



RAPID RISK ASSESSMENT

Severe respiratory disease associated with Middle East respiratory syndrome coronavirus (MERS-CoV) 16th update, 05 June 2015

Main conclusions and options for response

This update of the risk assessment was triggered by a large cluster of confirmed MERS-CoV cases in South Korea generated by a primary case that was imported from the Middle East.

The importation of a MERS-CoV case to South Korea is not an unexpected event. MERS-CoV cases with travel history to the Arabian Peninsula have been diagnosed outside of the Middle East in the past. Cases should also be expected in the future given the ongoing transmission in the region and frequent international travel to and from the region. On several occasions, notably in France, the United Kingdom and Iran, such importations have resulted in secondary transmission to patients, healthcare workers and visitors who were in contact with the primary imported cases and/or close relatives of a case.

Although the MERS-CoV cluster in South Korea is the largest that has so far been observed outside of the Arabian Peninsula, the cluster remains limited to patients, visitors to patients and healthcare workers in a few healthcare facilities and close relatives of the cases. The outbreak does not represent an increased risk of infection for travellers or visitors to South Korea. However, patients who present with severe acute respiratory disease in the EU and have recently been in contact with healthcare services in South Korea should be considered for MERS-CoV assessment, similar to patients having been in contact with healthcare services in the Arabian Peninsula.

The fact that the index case in the South Korean cluster does not have a documented history of exposure to camels or healthcare settings in the Arabian Peninsula is cause for concern. Continuous vigorous efforts are required to determine the likely source of infection and to ensure that other, undetected, transmission chains are not ongoing.

WHO has stated that there is currently no indication that the virus is behaving differently to how it has behaved in the past and that there is no indication of sustained transmission from person to person. However, further details of the virus characterisation in South Korea are pending.

ECDC's assessment continues to be that the MERS-CoV outbreak poses a low risk to the EU. Because of the continued risk of case importation to Europe after exposure in the Middle East or South Korea, international surveillance for MERS-CoV cases among travellers remains essential. Moreover, rapid efforts to contain nosocomial clusters in the affected countries are vital to prevent broader transmission patterns. Although sustained human-to-human transmission is unlikely, secondary transmission to unprotected close contacts, especially in healthcare settings, remains possible, as now documented in South Korea. The vast majority of cases detected in the Middle East and South Korea continue to be due to nosocomial exposure.

The importance of eliciting a travel history from patients with severe respiratory disease cannot be overemphasised. The immediate, systematic and strict implementation of infection prevention and control measures in the hospital setting are essential to interrupt transmission and prevent clusters of healthcare-associated infection. Furthermore, the challenges of detecting rare imported cases of respiratory infection early on highlight the need for adequate infection

prevention and control measures for all patients showing symptoms of acute respiratory infection.

WHO recommends that probable and confirmed cases should be admitted to adequately-ventilated single rooms or airborne precaution rooms. Healthcare workers caring for probable or confirmed cases of MERS-CoV infection should use contact and droplet precautions (medical mask, eye protection – i.e. goggles or face shield – gown and gloves) in addition to standard precautions. Airborne precautions should be taken when performing aerosol-generating procedures [1].

An overview of MERS-CoV infection is presented in an ECDC fact sheet [2], which also provides details of measures to be taken by health professionals for case management and treatment.

Source and date of request

ECDC Internal Decision and Request of the European Commission, 1 June 2015.

Public health issue

This update of the risk assessment was triggered by a large cluster of confirmed MERS-CoV cases in South Korea generated by a primary case imported from the Middle East.

Consulted experts

Internal consulted experts: Kaja Kaasik Aaslav, Niklas Danielsson, Pasi Penttinen, Diamantis Plachouras, René Snacken.

External consulted experts: World Health Organization (WHO) was consulted, however the views expressed in this document do not necessarily represent the views of WHO.

Disease background information

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

Clinical presentation of MERS-CoV infection ranges from asymptomatic to very severe pneumonia with acute respiratory distress syndrome (ARDS), septic shock and multi-organ failure resulting in death. The clinical course is more severe in immunocompromised patients.

Although it is likely that a zoonotic transmission is the starting point of some clusters, human-to-human transmission is currently 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 has been reported from hospital outbreaks in Saudi Arabia and United Arab Emirates (UAE).

There is growing evidence that the dromedary camel is a host species for the virus and that camels might play an important role in the direct or indirect transmission to humans.

See more at: <http://ecdc.europa.eu/en/healthtopics/coronavirus-infections/mers-factsheet/Pages/default.aspx#sthash.tTUYqixK.dpuf>

Recent evidence

In a recent cross-sectional seroprevalence study that included 10 009 subjects in Saudi Arabia, the presence of antibodies against MERS-CoV was found to be 23 times higher (3.6% vs 0.15%, $p < 0.001$) in slaughterhouse workers who are occupationally exposed to camels than in the general population [3]. The authors note that the higher prevalence in young males observed in this study is an indication of unrecognised infections with mild or no symptoms. These subclinical infections could then presumably act as a source of infection for patients not having been exposed to camels.

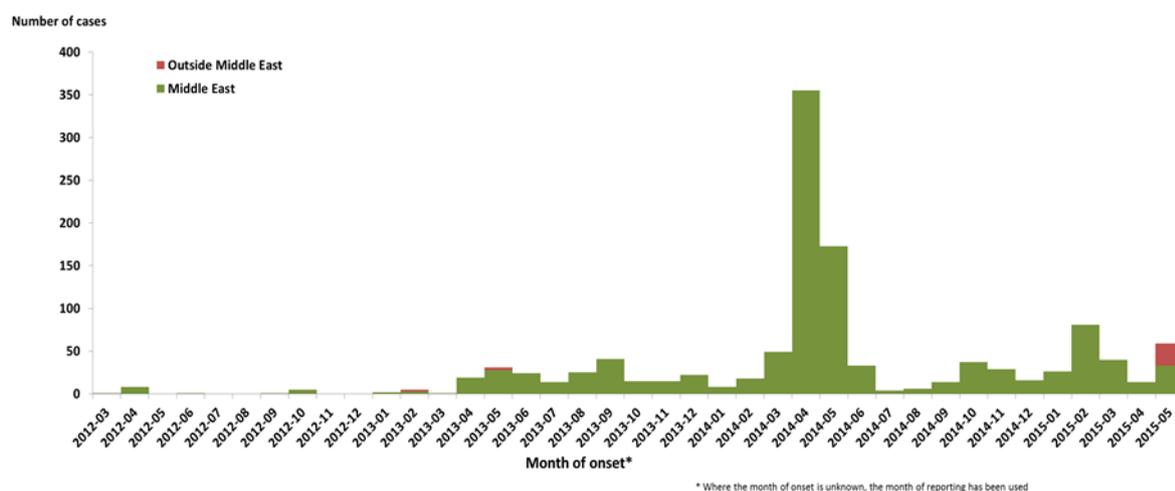
A serological study in Qatar [4] demonstrated the presence of neutralising antibodies in seven out of 109 persons with occupational exposure to dromedary camels, a proportion similar to that found among slaughterhouse workers in the seroprevalence study in Saudi Arabia. The findings of these studies strengthen evidence of the role of dromedary camels as a source of infection and indicate that unrecognised asymptomatic or mild infections are likely to occur at low rates in occupationally exposed persons.

Event background information

Worldwide situation

Since April 2012 and as of 5 June 2015, 1 211 cases of MERS-CoV (including 492 deaths) have been reported by health authorities worldwide (Figure 1, Table 1).

Figure 1. Distribution of confirmed cases of MERS-CoV by month and probable place of infection, March 2012 – 31 May 2015 (n=1 192)



* If the month of onset is unknown, month of reporting has been used.

Geographical distribution

Most of the cases have occurred in the Middle East: Saudi Arabia, United Arab Emirates, Qatar, Jordan, Oman, Kuwait, Egypt, Yemen, Lebanon and Iran (Table 2).

Table 1. Confirmed MERS-CoV cases and deaths, by country of reporting, March 2012 – 5 June 2015

Reporting country	Cases	Deaths
Middle East		
Saudi Arabia	1 019	450
United Arab Emirates	76	10
Qatar	13	5
Jordan	19	6
Oman	6	3
Kuwait	3	1
Egypt	1	0
Yemen	1	1
Lebanon	1	0
Iran	6	2
Europe		
Turkey	1	1
Austria	1	0
United Kingdom	4	3
Germany	3	1
France	2	1
Italy	1	0
Greece	1	1
Netherlands	2	0
Rest of the world		
Tunisia	3	1
Algeria	2	1
Malaysia	1	1
Philippines	2	0
South Korea	40	4
United States of America	2	0
China	1	0
Total	1 211	492

All cases reported from outside the Middle East have a recent travel history to the Middle East or are linked to a case with a travel history to the Middle East (Figure 2).

Figure 2. Geographical distribution of confirmed MERS-CoV cases and place of probable infection, as of 5 June 2015 (n=1 211)

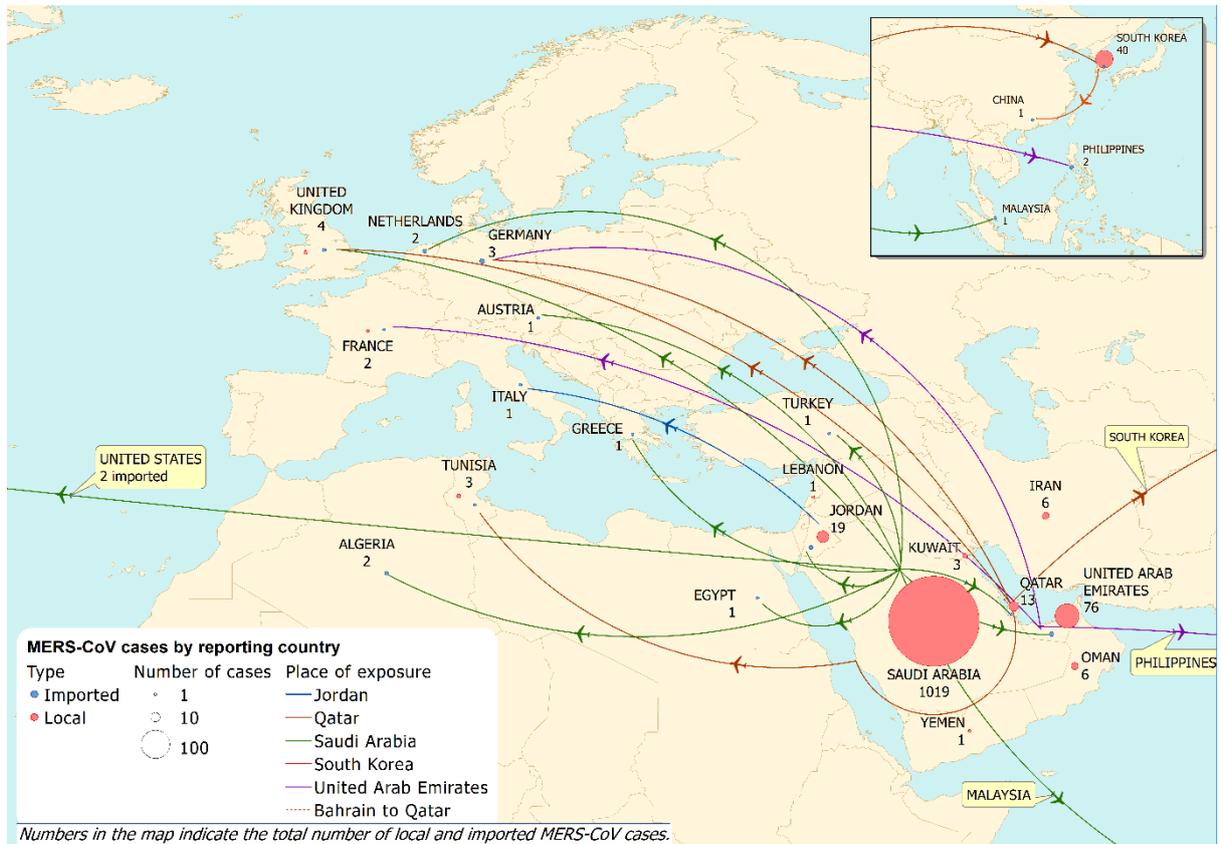
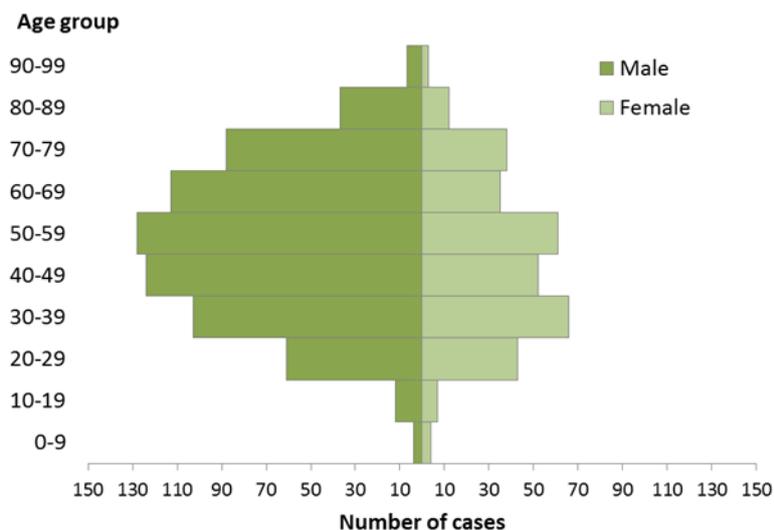


Figure 3. Age and gender distribution among confirmed cases of MERS-CoV (n=998)



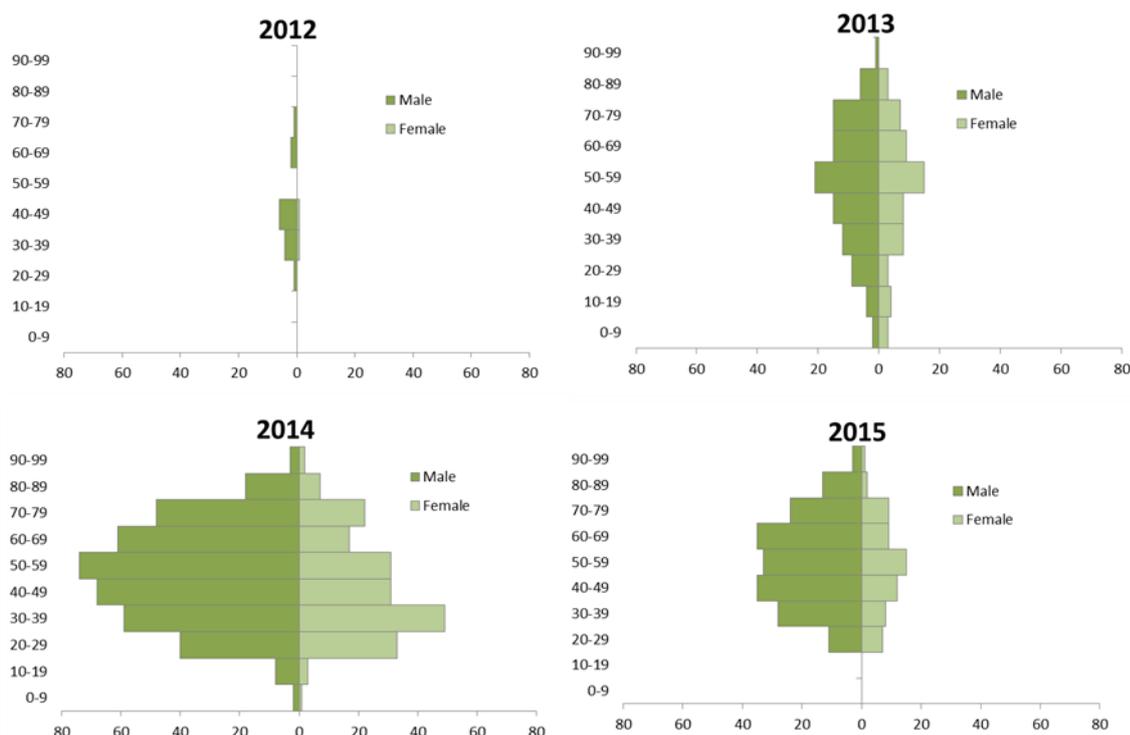
*213 cases for which age or sex data is missing have been excluded

Of the 998 cases with known age and gender 497 (50%) were male above the age of 40 (Figure 3). The average age for both females and males remains above 40 years (for cases with known age), with a range between 1 and 99 years of age.

Table 2. Distribution of confirmed MERS-CoV cases by reporting year and gender, as of 5 June 2015

	2012	2013	2014	2015	Overall
Male	14	100	381	182	677
Female	2	60	196	63	321
Total number of cases	16	160	577	238	998
Male–female ratio	7:1	1.7:1	1.9:1	2.8:1	2.1:1
Mean age of males	44	52	48	54	53
Mean age of females	42	48	40	54	46

Figure 4. Distribution of confirmed MERS-CoV cases by age, gender and year of reporting



Current epidemiological situation

Since the previous update of the ECDC Rapid Risk Assessment on severe respiratory disease associated with MERS-CoV dated 8 March 2015, there have been 129 new cases and 53 additional deaths from MERS-CoV reported globally: Saudi Arabia (81 cases and 48 deaths), Qatar (3 cases and one death), Oman (one case) United Arab Emirates (two cases), Iran (one case) South Korea (40 cases and four deaths) and China (one case).

South Korea and China

South Korea

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

According to WHO, the man had the following travel history: 18–29 April, Bahrain; 29–30 April, United Arab Emirates; 30 April to 1 May, Bahrain; 1–2 May, Saudi Arabia; 2 May, Bahrain; and 2–3 May, Qatar. The case arrived at Korea’s Incheon International airport via Qatar on 4 May and was asymptomatic on arrival. The patient has no history of exposure to camels or contacts with MERS-CoV patients, and he did not visit any healthcare facilities while travelling in the Middle East. Investigation of the source of infection is ongoing [5].

As of 5 June, this primary case has resulted in 30 secondary cases. All secondary cases were exposed to the primary case before he had been diagnosed with MERS-CoV and before appropriate infection prevention and control measures had been implemented. Of the 30 secondary cases:

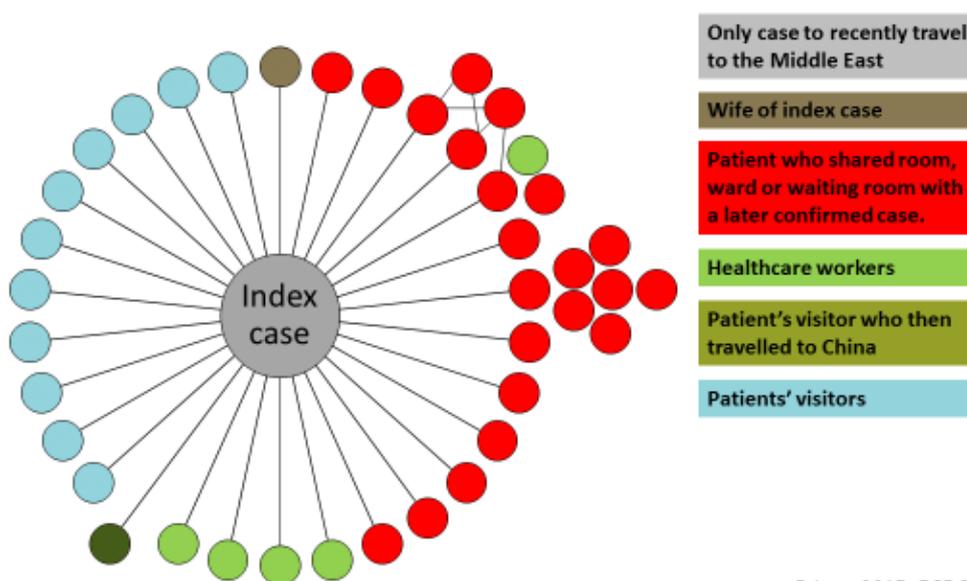
- Thirteen were admitted in the same ward or had contact with the index case as patients;
- Four healthcare workers provided care for him;
- Thirteen were family contacts or visitors to patients admitted to the same ward or sharing the same room with the index case: the wife of the index case, and twelve visitors, one of whom travelled to China.

On 2–5 June the health authorities in South Korea reported ten additional cases with no history of contact with the index case but contact with two secondary cases. One of these cases was a healthcare worker.

Furthermore, the health authorities are reporting four fatal cases.

Onset dates range from 11 May for the index case, until 01 June for the most recent nosocomial cases where the onset date is indicated, according to the [Korea Centers for Disease Control and Prevention](#).

Figure 5. Transmission chain of 41 confirmed MERS-CoV cases in South Korea and China reported from 20 May to 5 June 2015



5 June 2015, ECDC

China

On 30 May, WHO notified of a case of MERS-CoV in China. The case is a 44 year-old male from South Korea. The patient is the son of the third MERS-CoV case in South Korea and the younger brother of the fourth MERS-CoV case. He visited his father in the hospital, while the father was sharing a room with the index case. He developed symptoms on 21 May but decided to fly to Hong Kong, China on 26 May where he continued to Huizhou through an entry point in Shenzhen City, Guangdong Province. The local health authority found him on 27 May and immediately transferred him to a designated hospital for isolation. This patient was confirmed positive for MERS-CoV infection on 29 May [6].

Of the 41 cases reported from South Korea and China 68% (28 cases) were males. Of the 28 male cases; one is the index case, two are healthcare workers, nine are visitors and sixteen are patients. Three of the male cases have died.

Of the 41 cases reported 32% (13 cases) were females. Of the 13 female cases; three were healthcare workers, one is a close contact to the index case, three are visitors and six are patients. One of the female patients has died.

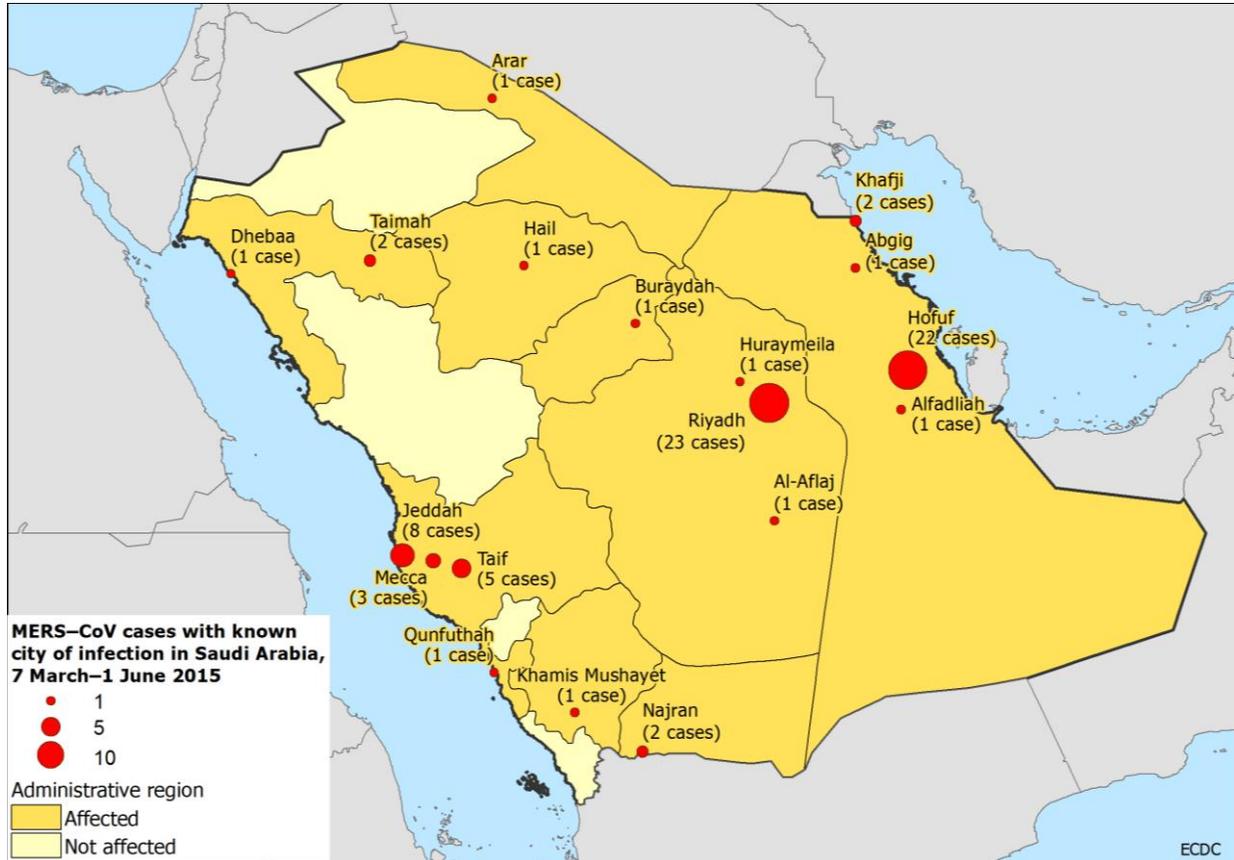
Saudi Arabia

Since the last risk assessment on 8 March 2015 and as of 5 June 2015, Saudi Arabia has reported 81 additional cases of MERS-CoV (Figure 4). Of the 81 cases, five were identified as healthcare workers. Thirty-one reportedly had contact with suspected or confirmed cases in hospitals or clinics or in the community. Six of the thirty-one were clearly indicated as a nosocomial transmission, while three are currently under investigation for possible nosocomial transmission and the source of the infection is unknown for forty-seven cases.

Of the 79 cases, where age and sex is known, 78% are male (62), while 22% are female (17). The age ranged from 20 to 93 years, with a mean age of 54 for males. For females the age ranged between 24 and 77 years, with a mean age of 55 years.

Eleven of the 81 cases reported animal contact and ten are reported to have drunk camel milk and to have had contact with to camels.

Figure 6. MERS-CoV cases with known city of infection in Saudi Arabia, 8 March – 2 June 2015



United Arab Emirates

On 18 and 24 May 2015, WHO notified of two additional cases of MERS-CoV infection in the United Arab Emirates. Both cases were asymptomatic and found through enhanced surveillance. According to WHO, both cases had a recent history of contact with MERS-CoV infected camels imported from Oman.

Qatar

Since the last ECDC Rapid Risk Assessment update on 8 March, there have been three additional cases and one death of MERS-CoV in Qatar. All the cases are males between the ages of 29 and 73 years. Two of the cases have had frequent contact with camels. One of the two cases frequently drinks camel milk. A relative of the third case owns a camel farm and drinks raw camel milk, however he does not have direct contact with camels. The third case has died.

Oman

On 31 May 2015, the health authorities in Oman reported a case of MERS-CoV in a 75-year-old male.

Iran

On 8 May 2015, the WHO notified of an additional case of MERS-CoV in a 61-year-old male with onset of symptoms on 18 March.

ECDC threat assessment for the EU

Continuing transmission of MERS-CoV is being observed in the Arabian Peninsula. The transmission pattern is consistent with what has been observed since 2013: sporadic cases detected throughout the years occasionally leading to small or large nosocomial clusters and outbreaks.

There is an ongoing risk of MERS-CoV infection being imported into the EU, especially during periods of increased activity in the Arabian Peninsula. Although sustained human-to-human transmission has not been observed, transmission to unprotected close contacts, including healthcare workers and other patients in hospital settings, is frequently reported.

The evolving cluster in the South Korea that originated from a single traveller returning from the Arabian Peninsula is the largest cluster of cases outside of the Middle East. Although the number of confirmed secondary cases associated with this primary case is high, clusters of healthcare-associated infections have previously been observed in Saudi Arabia. To date sustained human-to-human transmission has not been observed, however the occurrence of tertiary cases is of concern, although not unexpected.

The possibility of changes in the potential for transmission of the virus or genetically determined differences in susceptibility at population level are being investigated. In addition, more details of the potential exposures of the index case would be useful, both to elucidate the potential source of infection and the cause of high numbers of secondary cases. 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.

Conclusions and options for response

The importation of a MERS-CoV case to South Korea is not an unexpected event. MERS-CoV cases with travel history to the Arabian Peninsula have been diagnosed outside of the Middle East in the past. Cases should also be expected in the future given the ongoing transmission in the region and frequent international travel to and from the region. On several occasions, notably in France, the United Kingdom and Iran, such importations have resulted in secondary transmission to patients, healthcare workers and visitors who have been in contact with the primary imported cases, as well as to close relatives of a case.

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