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

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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)

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<tr>
<th>Country</th>
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Middle East respiratory syndrome coronavirus (MERS-CoV): Summary of Current Situation, Literature Update and Risk Assessment, 7 July 2015

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

**CONFIRMED CASES OF MIDDLE EAST RESPIRATORY SYNDROME - CORONAVIRUS 2012 - 2015**

- Saudi Arabia
- Republic of Korea
- All other countries reporting cases to date: Egypt, Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, United Arab Emirates, Yemen, Algeria, Tunisia, Austria, France, Germany, Greece, Italy, the Netherlands, Turkey, United Kingdom, Malaysia, Philippines, Thailand, and United States of America

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, Egypt, 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 Korea and 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-6june2015/en/index.html.


- 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:
  - Investigation of cases of human infection with Middle East respiratory syndrome coronavirus (MERS-CoV) (http://www.who.int/csr/disease/coronavirus_infections/mers-investigation-cases/en/)
  - Laboratory testing for Middle East Respiratory Syndrome Coronavirus (http://www.who.int/csr/disease/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 (http://www.who.int/csr/disease/coronavirus_infections/ipc-mers-cov/en/)
  - Clinical management of severe acute respiratory infections when novel coronavirus is suspected (http://www.who.int/csr/disease/coronavirus_infections/case-management-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 MERS- and 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, 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). 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 Korea or 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 camel-related 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 (http://www.who.int/mediacentre/mers-hmsg/en/), 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 transmission in the community or evidence of airborne transmission.

Therefore, the overall transmission patterns previously observed remain unchanged. WHO bases this assessment on the evidence that:

1. The clinical picture seen in recent outbreaks appears similar to that observed throughout previous outbreaks; secondary cases in the absence of comorbidities tend to present with milder disease than primary cases, and many of the recently reported secondary cases have been mild, or were people who tested positive for MERS-CoV but were reported to be asymptomatic;
2. The cases recently exported to countries outside the Middle East have not resulted in sustained onward transmission to persons in close contact with these cases in the community; this is true for all affected countries, including the Republic of Korea and China;
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 occupational settings and health care settings; and enhancing community studies and surveillance for community-acquired pneumonia. Collaboration between human and animal health sectors in affected countries is essential to understand the risk of transmission of MERS-CoV between animals and humans, whether there is any seasonal variation in the circulation of the virus in animals, and the natural reservoir(s) of MERS-CoV.

In addition, a better understanding of transmission in health care settings, especially the exposures that result in human-to-human transmission and the potential role of asymptomatic PCR-positive health care workers, is urgently needed.

Enhancing infection prevention and control awareness and implementation measures is critical to prevent the possible spread of MERS-CoV in health care facilities. It is not always possible to identify patients with MERS early
because some have mild or non-specific symptoms. For this reason, it is important that all health care facilities establish and implement clear triage policies for rapid screening and assessment of potential MERS cases and all cases with acute respiratory symptoms. It is also important that workers apply standard precautions consistently with all patients, regardless of their diagnosis, in all work practices all the time. Droplet precautions should be added to the standard precautions when providing care to any patient with symptoms of acute respiratory infection.

Health care facilities that provide care for patients suspected or confirmed to be infected with MERS should take appropriate measures to decrease the risk of transmission of the virus from an infected patient to other patients, health care workers and visitors. These measures involve interventions at the patient-carer interface and other general measures such as linen management, cleaning and disinfection and waste management. Contact precautions and eye protection should be added when caring for probable or confirmed cases of MERS, and airborne precautions should be applied when performing aerosol-generating procedures.

Until more is understood about MERS, people at high risk of developing severe disease (those with diabetes, renal failure, chronic lung disease, and immunocompromised persons), should take precautions when visiting farms and markets where dromedary camels are present (especially in the Middle East and Africa). These precautions include: avoiding contact with camels; not drinking raw camel milk or camel urine; and not eating meat that has not been thoroughly cooked.

Preliminary results from recent studies in Qatar, Saudi Arabia and UAE indicate that people handling or working with dromedary camels in these countries are at increased risk of infection compared with people who do not have contact with camels. Until more evidence is gathered, it is prudent for camel farm workers, slaughterhouse workers, market workers, veterinarians and those handling dromedary camels to practice good personal hygiene, including frequent hand hygiene. Hands should be washed with soap and water or alcohol gel after every contact with animals. Workers should wear facial protection where feasible and protective clothing that should be removed after work (followed by hand hygiene) and washed daily.

Workers should also avoid exposing family members to soiled work clothing, shoes, or other items that may have come into contact with camel secretions and excretions. It is recommended that these clothes and items remain at the workplace for daily washing and that workers have access to and use shower facilities at their workplaces before leaving the premises.

Camels infected with MERS-CoV may not show any signs of infection. It is therefore not possible to know whether an animal on a farm, in a market, race track or slaughterhouse is excreting MERS-CoV that can potentially infect humans. However, infected animals may shed MERS-CoV through nasal and eye discharge, faeces, and potentially in their milk and urine. The virus may also be found in the raw organs and meat of an infected animal. Therefore, until more is known about infection in animals, the best protection is to practice good hygiene and avoid direct contact with all of these. Obviously sick animals should never be slaughtered for consumption; dead animals should be safely buried or destroyed.

Unless protected, people should avoid contact with any animal that has been confirmed positive for MERS-CoV until subsequent tests have confirmed that the animal is free of the virus.

Countries outside the affected region should maintain a high level of vigilance, especially those with large numbers of travellers or migrant workers returning from the Middle East. Surveillance should continue to be enhanced in these countries according to WHO guidelines, along with infection prevention and 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 does not advise special screening at points of entry nor does it currently recommend the application of any travel or trade restrictions.

WHO guidelines and tools on epidemiologic investigations can be found at http://www.who.int/csr/disease/coronavirus_infections/technical-guidance-surveillance/en/.

Selected literature

- Korean researchers from Gyeonggi summarize the results of a detailed epidemiologic investigation of 37 MERS cases associated with a single hospital in Pyeongtaek, Gyeonggi Province. The researchers found that the median incubation period was 6 days (95% CI 4-7 days) and that the delay from symptom onset to laboratory confirmation was 6.5 days (95% CI 4-9 days). A line list of the cases was compiled from case investigation forms used during the investigation. Park HY, et al. Epidemiological investigation of MERS-CoV spread in a single hospital in South Korea, May to June 2015. Eurosurveillance. 2015;20(25):pii=21169. Available at http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21169.
- A preliminary assessment of the epidemiologic patterns of the MERS-CoV outbreak in the Republic of Korea was conducted by researchers from China, Hong Kong SAR, using publicly available data provided online by the Korean Ministry of Health and Welfare. The researchers illustrates transmission patterns, estimated the incubation period to be 6.7 days, the serial interval as 12.6 days and the case fatality ratio to be 21%. Cowling BJ, et al. Preliminary epidemiological assessment of MERS-CoV outbreak in South Korea, May to June 2015. Eurosurveillance. 2015;20(25):pii=21163. Available at http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21163.
- Two complete MERS-CoV genomes, one from China and one from the Republic of Korea have been published in GenBank: http://www.ncbi.nlm.nih.gov/news/06-10-2015-MERS-genomes-genbank/.
- A detailed clinical, laboratory and epidemiological description of the MERS case imported from the Republic of Korea to China has been published by researchers in China. Laboratory findings, including the
results of serial sampling from the patient are provided. The researchers identified 78 close contacts, all of whom tested negative for MERS-CoV.


- Researchers from China, Hong Kong SAR and Mongolia conducted a MERS-CoV serosurvey in Bactrian camel herds in southern Mongolia in November 2014. They sampled 200 animals from 11 herds in Umnugovi Province and Dundgovi Province and found no evidence of MERS-CoV using serologic assays and PCR testing.
  

- Researchers from the University of Bonn and Saudi Arabia conducted a cross-sectional serosurvey looking for the presence of MERS-CoV antibodies in more than 10,000 human serum samples obtained from healthy persons between 2012 and 2013. Antibodies to MERS-CoV were found in 15 (0.15%) of the samples. The seroprevalence was significantly higher in camel-exposed individuals than in the general population. The researchers suggest that if the results were extrapolated to the general population, the number of seropositive individuals in Saudi Arabia would exceed 45,000.
  

- An outbreak of MERS-CoV in Jeddah, Saudi Arabia, around April 2014, raised international concern and prompted speculation about the nature of the outbreak. A study conducted to investigate the possible sources of exposure found that the vast majority of symptomatic cases had contact with a health care facility, other patients, or both. Most of the reportedly asymptomatic cases included in this study had at least one symptom consistent with a viral respiratory illness.


- A case is reported of prolonged nasal virus RNA detection (more than 5 weeks) from one asymptomatic RT-PCR positive health care worker.
  

- Researchers from Saudi Arabia and the USA evaluated MERS-CoV in adult and juvenile dromedary camels in Al-Hasa Province between April 2013 and May 2014. The researchers found that samples from younger camels were more often PCR positive than adult camels (<4 vs ≥4 years old). PCR positivity in camels varied, with the highest proportion of positive samples between November 2013 and January 2014.
  