



## **Middle East respiratory syndrome coronavirus (MERS-CoV) summary and literature update – as of 22 November 2013**

Since April 2012, 157 laboratory-confirmed and 19 probable cases of human infection with Middle East respiratory syndrome coronavirus (MERS-CoV) have been reported to WHO. Three new countries—Spain, Kuwait, and Oman—have reported patients with MERS-CoV since the last update. Infections in Kuwait and Oman were likely acquired locally, while the two probable cases reported by Spain were both recent travellers to the Middle East. The cases in Spain have not yet been confirmed, pending finalization of the laboratory testing. To date, affected countries in the Middle East include Jordan, Kingdom of Saudi Arabia, the United Arab Emirates (UAE), Qatar, Oman and Kuwait. Europe countries reported include: France, Germany, the United Kingdom (UK), Italy and Spain, and in North Africa: Tunisia (Figure 1).

Eighteen of the 27 new cases reported since the last update cases were sporadic, that is, cases that were reported to have no prior contact with another known case and including cases that were the first case within a cluster. Seven cases reported contact with previous confirmed cases and two are unclassified due to lack of information.

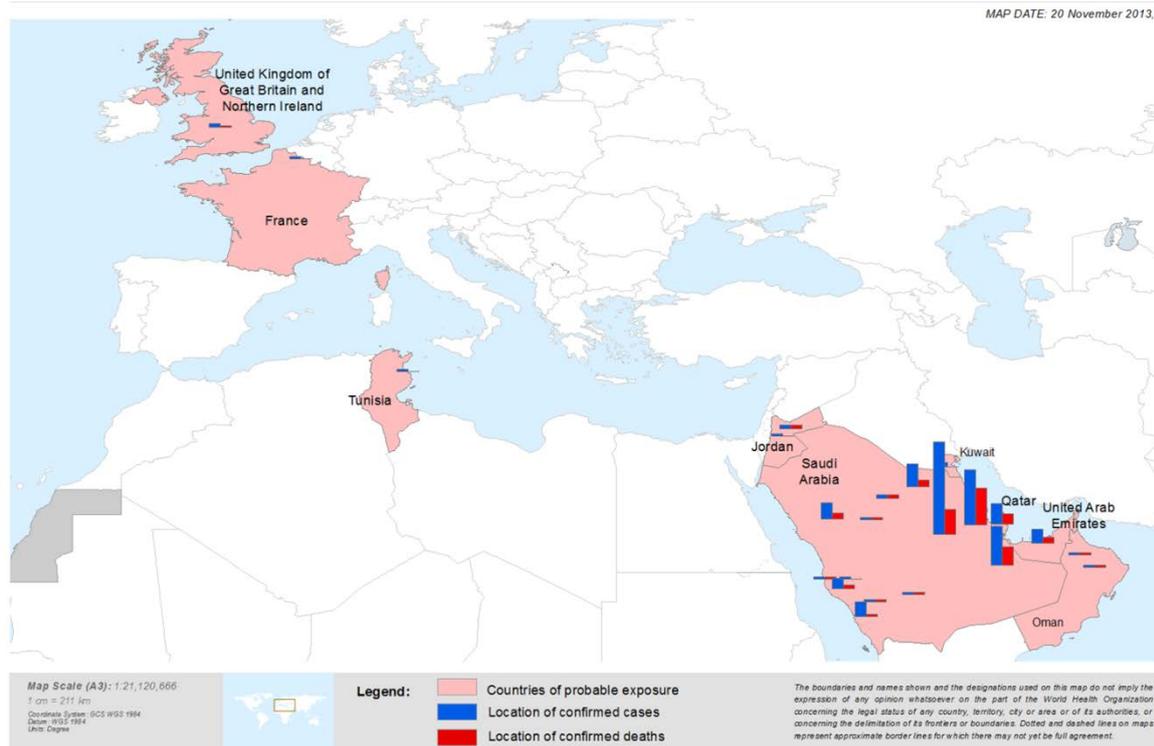
Of note, all four recently confirmed cases from Qatar were reported to have farm contact. The first case was a 61-year-old Qatar national without history of travel or contact with confirmed cases. The farms include a variety of animals, including camels, sheep and poultry. The second case is a 23-year-old male resident who worked on the farm owned by the first case. He displayed very mild symptoms and was discovered as part of contact screening. The third and fourth cases are a 48-year-old man and a 61-year-old man, respectively. Both had no history of contact with previously laboratory-confirmed cases but a preliminary investigation indicated that they had frequent interactions with farm animals. A comprehensive investigation into animal exposures of the cases has been launched by the Supreme Council of Health of Qatar.

On 10 November 2013, the Ministry of Health of Saudi Arabia announced the detection of MERS-CoV in a specimen taken from an ill camel owned by a laboratory-confirmed case from Jeddah. This case had direct contact with the ill camel. If confirmed, this will represent the first detection of MERS-CoV in camels.

Of the 176 laboratory-confirmed and probable reported cases to date, 69 (39.2%) have died and 65.3% of those for which sex is known were male (111/170). The median age of the cases with reported age is 51 years (range 14 months - 94 years; n=172). Sporadic cases (n=62) are more likely to be male (76% vs. 58%) and above the age of 50 years old (66% vs. 39%) compared with secondary cases (n=97).

Among secondary cases, infected individuals are believed to have acquired the virus in household settings, health care settings (HCS), and one in a workplace other than a HCS. Cases associated with HCS in Jordan, France, KSA, UK, UAE, and Qatar included health care workers treating MERS-CoV patients, patients seeking treatment in hospitals for conditions unrelated to MERS-CoV, and visitors. In households and the non-HCS workplace, secondary cases occurred among family contacts or co-workers. The specific types of exposure resulting in transmission are currently unknown. Altogether, at least 60 (49 confirmed and 11 probable) of the 97 secondary cases for whom the setting of their most likely exposure is known, are thought to have been infected in a health care setting.

**Figure 1 Number of laboratory confirmed MERS-CoV cases by country of probable exposure**



## WHO recent guidelines and tools

WHO has published an investigation protocol entitled: “Seroepidemiological Investigation of Contacts of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Patients”. This protocol describes a cohort study design for a comprehensive assessment of all contacts of confirmed and probable MERS-CoV cases, including household, familial, social, and occupational contacts, to evaluate the spectrum of illness and risk factors associated with infection, routes and risk of transmission. The protocol is available

here: [http://www.who.int/csr/disease/coronavirus\\_infections/WHO\\_Contact\\_Protocol\\_MERSCoV\\_19\\_November\\_2013.pdf](http://www.who.int/csr/disease/coronavirus_infections/WHO_Contact_Protocol_MERSCoV_19_November_2013.pdf)

## Selected literature published since last update

- The WHO MERS-CoV Research Group. State of Knowledge and Data Gaps of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Humans. PLOS Currents Outbreaks. 2013 Nov 12. Edition 1 Available at: <http://currents.plos.org/outbreaks/article/state-of-knowledge-and-data-gaps-of-middle-east-respiratory-syndrome-coronavirus-mers-cov-in-humans-2/>

WHO, in collaboration with affected Member States and an informal network of academic compiled information on MERS-CoV. The report summarizes the current state of knowledge about the epidemiology, demographic characteristics, clinical features and treatment strategies, and the virology of the MERS-CoV. In addition to summarizing data on reported cases, the report reviews published literature.

- Cauchemez S, Fraser C, Van Kerkhove MD, Donnelly CA, Riley S, Rambaut A, Enouf V, van der Werf S, Ferguson NM. Middle East respiratory syndrome coronavirus: quantification of the extent of the epidemic, surveillance bias, and transmissibility. The Lancet Infectious Diseases, Early Online Publication, 13 November 2013 doi:10.1016/S1473-3099(13)70304-9. Available at: <http://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2813%2970304-9/abstract>

Cauchemez and colleagues undertook independent analyses to assess the transmissibility and extent of spread of MERS-CoV to date. Using publicly available epidemiological data on 111 confirmed and probable MERS-CoV patients and genetic sequence data from 10 cases, the study found central estimates of  $R_0$  between 0.8 and 1.3. This work suggests that current data are consistent with two scenarios: (a) a sustained epidemic in an animal reservoir with sporadic spill-over into humans, or (b) sustained human-to-human transmission causing a slowly growing human epidemic. The authors also used epidemiological and genetic data to evaluate the underlying scale of the epidemic so far. Analyses using numbers of exported cases of returning travellers from countries in the Middle East ( $n=4$ ) and average length of visitor stays to Jordan, Qatar, KSA and UAE suggest that by now at least 900 symptomatic cases of MERS-CoV have occurred.

- Goh GK, Dunker AK, Uversky V. Prediction of Intrinsic Disorder in MERS-CoV/HCoV-EMC Supports a High Oral-Fecal Transmission. PLOS Currents Outbreaks. 2013 Nov 13. Edition 1. Available at: <http://currents.plos.org/outbreaks/article/mers-covhcov-emc-and-protein-intrinsic-disorder-model-detects-higher-oral-fecal-transmission-component/>

Goh and colleagues categorized coronaviruses using protein intrinsic disorder prediction – a model that evaluates the hardness of the coronavirus shells. MERS-CoV was categorized as having a hard inner and outer shell, implying that the virus can persist in the environment. The finding is consistent with observations of other viruses that transmit through a fecal-oral route.

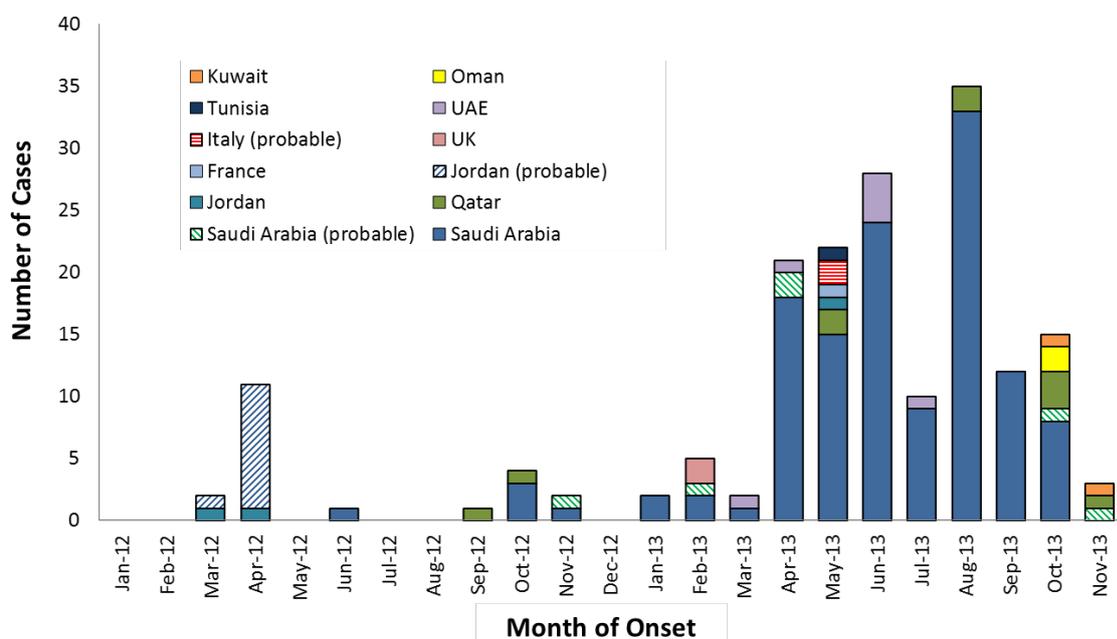
- Aburizaiza AS, Mattes FM, Azhar EI, Hassan AM, Memish ZA, Muth D, Meyer B, Lattwein E, Müller M, Drosten C. Investigation of anti-MERS-Coronavirus antibodies in blood donors and abattoir workers in Jeddah and Makkah, Kingdom of Saudi Arabia, Fall 2012. Journal of Infectious Diseases, Advance Access published November 11, 2013. Available at: <http://jid.oxfordjournals.org/content/early/2013/11/10/infdis.jit589.short>

Aburizaiza and colleagues conducted a serologic survey of 130 blood donors from Jeddah sampled during 2012 and 226 abattoir workers from Jeddah and Makkah sampled in

October 2012 during the Hajj pilgrimage. The authors found that none of the subjects were positive for MERS-CoV antibodies using immunofluorescence assay (IFA), differential recombinant IFA, and plaque reduction serum neutralization assay.

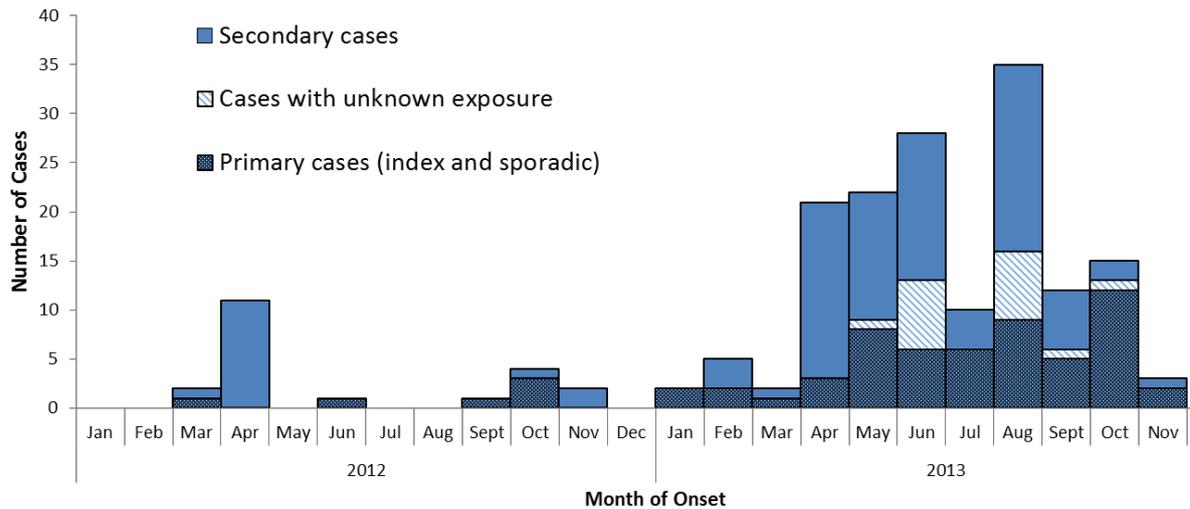
## Summary

MERS-CoV laboratory-confirmed cases continue to be reported from countries in the Middle East, mainly from Saudi Arabia and have been reported in two new countries —Oman and Kuwait—in recent weeks (Figure 2). This appearance of the virus in new countries and the steady increase in sporadic cases (Figure 3) continues to raise concerns about possible expansion of virus in the as yet unknown reservoir. It is clear that human-to-human transmission is occurring. However, the continuing of reports of sporadic cases from Middle Eastern countries suggests that cases continue to be infected from non-human source(s) as well. Although the two probable cases reported by Spain both performed the Hajj during their stay in Saudi Arabia, no other pilgrimage related cases have been detected in the period following the Hajj. The complete investigation of other potential exposures that the two had during their trip, and confirmation of their infections is still pending.



**Figure 2 Month of onset of 176 confirmed and probable MERS-CoV cases by country of most likely exposure**

*Note: \*After week 24 in 2013, 58 cases were not reported with date for symptom onset. For these 58 cases, the symptom onset date was estimated (date of reporting to WHO minus median of difference between onset date and reporting date of those cases that had both of these dates available; the median difference was calculated by country). Cases are reported by the location where infection is believed to have occurred.*



**Figure 3 Month of onset of 176 confirmed and probable MERS-CoV cases by case type**

MERS-CoV surveillance is focused on severe disease in much of the Middle East and it is likely that many milder cases are undetected. In addition, WHO has reports of a number of examples of laboratory confirmed MERS-CoV cases who initially tested negative from upper respiratory samples, while lower respiratory samples tested positive for MERS-CoV. The large number of transmissions that occur in hospitals raises concerns about transmission occurring in this setting when infection with MERS-CoV is not recognized either because cases are not tested or the tests are falsely negative. There are several specific measures that could help prevent nosocomial transmission. These include the following:

- Ensure that the quality of specimen is high. Obtain lower respiratory specimens when possible and oropharyngeal in addition to nasopharyngeal when not possible. Oropharyngeal and nasopharyngeal specimens can be tested together to reduce costs and demand on laboratory resources.
- Consider repeat testing when clinical suspicion of MERS-CoV infection is high if initial test is negative.
- Continue strict adherence to appropriate infection control procedures, even if a test is negative, when the clinical presentation and epidemiological picture is consistent with MERS-CoV.
- Consider sending negative specimens to a reference laboratory for further testing, in suspect cases. WHO can facilitate collaboration with a reference laboratory, if requested.
- Countries in the affected area should strongly consider expanding testing to include community-acquired pneumonias that are admitted to hospital, even if they do not require mechanical ventilation or intensive care, especially if no alternate diagnosis explains the illness. Testing for MERS-CoV should be considered for incorporation into routine diagnostic algorithms for community-acquired pneumonias and not limited to severe cases in ICU ([http://www.who.int/csr/disease/coronavirus\\_infections/en/index.html](http://www.who.int/csr/disease/coronavirus_infections/en/index.html)).

The finding of MERS-CoV virus in a camel in Saudi Arabia is consistent with previously published reports of MERS-CoV reactive antibodies in camels, and adds another important piece of information to our understanding of MERS-CoV ecology. However, this finding does not necessarily implicate camels directly in the chain of transmission to humans. The critical remaining question about this virus is the route by which humans are infected. A large portion of the human cases that did not have an apparent human source of their infection, also did not have direct camel exposure. Specifically, the remaining questions include 1) the specific behaviors and exposures that bring humans into contact with sources of the virus, 2) whether camels are a part of the chain of transmission to humans or whether they are coincidentally infected, and 3) whether other animals may also play a role in transmission or act as a reservoir.

Until more information is gathered, it is prudent for individuals at high risk of severe disease, including those with diabetes, chronic lung disease, pre-existing renal failure or who are immunocompromised, take appropriate precautions when visiting farm environments in the affected area. These might include good hand hygiene, avoiding sick animals, and avoiding food that may be contaminated with animal secretions or products unless they are properly washed, peeled, or cooked.

Countries outside of the affected region should maintain a high level of vigilance, especially those with large numbers of travellers or guest workers returning from the Middle East. Surveillance should continue to be enhanced in these countries according to WHO guidelines along with infection control procedures in health care facilities. 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, case-control studies for index cases and intensive follow-up of contacts with serological testing to improve knowledge of the critical features of MERS-CoV infection.

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](#)