

# Middle East Respiratory Syndrome Coronavirus: A Review

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**Context:** Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection is an emerging human disease that has been reported from the Arabian Peninsula and Middle East countries since 2012. Although zoonotic transmission was postulated, virological and serological findings suggest that the dromedary camels act as the potential reservoirs of MERS-CoV infection to humans. As of October 2014, a total of 855 confirmed cases with 333 related deaths were reported to WHO. All cases occurred in or epidemiologically linked to affected countries. The virus ability to induce a pandemic attack is limited. The clinical presentations vary and range from asymptomatic infection to severe respiratory disease and death. However, most severe disease occurs in elderly and in those with underlying conditions. Infection prevention and control measures are critical to prevent the possible spread of MERS-CoV infection in health care facilities and in the community. The WHO encourages all member states to perform surveillance of patients with acute severe respiratory infection and to carefully monitor any unusual patterns. This paper aims to review the current key characteristics of MERS-CoV infection in human and update the WHO recommendations about this illness.

**Keywords:** MERS-COV; Infection; Measures

## 1. Context

Coronaviridae are enveloped RNA viruses named after their corona or crown-like projection seen on electron microscopy. The subfamily of coronaviridae is currently divided into three genera; alpha, beta and gamma coronaviruses (CoVs). They are widespread pathogens in animals and cause a wide variety of important diseases. Human coronaviruses (h CoV) belonged to alpha and beta genera. Since the first report of h CoV isolation in 1966, h CoV group has been repeatedly confirmed as an important and frequent cause of common cold, exacerbation of asthma, contributors to lower respiratory tract infections in children and elderly and diarrhea in some. Human CoV are found worldwide and predominantly are active in winter and early months of spring in temperate climates (1, 2). In November 2002, a novel coronavirus was found to be responsible for a global outbreak of an Acute Severe Respiratory Syndrome (SARS) as the prominent symptoms. The outbreak spread worldwide from its origin in China and probably represented transmission from an animal species, possibly bats to human. The novel virus named as SARS related Coronavirus (SARS r-CoV), ended after 9 months (1). More recently, in 2012, a highly pathogenic novel CoV appeared in Saudi Arabia and neighbor countries named as Middle East Respiratory Syndrome Coronavirus (MERS) (3, 4). This virus with a case fatality of approximately 50% and ability to spread at least to a limited extent in families and among patients

and health care workers in hospitals, originated from an animal source, possibly camels (5-9). Our aim in this paper is to review the key clinical and epidemiologic characteristics of MERS-CoV and updated recommendations about this emerging infection.

## 2. Evidence Acquisition

To review the current key characteristics of MERS-CoV infection in human and update the WHO recommendations about this illness, several sources of information and the international databases such as PubMed and Google scholar using the following keywords were searched: Middle East Respiratory Syndrome Coronavirus, MERS, MERS-COV. Here in, the qualitative results derived from the reviewed articles are presented and discussed.

## 3. Results

### 3.1. Middle East Respiratory Syndrome Coronavirus

Middle East Respiratory Syndrome (MERS) is a new human disease; first reported from Saudi Arabia in September 2012, after isolation of a novel CoV from sputum of a 60-year-old man who died with severe respiratory distress and multiorgan dysfunction (3, 4). Subsequently, similar cases have been recorded in Saudi Arabia and

neighbor countries (10-13). In retrospective reports, similar cases were identified in a hospital outbreak occurred in Jordan in June 2012 (10). Most reported cases presented with severe respiratory distress and pneumonia. Animal sources and zoonotic transmission was suggested (11-13). The novel virus was named Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Human to human transmission of MERS-CoV has been documented in several clusters of cases, including among family members and in hospital facilities (5-13). Although human to human transmission does occur, it seems that the transmission ability of the virus is limited to family contacts and health care settings (9,10). However a large proportion of cases had caught the disease by a “community acquired” form with suspected zoonotic transmission (1, 12, 13). As of October 2014, globally 855 laboratory-confirmed cases of infection with MERS-CoV, including at least 333 related deaths, have officially been reported to the World Health Organization (WHO) (14). Among reported cases, there were familial clusters and hospital outbreaks. All cases have been epidemiologically linked to the countries in Arabian Peninsula and Middle East countries with confirmed cases from Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, United Arab Emirates and Yemen (13).

### 3.2. Sources of Infection and Transmission Routes

The epidemiological characteristics of MERS-CoV infections have not been well described. Based on the current reports, the virus has limited ability for transmission from person to person and has no potential for causing a pandemic (15). There is growing evidences that the dromedary camel is host species for MERS-CoV and plays an important role in the transmission of the viruses to human (15-20). In August 2013, for the first time, dromedary camels were implicated as a possible source of virus causing human infection because of the presences of MERS-CoV specific neutralizing antibodies in dromedary camels from Oman and other countries in the Arabian Peninsula and North Africa (15-19). An analysis of an outbreak of MERS-CoV infection in humans in Qatar in October 2013 found that dromedary camels and humans were infected with a nearly identical strain of MERS-CoV (18). Further studies from Saudi Arabia supported the hypothesis that dromedary camels act as reservoirs of MERS-CoV (17, 19). Widespread circulation of different genetic variants of MERS-CoV has been found in camels and the presence of MERS-CoV specific antibodies in samples taken from camels, years earlier. Although dromedary camels are suspected to be the primary source of MERS-CoV leading to human infections, the true routes of zoonotic transmission remain to be determined. MERS-CoV has been repeatedly demonstrated in nasal and rectal swabs of the infected camels. The current patterns of virus transmission and disease appear to be the combination of repeated introduction of the MERS-CoV from camels to people resulting in limited unsustained human to human transmission.

Detection of viral RNA in the air of a camel barn where transmission occurred with the same strain as that detected in the infected owner 16 suggesting the airborne transmission via droplets, as well as contacts transmission with fomites. In a recent study, viral RNA and specific antibodies were detected in milk collected from dromedary camels. This finding suggested that consumption of dromedary camel milk may play a role in transmission of virus to people (17).

### 3.3. Clinical Presentation, Case Definitions and Surveillance

MERS is an emerging infectious disease and its true clinical manifestations are not completely described. Most but not all identified cases have presented with fever, cough, shortness of breath and rapidly developing respiratory distress and pneumonia. Some of infected subjects including children and adolescents have been a symptomatic or only mildly infected. Other common symptoms have been diarrhea, sore throat, myalgia and headache (1, 21, 22). The WHO case definition for surveillance is based on the clinical pictures, history of exposure and results of laboratory tests. The WHO recommends early submission of respiratory samples preferably from the lower respiratory tract for Polymerase Chain Reaction (PCR) and sera for specific antibodies. The primary objectives of WHO surveillance recommendation are to detect early sustained human to human transmission and determine the geographic risk areas for infection with the virus. In addition, description of key clinical characteristics of the illness such as incubation periods, spectrum of disease and infection, natural history of illness, determination the key epidemiological characteristics of the virus - such as exposure that result in infection -, risk factors, secondary attack rates and mode of transmission could be obtained. These should be continuously revised in response to new information (13-15, 21, 22).

### 3.4. Case Finding

#### 3.4.1. Clinical Cases that Should be Evaluated for MERS-CoV Infection Include:

1) Any person with fever and pneumonia or acute respiratory distress syndrome based on clinic or radiologic findings and one of the following; i: visiting affecting countries (Arabian peninsula and Middle East countries) within 14 days before onset of illness, unless another etiology has been identified; ii: member of cluster of patients that occurs within 14 days period, without regard to place of residence or history of travel unless another etiology has been identified; iii: disease occurring in a health care provider who has been working in an environment where patients with severe acute respiratory infections are being cared for, particularly patients requiring intensive care management without regard to place

of residence or history of travel, unless another etiology has been identified; iv) persons who develop an unusual or unexpected clinical course, especially sudden deterioration despite appropriate treatment regardless to place of residence or history of travel, even if another etiology has been identified, which that alternate etiology does not fully explains the presentation or clinical course of the patient.

2) Individuals presenting acute respiratory illness with any degree of severity who were in close contact with a confirmed or probable case of MERS-CoV infection within 14 days before onset of illness. [A close contact is defined as: anyone who provided care for patient including a health care worker on family member who had other similarly close physical contact or anyone who stayed at the same place (visited or lived) as a probable or confirmed case while the index case was ill.]

3) For countries in the Middle East, the minimum standard for surveillance should be testing of patients with severe respiratory disease requiring mechanical ventilation. The minimum standard should also include investigation of all those in the three categories listed above - patients with unexplained pneumonia or Acute Respiratory Distress Syndrome (ARDS) occurring in clusters, health care workers requiring admission for respiratory disease and patients with unusual presentations or clinical course. Countries in the Middle East 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 if local capacity can support it and also some testing of patients with milder unexplained community acquired pneumonia requiring admission to hospital. WHO does not advise special screening at point of entry (13-15).

### 3.5. Laboratory Testing and Diagnosis

MERS-CoV infection is confirmed by Real Time Polymerase Chain Reaction (RT-PCR) targeting two or three available RNA targets or alternatively by sequencing (12-15). When the molecular methods of diagnosis are negative, serology can be used to detect specific antibodies in patients and contacts in available human and animal samples. Because of widespread circulation of other hCoV, interpretation of serological results may be problematic. Therefore, different screening assays have been developed (12-15, 23, 24).

### 3.6. Treatment

The main methods of treatment of patient with MERS-CoV infection are supportive. However, based on the available data, administration of convalescent patient sera, interferon and lopinavir may be considered for specific therapy. Monoclonal and polyclonal specific antibodies are currently in development. There is no evidence for efficacy of other therapy, particularly antiviral agents (13, 14).

### 3.7. Infection Control and Preventive Measures

Since there are currently no effective drug therapies to treat or prevent the infection, and also there is no natural immunity or vaccines against MERS-CoV infection, the only means available to limit the spread of MERS-CoV infection, are public health measures. These measures are to identify infected persons rapidly and implement full barrier precautions and transmission control methods. In addition, surveillance for cases or suspicious clusters of acute severe respiratory disease by using appropriate diagnostic testing, rapid isolation, strict adherence to infection control precautions and prompt identification and careful monitoring of close contacts are essential. Close contacts are defined as 1) those who providing care for ill patients or 2) those having similar close physical contact or staying or visiting the same place at the patient. The WHO advice for home-care management of patients with MERS-CoV infection, presenting with mild symptoms and management of contacts is targeted toward public health measures and infection control measures the same as those for health care providers. WHO does not recommend special screening at point of entry for travelers from Arabic Peninsula or the application of any travel on trade restrictions (1, 13-15)

## 4. Conclusions

MERS as an emerging human disease first was reported from Saudi Arabia in September 2012. Animal sources were suggested, and human to human transmission was documented. As October 2014, a total of 855 confirmed cases with 333 related deaths have been reported, all from Middle East countries. The two clinical presentation of illness are not completely described. To detect early the cases and describe key clinical characteristics of illness, determine key epidemiological points of infection, a case definition for surveillance was developed by WHO.

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