

Middle East respiratory syndrome coronavirus (MERS-CoV) Summary and literature update – as of 27 March 2014

Since April 2012, 206 laboratory confirmed cases of human infection with Middle East respiratory syndrome coronavirus (MERS-CoV) have been reported to WHO, including 86 deaths (Figure 1).

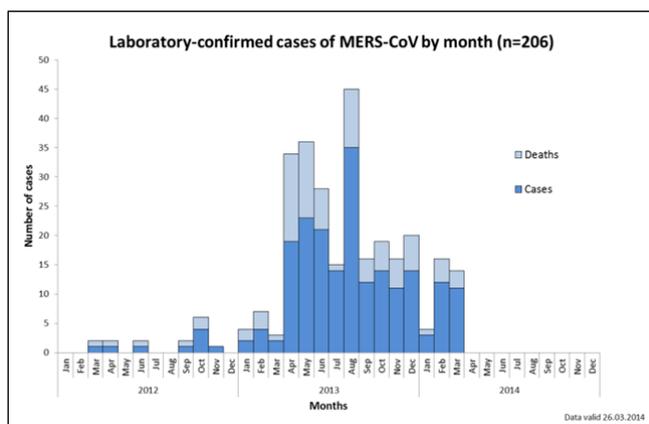


Figure 1. Laboratory confirmed cases of MERS-CoV infection by approximate time of onset, March 2012 through March 2014.

The age and gender distribution of cases vary depending on the presumed type of exposure that led to infection. Primary cases, those who have no history of prior exposure to other human cases, are on average older and a larger percentage of them are men than secondary cases (Table 1). Secondary cases are those who appear likely to have been infected by other humans.

Table 1. Demographic distribution of laboratory-confirmed cases of MERS-CoV

	Median age (years)	% male
Primary cases	58	80
Secondary cases	45	58
All cases	52	67

Thus far, the affected countries in the Middle East include Jordan, Kuwait, Oman, Qatar, Saudi Arabia and the United Arab Emirates (UAE), all of which appear to have had primary transmission events from non-human sources. Other affected countries include France, Germany, Italy and the United Kingdom (UK), in Europe; and Tunisia, in North Africa. In these countries, cases have been imported from the Middle East with some secondary transmission (Figure 2). All primary cases have had their exposure to MERS-CoV in the Middle East.

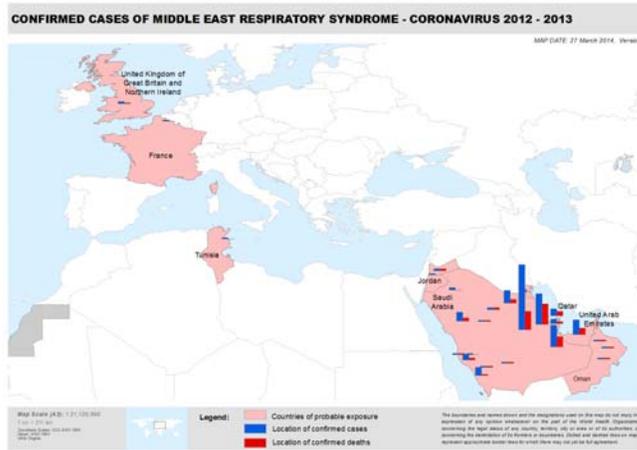


Figure 2. Location of laboratory confirmed cases of MERS-CoV infection by country of presumed exposure, March 2012 through March 2014.

Since the last update of 20 January 2014, 28 laboratory-confirmed cases, including 10 deaths, have been reported to WHO. Countries in which the presumed exposure of these cases occurred are shown in Table 2 below.

Table 2. Geographic distribution of laboratory-confirmed cases by country of presumed exposure since 20 January 2014

	Cases	Deaths
Jordan	1	1
Kuwait	1	1
Oman	2	1
Saudi Arabia	22	7
United Arab Emirates	2	0
Total	28	10

It is notable that the cases from Jordan, Kuwait, and one of the cases from UAE appear to have acquired infection in a health care setting. Among the 22 cases reported from Saudi Arabia, 19 were in Riyadh, and one appears to have acquired his infection in a health care setting. Among the four cases that acquired infection in a health care setting, three appear to have had exposure to an unidentified primary case. Additionally, four of the cases from Riyadh were members of the same household: the index case, a 19-year-old male, died as a result of infection with MERS-CoV, and three presumed secondary cases—a 53-year-old male, an 18-year-old female and a 22-year-old female—exhibited mild or no symptoms.

Recent MERS-CoV animal studies

An investigation in Egypt, using real time polymerase chain reaction (RT-PCR) detected MERS-CoV in 3.6% (4 of 110) apparently healthy dromedary camels in a slaughterhouse. Genetic sequence of the viruses demonstrated small differences from a reference strain previously taken from a human case. The investigators also tested sera collected from 52 of the camels and from 179 slaughterhouse workers. MERS-CoV reactive antibodies were detected in 92% of camels but none of the workers. The camels that tested positive were all imported from either Sudan or Ethiopia.

Reference: Chu DKW, et al. MERS Coronaviruses in Dromedary Camels, Egypt. *Emerg Infect Dis*, 2014 Jun, Vol 20, 6. Available at: <http://dx.doi.org/10.3201/eid2006.140299>.

A recent publication in *Emerging Infectious Diseases* reported the results of an investigation of a human case of MERS-CoV infection with exposure to an infected camel in Saudi Arabia. The human-derived virus and a partly sequenced virus from the camels shared single nucleotide change that occurred in no other known MERS-CoV sequences. The close relationship between the human and camel-derived viruses is consistent with a transmission event occurring between the two.

Reference: Memish ZA, et al. Human Infection with MERS Coronavirus after Exposure to Infected Camels, Saudi Arabia, 2013. *Emerg Infect Dis*, 2014 Jun (Early online release). Available at <http://dx.doi.org/10.3201/eid2006.140402>.

A second study from Saudi Arabia found MERS-CoV in a large number of camels from across the country, using molecular diagnostics. MERS-CoV nucleic acids were found more frequently in juveniles (36/104, 35%) than in adults (15/98, 15%). A large proportion of dromedary camels sampled in 2013 also had antibodies to MERS-CoV. The prevalence of seropositivity was higher in camels older than 2 years (93/98, 95%) than in camels younger than 2 years; (57/104, 55%). In addition, the investigators found antibodies against MERS-CoV in archived specimens dating from 1992 through 2010. Serum samples collected from goats (n = 36) and sheep (n = 112) in 2013 did not have antibodies reactive with MERS-CoV but did have antibodies reactive with a bovine coronavirus (25% of goats, n=36; 54% of sheep, n=24). Nasal swabs from 36 goats and 78 sheep were negative in RT-PCR assays for MERS-CoV uPE.

Reference: Alagaili AN, et. al. Middle East Respiratory Syndrome Coronavirus Infection in Dromedary Camels in Saudi Arabia. *mBio*. 2014. 5(2):doi:10.1128/mBio.00884-14 available at : <http://mbio.asm.org/content/5/2/e00884-14.full.html>.

Recent WHO activities

A meeting of countries of the Middle East that have had primary transmission of MERS-CoV was held in Riyadh, Saudi Arabia 2-3 March 2014. The purpose of the meeting was to finalize a protocol for a case-control study to determine significant exposure factors for MERS-CoV infection. After the meeting, the protocol was finalized and distributed to the affected countries.

Discussion

Recent studies support the premise that camels serve as the primary source of the MERS-CoV infecting humans and that other livestock are not involved. Although bats may have been the ultimate reservoir of the progenitor virus, epidemiologically it seems much more likely that camels would be the source of infection for humans. The evidence for this includes the frequency with which virus has recently been found in camels to which human cases have been exposed, the serological data that indicate widespread transmission in camels, the similarity of the camel-derived virus to human-derived virus collected in the same area, and the frequency of either direct or indirect contact between camels and humans in the region. The available genetic sequence data not only demonstrate a close link between the virus found in camels and that found in humans, but also suggest the current observed pattern of disease in humans is the result of repeated introductions into human populations from camels, with subsequent limited human-to-human transmission, rather than sustained community transmission among humans. As such, discovery of the route of transmission between camels and humans remains critical to stopping the initial introduction into

human populations. The limited data available on exposures of primary cases - that is, those patients who do not appear to have contracted the infection from other humans - suggest that transmission is often indirect, as most do not have a recent history of direct contact with camels. Until more information is gathered, it is prudent for persons at high risk of severe disease, including those with diabetes, chronic lung disease, pre-existing renal failure, or those who are immunocompromised, to take appropriate precautions when visiting farm and market environments where camels are present. These measures might include good hand hygiene, avoiding contact with camels, and avoiding food that may be contaminated with animal secretions or products unless they are properly washed, peeled, or cooked.

Serological evidence suggests that the virus is widespread in camel populations throughout the region. Although exposure behaviours may differ markedly from country to country, it is likely that small numbers of cases are being missed in countries with sizable camel populations. Countries in the region that have large camel populations are reminded of the need for surveillance and testing of persons with severe respiratory disease, including community-acquired pneumonia, according to current WHO surveillance guidelines and without respect to their history of travel.

The continued occurrence of transmission between humans in health care settings and in households is an ongoing concern. The outbreaks appear to be self-limited or extinguishable with rigorous implementation of appropriate infection control guidelines; however, it is likely that these will continue to occur until the primary route of transmission to humans is interrupted. The occurrence of nosocomial transmission from unrecognized primary cases illustrates the need for rigorous adherence to appropriate infection control practices when managing patients with respiratory tract infections, even when MERS-CoV is not yet diagnosed. Countries in which primary transmission is occurring are strongly urged to expand testing to patients hospitalized with mild community-acquired pneumonia, as resources permit. In addition, for patients in whom there is a high index of suspicion of MERS-CoV infection, retesting is recommended if the initial test is negative, particularly if it is based on a single nasopharyngeal swab. Clinicians should be encouraged to collect and submit lower respiratory tract specimens, such as sputa, endotracheal aspirates, or broncho-alveolar lavage, when lower respiratory disease is present. Countries that have large numbers of travellers to the region, including workers, are reminded of the need for vigilance in the form of surveillance, and the importance of good infection control practices in managing patients with acute respiratory infections.

WHO continues to request that Member States report all confirmed and probable cases, along with information about their exposures, testing, and clinical course, to inform the most effective international preparedness and response. WHO strongly recommends detailed case investigations for every case and case-control studies for index cases. In addition, more information is needed to determine the risk factors for in-hospital transmission.

WHO provides guidance and tools for carrying out investigations into human cases of MERS-CoV:

- WHO guidelines for investigation of cases of human infection with Middle East Respiratory Syndrome Coronavirus (MERS-CoV) pdf, 359kb
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Initial Interview Questionnaire of Cases pdf, 114kb
- Case-control study to assess potential risk factors related to human illness caused by Middle East Respiratory Syndrome Coronavirus (MERS-CoV) pdf, 257kb
- Seroepidemiological Investigation of Contacts of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Patients