

**Review Article**

# Middle East Respiratory Syndrome Coronavirus (Mers-Cov) - An Emerging Threat

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## Abstract

Middle East Respiratory Syndrome (MERS) is a severe acute respiratory illness (SARI) first reported from Saudi Arabia, caused by a novel beta corona virus. This virus is now named as Middle East Respiratory Syndrome Corona Virus (MERS-COV) by international committee on taxonomy of viruses. This virus has a strong tropism for non ciliated bronchial epithelial cells and dipeptyl peptidase 4 (dpp-4) is functional cellular receptor for this virus. Cases of virus infection are reported from 9 countries so far with fatality rate of almost 50 %. No vaccine or specific anti viral drug is available so far. This virus is a emerging global threat in view of massive pilgrimage to Saudi Arabia in recent future.

## Introduction

A previously unknown corona virus was isolated from the sputum of a 60-year-old man who presented with acute pneumonia and subsequent renal failure with a fatal outcome in Saudi Arabia. The virus replicated readily in cell culture, producing cytopathic effects of rounding, detachment, and syncytium formation. The virus represents a novel beta corona virus species. The closest known relatives are bat coronaviruses HKU4 and HKU5. The clinical picture was remarkably similar to that of the severe acute respiratory syndrome (SARS) outbreak in 2003.<sup>1</sup> Since the initial discovery, isolates of the virus have been described in the scientific literature, databases, and popular press under various names (e.g., human betacoronavirus 2c EMC, human betacoronavirus 2c England-Qatar, human betacoronavirus 2C Jordan-N3, betacoronavirus England 1). After careful consideration and broad consultation, the International Committee on Taxonomy of Viruses has decided to call the new corona virus Middle East respiratory syndrome corona virus (MERS-CoV). This name is now accepted by WHO, CDC and by consensus all over world.<sup>2</sup>

## Virology

The virus MERS-CoV belongs to the genus Betacorona virus, as does SARS-CoV. Corona viruses are a large family of viruses that can cause a range of illnesses in humans, from the common cold to severe acute respiratory syndrome (SARS). These viruses also cause disease in a wide variety of animal species.<sup>3</sup> It is

hypothesize that, one or more species of animals, possibly bats, are the reservoir host of this new coronavirus.<sup>1</sup> In humans, the virus has a strong tropism for nonciliated bronchial epithelial cells, and it has been shown to effectively evade innate immune responses and antagonize interferon (IFN) production in these cells. This tropism is unique in that most respiratory viruses target ciliated cells.<sup>4</sup> Due to the clinical similarity between MERS-CoV and SARS-CoV, it was proposed that they may use the same cellular receptor; the exopeptidase, angiotensin converting enzyme 2 (ACE2). However, it was later discovered that neutralization of ACE2 by recombinant antibodies does not prevent MERS-CoV infection. Further research identified dipeptyl peptidase 4 (DPP4; also known as CD26) as a functional cellular receptor for MERS-CoV. Unlike other known coronavirus receptors, the enzymatic activity of DPP4 is not required for infection. As would be expected, the amino acid sequence of DPP4 is highly conserved across species and is expressed in the human bronchial epithelium and kidneys.<sup>5</sup> The risk of sustained person-to-person transmission appears to be very low. The cells MERS-CoV infects in the lungs only account for 20% of respiratory epithelial cells, so a large number of virions are likely needed to be inhaled to cause infection.<sup>6</sup>

## Epidemiology

Globally, from September 2012 to 1<sup>st</sup> August 2013, WHO has been informed of a total of 94 laboratory-confirmed cases of infection with MERS-CoV, including 46 deaths. Thus showing fatality of 49%. Cases found so far are from Saudi Arabia, Qatar, Jordan, Tunisia, UAE, UK, Italy and France. Highest numbers of cases reported are from Saudi Arabia.<sup>7</sup> Most patients had underlying diseases, with a remarkable number having diabetes. The average

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incubation period seen is 5.2 days. Patients with diabetes or chronic renal failure appear to be at especially high risk for severe MERS-CoV infection. An immediate concern is that the MERS-CoV will infect pilgrims traveling to Saudi Arabia this October for the Hajj pilgrimage<sup>8,9</sup>

### Case Definitions<sup>10</sup>

#### Patient Under Investigation (PUI)

A patient under investigation (PUI) is a person with the following characteristics:

fever ( $\geq 38^{\circ}\text{C}$ ,  $100.4^{\circ}\text{F}$ ) and pneumonia or acute respiratory distress syndrome (based on clinical or radiological evidence);

#### ANDEITHER

History of travel from countries 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 (not necessarily pneumonia) within 14 days after traveling from countries in or near the Arabian Peninsula;<sup>1</sup>

#### OR

is 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.

### Confirmed Case

A confirmed case is a person with laboratory confirmation of MERS-CoV infection.

### Probable Case

A probable case is a PUI with absent or inconclusive laboratory results for MERS-CoV infection who is a close contact of a laboratory-confirmed MERS-CoV case.

### Biological specimen collection and laboratory testing<sup>3</sup>

#### Specimen Collection

To confirm the presence of MERS-CoV in suspect cases, collect appropriate clinical specimens for testing: Available evidence suggests that lower respiratory tract specimens contain higher virus titres than upper respiratory tract specimens and are more sensitive for detecting the presence of the virus. Lower respiratory tract specimens include: Sputum, induced or non-induced.

Endotracheal aspirate for patients on mechanical ventilation.

Bronchial alveolar lavage for those in whom it is indicated for patient management.

Upper respiratory tract specimens such as nasopharyngeal and oropharyngeal swabs should be collected if lower respiratory tract specimens cannot be collected. If initial testing of an upper respiratory specimen is negative in a patient suspected of having MERS-CoV infection, repeat testing should be performed.

Collect blood for serological testing. For recent cases, an initial blood specimen should be collected and a repeat specimen taken after a period of at least 3 weeks. For cases that had symptom onset more than 3 weeks prior to being investigated, a single blood sample is sufficient (note: results of single sera will need to be interpreted with caution as the extent of cross reactivity of currently available serological assays is unknown).

MERS-CoV has been identified in other body fluids including blood, urine, and stool of infected patients. However, titres of virus in these body fluids are quite low and they may not be useful for diagnostic testing. The presence of virus in these body fluids could have public health implications and could be part of an ancillary study of a case.

### Clinical features and Management:-

Pneumonia has been the most common clinical presentation; some patients developed Acute Respiratory Distress Syndrome (ARDS). Renal failure, pericarditis and disseminated intravascular coagulation (DIC) have also occurred. All confirmed cases reported to date have occurred in adults. At present, no virus-specific prevention or treatment (e.g. vaccine or antiviral drugs) is available. Clinicians should provide supportive management to patients who have acute respiratory failure and septic shock as a consequence of severe infection. Because other complications have been seen (renal failure, pericarditis, DIC, as above) clinicians should monitor for the development of these and other complications of severe infection and treat them according to local management guidelines.<sup>9</sup>

### Advice for Pilgrims to Saudi Arabia:<sup>11,12</sup>

The Saudi Ministry of Health recommends that elderly (above 65 years of age) and those with chronic diseases (e.g. heart disease, kidney disease, respiratory disease, diabetes) and pilgrims with immune deficiency (congenital and acquired), Malignancy and terminal illnesses, pregnant women and children (under 12) coming for Hajj and Umrah this year, to postpone the performance of the Hajj and Umrah for their own safety.

The Saudi Ministry of Health also advises all pilgrims to comply with common public health guidelines to curb the spread of respiratory infectious disease, which can be summarized as follows:

- A– Wash hands with soap and water or disinfectant, especially after coughing and sneezing.
- B- Use disposable tissues when coughing or sneezing and dispose it in the waste basket.
- C- Try as much as possible to avoid hand contact with the eyes, nose and mouth.
- D- Avoid direct contact with the infected persons (people with symptoms such as cough, sneeze, expectoration, vomiting, and diarrhea) and do not share their personal gadgets.
- E- Wearing masks, especially when in crowded places.
- F- Maintain good personal hygiene.

**WHO global alert:-**

Who issued global alert on MERS-COV infection. WHO encourages all Member States to continue their surveillance for severe acute respiratory infections (SARI) and to carefully review any unusual patterns. Health care providers are advised to maintain vigilance. Recent travelers returning from the Middle East who develop SARI should be tested for MERS-CoV. Specimens from patient's lower respiratory tracts should be obtained for diagnosis where possible. Clinicians are reminded that, MERS-CoV infection should be considered even with atypical signs and symptoms, such as diarrhoea, in patients who are immuno compromised. All Member States are reminded to promptly assess and notify WHO of any new case of infection with MERS-CoV, along with information about potential exposures that may have resulted in infection and a description of the clinical course. Investigation into the source of exposure should promptly be initiated to identify the mode of exposure, so that further transmission of the virus can be prevented.<sup>7</sup>

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