

Summary report on the

Consultative meeting to determine a public health research agenda on MERS-CoV

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Cairo, Egypt
15–16 December 2013



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Organization**

Regional Office for the Eastern Mediterranean

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1. Introduction

Since the emergence of Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012, collaborative work of WHO with other national health authorities, particularly with the countries where cases have occurred, have resulted in steady increase of knowledge surrounding the origin and transmissibility of this novel virus. Nonetheless, the reservoir of this virus, its transmission risk factors as well as other aspects of its ecology remain unknown.

During November–December 2013, two new developments were noted to have occurred in the WHO Eastern Mediterranean Region surrounding the spread of MERS-CoV with significant public health importance. Following a joint and comprehensive epidemiological field investigation done by the Public Health Department and Department of Animal Resources of Qatar and WHO, the MERS-CoV was detected in a herd of camels in Qatar that were linked to two recent confirmed human infections in the country. Saudi Arabia reported a similar incident of detection of MERS-CoV in camels. The second important development was that the outbreak appeared to have spread geographically. Two more countries in the Region (Oman and Kuwait) reported laboratory-confirmed cases during this period with no contact history of animals and initial findings suggested that these new cases were locally acquired.

These findings suggested that the virus was circulating in the Region in animal or environmental sources, or both, which could trigger further spread and accelerate further transmission opportunities. At this point, it was essential to address some of the critical knowledge gaps like exposure risk in humans, transmission chain and the extent of spread of the virus. Given this situation, a two-day consultative meeting was held in Cairo, Egypt on 15–16 December 2013. A total of

24 participants from the affected countries (Kuwait, Oman, Qatar, Saudi Arabia and Tunisia) attended the meeting to discuss a public health research agenda that could help in answering these research questions. The meeting was also attended by representatives from the Food and Agriculture Organization of the United Nations (FAO), Public Health England (PHE), U.S. Naval Medical Research Unit No. 3 (NAMRU-3) and the World Organisation for Animal Health (OIE) as well as WHO staff from headquarters and the Regional Office for the Eastern Mediterranean.

The objective of the meeting was to:

- Discuss and agree on the urgent need for conducting a multi-national case-control study to better understand and identify risk factors and types of exposure that result in infection; a sero-epidemiological investigation to evaluate the extent of infection in contacts, risk factors for infection and detect sub-clinical human infection; and further animal studies to identify the animal reservoir of the virus, including the intermediate host, if any;
- Determine an implementation plan and identify roles and responsibilities for conducting the agreed research studies on MERS-CoV; and
- Review the current public health recommendations in view of the recent findings and develop a set of rapid recommendations as part of an interim guidance on appropriate measures for prevention of risk of infection among high risk groups.

2. Summary of discussions

During the two-day meeting a general consensus was reached on the need to undertake selective epidemiological and animal studies on

MERS-CoV in order to find answers regarding its origin, animal reservoir, exposure risk and also to determine the geographic spread of the virus. The following discussion points were noted.

Case-control study: Following the detection of MERS-CoV in camels, the key question that needed to be answered was how the virus is transmitted to humans from animals, particularly from camels. Well designed and methodologically sound case-control studies involving countries where cases have occurred may provide data to evaluate exposures that result in transmission of infection from non-human sources and also help in determining risk factors that present opportunities for transmission. By comparing the rates of recent exposures to variety of potential sources between known cases and individuals of similar age and gender (controls) and by comparison of other risk factors (such as medical conditions) in cases and controls, such information can be made available. Global public health measures will not be effective in preventing infection in humans unless such knowledge is available on how transmission occurs and who are at greatest risk of infection. Although many additional questions remain to be answered – e.g. interactions between humans result in transmission –preventing primary introduction would be the key. Despite some study limitations inherent in all case-control studies where cases are not many and the fact that recent cases need to be included in the study to avoid “recall bias”, it is prudent to conduct a multinational study rather than one national case-control study (as cases in many countries are very few in number) as inclusion of many cases in the study would strengthen the confidence in any positive associations and allow some examination of reasons for differences between countries. Study protocols and questionnaires have been developed and are currently available and may need refinement based on the discussions held in the meeting.

Sero-epidemiological investigation: Sero-epidemiological studies will be required to be conducted amongst known contacts – household, familial, social and occupational – of confirmed and probable MERS-CoV cases to determine the extent of MERS-CoV infections, identify potential viral sources and to understand transmission dynamics which will help in guiding public health prevention and control efforts. Thus, the sero-epidemiological study will be another essential and complimentary to the case-control study which can provide additional information on exposures and infection rates to complement the findings of the case-control study as infection rates are important to understand transmissibility. This study will also provide insight into spectrum and extent of severity. Protocols are developed and currently available for conducting such study. As with the case-control study, compatible data from different countries can provide invaluable insight into transmission factors and apparent differences in rates of infection although such studies can be done individually by the countries concerned. The key practical step for sero-epidemiological studies will be that the participating countries and WHO work together to develop a standardized panel of sera to compare available serological assays. In addition, study protocols must be agreed upon which includes the conditions under which the serum panel may be used, the roles of laboratories and investigators, and a standardized testing algorithm.

Animal studies: Virological and serological investigations in animal populations in contact with confirmed cases are required to be carried out during outbreak investigation of human infections and as part of the research to find out the animal reservoir of MERS-CoV in the affected countries. However, during the current period, there is need to standardize protocols for conducting such animal studies as well as build capacities for shipment and transportation of animal samples to

FAO/OIE certified reference laboratories. It is also not clear what policy measures need to be taken when the virus is detected in animals (like restriction of movement, quarantine period, culling, etc). The challenges are huge for conducting experimental animal studies for which capacity of the animal health laboratories and countries need to be assessed along with standardization of study protocols. In the interim period, small scale field studies can be conducted in areas where human infections have been confirmed and in its surroundings through the use of a standardized study protocols.

Case-definition: Based on the suggestion from the representative of Saudi Arabia, the revised interim case-definition of probable case of MERS-CoV for reporting to WHO which was published on 3 July 2013 was discussed. Following the discussion, it was agreed to remove the part concerning the travel history of cases to the Middle Eastern countries (where MERS-CoV virus is believed to be circulating in the 14 days before the onset of illness) from the case definition of the “probable” case of MERS-CoV.

Study governance: A governance structure to oversee the implementation of the epidemiological studies was also proposed at the meeting (Figure 1). Participating countries agreed to nominate a technical focal point for the Technical Study Development Group. Their role will be to coordinate the finalization of study protocols and other questionnaires and to act as a liaison between international organizations, countries implementing these studies and international reference laboratories to be set up for the purpose of testing samples or for development of convalescent serum panel to compare available serological assay.

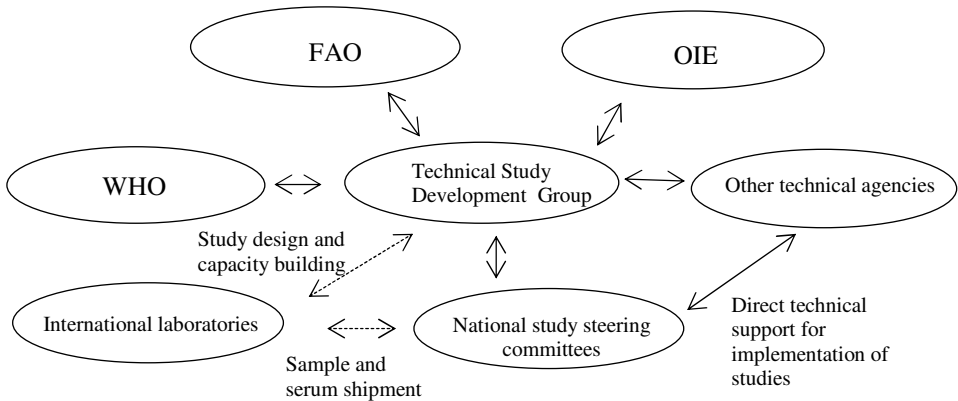


Figure 1. Structure for oversight of epidemiological studies

3. Next steps

Two major conclusions came out of the meeting. One was that all the affected countries would participate in an international multicountry case–control study in collaboration with WHO and other international health partners. The other was that all the affected countries would participate in national sero-epidemiological studies to be coordinated by WHO and other international health partners.

In addition, it was also agreed that the “probable” case definition for MERS-CoV which is used for reporting purposes would be revised in view of the discussions held in the meeting. To facilitate the implementation of the selected epidemiological studies for which a consensus was reached in the meeting, it was agreed the following actions would be taken.

- The participating countries will identify individuals/experts to serve on a technical study development group and also on the international technical advisory committee for implementation of the selected studies.
- In order to facilitate the work of both technical study development group and the international technical advisory committees, WHO will be responsible for:
 - drafting a concept note including the terms of reference of these groups;
 - developing a concept note summarizing the objectives and methodology of both case–control and sero-epidemiological studies that have been agreed upon by the countries for implementation;
 - revising the study protocols and questionnaires of the case–control study in accordance with the discussions that were held in the meeting. These revised study protocols will be reviewed by the technical study development group and the international technical advisory group for finalization;
 - developing an implementation plan for the selected epidemiological studies including a timeline for training, data collection, sample collection and testing, data analysis and report generation for consideration by the countries;
 - identifying and recruiting international experts and laboratories to provide guidance and support to the countries for implementation of the research studies as needed
 - finalizing the standardized protocol for undertaking the sero-epidemiological study which will include the conditions under which the serum panel may be used, the roles of laboratories

and investigators, and a standardized testing algorithm and logistical arrangements;

- following up with the affected Member States regarding creation of a convalescent serum panel;
- supporting, with partners, capacity-building activities in Member States to develop serological testing capabilities and facilitate linkages with international reference laboratories.

For conducting animal studies it was agreed that FAO/OIE would support the implementation of animal studies through:

- identifying reference laboratories for animal virological and serological testing;
- identifying laboratories with facilities to conduct experimental animal research studies in partnership with participating countries, e.g. transmissibility studies, challenge studies, etc.
- providing guidance related to the duration of quarantine for laboratory confirmed MERS-CoV infections in camels.

WHO will organize a meeting of the technical study development group and international technical advisory committee in Geneva in January 2014. Technical staff designated by affected countries will gather in Geneva during this meeting with WHO and other invited international experts to finalize the study protocol for the case-control study including the questionnaire. WHO will provide a draft protocol to the affected Member States to facilitate internal national discussions and consensus in preparation for the meeting of the technical study development group.



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