Case definition for reporting to WHO Middle East respiratory syndrome coronavirus
Interim case definition
14 July 2014

Introduction

These case definitions have been revised based on new information collected since the previous definitions were published. WHO will continue to review and update them as new information becomes available.

Note that these definitions are for classification and reporting. As such, they should not be taken as recommendations for when and whom to test. Surveillance recommendations can be found on the WHO coronavirus website (http://www.who.int/csr/disease/coronavirus_infections/en/).

The key change in this 14 July 2014 update

- A case can be confirmed by the demonstration of seroconversion in 2 samples ideally taken at least 14 days apart, by a screening (ELISA, IFA) and a neutralization assay.

Confirmed case

A person with laboratory confirmation of MERS-CoV infection¹, irrespective of clinical signs and symptoms.

Probable case

Definition 1

- A febrile acute respiratory illness with clinical, radiological, or histopathological evidence of pulmonary parenchymal disease (e.g. pneumonia or Acute Respiratory Distress Syndrome); and
- Direct epidemiologic link² with a confirmed MERS-CoV case; and
- Testing for MERS-CoV is unavailable, negative on a single inadequate specimen¹ or inconclusive. ³

Definition 2

- A febrile acute respiratory illness with clinical, radiological, or histopathological evidence of pulmonary parenchymal disease (e.g. pneumonia or Acute Respiratory Distress Syndrome); and
- The person resides or travelled in the Middle East, or in countries where MERS-CoV is known to be circulating in dromedary camels or where human infections have recently occurred; and
- Testing for MERS-CoV is inconclusive. ⁴

Definition 3

- An acute febrile respiratory illness of any severity; and
- Direct epidemiologic link² with a confirmed MERS-CoV case; and
- Testing for MERS-CoV is inconclusive. ⁴

Notes

¹ A case may be laboratory confirmed by detection of viral nucleic acid or serology. The presence of viral nucleic acid can be confirmed by either a positive rRT-PCR result on at least two specific genomic targets or a single positive target with sequencing of a second target. A case confirmed by serology requires demonstration of seroconversion in 2 samples ideally taken at least 14 days apart, by a screening (ELISA, IFA) and a neutralization assay. However, the interim recommendations for laboratory testing for MERS-CoV should be consulted for the most recent standard for laboratory confirmation.

² A direct epidemiological link with a confirmed MERS-CoV patient may include:
  - 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 individuals infected with MERS-CoV.
  - Working together in close proximity or sharing the same classroom environment with individuals infected with MERS-CoV.
  - Traveling together with individuals infected with MERS-CoV in any kind of conveyance.
  - Living in the same household as individuals infected with MERS-CoV.
  - The epidemiological link may have occurred within a 14-day period before or after the onset of illness in the case under consideration.

³ An inadequate specimen would include a nasopharyngeal swab without accompanying lower respiratory specimen, a specimen that has had improper handling, is judged to be of poor quality by the testing laboratory, or was taken too late in the course of illness.

⁴ Inconclusive tests may include:
  - A positive screening test on a single rRT-PCR target without further confirmation.
  - Evidence of sero-reactivity by a single convalescent serum sample ideally taken at least 14 days after exposure by a screening assay (ELISA or IFA) and a neutralisation assay, in the absence of molecular confirmation from respiratory specimens.

Inconclusive testing

Patients with an inconclusive initial test should undergo additional virologic and serologic testing to determine if the patient can be classified as a confirmed MERS-CoV case. It is strongly advised that multiple lower respiratory tract specimens such as sputum, endotracheal aspirate, or bronchoalveolar lavage fluid be collected and tested when possible. If patients do not have signs or symptoms of lower respiratory tract disease and lower tract specimens are not available or clinically indicated, both nasopharyngeal and oropharyngeal swab specimens should be collected.

If initial testing of a nasopharyngeal swab is negative in a patient who is strongly suspected to have MERS-CoV infection, patients should be retested using a lower respiratory specimen tract or a repeat nasopharyngeal specimen with additional oropharyngeal specimen if lower respiratory tract specimens are not possible, and appropriately timed paired acute and convalescent sera.

Other types of clinical specimens could also be considered for molecular testing if necessary, including blood/serum, urine and stool. These generally have lower titres of virus than respiratory tract specimens but have been used to confirm cases when other specimens were inadequate or unobtainable. Laboratories which obtain discordant PCR testing results and have limited experience in detecting MERS-CoV should consider referring their specimens to laboratories with greater experience for confirmation.