Middle East respiratory syndrome coronavirus (MERS-CoV) Summary of Current Situation, Literature Update and Risk Assessment

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Summary

Since 1 January 2015, 423 laboratory-confirmed cases of MERS have been reported to WHO, notably from the Kingdom of Saudi Arabia and the Republic of Korea. The ongoing outbreak in the Republic of Korea – resulting from a single exported case with travel history in the Middle East (Saudi Arabia, Qatar, United Arab Emirates (UAE) and Bahrain) and subsequent human-to-human transmission to close family contacts, to patients who shared a room or ward with infected patients, to health care workers providing care for patients before MERS was suspected or diagnosed – is similar to nosocomial outbreaks in other countries (e.g., Saudi Arabia and UAE).

An unrelated exportation of MERS in an Omani national to Thailand in June 2015 has not thus far resulted in any further transmission in Thailand. Concurrently, an outbreak of MERS is ongoing in Hofuf, Eastern Province, in Saudi Arabia. This outbreak has been associated with 13 health care facilities and 44 cases to date since 1 January.

Transmission in some of these events, particularly the outbreak in the Republic of Korea, which occurred before adequate infection prevention and control procedures were applied and cases were isolated and managed, is of great concern, but is not unexpected given that MERS is still a relatively rare disease and little known outside the Arabian Peninsula. Cases can therefore be easily missed initially. Thus far, no sustained human-to-human transmission has occurred anywhere in the world. WHO's understanding is that health authorities in countries where MERS has been reported in recent weeks are aggressively investigating cases and contacts.

A great deal of knowledge about MERS has been gained in recent months, especially, prevalence in animals and humans, transmission and how to manage nosocomial outbreaks. WHO is continuing to work with ministries of health in all affected countries and with international partners to better understand transmission patterns and risk factors for infection and severe outcomes, as well as to develop mitigation measures to prevent human infections and to support the timely release of research findings. WHO's risk assessment remains unchanged from the global risk assessment published on 5 February 2015¹ and the Republic of Korea/China specific risk assessment published on 19 June 2015.²

Background

Between 2012 and 7 July 2015, 1368 laboratory-confirmed cases of human infection with Middle East respiratory syndrome coronavirus have been reported to WHO, including at least 487 deaths (Figure 1). Overall, 65% of cases where gender has been reported (n=1359) are male and the median age is 50 years (range 9 months–99 years; n=1365).

Since 2012, 26 countries have been affected (Figure 2), including countries in the Middle East: Egypt, Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, United Arab Emirates and Yemen; in Africa: Algeria, and Tunisia; in Europe: Austria, France, Germany, Greece, Italy, the Netherlands, Turkey and the United Kingdom; in Asia: China, the Republic of Korea, Malaysia, Philippines and Thailand; and in North America: the United States of America. The majority of cases (approximately 75%) have been reported from Saudi Arabia (Table 1).

Table 1. Number of MERS-CoV cases by country and year (as of 7 July 2015)

| | 2012 | 2013 | 2014 | 2015 | Total |
|--------------------------|------|------|------|------|-------|
| Algeria | 0 | 0 | 2 | 0 | 2 |
| Austria | 0 | 0 | 1 | 0 | 1 |
| China | 0 | 0 | 0 | 1 | 1 |
| Egypt | 0 | 0 | 1 | 0 | 1 |
| France | 0 | 2 | 0 | 0 | 2 |
| Germany | 1 | 1 | 0 | 1 | 3 |
| Greece | 0 | 0 | 1 | 0 | 1 |
| Iran | 0 | 0 | 5 | 1 | 6 |
| Italy | 0 | 1 | 0 | 0 | 1 |
| Jordan | 2 | 0 | 10 | 0 | 12 |
| Kuwait | 0 | 2 | 1 | 0 | 3 |
| Lebanon | 0 | 0 | 1 | 0 | 1 |
| Malaysia | 0 | 0 | 1 | 0 | 1 |
| Netherlands | 0 | 0 | 2 | 0 | 2 |
| Oman | 0 | 1 | 1 | 4 | 6 |
| Philippines | 0 | 0 | 0 | 2 | 2 |
| Qatar | 0 | 7 | 2 | 4 | 13 |
| Republic of Korea | 0 | 0 | 0 | 185 | 185 |
| Saudi Arabia | 5 | 136 | 679 | 217 | 1037 |
| Thailand | 0 | 0 | 0 | 1 | 1 |
| Tunisia | 0 | 3 | 0 | 0 | 3 |
| Turkey | 0 | 0 | 1 | 0 | 1 |
| United Arab Emirates | 0 | 12 | 57 | 7 | 76 |
| United Kingdom | 1 | 3 | 0 | 0 | 4 |
| United States of America | 0 | 0 | 2 | 0 | 2 |
| Yemen | 0 | 0 | 1 | 0 | 1 |
| Total | 9 | 168 | 768 | 423 | 1368 |

¹ Available at <u>http://who.int/csr/disease/coronavirus_infections/mers-5-february-2015.pdf?ua=1</u>

² Available at <u>http://www.who.int/csr/disease/coronavirus_infections/risk-assessment-19june2015/en/</u>



Figure 1. Epidemic curve of MERS-CoV cases (n=1368) (as of 7 July 2015)



Figure 2. Number of laboratory-confirmed MERS-CoV cases reported by countries by year since 2012

Since 1 January 2015, WHO has been made aware of 423 laboratory-confirmed cases of MERS, including one case each reported from China, Germany, Iran, and Thailand; two cases reported from the Philippines; four cases reported from both Oman and Qatar; 7 cases reported from UAE, 185 cases reported from the Republic of Korea; and 217 cases reported by Saudi Arabia. This is the first reporting of cases from the Republic of Korea(Seoul), China (Guangdong) and Thailand (Bangkok). Among the 217 cases from Saudi Arabia, cases were reported from many different regions including, Jeddah, Riyadh, Taif, Mecca, and Hofuf.

Since 1 January 2015, five exported cases (suspected exposure within and diagnosis outside the Middle East) were reported to WHO. The **first exported case** was reported by the Philippines in February 2015. The case, a 31-year-old woman working as a health care professional in Riyadh, Saudi Arabia, developed symptoms on 26 January. After extensive contact tracing in the Philippines and among travel contacts, no additional cases were identified.

A **second exported case** was reported by the Philippines in July 2015. The case, a 36-year-old Finnish national, recently travelled to the Philippines from Saudi Arabia via the UAE. Investigations are ongoing as to the source of his infection, but at present, no contact with camels or camel products, confirmed MERS patients, or a health care facility in Saudi Arabia has been reported.

The **third exported case**, a 65-year-old German citizen, was reported by Germany on 7 March 2015. This case had recently returned from UAE (Abu Dhabi). No additional MERS cases were reported among some 200 contacts.

On 20 May 2015, the fourth exported case, who had recent travel history to Saudi Arabia, Qatar, UAE and Bahrain, was reported by the Republic of Korea. As of 7 July, an additional 185 laboratory-confirmed cases (including 33 deaths) among health care workers caring for MERS patients, patients who were being cared for at the same health care facilities and family members have been identified. At present, contact tracing is ongoing and more than 16,000 contacts have been identified, monitored for symptoms and/or tested for MERS-CoV. There is evidence of tertiary transmission in the Republic of Korea (this has also been seen in nosocomial outbreaks in the Middle East), but it will be some time before researchers understand transmission chains in the affected hospitals. Researchers in the Republic of Korea, as in other countries (e.g., Saudi Arabia and UAE), are performing a number of investigations to better understand the potential role of poor infection prevention and control practices, environmental contamination, poor ventilation in one hospital and asymptomatic or mild cases in transmission of MERS in health care settings.

One person who was infected in the Republic of Korea travelled to China, first by plane to China, Hong Kong Special Administrative Region (SAR), and then by bus to Guangdong. The case was symptomatic while travelling. Chinese authorities were able to find this person rapidly and provide care under isolation conditions and to identify contacts in China. No additional cases have been identified among contacts in China, Hong Kong SAR (n=28) or in Guangdong (n=75). This is the first MERS case reported in China.

The **fifth exported case** was reported on 18 June 2015 when Thailand reported its first case of MERS in an Omani national who travelled to Bangkok for medical treatment for an unrelated underlying condition. This case, who had travelled with three family members by plane while symptomatic, was immediately placed in isolation for reasons unrelated to MERS. To date, all identified contacts in Thailand have been isolated and followed up. No further cases have been identified in Thailand. Investigations into the source of infection in Oman are underway.

Since 1 January 2015, 217 laboratory-confirmed cases have been reported by Saudi Arabia. Among them, at least 44 have been reported from Hofuf, Eastern Province. Thus far, these cases have been associated with 13 health care facilities in Hofuf. The majority of the cases reported are male (63.6%) and the median age is 54.5 years (range 24-77). Among these 44 cases, 6 are believed to have acquired infection in the community from non-human sources, 18 are secondary cases who acquired infection while in a health care facility, 6 are health care workers, 8 are household contacts of cases, and the source of infection for 6 cases is still under review. Our current understanding is that the outbreak began in the community through a person who had contact with dromedary camels. Cases from this household were treated at several health care facilities, including a cardiac care center where human-to-human transmission was reported.

WHO MERS activities and guidance

- A mission of international experts from WHO, the Food and Agriculture Organization (FAO), the World Organisation for Animal Health (OIE), and Institut Pasteur participated in a mission to Riyadh, Saudi Arabia 17-20 February 2015 at the request of the Ministry of Health. The Mission team, led by WHO, met with senior Ministry of Health and Ministry of Agriculture officials and were presented with the latest research the country is conducting in animals and humans. The Mission assessed progress in the prevention and control of MERS outbreaks in Saudi Arabia and provided public health recommendations so that future cases can be prevented or controlled. Particular focus was drawn to understanding and assessing the current epidemiologic situation in the country; progress and gaps in infection prevention and control procedures; ongoing research studies; interaction and engagement among groups working at the animal, human and environmental interface; risk communications and community engagement; and coordination of national, ministerial, and international partners involved in the investigation and management of MERS cases in Saudi Arabia.
- Two technical meetings on MERS-CoV were held in Doha, Qatar, on 27-29 April 2015 (hosted by FAO and the Supreme Council of Health of Qatar) and in Cairo, Egyp,t from 5-6 May 2015 (hosted by WHO/EMRO). Participants in both meetings were from the human and animal health sectors in affected countries, international experts from OIE, FAO, WHO and a number of international institutions.

During the Doha and Cairo meetings, participants shared published and unpublished research findings; discussed the urgent need to modify control measures and to develop evidence-based measures and risk communication materials based on the accumulation of evidence linking camels to human infection; discussed the enhancement of joint collaboration between human and animal health sectors in field investigations, surveillance and research; and agreed on regular meetings to discuss and disseminate information to affected countries and the international community.

The Qatar meeting concluded with the "Doha Declaration", which calls for more joint animal/human investigations of cases and recommended that all animals that test PCR positive for MERS-CoV, regardless of an epidemiologic link to humans, be reported immediately to OIE and to national health authorities. The Doha Declaration can be found at http://www.fao.org/ag/againfo/ /programmes/en/empres/news 220515b.html.

- WHO has organized a number of teleconferences with the Republic of Korea, China and Thailand, other affected countries and international experts with MERS-CoV experience. These have addressed the clinical management of patients, genetic sequences of MERS-CoV from patients identified in the Republic of Koreaand China, and the overall epidemiology and management of MERS in Asia. A summary of discussions on sequences from MERS viruses isolated from two patients in the Republic of Korea and China can be found at http://www.who.int/entity/csr/disease/coronavirus __infections/risk-assessment-9june2015/en/index.html.
- A joint WHO and Ministry of Health and Welfare mission took place in the Republic of Korea 8-13 June 2015. More information about the Mission and its initial recommendations can be found at <u>http://www.wpro.who.int</u> /mediacentre/releases/2015/20150613/en/.
- A panel of convalescent sera is being assembled to enable a comparison of available serological assays. The National Institute for Biological Standards and Control in the United Kingdom, a WHO Collaborating Centre, is coordinating the study and is currently preparing the panel from donated sera.
- WHO has updated the following guidance on MERS:
 - Surveillance for human infection with Middle East respiratory syndrome coronavirus (MERS-CoV) (<u>http://www.who.int/csr/disease/coronavirus_infections/surveillanc</u> <u>e-human-infection-mers/en/</u>)
 - Investigation of cases of human infection with Middle East respiratory syndrome coronavirus (MERS-CoV) (<u>http://www.who.int/csr/disease/coronavirus_infections/mers-investigation-cases/en/</u>)
 - Laboratory testing for Middle East Respiratory Syndrome Coronavirus (<u>http://www.who.int/csr/disease</u> /coronavirus_infections/mers-laboratory-testing/en/)
 - Infection prevention and control during health care for probable or confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection (<u>http://www.who.int/csr/disease/coronavirus</u> <u>infections/ipc-mers-cov/en/</u>)
 - Clinical management of severe acute respiratory infections when novel coronavirus is suspected (http://www.who.int/csr/disease/coronavirus_infections/casemanagement-ipc/en/)

Risk assessment

WHO is continuing to work with ministries of health in affected countries and with international partners to better understand transmission patterns and risk factors of MERSand to develop mitigation measures to prevent human infections. WHO's global risk assessment remains unchanged from the last publication on 5 February 2015.

The ongoing outbreak in the Republic of Korea-resulting from a single exported case with travel history in the Middle East (Saudi Arabia, Oatar, United Arab Emirates (UAE) and Bahrain) and subsequent human-to-human transmission to close family contacts, to patients who shared a room or ward with infected patients, to health care workers providing care for patients before MERS was suspected or diagnosed-is similar to nosocomial outbreaks in other countries (e.g., Saudi Arabia and UAE). The occurrence of such a large nosocomial outbreak outside of the Middle East is new and the further exportation to a third country (China) is also new. However, the index case in this outbreak travelled while symptomatic, against the guidance of health authorities. These events, which occurred before adequate infection prevention and control procedures were applied, including tertiary transmission, are of concern but are not unexpected. No sustained human-to-human transmission is occurring in the Republic of Koreaor China.

Sequencing of the virus isolated from patients in the Republic of Korea and China has been completed and shared. Initial results indicate that the virus in Asia has not changed significantly from the viruses circulating in the Middle East.

Our current understanding of MERS-CoV is that it is a zoonotic virus, which has entered the human population in the Arabian Peninsula on multiple occasions from direct or indirect contact with infected dromedary camels or camelrelated products (e.g. raw camel milk). Several studies have shown that MERS-CoV-specific antibodies are widespread in dromedary camel populations in the Middle East and Africa. The evidence from animal seroepidemiologic surveys suggests that MERS-CoV has been circulating in camels for decades. However, the reason that human cases were first detected only in 2012 is unknown, and the specific exposures resulting in and modes of transmission from animals to humans have not been fully elucidated. It is likely that MERS-CoV infected humans earlier than 2012, but WHO is not aware of any testing of stored human sera before 2012.

The evidence linking MERS-CoV transmission between camels to humans is irrefutable. A significant amount of knowledge of MERS has accumulated in the last 12 months. The main highlights include:

- MERS-CoV has been detected in dromedary camel populations where human cases in the Middle East have been reported. Phylogenetic analyses show that the human and camel viruses are nearly identical.
- Several serologic studies conducted in humans in Saudi Arabia, Qatar and UAE have found higher levels of prevalence of antibodies against MERS-CoV among populations in close, regular occupational contact with dromedary camels (e.g., farmers, slaughterhouse workers, market workers) when compared with the general population. Risk factors for infection between

animals and humans have not yet been evaluated in seroprevalence studies.

• Risk factors for non-human transmission have been evaluated in a case-control study conducted by the Ministry of Health in Saudi Arabia and international partners. This study, which is unpublished but has been presented at recent scientific meetings in the Middle East, has found evidence that persons with direct and indirect contact with dromedary camels had a significantly higher risk of infection compared with controls.

Human-to-human transmission has been observed to a limited extent in households. However, the majority of human cases reported to date have resulted from human-to-human transmission in health care settings. Failures in infection prevention and control in health care settings have resulted in sometimes large numbers of secondary cases, as was seen in Saudi Arabia in April-May of 2014, and has recently been seen in the Republic of Korea. To date, there is no evidence of sustained human-to-human transmission. Although it will take some time before health officials understand clearly how cases were infected in the hospitals, evidence supports a median incubation period of approximately 5.5-6.5 days. A maximum 14-day incubation period remains valid for contact tracing and management.

In 2015, the same epidemiologic patterns of MERS-CoV are observed: multiple introductions from animals to humans and secondary transmission in health care settings. What is different, however, is that the hospital outbreaks in Saudi Arabia are smaller in size, but more frequent. Until zoonotic transfer of the virus from animals into the human population is stopped, the risk of further nosocomial outbreaks in the Middle East and beyond remains. The repeated and ongoing hospital outbreaks in Saudi Arabia are of concern; more work to better understand the reasons behind these outbreaks is needed.

Imported cases have been recorded in a number of countries and could happen again anywhere. The combination of factors, which have been previously described (<u>http://www.wpro</u> <u>.who.int/mediacentre/mers-hlmsg/en/</u>), show that low awareness and the inability to rapidly limit exposure to MERS patients can lead to large outbreaks.

Have the transmission patterns of MERS-CoV changed ?

There is no evidence of sustained human-to-human

- 3. Intensive screening of MERS contacts revealed very few instances of household transmission and there has been no identified transmission on airplanes;
- 4. There has been no increase in the size or number of observed household clusters; and
- 5. The overall reproduction number of MERS is less than 1, but can be higher in health care settings. Experience in Saudi Arabia, UAE, China and Thailand has shown that the reproduction number can be brought under one with early isolation of cases and adequate infection prevention and control measures.

Can we expect additional cases of MERS in the Middle East? And can we expect additional cases exported to other countries?

WHO expects that additional cases of MERS infection will be reported from the Middle East, and that cases will continue to be exported to other countries by persons who might become infected after exposure to an animal (for example, while visiting farms or markets) or a human source (possibly in a health care setting).

Until more is understood about mode of transmission and risk factors for infection, cases resulting from zoonotic transmission will continue to occur, and will eventually lead to limited community transmission within households and possibly significant hospital-associated outbreaks such as the one in the Republic of Korea. Consistent application of adequate infection prevention and control measures has been used to end transmission in previous clusters.

Among the all exported cases who reported performing Umrah in Saudi Arabia, investigation into their activities revealed that they had either visited a health care facility or had come into contact with camels or raw camel products while in Saudi Arabia.

Recommendations

A number of epidemiologic investigations to better understand the transmission patterns of MERS-CoV have been conducted. WHO hopes that these investigations can be shared with affected countries dealing with MERS-CoV and published as soon as possible. The most urgent needs remain: a better understanding of how humans become infected from animal or environmental source(s); identifying risk factors for infection in convertional satisfies and health

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