RAPID RISK ASSESSMENT

Severe respiratory disease associated with Middle East respiratory syndrome coronavirus (MERS-CoV)

18th update, 30 June 2015

Main conclusions and options for response

The Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak continues to pose a low risk to the EU with regards to the importation of MERS cases. Although sustained community transmission has not been observed, transmission to close contacts of imported cases, including to healthcare workers, other patients and visitors in hospitals has been reported, most recently in South Korea but also in France, the United Kingdom and Iran.

The risk for visitors to South Korea is extremely low, unless visitors have had contact with healthcare facilities, in particular in the 13 affected districts. The risk for participants in Universiade events (an international multi-sport event, organised for university athletes) in South Korea in July 2015, is similarly extremely low as no MERS cases have been reported from the districts where Universiade events will take place.

The risk for visitors to Saudi Arabia is low, and related to exposures either to live camels and camel products or to healthcare facilities. The risk is considered higher than in South Korea because of the high number of nosocomial clusters identified in Saudi Arabia, the persistence of transmission in healthcare settings for more than two years, the suspicion of infections occurring through unrecognised chains of transmissions and the risk related to exposure to camels and camel products.

WHO does not recommend travel restrictions with regards to MERS-CoV, but rather to raise awareness among travellers to and from affected countries. EU citizens travelling to the affected countries in the Middle East and to South Korea need to be made aware that MERS-CoV is circulating in these areas and should be reminded of general travel advice of good hand and food hygiene.

Participants in the Universiade in South Korea in July 2015 should follow the recommendation published by the organiser of the event, International University Sports Federation (FISU), which states that "*all persons involved in the FISU Summer Universiade should take strict precautions for good health procedures (i.e. wash hands, do not cough on others, make sure bodily fluids are self-contained). No-one is to travel to these Games or from your country if they have symptoms of any illness or have fever, cough or signs/symptoms of respiratory infection.*"

The organisers of Universiade have taken preventive measures, including entry control, personnel control and the establishment of a special inspection team, as well as identifying MERS designated medical facilities. One MERS designated examination centre and two MERS quarantine facilities have been set up to receive suspected patients.

Early detection of MERS-CoV infection among travellers exposed to camels or healthcare facilities in the Middle

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East or in South Korea remains essential. The outbreak in South Korea highlights the continued risk of healthcare-associated transmission and the need for timely diagnosis and implementation of prevention and control measures.

In light of the ongoing outbreak, travellers returning from the Middle East and South Korea should be made aware that if they develop respiratory symptoms or diarrhoea, either during travel or up to 14 days after their return, they should seek medical attention and report their travel history. Patients presenting with severe acute respiratory disease in the EU and having recently been in contact with MERS patients, healthcare services or camels in South Korea or the Middle East should be investigated for MERS-CoV infection.

Healthcare workers in the EU should be made aware of the risk related to travellers from affected areas, the presentation of the disease, and the need to promptly investigate travellers returning from affected areas presenting with severe respiratory illness.

WHO recommends that probable and confirmed cases should be admitted to adequately ventilated single rooms or rooms with airborne transmission precautions. Healthcare workers caring for probable or confirmed cases of MERS should use contact and droplet precautions (medical mask, eye protection such as goggles or face shield, gown, and gloves) in addition to standard precautions. Airborne transmission precautions should be applied when performing aerosol-generating procedures.

Source and date of request

ECDC internal decision, 22 June 2015.

Public health issue

This update was prompted by the epidemic of confirmed MERS cases reported from South Korea in light of the upcoming Universiade, as well as the identification of a travel-related MERS case in Thailand.

The Summer Universiadeis, is an international sports event with an estimated 20 000 participants (athletes and officials) from 170 countries including EU countries, which takes place in Gwangju, South Korea from 3 to 14 July 2015 [1].

Consulted experts

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Disease background information

Since it was first identified in Saudi Arabia in September 2012, more than 1 000 MERS cases have been detected in over 20 countries. In Europe, seven countries have reported confirmed cases, all with direct or indirect connection with the Middle East.

The clinical presentation of MERS-CoV infection ranges from asymptomatic to very severe pneumonia with acute respiratory distress syndrome, septic shock and multi-organ failure resulting in death. The clinical course is more severe in immunocompromised patients. There is growing evidence that the dromedary camel is a host species for the virus and that camels play an important role as a source of human infection.

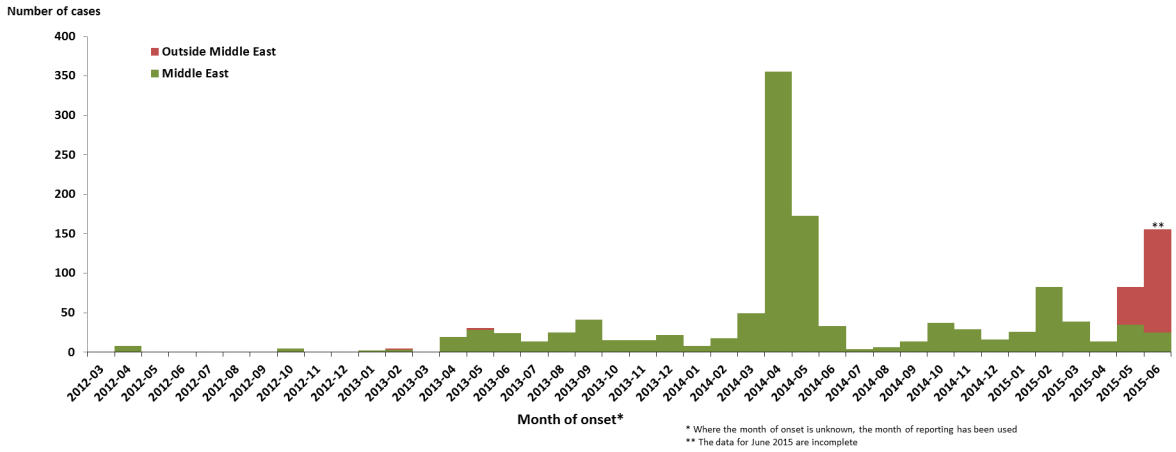
Although it is likely that zoonotic transmission is the starting point of most clusters, human-to-human transmission is the dominant mode of transmission for MERS-CoV, and almost all new cases are generated in healthcare facilities or among family members. Nosocomial transmission has been a hallmark of MERS, and the majority of cases have been reported from hospital outbreaks in Saudi Arabia, the United Arab Emirates (UAE) and most recently in South Korea.

Event background information

Worldwide situation

Since April 2012 and as of 29 June 2015, 1 379 cases of MERS (including 531 deaths) have been reported by health authorities worldwide (Figure 1 and Table 1).

Figure 1. Distribution of confirmed cases of MERS by month* and probable place of acquisition of infection, March 2012–28 June 2015 (n=1 379)



Current epidemiological situation

Since the previous update of the ECDC Rapid Risk Assessment on MERS-CoV (11 June 2015), 92 new cases and 33 deaths have been reported globally from: South Korea (74 cases and 23 deaths), Saudi Arabia (12 cases and 8 deaths), United Arab Emirates (4 cases and 1 death), Germany (one death in a travel-related case reported in March 2015) and Thailand who reported a travel-related MERS case from Oman to Bangkok on 18 June 2015.

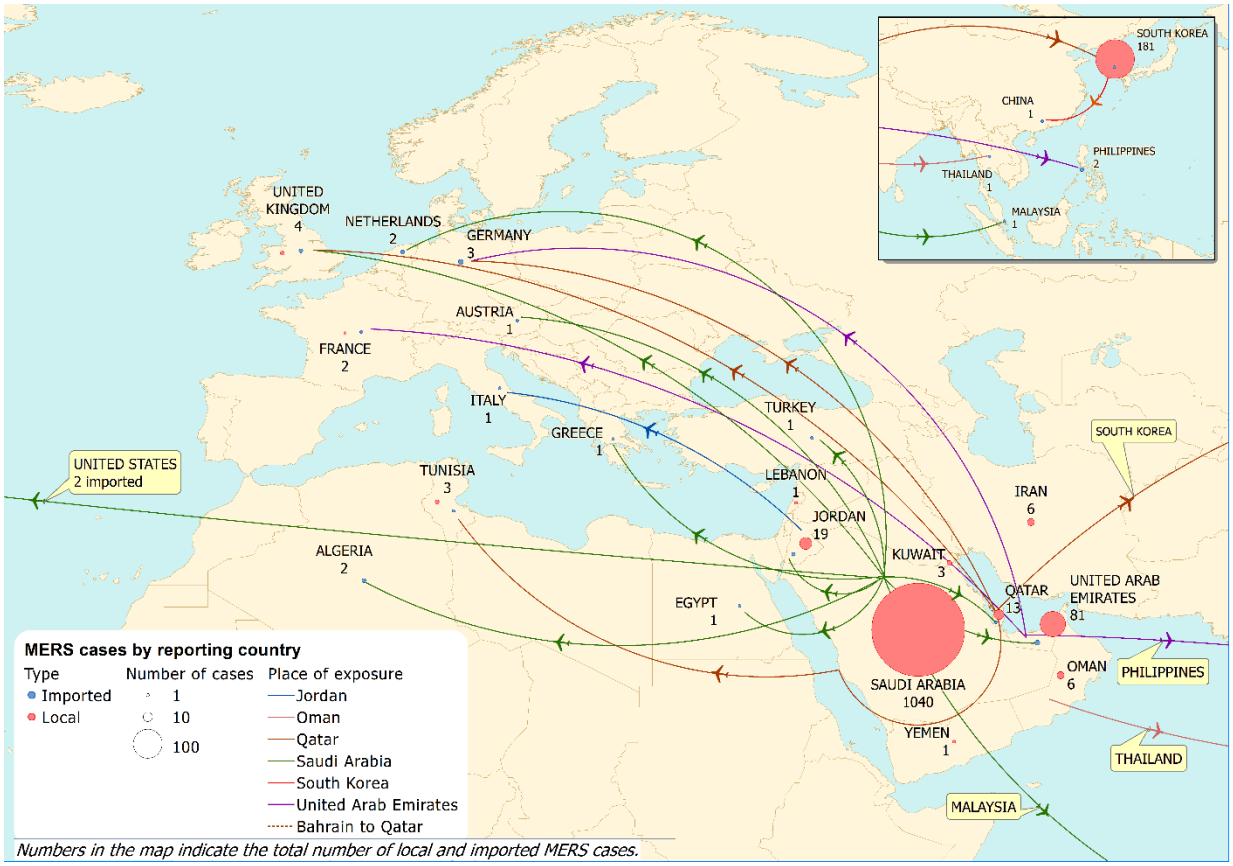
The majority of cases have occurred in the Middle East, most of them in Saudi Arabia and the United Arab Emirates (Table 1). However, South Korea is the country with the highest number of new cases reported since the start of the outbreak there in early May 2015.

Table 1. Confirmed MERS cases and deaths, by country of reporting, March 2012–28 June 2015

Reporting country	Cases	Deaths
Middle East	**1 171**	**488**
Saudi Arabia	1 040	459
United Arab Emirates	81	11
Jordan	19	6
Qatar	13	5
Oman	6	3
Iran	6	2
Kuwait	3	1
Egypt	1	0
Yemen	1	1
Lebanon	1	0
Europe	**15**	**8**
United Kingdom	4	3
Germany	3	2
France	2	1
Netherlands	2	0
Greece	1	1
Turkey	1	1
Austria	1	0
Italy	1	0
Asia	**186**	**33**
China	1	0
Malaysia	1	1
Philippines	2	0
South Korea	181	32
Thailand	1	0
Rest of the world	**7**	**2**
Algeria	2	1
Tunisia	3	1
United States of America	2	0
Total	**1 379**	**531**

All cases reported from outside the Middle East have either had a recent travel history to the Middle East or could be linked to a chain of transmission originating from a case with a travel history to the Middle East (Figure 2).

Figure 2. Distribution of confirmed MERS cases by probable place of acquisition of infection, as of 28 June 2015 (n=1 379)



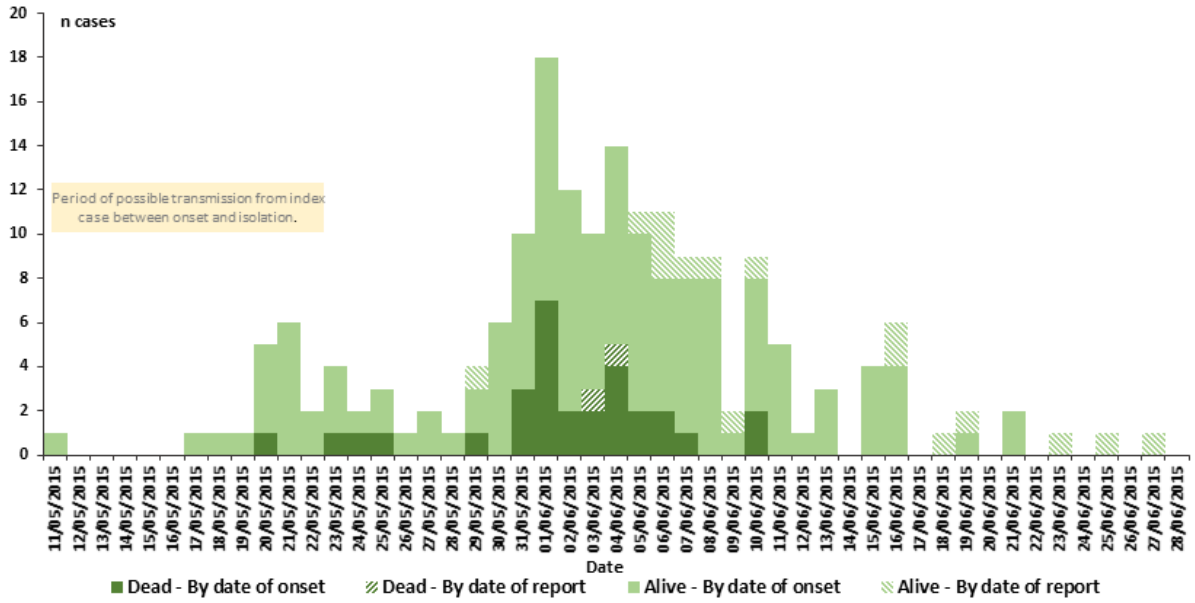
South Korea

On 20 May 2015, the Korea Centres for Disease Control and Prevention notified WHO of the first laboratory-confirmed case of MERS in a 68-year-old man with recent travel history to the Middle East [2].

On 29 June 2015, the South Korean Ministry of Health and Welfare reported 182 cases since the beginning of the outbreak in South Korea (including the index case and the South Korean case reported by China). Of these, 14 were in a severe condition, 43 in moderate condition, 93 have been discharged and 32 have died (Figure 3). Overall, 53% of the reported fatal cases had a comorbidity (n=17).

The median age for the 93 discharged cases is 49 years, while the median age for the 32 fatal cases is 69.5 years. The number of new reported cases has been decreasing over the past two weeks.

Figure 3. Distribution of confirmed cases of MERS by date of onset or reporting, South Korea and China, 11 May–28 June 2015 (n=182)

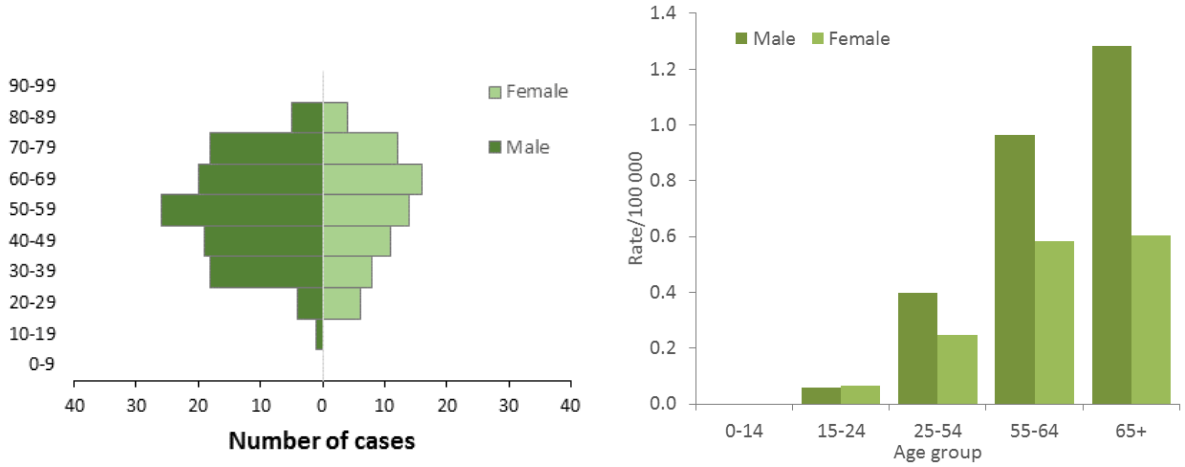


Men have been consistently overrepresented among the cases since the start of the outbreak in 2012, but this is less marked among the Korean cases (Table 2 and Figure 4). However, the age and gender-specific attack rates show that older men also have the highest risk of infection in Korea, and that people above 30 years of age are mostly affected.

Table 2. Distribution of confirmed MERS cases by reporting year and gender, as of 28 June 2015

	2012 Global	2013 Global	2014 Global	2015 Global	2015 South Korea
Male	14	101	381	277	111
Female	2	63	196	124	71
Male/female ratio	7.0	1.6	1.9	2.2	1.6

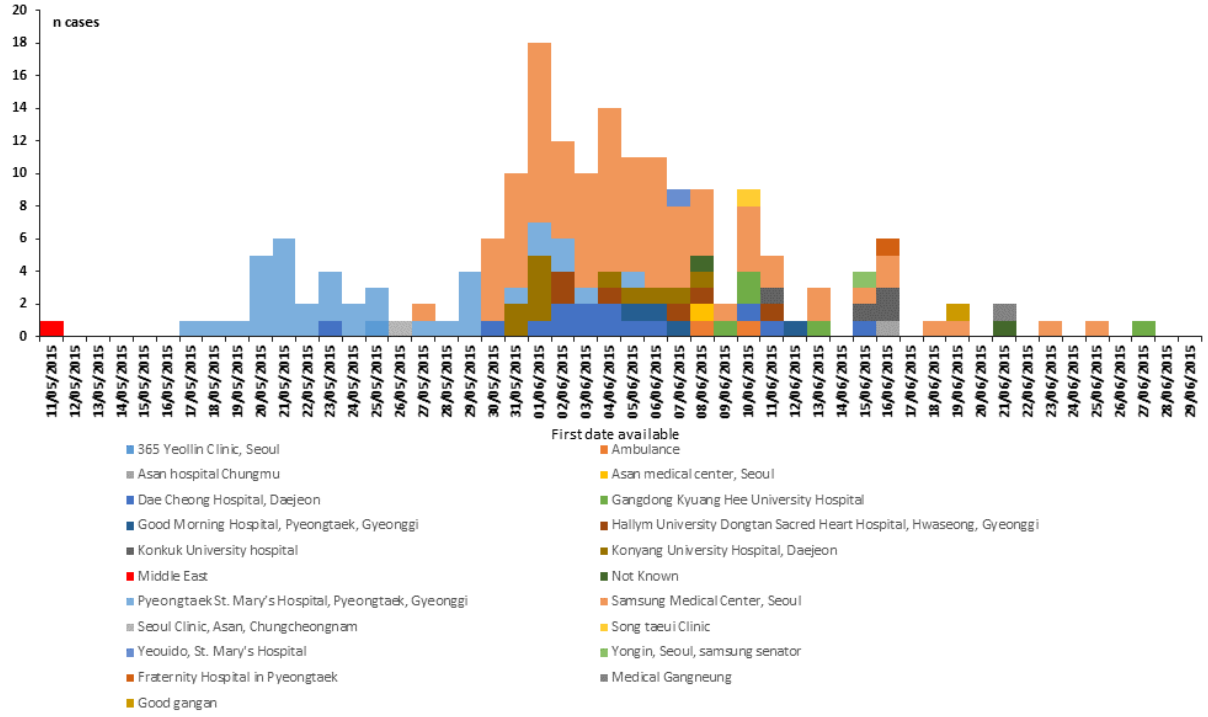
Figure 4. Distribution of confirmed MERS cases by age and gender, South Korea and China, as of 28 June 2015 (n=182)



Population source: 2015 World Fact Book of the United States Central Intelligence Agency

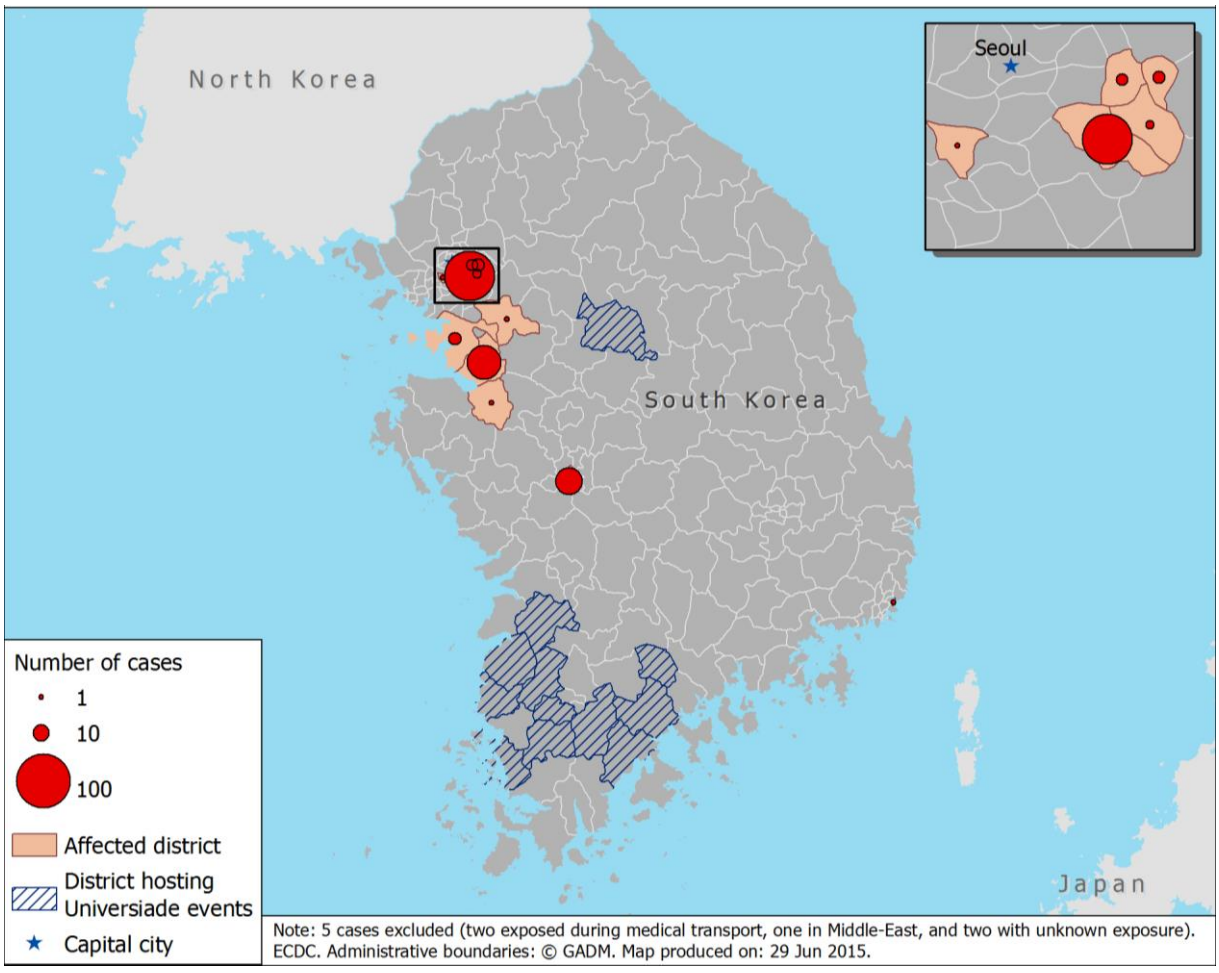
The index case in the South Korea outbreak had onset of symptoms on 11 May and was diagnosed and isolated on 20 May 2015. During the 10-day period from onset of illness until isolation (Figure 3, yellow box), the index case visited several healthcare facilities. So far, 17 hospitals have either reported MERS cases or cared for patients who were subsequently confirmed as having MERS-CoV infection (Figure 5 and Figure 6). These hospitals are located in 13 districts of South Korea, none of which are involved in the organisation of the Summer Universiade.

Figure 5. Distribution of confirmed cases of MERS infection by place of presumed exposure and date of onset or reporting*, South Korea and China, 11 May–28 June 2015 (n=182)



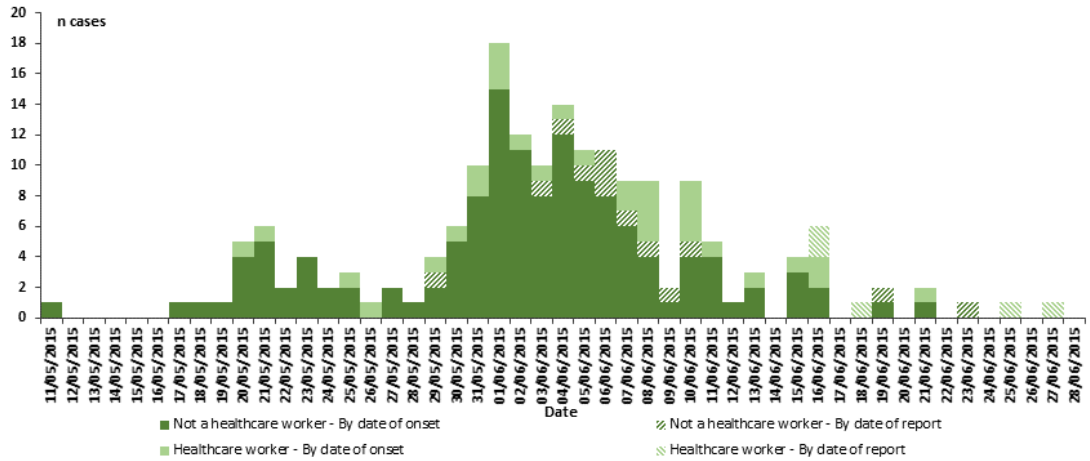
**Date of reporting is used when date of onset is unknown.*

Figure 6. Distribution of healthcare units with confirmed MERS-CoV transmissions as of 28 June 2015, and districts hosting the Universiade games, South Korea



All reported cases apart from two (the index case and the suspected household transmission) have been associated with nosocomial transmission in South Korea. As of 28 June 2015, the South Korean Ministry of Health reported, that 36 (20%) of the cases are healthcare workers: 20 doctors or nurses, eight caregivers and eight medical support staff (Figure 7) [4].

Figure 7. Distribution of confirmed cases of MERS infection by healthcare worker status and date of onset or reporting, South Korea and China, 11 May–28 June 2015 (n=182)



On 24 June, media sources quoting the South Korean Ministry of Health, reported a suspicion of community transmission in South Korea. A previously reported 74-years-old MERS case was hospitalised with symptoms and isolated on 21 June, and tested positive for MERS-CoV on 22 June. He is believed to have been infected by his wife who was confirmed to be infected with MERS-CoV on 10 June and died on 13 June. The couple had been quarantined at home until 10 June, and the husband remained asymptomatic after the death of his wife. Considering that the maximum incubation period of MERS is 14 days, it is most likely that the 74-years-old man was infected by his late wife at home.

China

On 30 May 2015, WHO notified a case of MERS in China with probable transmission in South Korea. The case is a 44-year-old son of the third MERS case in South Korea and the younger brother of the fourth MERS case. He visited his father at a time when he was hospitalised in the same room as the index case in South Korea. Later, he travelled from Seoul to Guangdong in China where he was hospitalised, and MERS-CoV infection was confirmed on 29 May [9]. No further cases of MERS linked to this patient have been identified to date. According to media sources, the patient was discharged from hospital on 26 June 2015.

Thailand

On 18 June 2015, a 75-year-old male Omani national with chronic heart disease was diagnosed with MERS-CoV infection in Thailand. According to the media in Oman quoting a Ministry of Health official, he was admitted to a hospital in Oman on 4 June for heart problems and discharged on 7 June. On 10 June, he developed respiratory symptoms and visited a health centre, and on 14 June he was referred to another hospital. On 15 June, he and three family members took a flight to Thailand. He had no fever upon arrival in Bangkok but he subsequently developed fever with suspected pneumonia. He was referred to the Bamrasnaradura Diseases Institute for treatment on 18 June 2015 and the three family members have been quarantined in the same institute. At present, his clinical condition is stable. On 18 June 2015, sputum was sent to two laboratories (National Institute of Health and the WHO Collaborating Centre for Viral Zoonoses, Faculty of Medicine, Chulalongkorn University), which revealed positive results for MERS-CoV by real-time PCR (UpE and ORF 1a) in both centres. Two of the accompanying family members are being tested for MERS-CoV after one was found to have a cough and the other a fever. So far, 175 contacts of this case have been identified.

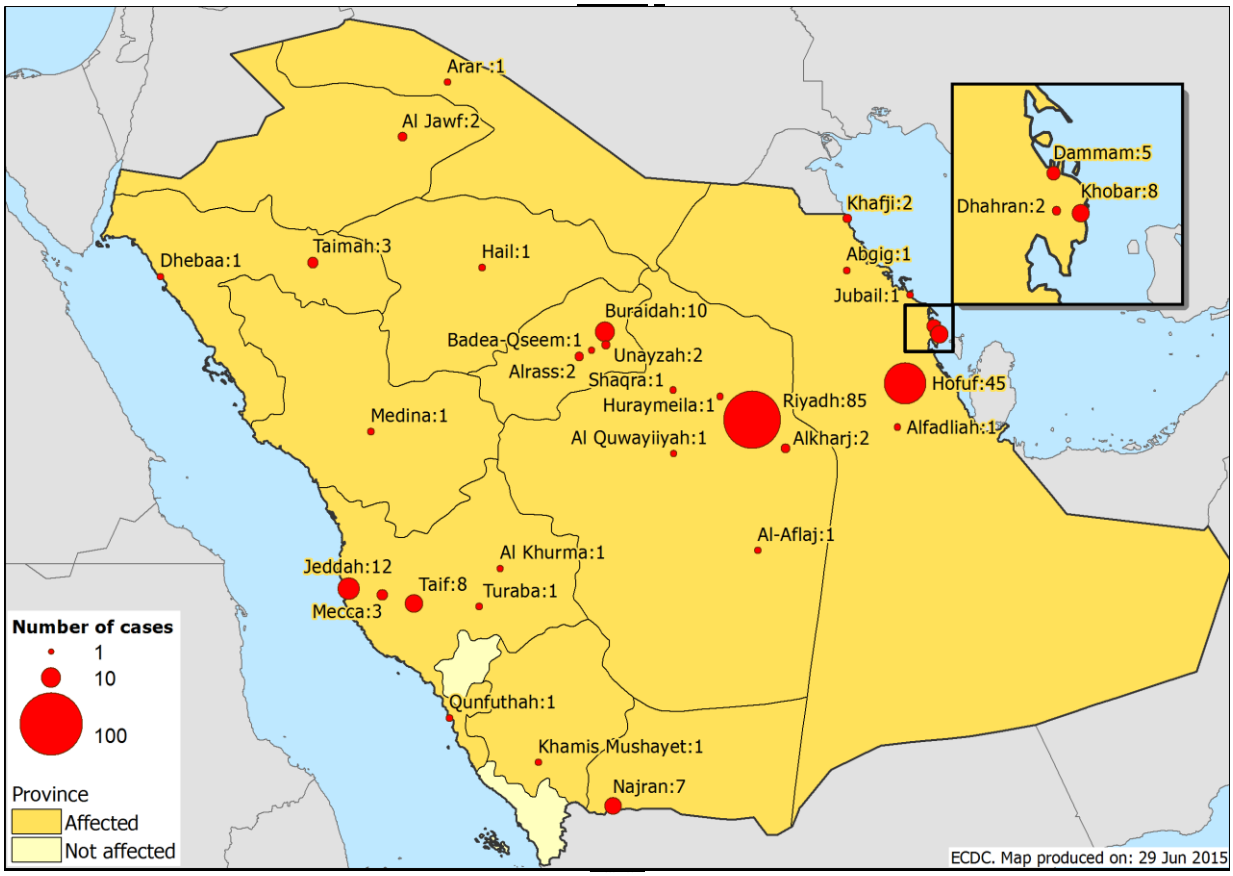
Oman

The latest MERS case was reported 31 May 2015 by the Ministry of Health. The case was reported to be a 75-years-old patient suffering from severe pneumonia and high fever. He is alive but his current condition is unknown.

Saudi Arabia

Since the beginning of 2015 and as of 29 June, Saudi Arabia has reported 214 infections with MERS-CoV (Figure 8). The WHO Regional Office for the Eastern Mediterranean published an overview of two hospital outbreaks and one household cluster of community-acquired infections with MERS-CoV from Hofuf City in the Al-Ahsa region in Saudi Arabia during the period from mid-April to the end of May 2015. This indicates that transmission of MERS-CoV is ongoing in the hospitals and in the community, and that most administrative regions are affected.

Figure 8. Distribution of MERS cases by reporting city, Saudi Arabia, 1 January–28 June 2015



Virological information

Two whole genome sequences have been produced from viruses isolated from cases linked to the cluster in South Korea. One sequence originates from a virus isolated from the patient diagnosed in Guangdong, and was sequenced by the Chinese CDC (GenBank KT006149). The other sequence was generated by the Korea National Institute of Health and Seoul National University from a virus isolated from a patient in South Korea. There is a small 22-nucleotide difference between the Korean and Chinese sequences which is likely to result from technical issues of sequencing and the fact that the Korean sequence was obtained from a cultured virus while the Chinese virus was sequenced directly from a patient swab [10].

Preliminary analysis suggests that the viruses from China and Korea are unlikely to be phenotypically different from the MERS-CoV currently circulating in the Middle East and are unlikely to present different virulence or transmission properties [10]. In particular, sequence analysis suggests that there are no significant differences in the amino acid composition of the spike protein – the glycoprotein mediating MERS-CoV virus entry into human cells and an important determinant of virulence [11]. A phylogenetic analysis of the Korean and Chinese MERS-CoV sequences clustered them closest to a recent outbreak in Riyadh in February–March 2015, but this does not necessarily link the two outbreaks as the level of diversity could be explained by a separate zoonotic infection [10].

It is unlikely that the performance of the laboratory assays for detection and confirmation of MERS-CoV infection that are widely used across the EU/EEA will be affected by the genetic changes detected in the viruses sequenced in South Korea and China (Drosten C, personal communication and [12-14]).

Conclusion

The detection of travel-related MERS cases in South Korea and Thailand is not an unexpected event. MERS-CoV infections with travel history to the Middle East have been diagnosed in the past in the EU and elsewhere. Although the MERS cluster in South Korea is the largest observed outside of the Middle East, there is no evidence of sustained community transmission of the virus. The transmission pattern observed in the Korean hospitals is similar to that observed in hospitals in the Middle East.

The number of new cases has been falling in South Korea over the last two weeks indicating that the public health measures are effective in interrupting the chains of transmission and controlling the outbreak.

WHO has stated that there is currently no indication that the MERS-CoV isolated in the South Korean outbreak is behaving differently to how it has behaved in the past, and that there are no indications of sustained transmission from person to person in the community. Transmission remains limited to patients, visitors and relatives of patients, and healthcare workers in several healthcare facilities. The incubation time is similar to previously reported clusters, and there is limited evidence of transmission before the onset of symptoms [5]. However, the number of tertiary cases is high in South Korea compared with previously documented outbreaks.

MERS-CoV transmission continues in the Middle East, with the highest number of cases reported from Saudi Arabia, UAE and Oman. The current transmission of MERS-CoV is consistent with the pattern that has been observed since 2013: sporadic primary zoonotic cases leading to nosocomial clusters of variable size. The fact that the Korean index case had no history of exposure to camels or healthcare settings in the Middle East, raises the possibility that there are unrecognised chains of human-to-human transmission in the Middle East. Müller et al have suggested that undetected low-level infection in people who are exposed to the animal reservoir could serve as source of infection for people without exposure to animals [15].

There is growing serological and molecular evidence that the dromedary camel (*Camelus dromedarius*) is a host species for MERS-CoV. Human serological and outbreak studies also support this [15]. It suggests that MERS-CoV or MERS-like coronaviruses have been circulating among dromedaries in Africa and the Middle East long before 2012. It is to be expected that sporadic cases will be seen in the vicinity of infected host species.

ECDC threat assessment for the EU

The MERS outbreak continues to pose a low risk to the EU with regards to the importation of MERS cases. Although sustained community transmission has not been observed, transmission to close contacts of imported cases, including to healthcare workers, and other patients and visitors in hospitals has been reported, most recently in South Korea, and in France, the United Kingdom and Iran.

The risk for visitors to South Korea is extremely low, unless the visitors have had contact with healthcare facilities, in particular in the 13 affected districts. The risk for participants in Universiade events in South Korea in July 2015 is similarly extremely low, as no MERS cases have been reported from the districts where Universiade events will take place.

The risk for visitors to Saudi Arabia is low, and related to exposure either to live camels and camel products or to healthcare facilities. The risk is considered higher than in South Korea because of the high number of nosocomial clusters identified in Saudi Arabia, the persistence of transmission in healthcare settings for more than two years, the suspicion of infections occurring through unrecognised chains of transmissions and the risk related to exposure to camels and camel products.

Options for response

Travellers

WHO does not recommend travel restrictions with regards to MERS-CoV, but rather to raise awareness among travellers to and from affected countries [18]. EU citizens travelling to the countries in the Middle East and to South Korea need to be made aware that MERS-CoV is circulating in these areas and should be reminded of general travel advice of good hand and food hygiene.

Participants in the Universiade in South Korea in July 2015 should follow the recommendation published by the organiser of the event, International University Sports Federation (FISU), which states that "*all persons involved in the FISU Summer Universiade should take strict precautions for good health procedures (i.e. wash hands, do not cough on others, make sure bodily fluids are self-contained). No-one is to travel to these Games or from your country if they have symptoms of any illness or have fever, cough or signs/symptoms of respiratory infection*[17]."

The organisers of Universiade have taken preventive measures, including entry control, personnel control and the establishment of a special inspection team, as well as identifying MERS designated medical facilities [16]. One MERS designated examination centre and two MERS quarantine facilities have been set up to receive suspected patients.

Returning travellers

Early detection of MERS-CoV infection among travellers exposed to camels or healthcare facilities in the Middle East or to healthcare facilities in South Korea remains essential. The outbreak in South Korea highlights the continued risk of healthcare-associated transmission and the need for timely diagnosis and implementation of prevention and control measures.

Therefore, travellers returning from the Middle East and South Korea should be made aware that if they develop respiratory symptoms or diarrhoea either during travel or up to 14 days after their return, they should seek medical attention and report their travel history. Patients presenting with severe acute respiratory disease in the EU and having recently been in contact with MERS patients, healthcare services or camels in South Korea or the Middle East should be investigated for MERS-CoV infection.

Healthcare workers in the EU should be made aware of the risk related to travellers from affected areas, the presentation of the disease, and the need to promptly investigate travellers returning from affected areas presenting with severe respiratory illness.

WHO recommends that probable and confirmed cases should be admitted to adequately ventilated single rooms or rooms with airborne transmission precautions. Healthcare workers caring for probable or confirmed cases of MERS should use contact and droplet precautions (medical mask, eye protection such as goggles or face shield, gown, and gloves) in addition to standard precautions. Airborne transmission precautions should be applied when performing aerosol-generating procedures [12].

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