

Surveillance for human infection with Middle East respiratory syndrome coronavirus (MERS-CoV)

Interim guidance

Updated June 2018

WHO/MERS/SUR/15.1 Revision 1



Update

This document summarizes WHO recommendations for surveillance for Middle East respiratory syndrome coronavirus (MERS-CoV) infection, which were first published in 2012. WHO will continue to update these recommendations as new information becomes available.

It is important to note that this guidance may be implemented in different countries with varying resources and epidemiological patterns, and should be adapted accordingly.

Current Update: The key change in the June 2018 version:

- Background information was updated and
- Links to WHO's Case Report and Initial Interview Forms have been added.

Previous Updates: The key change in the 30 June 2015 version:

- Guidance for surveillance in clusters of cases associated with health care facilities

Background

Since 2012 and as of 5 May 2018, more than 2200 cases of laboratory confirmed Middle East respiratory syndrome (MERS) have been reported to WHO. The virus is circulating widely throughout the Arabian Peninsula, and, to date, the largest number of human cases have been reported by Saudi Arabia.

Human-to-human transmission of MERS-CoV has been documented in several clusters of cases, including among family members and in health care facilities in several countries. While there have been large nosocomial outbreaks in the Middle East and in the Republic of Korea, so far, there has been no evidence of sustained human-to-human transmission.

The clinical spectrum of MERS-CoV infection ranges from asymptomatic to severe pneumonia presenting acute respiratory distress syndrome (ARDS) and other life-threatening complications such as septic shock and multi-organ failure. Approximately 36% of laboratory confirmed cases have had a fatal outcome. Co-infections with bacteria and with other respiratory viruses including parainfluenza, rhinovirus, influenza A & B, pneumococcus, and ventilator-associated pneumonia have been reported.

The average incubation period for cases in whom exposure is between 5.5–6.5 days, and evidence suggests that the incubation is less than 14 days.^{1,2}

Recommendations for specimen collection

Lower respiratory specimens have a higher diagnostic value than upper respiratory tract specimens for detecting MERS-CoV infection. Upper respiratory tract samples have yielded negative results in some symptomatic close contacts of confirmed cases, who later developed pneumonia and tested positive on lower respiratory specimens. WHO has strongly advised that lower respiratory specimens such as sputum, endotracheal aspirate, or bronchoalveolar lavage be collected for MERS-CoV testing where possible. If patients do not have signs or symptoms of lower respiratory tract disease and the collection of lower tract specimens is not possible or clinically indicated, upper respiratory tract specimens such as a nasopharyngeal aspirate or combined nasopharyngeal and oropharyngeal swabs should be collected.

If initial testing is negative in a patient who is strongly suspected to have MERS-CoV infection, the patient should be resampled and specimens collected from multiple respiratory tract sites. Paired acute and convalescent sera for antibody detection should also be collected. Virus has also been demonstrated in body fluids such as blood, urine, and stool, but usually at lower titres than in respiratory tract specimens. Such specimens may be collected when good quality respiratory tract specimens are unavailable, or to monitor the presence of virus in different body compartments.

Objectives of surveillance

The primary objectives of surveillance are to:

1. Detect early cases of MERS-CoV infection, clusters and any evidence of sustained human-to-human transmission;
2. Determine risk factors and the geographic risk area for infection with the virus.

Additional clinical and epidemiological investigations (see Table 1) are needed to:

1. Determine key clinical characteristics of the illness, such as incubation period, spectrum of disease, and the clinical course of the disease.
2. Determine key epidemiological characteristics of MERS-CoV infection, such as exposures that result in infection, risk factors, secondary attack rates, and modes of transmission.

The following people should be investigated and tested for MERS-CoV

Case definitions for surveillance

1. A person with an acute respiratory infection, with history of fever and cough and indications of pulmonary parenchymal disease (e.g. pneumonia or ARDS), based on clinical or radiological evidence, who requires admission to hospital, with no other etiology that fully explains the clinical presentation¹ (clinicians should also be alert to the possibility of atypical presentations in patients who are immunocompromised);

AND any of the following:

- a. the person resides in the Middle East², in particular where human infections have been reported, and in countries where MERS-CoV is known to be circulating in dromedary camels;
 - b. the patient is part of a cluster³ of acute respiratory illness that occurs within a 14 day period, without regard to place of residence or history of travel;
 - c. the disease occurs in a health care worker who has been working in an environment where patients with severe acute respiratory infections are being cared for, without regard to place of residence or history of travel;
 - d. the person develops an unusual or unexpected clinical course, especially sudden deterioration despite appropriate treatment, without regard to place of residence or history of travel, even if another aetiology has been identified that fully explains the clinical presentation.
2. A person with an acute respiratory infection, with history of fever and cough and indications of pulmonary parenchymal disease (e.g. pneumonia or ARDS), based on clinical or radiological evidence, and who has travelled within 14 days before onset of illness to the Middle East² or countries where MERS-CoV is known to be circulating in dromedary camels or where human infections have recently occurred.
 3. Individuals with acute respiratory illness of any degree of severity who, within 14 days before onset of illness, had any of the following exposures :
 - a. close physical contact⁴ with a confirmed or probable case of MERS-CoV infection, while that patient was ill;

- b. a healthcare facility in a country where hospital-associated MERS-CoV infections have been reported;
- c. direct contact with dromedary camels or consumption or exposure to dromedary camel products (raw meat, unpasteurized milk, urine) in countries where MERS-CoV is known to be circulating in dromedary camel populations or where human infections occurred as a result of presumed zoonotic transmission.

4. Countries in the Middle East² are also strongly encouraged to consider adding testing for MERS-CoV to current testing algorithms as part of routine sentinel respiratory disease surveillance and diagnostic panels for pneumonia.

WHO does not advise special screening at points of entry.

Recommendations for testing in clusters associated with health care settings

Human to human transmission of MERS-CoV can become amplified in health care settings, as has been seen in the large health care associated outbreaks in Jeddah and Riyadh in 2014 and outbreaks seen throughout Saudi Arabia, the United Arab Emirates and in the Republic of Korea in 2015. During such outbreaks WHO recommends that, if feasible, all close contacts⁴ of laboratory confirmed cases, especially health care worker contacts and inpatients sharing rooms/wards with confirmed cases, regardless of the development of symptoms, be tested for MERS-CoV using PCR. Serologic assays are also available and should be considered as part of the evaluation to understand extent of infection in the health care setting.

Public Health Actions

Reporting

WHO requests that probable and confirmed cases be reported within 24 hours of classification, through the regional contact point for International Health Regulations at the appropriate WHO regional office. See current definitions for probable and confirmed cases at: http://www.who.int/csr/disease/coronavirus_infections/case_definition/en/index.html.

The WHO case reporting form is available here: http://www.who.int/csr/disease/coronavirus_infections/mers-cov-interim-case-summary-form.pdf?ua=1.

Investigations around cases of MERS-CoV infection

Many of the critical questions regarding the clinical manifestation and epidemiological characteristics of MERS-CoV infection will be answered only by careful, detailed investigations around cases.

WHO has developed guidance on the types of studies that should be considered. In addition, WHO has updated the Initial interview form for MERS patients. The form is available [here](#) and is designed to gather initial information

¹ Testing should be according to local guidance for management of community-acquired pneumonia. Examples of other aetiologies include *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, *Legionella pneumophila*, other recognized primary bacterial pneumonias, influenza, and respiratory syncytial virus.

² For a map of the Middle East, see: <http://www.un.org/Depts/Cartographic/map/profile/mideastr.pdf>

³ A 'cluster' is defined as two or more persons with onset of symptoms within the same 14 day period, and who are associated with a specific setting such as a classroom, workplace, household, extended family, hospital, other residential institution, military barracks or recreational camp.

⁴ Close contact' is defined as:

- Health care associated exposure, including providing direct care for MERS-CoV patients, working with health care workers infected with MERS-CoV, visiting patients or staying in the same close environment of a MERS-CoV patient.
- Working together in close proximity or sharing the same classroom environment with a with MERS-CoV patient
- Traveling together with MERS-CoV patient in any kind of conveyance
- Living in the same household as a MERS-CoV patient

The epidemiological link may have occurred within a 14-day period before or after the onset of illness in the case under consideration.

about the potential exposures of a suspected or confirmed

patient in the 14 days before symptom onset.

Please check the WHO website for current investigation recommendations and protocols at http://www.who.int/csr/disease/coronavirus_infections/technical-guidance-surveillance/en/.

Table 1. Investigations of and around confirmed cases of MERS-CoV infection

Purpose	Investigation
Describe the clinical presentation and natural history of infection.	Complete data collection on clinical history, presentation, occurrence of complications, important laboratory and X - ray findings, and course of illness. Sequential sampling of laboratory confirmed cases (where resources permit): ideally, sampling upper and lower respiratory tract, blood, urine and stool every 1 - 3 - days until the patient is PCR negative.
Determine the source of infection and type of exposure.	Investigation of potential exposures in the last 14 days before onset of illness, including travel history, exposures to animals (type of animals, especially dromedary camels, and type of contact), exposures to other patients with acute respiratory infections, exposures in health care settings, and consumption of raw camel meat and camel products. Collect detailed information on time, duration, and intensity of exposure and type of contact.
Epidemiological evidence of human-to-human transmission; estimate secondary attack rates, duration of infectivity, and incubation period. Describe spectrum of disease, especially milder cases. Determine the epidemiological importance of asymptomatic cases.	Contact tracing, including contacts in household, workplace, school and social settings. Careful history should be taken with regard to the timing of contact with sick individuals and the onset of illness. Contacts should be tested with reverse transcription polymerase chain reaction (RT-PCR) and acute and convalescent serology if they become symptomatic. Complete investigation of asymptomatic contacts, including testing for rRT-PCR and acute and convalescent serology, could be done as a research protocol.
Epidemiological evidence of human-to-human transmission, effectiveness of PPE.	Survey of health care workers working in the environment where cases are cared for. Survey should include those not directly involved in care but working in the same ward or unit as well as those who provide intermittent care, such as radiologists, respiratory and physical therapists, etc. Include information on timing, duration, and intensity of contact, type of interaction, use of personal protective equipment (PPE), and other potential exposures outside of health care setting (e.g. animals in the home environment).
Detect signals of background transmission of MERS-CoV.	Investigations for recent increases in respiratory disease activity in the community. This would include review of local hospital admission records and outpatient records of selected general practitioners in the community where infection is thought to have been acquired.
Detect the pre-existence of virus in the community.	Retrospective testing of stored specimens from patients with respiratory disease.
Determine the animal reservoir and origin of the virus.	Retrospective testing of stored animal specimens for presence of MERS-CoV or antibodies.
Identify types of exposure that result in infection.	Serological surveys of potentially exposed groups of individuals such as animal workers, market workers, health care workers, and office workers (as a comparison group). Detailed information should be collected from each participant on the type and degree of exposure.

References

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2. Cowling BJ, Park M, Fang VJ, Wu P, Leung GM, Wu JT. Preliminary epidemiological assessment of MERS-CoV outbreak in South Korea, May to June 2015. *Euro Surveill*. 2015;20(25):pii=21163. Available at <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21163>

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