Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Infection

Signs and Symptoms	• Initial symptoms of fever, cough, and shortness of breath; diarrhea may occur • May progress to pneumonia, respiratory distress, and sometimes kidney failure
Incubation	Not definitively defined, up to 14 days

Case classification	**Person under investigation (PUI) – within 14 days of symptom onset:**
	• Fever AND pneumonia or acute respiratory distress syndrome AND:
	  ○ Travel in or near the Arabian Peninsula within 14 days before symptom onset, **or**
	  ○ Close contact with a symptomatic traveler who developed fever and acute respiratory illness within 14 days of travel in or near the Arabian Peninsula, **or**
	  ○ In a cluster of cases of severe acute respiratory illnesses (e.g., hospitalized with fever and pneumonia) with MERS-CoV considered in differential diagnosis
	• Fever AND respiratory illness (e.g., cough, SOB) AND was in a healthcare facility within 14 days of symptom onset in or near the Arabian Peninsula in which recent healthcare-associated cases of MERS identified
	• Fever or respiratory illness AND close contact with a confirmed MERS case while ill

	Probable: PUI with absent or inconclusive test results for MERS-CoV (e.g., single PCR target positive) who is a close contact of a laboratory-confirmed MERS-CoV case.
	Confirmed: Laboratory confirmation of MERS-CoV infection (positive PCR on at least 2 gene targets)
	Contact under investigation: Fever or symptoms of respiratory illness within 14 days of close contact with confirmed MERS case while the case was ill
Differential diagnosis	Other respiratory pathogens such as influenza A and B and other respiratory viruses, *Streptococcus pneumoniae*, and *Legionella pneumophila*.
Treatment	Supportive care. Case fatality rate is approximately 35%.
Duration	Depends on severity of illness
Exposure	Persons considered to be potentially exposed include those who were within 6 feet, or within a patient care room, of a confirmed MERS case for a prolonged period of time.

Laboratory testing	LHJ should coordinate with Office of Communicable Disease Epidemiology (CDE) for testing of MERS PUI and their contacts. All MERS testing is performed at CDC.
	• CDC performs PCR on both respiratory specimens and serum as below (send all three if possible):
	  ○ Sputum, bronchoalveolar lavage, tracheal aspirate, pleural fluid
	  ○ Nasopharyngeal and oropharyngeal swabs or nasal aspirate
	  ○ Serum
	See CDC Lab Test Menu for specimen collection and submission instructions.
	https://www.cdc.gov/laboratory/specimen-submission/list.html and
	https://www.cdc.gov/coronavirus/mers/guidelines-clinical-specimens.html

Public health actions **URGENT**	• Immediately report to OCDE any MERS PUI • Ensure proper infection control for a PUI-- standard, contact and airborne precautions • Ill close contacts should be isolated at home if not requiring medical attention

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Infection

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To identify infections due to Middle East Respiratory Syndrome Coronavirus (MERS-CoV).
2. To prevent the spread of MERS-CoV.

B. Legal Reporting Requirements

1. **Health care providers** and **Health care facilities**: *immediately* notifiable to **local health jurisdiction**
2. Laboratories: *immediately* notifiable to **local health jurisdiction**; submission on request – presumptive positive isolate or if no isolate specimen associated with positive result, within 2 business days
3. **Local health jurisdictions**: *immediately* notifiable to Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (CDE)

C. Local Health Jurisdiction Investigation Responsibilities

1. Contact CDE **immediately (206-418-5500 or 877-539-4344)** regarding suspected MERS-CoV infections. Determine exposures for the case. Facilitate the transport of specimens to the Washington State Public Health Laboratories (PHL) for testing at CDC. Ensure that appropriate infection control practices are implemented while testing is pending.
2. For laboratory positive cases, complete the https://www.cdc.gov/coronavirus/mers/downloads/mers-investigation-short-form.pdf and enter case data into Washington Disease Reporting System (WDRS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Coronaviruses are named for crown-like spikes on their surface. Human coronaviruses were first identified in the mid-1960s. The family includes common viruses that most people get some time in their lives, which usually involve mild to moderate upper-respiratory tract illnesses.

There are three main sub-groupings of coronaviruses: alpha, beta and gamma, and a fourth provisionally-assigned new group called delta coronaviruses. Middle East Respiratory Syndrome coronavirus (MERS-CoV) is a beta coronavirus that was first reported in 2012 in Saudi Arabia. It is different from the six other coronaviruses that have previously been found in humans: alpha coronaviruses 229E and NL63 and beta coronaviruses SARS-CoV-1 (cause of severe acute respiratory syndrome [SARS]), SARS-CoV-2 (cause of COVID-19 – see separate guideline), OC43, and HKU1.

Coronaviruses may also infect many different animals and cause them to have respiratory, gastrointestinal, liver, and neurologic diseases. Most of these coronaviruses usually infect only one animal species or, at most, a small number of closely related species. The reservoir for MERS-CoV is dromedary camels. However, the related SARS-CoV can infect people and several types of animals, including monkeys, Himalayan palm civets, raccoon dogs, cats, dogs, and rodents.

B. Description of Illness

Initial MERS symptoms are fever, cough, and shortness of breath. Other reported early symptoms include headache, chills, myalgia, nausea/vomiting, and diarrhea. Disease may progress to pneumonia, respiratory distress, septic shock, and multi-organ failure. The case fatality rate is about 35%. People with diabetes, kidney failure, or chronic lung disease, and people who have weakened immune systems are at a higher risk of severe disease, including death. Approximately 10-30% of cases are asymptomatic or have mild disease.

C. MERS-CoV Infections Globally

As of October 2022, 2600 laboratory-confirmed cases including at least 935 associated deaths have been reported to the World Health Organization (WHO). Of these, 2193 were reported from Saudi Arabia with 854 deaths.

To date, 27 countries have reported cases including countries in or near the Arabian Peninsula: Bahrain, Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia (KSA), United Arab Emirates (UAE) and Yemen. The only known US cases of MERS were reported in May 2014 in Indiana and Florida, with exposures in the Middle East. Other countries in Africa, Europe and Asia have also had travel-associated cases.

For updates on recently reported cases of infection with MERS-CoV see WHO MERS situation updates available at https://www.emro.who.int/health-topics/mers-cov/mers-outbreaks.html

D. Reservoirs

Current scientific evidence suggests that dromedary camels are a major reservoir host for MERS-CoV and an animal source of MERS infection in humans. The virus likely originated in a bat and transferred to camels. Genetic sequencing to date has determined the virus is most closely related to coronaviruses detected in bats. MERS-CoV gene sequences and serologic evidence of past infection have been found in camels in several countries in or near the Middle East.

E. Modes of Transmission

Studies have shown that humans are infected through direct or indirect contact with infected dromedary camels. MERS-CoV has been identified in dromedaries in several countries, including Egypt, Oman, Qatar, and Saudi Arabia, and MERS-CoV specific antibodies in dromedaries in the Middle East, Africa and South Asia.

Viral shedding may last weeks. The virus does not pass easily from one person to another unless there is close contact, such as providing unprotected care to an infected patient. There have been clusters of cases in healthcare facilities, where human-to-human transmission appears to have occurred, especially when infection prevention and control

practices are inadequate, as for example a large cluster of 186 cases reported from Republic of Korea (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5840604/). Human to human transmission has been limited to date, and has been identified among family members, patients, and health care workers. While the majority of MERS cases have occurred in health care settings, thus far, no sustained human to human transmission has been documented anywhere in the world.

F. Incubation Period

The current case definition uses an onset of illness within 14 days for travelers to the Arabian Peninsula or neighboring countries including patients or visitors who were present in a healthcare facility within 14 days before illness onset. See section 3.A.

G. Period of Communicability

The period of communicability for MERS-CoV is unknown at this time. Until further guidance is available, follow isolation recommendations used for SARS; persons with MERS should be isolated (for example, by not going to work or to school) until 10 days after fever has resolved, provided respiratory symptoms are absent or improving. See Appendix A in 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings available at: https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html

H. Treatment

Treatment is supportive: https://www.cdc.gov/coronavirus/mers/clinical-features.html

3. CASE DEFINITIONS

A. Case Classification see: https://www.cdc.gov/coronavirus/mers/interim-guidance.html

Person Under Investigation (PUI)

Consider a person with any of the three following sets of characteristics as a **person under investigation (PUI)**:

- Fever AND pneumonia or acute respiratory distress syndrome (based on clinical or radiologic evidence) AND EITHER:
  - Travel in or near the Arabian Peninsula within 14 days of symptom onset, **or**
  - Close contact[2] with a symptomatic traveler who developed fever and acute respiratory illness within 14 days of travel in or near the Arabian Peninsula, **or**
  - In a cluster of cases of severe acute respiratory illnesses (e.g., hospitalized with fever and pneumonia) with MERS-CoV considered in differential diagnosis
- Fever AND respiratory illness (e.g., cough, shortness of breath) AND was in a healthcare facility within 14 days of symptom onset in or near the Arabian Peninsula in which recent healthcare-associated cases of MERS identified
- Fever OR symptoms of respiratory illness (e.g., cough, shortness of breath) AND Close contact[2] with a confirmed MERS case while the case was ill.

Probable Case

A PUI with absent or inconclusive laboratory results for MERS-CoV infection who is a close contact[2] of a laboratory-confirmed MERS-CoV case. Examples of laboratory results that may

be considered inconclusive include a positive test on a single PCR target, a positive test with an assay that has limited performance data available, or a negative test on an inadequate specimen.

Confirmed Case

A person with laboratory confirmation of MERS-CoV infection. Confirmatory laboratory testing requires a positive PCR on at least two specific genomic targets or a single positive target with sequencing on a second.

Contact Under Investigation of a Confirmed Case of MERS

As part of investigation of confirmed cases, in consultation with a state or local health department, a person with fever or symptoms of respiratory illness within 14 days following close contact[2] with a confirmed case of MERS while the case was ill should be evaluated for MERS-CoV infection.

Footnotes

1. Countries considered in the Arabian Peninsula and neighboring include: Bahrain; Iraq; Iran; Israel, the West Bank and Gaza; Jordan; Kuwait; Lebanon; Oman; Qatar; Saudi Arabia; Syria; the United Arab Emirates (UAE); and Yemen.
2. Close contact is defined as: a) being within approximately 6 feet (2 meters), or within the room or care area, of a confirmed MDRS case for a prolonged period of time (such as caring for, living with, visiting, or sharing a healthcare waiting area or room with a confirmed MDRS case) while not wearing recommended personal protective equipment (e.g., gowns, gloves, NIOSH-certified disposable N95 respirator, eye protection) or b) having direct contact with infectious secretions (e.g., being coughed on) of a confirmed MDRS case while not wearing recommended personal protective equipment. See CDC's Interim Infection Prevention and Control Recommendations for Hospitalized Patients with Middle East Respiratory Syndrome Coronavirus (MERS-CoV) for more detail. Data to inform the definition of close contact are limited; considerations when assessing close contact include the duration of exposure (e.g., longer exposure time likely increases exposure risk) and the clinical symptoms of the person with MERS (e.g., coughing likely increases exposure risk). Special consideration should be given to those exposed in healthcare settings. For detailed information regarding healthcare personnel (HCP) please review CDC's Interim U.S. Guidance for Monitoring and Movement of Persons with Potential Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Transient interactions, such as walking by a person with MERS, are not thought to constitute an exposure; however, final determination should be made in consultation with public health authorities.

4. LABORATORY DIAGNOSIS AND SERVICES

A. Laboratory Diagnosis at Washington State Public Health Laboratories (PHL)

All testing must be discussed with and approved by local health and OCDE before submission to PHL.

Testing for MERS is performed at CDC using PCR assay to detect MERS-CoV in respiratory and serum specimens.

B. Specimen Collection

There is incomplete knowledge about pathogenic potential and transmission dynamics of MERS-CoV. To increase the likelihood of detecting infection, collect and submit lower respiratory, upper respiratory, and serum specimens. Lower respiratory samples include bronchoalveolar lavage, tracheal aspirate, pleural fluid, and sputum; upper respiratory samples include nasopharyngeal and oropharyngeal swabs. Lower respiratory samples from an intubated patient are preferred over upper, but upper respiratory are generally

preferred over sputum. CDC provides testing guidance at: http://www.cdc.gov/coronavirus/mers/guidelines-clinical-specimens.html

Use appropriate personal protective equipment (standard, contact and airborne precautions) when collecting clinical specimens for MERS-CoV testing.

Refrigerate all specimens at 2-8ºC up to 72 hours and ship cold; if exceeding 72 hours holding time, freeze at -70ºC. When shipping frozen specimens use a combination of dry ice and frozen gel ice-packs, not wet ice, to maintain temperatures over several days.

Lower Respiratory Tract:

- **Broncheoalveolar lavage, tracheal aspirate, pleural fluid**

  Collect 2-3 mL in a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container.

- **Sputum**

  Have the patient rinse the mouth with water and then expectorate deep cough sputum directly into a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container.

Upper Respiratory Tract:

- **Nasopharyngeal and oropharyngeal swabs (NP/OP swabs)**

  Use only synthetic fiber (e.g., Dacron, nylon, polyester) swabs with plastic shafts. Calcium alginate swabs or wooden shafted swabs may inhibit PCR tests. Place swabs immediately into sterile tube containing 2-3 mL viral transport media. NP/OP specimens should be combined, placing both swabs in the same vial.

  - **Nasopharyngeal swabs** -- Insert a swab in the nostril parallel to the palate. Leave in place for a few seconds to absorb secretions. Swab both nasal areas.
  - **Oropharyngeal swab** -- Swab the posterior pharynx, avoiding the tongue.

- **Nasal Aspirate**

  Collect 2-3 mL into a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container.

Serum:

- Serum for PCR testing should be collected during the first week after symptom onset, preferably within 3-4 days after symptom onset.
  - **Adults and children:** Collect 1 tube (5-10 mL) whole blood in a serum separator tube. Serum separator tubes should be stored upright for at least 30 minutes, and then centrifuged at 1000–1300 relative centrifugal force (RCF) for 10 minutes before removing the serum and placing it in a separate sterile tube for shipping (such as a cryovial). The minimum amount of serum required for testing is 200 µL.
  - **Infants:** A minimum of 1 mL of whole blood is needed for testing of pediatric patients. Collect at least 1 mL in a serum separator tube and process as above.

- Serum for serologic testing for MERS antibodies, collect serum during acute symptoms, preferably the first week after onset of illness, and again ≥ 3 weeks later.
    - **Adults, children and infants:** Collect and process as above. Note, if both MERS-CoV serology and rRT-PCR tests are planned, the minimum amount of serum required is 400 µL (200 µL for each test).

C. Shipping

Specimens should be stored and shipped at the temperatures indicated above.

Specimens from suspected MERS cases shipped within the United States must be packaged, shipped, and transported in accordance with the shipping regulations from the US Department of Transformation (USDOT). Packaging procedures can be found in the USDOT document entitled, *Transporting Infectious Substances Safely* at: https://www.phmsa.dot.gov/sites/phmsa.dot.gov/files/docs/Transporting_Infectious_Substances_brochure.pdf.

Package all specimens to prevent breakage and spillage. The primary container (containing specimen) must be leak-proof and sealed securely with either tape or Parafilm® and placed in zip-sealing, leak-proof bags with enough absorbent material to capture the contents of the primary container. Each requisition form should be attached to the zip-sealing bag with the primary container. Multiple primary containers (each in a zip-sealing bag with requisition slip attaches) may be placed in a secondary leak-proof container. The secondary container is then placed in an outer certified box. The outer box must be labeled with the specimen's bioterrorism agent category level. Clinical specimens for MERS-CoV testing are category B.

When shipping frozen specimens use a combination of dry ice and frozen gel ice-packs, not wet ice, to maintain temperatures over several days.

Avoid shipping problems:

- Do not place any dry ice in the primary container or secondary container, foam envelopes, ziplock bags, cryovial boxes, or hermetically sealed containers.
- Do not place primary containers sideways or upside down in zip-sealing bags.
- Do not place any paperwork in the zip-sealing bags, so as not to damage the paperwork.
- Do not use biohazard autoclave bags to prepack your materials due their inadequate sealing.

Note that PHL require all clinical specimens have **two** patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

5. CONTROLLING FURTHER SPREAD

A. Infection Control Recommendations in Healthcare Settings

Immediately implement standard, contact, and airborne precautions for MERS-CoV persons under investigation (PUI). For all patient care activities use gloves, gowns, eye protection and an N95 or higher respirator. These recommendations are consistent with those recommended for the coronaviruses that caused severe acute respiratory syndrome (SARS) and COVID-19.

Care for PUI in an Airborne Infection Isolation Room (AIIR). If this is not available, transfer the patient as soon as possible to a facility with an AIIR. Pending transfer, place a facemask on the patient, if tolerated, and house in a single-patient room with the door closed. The patient should not be placed in any room where room exhaust is recirculated without high-efficiency particulate air (HEPA) filtration. Once in an AIIR, the patient's facemask may be removed.

When outside of the AIIR, patients should wear facemasks to contain secretions. Limit transport and movement of a patient outside of the AIIR to medically-essential purposes. Implement staffing policies to minimize the number of personnel that must enter the room. Infection prevention recommendations may be updated as information about transmission and the severity of clinical illness caused by MERS-CoV becomes available.

For full details of these precautions, see:

https://www.cdc.gov/coronavirus/mers/infection-prevention-control.html

https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html

https://www.cdc.gov/coronavirus/mers/interim-guidance.html

B. Contact Management

Any person who has had close contact with a person under investigation (Section 3A), probable or confirmed case while the person was ill, should be carefully monitored for 14 days for the appearance of respiratory symptoms. Close contact is defined as: a) being within approximately 6 feet (2 meters) or within the room or care area, of a confirmed MERS case for a prolonged period of time (such as caring for, living with, visiting, or sharing a healthcare waiting area or room with a confirmed MERS case) while not wearing recommended personal protective equipment (i.e., gowns, gloves, NIOSH-certified disposable N95 respirator, eye protection) or, b) having direct contact with infectious secretions (e.g., being coughed on) while not wearing recommended personal protective equipment. See CDC's Infection Prevention and Control Recommendations for more detail. Transient interactions, such as walking by a person with MERS, are not thought to constitute and exposure; however, final determination should be made in consultation with public health authorities.

Use the DOH MERS Contact Investigation Form to investigate each contact. (http://www.doh.wa.gov/Portals/1/Documents/5100/420-106-CaseContactForm-MERS-CoV.pdf) The local health jurisdiction should provide contacts of a case with instructions to check daily temperature and other symptoms to watch for and should assess contacts for symptoms at the end of the 14 day period, at a minimum, and more frequently as resources allow. If the contact develops fever, cough, shortness of breath, or breathing

trouble, they should be told to: isolate at home until evaluated; wear a mask when around other people; and consult with their healthcare provider and report the MERS-CoV risk exposure. If the contact has an outpatient or emergency department visit they should be told to put on a mask before entering the facility and to report the potential MERS-CoV exposure. Infection control measures should continue until MERS-CoV testing is done. See: https://www.cdc.gov/coronavirus/mers/hcp/home-care-patient.html

If severe acute respiratory illness develops within the first 14 days following the contact, the individual should be considered a "Person Under Investigation" and reported to CDC.

Guidance for patients and contacts who are managed in in home settings is available at: https://www.cdc.gov/coronavirus/mers/hcp/home-care.html

If milder symptoms develop during this period, call the Office of Communicable Disease Epidemiology at (206) 418-5500 to discuss management of the contact.

C. Prevention and Environmental Measures

The approach to prevention and environmental cleaning and disinfection for MERS-CoV will follow the same principles used for controlling the spread of other infections in healthcare settings. See: https://www.cdc.gov/coronavirus/mers/infection-prevention-control.html

D. Travel Measures

CDC recommends that travelers practice general hygiene precautions such as frequent handwashing; avoiding touching the eyes, nose, and mouth; and avoiding contact with sick people. The World Health Organization (WHO) considers certain groups to be at high risk for severe MERS, including people with diabetes, kidney failure, chronic lung disease, or immunocompromised people. WHO recommends that these groups take additional precautions: avoid contact with camels, do not drink raw camel milk or raw camel urine, and do not eat undercooked meat, particularly camel meat.See CDC Travelers' Health https://wwwnc.cdc.gov/travel/diseases/mers for more detailed information.

CDC is recommending airline contact investigations if a case is known to have been symptomatic during or shortly after an air flight. Investigations will involve interviewing passengers and crew, referring symptomatic contacts for medical evaluation, and advising monitoring of asymptomatic contacts for 14 days. Any contacts developing symptoms should be isolated and undergo medical evaluation. After 14 days, contacts should have a final interview to assure that no symptoms occurred.

ACKNOWLEDGEMENTS

This document was created from information from the Centers for Disease Control and Prevention. http://www.cdc.gov/coronavirus/mers/index.html and adapted from Public Health – Seattle and King County.

UPDATES

May 2014: Section 2 was updated with case counts and epidemiologic information; section 3 with newer recommendations on evaluation for MERS-CoV in PUIs; and section 4 with newer testing recommendations from CDC.

July 2014: Section 2 was updated with case counts and affected countries; section 3 with updated case classification descriptions.

June 2015: Section 1 was updated with the CDC MERS PUI Report Form; section 2 with new countries affected.

August 2015: Section 2 was updated with new countries affected.

August 2017: Quick reference sheet added to Guideline. Section 2 was updated with case counts and countries affected.

September 2017: Corrected links to laboratory test requisition form and updated requirements for reporting PUI to CDC.

December 2021: Updated coronavirus information to include SARS CoV-2 (Section 2A); updated global case counts (Section 2C); updated definition for a person under investigation (Section 3A); linked to CDC for prevention and environmental measures (Section 5C).

December 2022: For 2023 WAC revision combined provider and facility reporting requirement (Section 1B2), updated laboratory submission (Section 1B3); updated regarding MERS testing is no longer available at PHL, only at CDC; updated global case counts (Section 2C).