (Bahrain; Iraq; Iran; Israel, the West Bank and Gaza; Jordan; Kuwait; Lebanon; Oman; Qatar; Saudi Arabia; Syria; the United Arab Emirates (UAE); and Yemen - see Figure 1, above) with acute lower respiratory symptoms within 14 days of travel, and for people who had close contact with someone diagnosed with MERS.

Specifically, testing should be considered in patients meeting any of the following three main criteria (indicated by the “•” symbol):

• Fever AND pneumonia or acute respiratory distress syndrome (based on clinical or radiological evidence) AND EITHER OF THE THREE CIRCUMSTANCES BELOW:
  a. History of travel from countries in or near the Arabian Peninsula within 14 days before symptom onset.
  OR
  b. Close contact with a symptomatic traveler who developed fever and acute respiratory illness (not necessarily pneumonia) within 14 days after traveling from countries in or near the Arabian Peninsula.
  OR
  c. Is part 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 considered in consultation with state and local health departments.

• Fever AND symptoms of respiratory illness (not necessarily pneumonia; e.g., cough, shortness of breath) AND 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 have been identified

• Fever OR symptoms of respiratory illness AND having had close contact with a confirmed symptomatic MERS case.

Each suspected case should be evaluated and discussed with public health departments especially if the clinical presentation or exposure history is equivocal. Note that fever may not be present in some patients, such as those who are very young, elderly, immunosuppressed, or taking certain medications. Full interim guidance for healthcare professionals is available on the CDC MERS web page.
Specimens and Testing

The preferred specimen for the detection of MERS-CoV is a lower respiratory tract specimen, if available, and if only one type of specimen is collected. However, the CDC recommends collecting lower respiratory, upper respiratory, and serum specimens for molecular and serological testing if possible. Note that collection of stool is no longer recommended by the CDC.

Serologic testing is not routinely utilized for diagnostic purposes, though it may be utilized for surveillance or to investigate ongoing outbreaks. It may also be of utility when patients are greater than 14 days from symptom onset. Serologic testing can be performed at the CDC utilizing a two-step screening and confirmatory assay approach. When performed, acute and convalescent samples should be obtained. Serologic positivity may reflect past exposure, and not necessarily active disease.

Table 1 summarizes the specimen requirements for potential MERS-CoV testing. Consult with your state or local public health laboratory for obtaining approval for testing and for specific instructions and shipping guidelines.

Table 1. CDC Specimen Collection and Transport Guidance for MERS-CoV

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Optimal Collection Time</th>
<th>Specimen Collection Container and Volume</th>
<th>Shipping Conditions</th>
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<tr>
<td>Lower respiratory (bronchoalveolar lavage, sputum, tracheal aspirate) is the preferred specimen if only one specimen type collected</td>
<td>Respiratory specimens should be collected as early as possible after symptom onset. Multiple specimens from different sites at different times after symptom onset is recommended.</td>
<td>2-3 mL in a sterile leak-proof cup</td>
<td>Refrigerated (4°C) or placed on cold packs if specimen will be tested within 72 h of collection. If &gt;72 h, freeze specimen at -70°C as soon as possible after collection and ship on dry ice.</td>
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<tr>
<td>Upper respiratory tract (nasopharyngeal and/or throat swab; nasopharyngeal wash/aspirate; nasal aspirate)</td>
<td>Nasopharyngeal and throat swabs (synthetic fiber with plastic shafts) can be combined in 2-3 mL of viral transport media Wash/aspirate: 2-3 mL in sterile leak-proof cup</td>
<td>Adults: 5-10 mL Infants: 1 mL Serum separator tube</td>
<td></td>
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<tr>
<td>Serum (for rRT-PCR testing)</td>
<td>Within 10-12 days of symptom onset</td>
<td>Adults: 5-10 mL Infants: 1 mL Serum separator tube</td>
<td></td>
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<tr>
<td>Serum (for surveillance serologic testing)*</td>
<td>≥14 days post onset</td>
<td>Adults: 5-10 mL Infants: 1 mL Serum separator tube</td>
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*Serologic testing is currently only available at the CDC for research/surveillance purposes and not for diagnostic purposes. Contact CDC’s Emergency Operations Center (EOC) (770-488-7100) for consultation and approval if serologic testing is being considered.
Real-time RT-PCR (rRT-PCR) testing is carried out by public health laboratories and/or the CDC using the “CDC Novel Coronavirus 2012 Real-time PCR Assay.” The test is available to public health laboratories through Emergency Use Authorization (EUA) provided by the FDA. There are 3 targets in the assay: NCV.N2 (nucleocapsid protein gene), NCV.N3 (nucleocapsid protein gene) and NCV.upE (region upstream of envelope protein gene). Most state public health laboratories and some local public health laboratories have been provided the primers and probes by CDC and demonstrated competency in performing the test. Clinical laboratories should contact their state or local public health laboratory to determine if the test is available locally or if it will be performed by the CDC. Timely communication between clinical laboratories and public health laboratories is essential to ensure accurate and efficient testing. Once testing is coordinated, specimens should be packaged and shipped to public health laboratory or the CDC as UN 3373 Biological Substance, Category B.

Note that it is strongly recommended to test for other common respiratory pathogens using molecular or antigen detection based on clinical presentation, epidemiology, and time of year of testing. Laboratories should NOT attempt viral isolation in cell culture unless performed in a BSL-3 facility.

**Biosafety**

Since little is known about MERS-CoV transmission, caution must be practiced when handling potentially infectious specimens in the laboratory. Specimens from patients suspected of having MERS-CoV must be handled in a BSL-2 laboratory using standard BSL-2 practices, and specimen manipulation must be performed in a class II biosafety cabinet. Any propagation of MERS-CoV virus or manipulation of MERS-CoV virus cultures must be performed in a BSL-3 laboratory using BSL-3 practices, including a respirator and eye protection. Specific MERS-CoV biosafety guidelines can be found here: [https://www.cdc.gov/coronavirus/mers/guidelines-lab-biosafety.html](https://www.cdc.gov/coronavirus/mers/guidelines-lab-biosafety.html). Laboratories may also consult the updated Biosafety in Microbiological and Biomedical Laboratories (BMBL) for guidance on how to safely handle potential MERS-CoV specimens.

**Conclusion**

Clinical laboratories should contact their state or local public health laboratory for assistance with collection of specimens and transport of specimens for MERS-CoV testing. The CDC continues to work with the World Health Organization to better understand the pathogenicity and epidemiology of the virus, how it is spread, ways to prevent spread and the risk it poses to the general public.

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References