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WHO Collaborating Centre for Research and Training in Viral Diagnostics

**Guidelines for the Prevention, Control and Management of**  
**Middle East Respiratory Syndrome-Coronavirus (MERS-CoV)**  
(Updated 19<sup>th</sup> July 2013)

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***Developed by the Epidemic Investigation Cell of NIH in collaboration with the WHO Pakistan with the following Objectives:***

- i. Provide updated information about the spread on Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection to various categories of professionals in the health sector
- ii. Guide healthcare staff in suspecting MERS-CoV infection among Pakistani population and the subsequent case management
- iii. Facilitate health managers in advance preparations

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Middle East Respiratory Syndrome Coronavirus (MERS-CoV)**

**1. Introduction:**

Named for the crown-like spikes on their surface, Coronaviruses are found worldwide and causing a range of illnesses in humans, animals and rodents. In humans, coronaviruses can cause mild to severe illness like common cold as well as severe acute respiratory syndrome (SARS). The new strain of Coronavirus MERS-CoV (formerly called “novel coronavirus”) was first identified in September 2012 among individuals with severe acute respiratory illness in Kingdom of Saudi Arabia. The infected individuals developed severe acute respiratory illness with symptoms of fever, cough, and shortness of breath. A small number of the reported cases however also had a mild respiratory illness.

The MERS-CoV appears similar to coronaviruses found in bats however; genetic sequence analyses have shown that the new virus is different from other known human coronaviruses, including SARS. No vaccines and specific antivirals have been developed as yet and therefore, the supportive treatment remains the mainstay of case management.

The available evidence suggests that the virus is capable of limited human to human transmission. The WHO however, neither recommends any travel restrictions to the affected countries nor any special screening at the airports. The current global efforts are accordingly aimed at strengthening Severe Acute Respiratory Infection (SARI) surveillance especially among people traveling to Arabian Peninsula. Considering the large number of Pakistani travelers visiting the identified high risk countries and the large number of Umrah attendees during Ramadan and the subsequent Hajj, necessary preparations need to be undertaken by all stakeholders.

Notwithstanding the need for preparedness highlighted above, it is pertinent that 2nd Meeting of the IHR Emergency Committee on MERS-CoV held on 17 Jul 2013, based on the information available till date, and using a risk-assessment approach, has unanimously decided that the conditions for a Public Health Emergency of International Concern (PHEIC) have not yet been met.

**2. Global Epidemiological Update:**

Globally, as on 18<sup>th</sup> July 2013, WHO has been informed of a total of 84 laboratory-confirmed cases of MERS-CoV infection resulting in 45 deaths.

Disease is mostly affecting old age as the median age of cases is 51 years (Range 14 months to 94 years).

Males are predominant among reported cases (65%) as well as deaths

The cases started originating from the Middle-East i.e. Jordan, Qatar, Saudi Arabia, and the United Arab Emirates (UAE) and have now spread to France, Germany, Italy, Tunisia and the United Kingdom.

<b>Countries</b>	<b>Cases</b>	<b>Deaths</b>	<b>CFR</b>
France	2	1	50%
Italy	3	0	0
Jordan	2	2	100
Qatar	2	1	50
Saudi Arabia	68	38	56
Tunisia	2	0	0
United Kingdom	3	2	66.6
UAE	2	1	50
<b>Total</b>	<b>84</b>	<b>45</b>	<b>53.6</b>

All reported cases directly or indirectly linked to one of four countries (KSA, Jordan, Qatar, UAE).

Most of the confirmed patients developed severe respiratory illness and their symptoms included shortness of breath, coughing, and pneumonia. Acute renal failure, pericarditis and disseminated intravascular coagulation were also observed in fatal cases.

### **3. Transmission:**

Mode of transmission of viral Infection is yet not clear and investigations are underway to determine the source of the virus, the types of exposure that lead to infection, the mode of transmission, and the clinical pattern and course of disease. A Camel, whose human contact had died in UAE, is known to have recovered after illness. It is considered likely that the new strain originated from an animal source.

The efficiency of person-to-person transmission of MERS-CoV is not well characterized but appears to be low. Occurrence of eight clusters among close contacts and healthcare settings point towards limited human-to-human transmission however, so far there has been no evidence of sustained transmission beyond the immediate clusters.

### **4. Incubation Period:**

The presumed incubation period is between 9 and 12-days. The observed incubation period is generally less than one week however, in at least one case, the known exposure occurred 9 to 12 days prior to onset of illness. Further evidence in exposed cases suggests that in a minority of cases, incubation period may exceed one week but is less than two weeks.

### **5. Surveillance Recommendations:**

The primary objectives of enhanced surveillance and epidemiological investigations are to:

- i. Detect early, sustained human-to-human transmission.
- ii. Determine the geographic risk area for infection with the virus.
- iii. Understand the spectrum, natural history as well as dynamics of disease transmission

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

1. A person with an acute respiratory infection, which may include history of fever and cough and indications of pulmonary parenchymal disease (e.g. pneumonia or ARDS), based on clinical or radiological evidence of consolidation, who requires admission to hospital. In addition, clinicians should be alert to the possibility of atypical presentations among immunocompromised patients.

AND any of the following:

- The disease is in a cluster that occurs within a 14 day period, without regard to place of residence or history of travel, unless another aetiology is identified.
  - 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, particularly patients requiring intensive care, without regard to place of residence or history of travel, unless another aetiology has been identified.
  - The person has history of travel to the Middle East within 14 days before onset of illness, unless another aetiology has been identified.
  - 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 but it does not fully explain the presentation or clinical course of the patient.
2. Individuals with acute respiratory illness of any degree of severity who, within 14 days before onset of illness, were in close physical contact with a confirmed or probable case of MERS-CoV infection, while that patient was ill.

## 6. Case Definitions:

The WHO recommends following case definitions for surveillance of MERS-CoV infections:

### **Probable case**

Combinations of clinical, epidemiological and laboratory criteria can define a probable case:

- A person with a febrile acute respiratory illness with clinical, radiological, or histopathological evidence of pulmonary parenchymal disease (e.g. pneumonia or Acute Respiratory Distress Syndrome)

**AND**

Testing for MERS-CoV is unavailable or negative on a single inadequate specimen

**AND**

The patient has a direct epidemiologic-link with a confirmed MERS-CoV case.

- A person with a febrile acute respiratory illness with clinical, radiological, or histo-pathological evidence of pulmonary parenchymal disease (e.g. pneumonia or Acute Respiratory Distress Syndrome)

**AND**

An inconclusive MERS-CoV laboratory test (that is, a positive screening test without confirmation)

**AND**

A resident of or traveler to Middle Eastern countries where MERS-CoV virus is believed to be circulating in the 14 days before onset of illness.

- A person with an acute febrile respiratory illness of any severity

**AND**

An inconclusive MERS-CoV laboratory test i.e. a positive screening test without confirmation

**AND**

The patient has a direct epidemiologic-link with a confirmed MERS-CoV case.

### **Confirmed case**

A person with laboratory confirmation of MERS-CoV infection.

### **Close contact is defined as:**

- Any person who provided care for the patient, including a healthcare worker or family member, or had similarly close physical contact.
- Any person who stayed at the same place e.g. lived with, visited as the patient while the patient was ill.

## 7. Clinical Features:

All confirmed cases presented with respiratory disease and most of them had pneumonia. However, one immunocompromised patient presented initially with fever and diarrhoea, and was only incidentally found to have pneumonia on a radiograph. Complications during the course of illness included severe pneumonia with respiratory failure requiring mechanical ventilation, acute respiratory distress syndrome (ARDS) with multi-organ failure, renal failure requiring dialysis, consumptive coagulopathy and pericarditis. A number of cases have also had gastrointestinal symptoms like diarrhoea.

One immunocompromised patient presented primarily with gastrointestinal signs and symptoms along with MERS-CoV infection. Co-infections include influenza, herpes simplex, and pneumococcus. More than half of all confirmed cases became fatal.

#### **8. Laboratory Diagnosis:**

Lower respiratory specimens (sputum, bronchoalveolar lavage, endotracheal) are a priority respiratory specimen for RT-PCR testing. If not possible or clinically indicated, both nasopharyngeal and oropharyngeal specimens can 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 or a repeat nasopharyngeal specimen with additional oropharyngeal specimen if lower respiratory specimens are not possible.

Virus has also been demonstrated in other body fluids such as blood, urine, and stool but the usefulness of those body fluids in diagnosing MERS-CoV infection is uncertain. Routine confirmation of cases of novel coronavirus infection will be based on detection of unique sequences of viral RNA by real-time reverse-transcriptase polymerase chain reaction (RT-PCR) and sequencing.

#### **9. Sample Collection and Transportation within Pakistan:**

- Specimens being sent for MERS-CoV testing should preferably be tested at local facility to exclude the presence of other known respiratory pathogens before dispatch.
- Exercising standard, contact, droplet and airborne precautions, samples must be transported to NIH; duly labeled / packed in triple packaging to the Department of Virology, Public Health Laboratories Division, National Institute of Health, Islamabad along with detailed clinical information and travel / contact history.
- Lower respiratory tract specimens (tracheal aspirates and bronchoalveolar lavage) appear to have the highest virus titre however, upper respiratory tract specimens may be collected when lower respiratory tract specimens are hard to obtain.
- For any likely delay in reaching referral laboratory, the respiratory tract specimens or serum may be frozen on dry ice.

#### **10. Case Management:**

No vaccines has been developed yet, no antivirals identified and only the supportive treatment is the mainstay. Pillars of the case management include:

- i) Supplemental oxygen
- ii) Empiric antimicrobials for community-acquired pathogens
- iii) conservative fluid management

Use of systemic high-dose corticosteroids can result in serious adverse events in patients with SARI, including opportunistic infection, avascular necrosis, new health-care-associated bacterial infection and possibly prolonged viral replication. Therefore, corticosteroids should be avoided unless they are indicated for another reason

#### **11. Infection control recommendations for healthcare settings:**

Standard, contact, and airborne precautions are recommended for the management of hospitalized patients with known or suspected MERS-CoV infection as follows:

##### **i. Standard Precautions:**

##### ***Must apply routinely in all health-care settings for all patients:***

Hand hygiene and use of personal protective equipments (PPEs) to avoid direct contact with patients' blood, body fluids, secretions (including respiratory secretions) and non-intact skin. Use

eye protection while providing care in close contact with a patient with respiratory symptoms e.g. coughing or sneezing because sprays of secretions may occur.

Standard precautions also include: prevention of needle-stick or sharps injury; safe waste management; cleaning and disinfection of equipment; and cleaning of the environment.

**ii. Droplet precautions**

Use a medical mask if working within one meter of the patient. Place patients in single rooms, or group together those with the same etiological diagnosis. If an etiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation of at least one meter. Limit patient movement and ensure that patients wear medical masks when outside their rooms.

**iii. Airborne precautions**

Ensure that healthcare workers performing aerosol-generating procedures use PPE, including gloves, long-sleeved gowns, eye protection and particulate respirators (N95 or equivalent). Whenever possible, use adequately ventilated single rooms when performing aerosol-generating procedures.

**iv. Patient placement:**

Place confirmed patient in a negative pressure airborne infection isolation room (AIIR), and probable case in a Single Airborne Infection Isolation Room. While the patient is hospitalized efforts should be made to limit the transportation and movement outside of the AIIR to medically essential purposes. And staffing policies should be implemented to minimize the number of persons who must enter the room.

**v. Decontamination of equipment:**

Dedicated individual or disposable equipments are generally recommended. Shared equipment if any must be decontaminated before use on the next patient. Re-usable equipment is packed and sent for decontamination according to the standard protocols.

**vi. Environmental Decontamination:**

Clean and disinfect the environment at least once daily and terminally disinfect at discharge as well. Use 1:49 hypochlorite (1,000 ppm) solution; then rinse and dry. For blood spills, use 1:4 hypochlorite (10,000 ppm) solution, leave for 10 minutes and then rinse with water. Use 70% alcohol for metallic items.

**vii. Transport of patients:**

Patient should wear a surgical mask and attendants should practice standard, contact, droplet and airborne precautions.

**viii. Waste Management:**

All wastes related to the patient care should be considered as clinical waste using the red bags and be disposed properly.

**12. Advice to Travelers / Those Intending to Perform Hajj / Umrah:**

Based on the information available, WHO currently does not recommend the application of any travel or trade restrictions nor does it advise special screening at points of entry with regard to this event.

The Kingdom Saudi Arabia on 13<sup>th</sup> Jul 2013, recommended to postpone the Umrah and Hajj this year [2013] for the elderly and those suffering chronic illnesses, like heart, kidney, respiratory

diseases, and diabetes and people with immunity deficiency, as well as children and pregnant women.

Although the source of the virus and the mechanism of transmission is unknown, it would be prudent to try to reduce the general risk of infection while travelling, by:

- Avoiding direct contact with ill individuals, and wear masks in crowded locations, maintaining personal hygiene as a whole
- Washing hands thoroughly with soap and water or disinfectant, especially after coughing and sneezing, and cover while coughing or sneezing; dispose of the waste in a basket; do not touch your eyes, nose, or mouth with your hands
- Adhering to food safety and hygiene rules such as avoiding undercooked meats, raw fruits and vegetables unless they have been peeled, or unsafe water.
- Avoiding close contact with live farm or wild animals.
- Seeking immediate medical attention in case of sickness, observing respiratory etiquettes and avoiding contact with other people

***Travelers to the Middle East who develop respiratory symptoms either during travel or after their return are encouraged to seek medical attention and to share their history of travel. People with symptoms of acute respiratory infection should practice cough etiquette (maintain distance, cover coughs and sneezes with disposable tissues or clothing, and wash hands) and to delay travel until they are no longer symptomatic.***

### **13. Advice to Crew Members and Airport Health Authorities:**

- Crew may report to local airport health authorities about patients with respiratory illness among travelers arriving from countries in and near the Arabian Peninsula (Bahrain, Iraq, Iran, Israel, Jordan, Kuwait, Lebanon, Oman, Palestinian territories, Qatar, Saudi Arabia, Syria, the United Arab Emirates (U.A.E.), and Yemen).
- Airport health authorities must establish liaison with tertiary care hospitals for referral, isolation, diagnosis and case management of the suspected patients
- Arrival of any such case must also be reported to local Executive District Officer (Health) for necessary arrangements

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8. MERS - CoV - Eastern Mediterranean (43): WHO, Saudi Haj Recommendations
9. WHO Statement on the 2nd Meeting of the IHR Emergency Committee concerning MERS-CoV convened by the Director-General under the International Health Regulations (2005) held by teleconference on 17 July 2013
10. WHO Interim guidance document "Clinical Management of SARI when novel coronavirus is suspected"

11. US CDC Middle East Respiratory Syndrome (MERS) Interim Guidance for Airline Crew

***Detailed guidelines on for surveillance, laboratory testing, Case management and infection control are available at [http://www.who.int/csr/disease/coronavirus\\_infection/en/index.html](http://www.who.int/csr/disease/coronavirus_infection/en/index.html)***