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Guidelines for the Prevention, Control and Management of Middle East Respiratory Syndrome-Coronavirus (MERS-CoV) (Updated May 2014)

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

- i. Update various categories of health professionals about the spread of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection.
- ii. Guide healthcare staff for suspecting MERS-CoV infection and undertaking follow up actions including; lab confirmation, treatment, safety precautions as well as contact monitoring.
- iii. Facilitate stakeholders 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. Besides spread among close family contacts and healthcare workers, MERS has also been transmitted to other countries through travelers infected in Arabian Peninsula and neighboring countries. 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, it is pertinent that based on the information available till date, WHO-IHR Emergency Committee concerning MERS-CoV in its meeting held on May 14, 2014; has observed that the conditions for a Public Health Emergency of International Concern (PHEIC) have not yet been met. It was however felt that the seriousness of the situation had increased in terms of public health impact. The Committee emphasized its concern about the recent sharp rise in cases due to systemic weaknesses in infection prevention and control. The Committee reinforced its previous advice for consideration by WHO and Member States and strongly urged to take immediate steps to:

- Improve national policies for infection prevention and control, and implement them in health-care facilities
- Strengthen case and contact identification and management
- Greatly enhance awareness and effective risk communication concerning MERS-CoV to the general public, health professionals, at-risk groups, and policy makers
- Strengthen inter-sectoral collaboration and information sharing across ministries and with relevant stakeholders
- Strengthening surveillance
- Increasing relevant diagnostic testing capacities
- Timely sharing of information in accordance with IHR 2005

2. Global Epidemiological Update:

As of 16th May 2014, there have been 572 confirmed cases of MERS in 16 countries resulting in 173 deaths. Though Saudi Arabia remains the most affected country with 514 cases and 160 deaths, all cases reported globally have either occurred in the Middle East or have direct links to a primary case infected in the Middle East.

Countries with Cases in Arabian Peninsula	Countries with Travel-associated Cases
Saudi Arabia, United Arab Emirates, Qatar, Oman, Jordan, Kuwait, Yemen, Lebanon	United States, United Kingdom, Germany, France, Italy, Greece, Tunisia, Italy, Malaysia, Philippines, Turkey, Egypt, Netherland.

Whereas between March 2013 - March 2014, about 15 cases were being reported monthly on average, the number of cases increased markedly in April 2014 with 261 cases - essentially in KSA and UAE, where healthcare-associated outbreaks are occurring. Additional five countries (Philippines, Greece, Malaysia, Netherland and Egypt) notified imported cases in April and two (United States) reported its first imported case in May 2014. Among cases reported so far, males are predominant (ratio of 2:1). Moreover, with mean and median age of 49 and 50 years (range 1-94 years) respectively, the disease is mainly affecting old people.

3. Transmission:

Mode of transmission of viral Infection is yet not fully clear and investigations are underway to determine the possible sources of the virus, types of exposure that lead to infection, mode of transmission, and the clinical pattern and course of disease. However, the MERS-CoV has been detected in camels from multiple countries including Qatar, Egypt and Saudi Arabia. Moreover, camels in a few other countries have also tested positive for antibodies.

The efficiency of person-to-person transmission of MERS-CoV is not well characterized but appears to be low. Limited Human-to-human transmission of MERS-CoV has now been documented in several clusters of cases, including among family members and in health care facilities 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:

- i. 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 some other etiology 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 aetiology has been identified.
 - The person has history of travel to the Middle East within 14 days before onset of illness, unless 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.
- ii. 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/CDC recommends following case definitions for surveillance of MERS-CoV infections:

Patient Under Investigation (PUI):

A person with the following characteristics:

A. Fever ($\geq 38^{\circ}\text{C}$, 100.4°F) and pneumonia or acute respiratory distress syndrome (based on clinical or radiological evidence) AND EITHER:

- 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 OR
- 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

OR

B. Close contact with a confirmed or probable case of MERS while the case was ill AND

- Fever ($> 100^{\circ}\text{F}$) or symptoms of respiratory illness within 14 days following the close contact.

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.

Confirmed case:

A person with laboratory confirmation (positive PCR) of MERS-CoV infection.

Close contact is defined as:

- a) Any person who provided care for the patient, including a healthcare worker or family member, or had similarly close physical contact; OR
- b) 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. Observed co-infections include influenza, herpes simplex, and pneumococcus.

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.
- To increase the likelihood of detecting the virus, multiple samples from multiple sites should be collected over the course of the illness.
- 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.
- For any likely delay in reaching referral laboratory, the respiratory tract specimens or serum may be frozen on dry ice.

10. Case Management:

A suspected patient should be managed as potentially infected observing recommended bio-safety precautions.

In the absence of any vaccine developed or antivirals identified, the supportive treatment remains 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:

The recent large outbreaks in Jeddah and Riyadh, and the reports of smaller hospital associated cases in other countries, emphasize the importance of infection control strategies and practices. The implementation of standard precautions at all levels must therefore be ensured along with additional precautions according to the risk assessment.

Droplet precautions should be added to the standard precautions when providing care to all patients with symptoms of acute respiratory infection. Contact precautions and eye protection should be added when caring for probable or confirmed cases of MERS-CoV infection. Airborne precautions should be applied when performing aerosol generating procedures.

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. However, during Hajj 2013, the Kingdom Saudi Arabia recommended to postpone the Umrah and Hajj 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.
- 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

References:

1. WHO MERS CoV page: http://www.who.int/csr/disease/coronavirus_infections/en/
CDC guidelines for MERS CoV; <http://www.cdc.gov/CORONAVIRUS/MERS/INDEX.HTML>
2. European Centre for Disease Prevention and Control. Rapid Risk Assessment and updates on MERS-CoV. Available from: <http://ecdc.europa.eu/en/healthtopics/coronavirus-infections/Pages/publications.aspx>.
3. "A Novel Coronavirus Called "MERS-CoV" in the Arabian Peninsula" CDC document.
4. "WHO Coronavirus Infection" interim guidelines
5. "Novel coronavirus: interim recommendations for laboratory biorisk management" WHO
6. Infection prevention and control during health care for probable or confirmed cases of novel coronavirus (nCoV) infection. WHO
7. Naming of the Novel Coronavirus, May 2013, WHO
8. Interim surveillance recommendations for human infection with Middle East respiratory syndrome coronavirus. June 2013, WHO
9. Laboratory testing for novel coronavirus; Interim recommendations. WHO
10. Revised interim case definition for reporting to WHO – Middle East respiratory syndrome coronavirus (MERS-CoV). July 2013
11. MERS - CoV - Eastern Mediterranean (43): WHO, Saudi Haj Recommendations
12. 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
13. WHO Interim guidance document "Clinical Management of SARI when novel coronavirus is suspected"
14. 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