UPDATED RAPID RISK ASSESSMENT

Severe respiratory disease associated with Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
6th update
19 July 2013

Main developments in this update

- The number of new cases per month in Saudi Arabia increased ten-fold since April 2013 and more asymptomatic and mild secondary cases have been detected through contact tracing.
- Ten asymptomatic cases have been reported since 8 June, eight by Saudi Arabia and two by the United Arab Emirates (UAE). Six of these asymptomatic cases have been health care workers. All the new cases reported since the previous update have been reported by Saudi Arabia and UAE.
- The skewed age and sex distribution with a higher incidence in older men has become less accentuated since the last update as more mild and asymptomatic cases are detected through contact tracing.
- The Ministry of Health Saudi Arabia updated its Health Regulations for travellers to Saudi Arabia for Umrah and Hajj pilgrimage regarding MERS-CoV: '...recommends that elderly (above 65 years of age) and those with chronic diseases (e.g. heart disease, kidney disease, respiratory disease, diabetes) and pilgrims with immune deficiency (congenital and acquired), malignancy and terminal illnesses, pregnant women and children (under 12) coming for Hajj and Umrah this year, to postpone the performance of the Hajj and Umrah for their own safety.' [1].
- WHO published Revised interim case definition for reporting to WHO – Middle East respiratory syndrome coronavirus (MERS-CoV) on 3 July 2013.
- An Emergency Committee concerning Middle East Respiratory Syndrome Coronavirus (MERS-CoV) was set up by WHO in accordance with the International Health Regulations. The Committee held its second meeting on 17 July. It concluded that '...the conditions for a Public Health Emergency of International Concern have not at present been met.'
- Modelling results of MERS-CoV transmission have been published in *The Lancet*. They indicate that the virus currently has a low potential pandemic spread [2].

Epidemiological summary

- As of 18 July 2013, 88 confirmed cases of MERS-CoV had been reported worldwide of which 45 have been fatal. The age ranges from 2 to 94 years with a median of age 51 years. As of 18 June, 62% of the cases with known sex (51 of 82) have been male. To date, all cases have either occurred in the Middle East or have had direct links to a primary case infected in the Middle East. Saudi Arabia has reported 68 cases including 38 deaths, Jordan two cases, who both died, and United Arab Emirates five cases. Thirteen cases have been reported from outside of the Middle East in the UK (4), Italy (3), France (2), Germany (2) and Tunisia (2). These 13 cases resulted from seven separate chains of transmission. The primary case for each chain had been infected in the Middle East and local secondary transmission was reported from four countries: UK, France, Italy and Tunisia. The primary case in the cluster in Tunisia was never confirmed and remains a probable case.

Conclusions

- The risk of importation of MERS-CoV to the EU is unchanged and sporadic importation of cases is expected to continue. The precise risk of importation is difficult to estimate as long as the reservoir of the virus is unknown and behavioural risk factors that are critical for transmission in the Middle East have not been established. It is possible that the risk of importation may increase as a result of more transmission in the Middle East and the influx of visitors from the EU to Saudi Arabia during Ramadan, which started on 9 July, and during the Hajj pilgrimage in October.
- The risk of secondary transmission in the EU remains low and could be reduced further through screening for exposure among patients presenting with respiratory symptoms and their contacts, and strict implementation of infection prevention and control measures for patients under investigation.
- Person-to-person transmission has occurred in many clusters, both among household contacts and within health care facilities. However, with the exception of the health facility associated cluster in Al-Ahsa, the number of confirmed secondary cases per cluster has remained low and there is no convincing evidence of the virus becoming more infective over time.
- MERS-CoV has been transmitted in healthcare settings, both in Europe and in the Middle East. The Al-Ahsa outbreak with 23 confirmed cases in four facilities, the transmission in France between two people who shared a room and toilet, and the transmission in London from an intubated case to a visiting relative are the best documented occasions and indicate a significant risk for nosocomial transmission.
- The pandemic potential of MERS-CoV remains low. A modelling study published in *The Lancet* on 5 July 2013 estimated the basic reproduction number (R0) to be 0.69, lower than for pre-pandemic SARS-CoV (0.80) and well below the epidemic threshold.
- The Al-Ahsa cluster is a significant event, an 'outlier' that breaks the established pattern of transmission in the outbreak. This cluster could have been caused by lack of appropriate infection prevention measures in the health facilities but also raises concerns about the possibility of super-spreaders, a phenomenon that played an important role for the spread of the SARS-CoV pandemic.
- The virus reservoir remains unknown. The transmission pattern in Saudi Arabia, with many sporadic cases distributed over a large geographical area, points to infrequent introductions of the virus from a continuous non-human source, but unrecognised circulation among humans should not be ruled out. Finding the source of the virus transmission is key to formulating advice on how to reduce the risk of exposure.

Recommendations

Travel advice

ECDC endorses the WHO travel advice for MERS-CoV, which does not impose any travel or trade restrictions. In view of the on-going Umrah, the forthcoming Hajj in October and the large number of European Muslims who visit Saudi Arabia at all times of the year, Member States should consider disseminating specific advice through dedicated travel agencies and religious organisations.

Travellers to the Middle East should:

- Avoid contacts with animals and their waste products.
- Limit contacts with others and practise cough etiquette (maintain distance, cover coughs and sneezes with disposable tissues or clothing, and wash hands) if they develop respiratory illness.
- Avoid close contact with sick people, especially with those suffering from acute respiratory infections.
- Practise good hand hygiene, especially if respiratory symptoms develop and after direct contact with ill people or their environments.

Travellers from the EU who plan to visit Saudi Arabia for the Umrah and Hajj pilgrimage should consult the recommendations made by the Saudi Ministry of Health under Health Regulations for travellers to Saudi Arabia regarding MERS-CoV which '...recommends that elderly (above 65 years of age) and those with chronic diseases (e.g. heart disease, kidney disease, respiratory disease, diabetes) and pilgrims with immune deficiency (congenital and acquired), malignancy and terminal illnesses, pregnant women and children (under 12) coming for Hajj and Umrah this year, to postpone the performance of the Hajj and Umrah for their own safety'.

General travel health advice, including avoiding unsafe water, undercooked meats, and raw fruits and vegetables unless freshly peeled and washed, remain important for travel in the Middle East.

Case finding

Travellers to the Middle East who develop respiratory disease within 14 days after their return to Europe should seek medical attention and immediately communicate their travel history to the healthcare provider. They should practice cough etiquette, avoid contact with others and avoid public transport until assessed by a healthcare worker.

Clinicians should consider MERS-CoV infection in all patients, who have developed severe respiratory or other infectious disease symptoms and who have been to the Middle East in the preceding 14 days.

Patients presenting with acute respiratory infections in the EU should be screened for travel history to Saudi Arabia and the Middle East and for contact with MERS-CoV patients at first contact with the health system. Patients who have a history of possible exposure should, as far as possible, wait and be examined in a single room.

Clinicians should be familiar with the most recent WHO: surveillance guidance, case investigation guidelines and WHO case definitions for MERS-CoV which can all be found at the WHO Global Alert and Response page for coronavirus page.

Clinicians and laboratory personnel should be familiar with the most recent infection prevention and control recommendations for MERS-CoV, also found on the WHO coronavirus page.

There is growing evidence that viral loads are higher in lower respiratory tract specimens and low in nasopharyngeal samples. Consequently, routine microbiological sampling through nasopharyngeal swabs may give negative results in persons later shown to be infected with the coronavirus and tests should be repeated on deeper respiratory samples if a person meets the criteria for investigation, especially if their condition is worsening.

Patients who are evacuated from the Middle East deserve special attention. Receiving hospitals in the EU should screen patients for MERS-CoV infection and apply strict infection prevention and control measures, including administrative and environmental controls and personal protective equipment until MERS-CoV infection has been ruled-out. Companies undertaking medical evacuations from the Middle East should be reminded of their obligations to protect staff engaged in the transfer and the need to inform receiving hospitals of the risk of MERS-CoV infection.

Contact tracing

All close contacts of probable and confirmed MERS-CoV cases should be followed-up and monitored for symptoms for 14 days after last exposure. A close contact is defined as a healthcare worker or family member providing direct patient care or anyone who spent some time in the same place as the probable or confirmed case.

Close contacts should have a base-line serum sample collected and stored which can be used for comparison of paired sera, if later required. Airway specimen should be tested with PCR if a contact develops symptoms. When collecting specimens, it should be considered that lower respiratory specimens generally have higher viral load than upper respiratory specimens. [Guidance PHE, UK].

Aircraft contact tracing

Countries should trace contacts of confirmed MERS-CoV cases on aircrafts according to the guidelines for SARS contact tracing in RAGIDA. There should be no limit to the flight time.

Priority for contact tracing efforts should be given to:

- passengers seated in the same row as the index case;
- passengers seated three rows in front or behind the index case;
- all crew members;
- passengers providing care for the index case;
- passengers having had >15 minutes of face-to-face contact with the index case;
- passengers having had contact with respiratory secretions of the index case; and
- passengers living in the same household with the index case.

Depending on the clinical presentation of the case during the flight and feasibility, Member State officials may consider extending the tracing of contacts beyond three rows, possibly including all passengers and crew members. Lacking firm evidence of on-board MERS-CoV transmission, efforts should be made for extensive contact tracing in order to inform future public health decisions. If a crew member is the index case and if all passengers cannot be contacted, contact tracing efforts should at least concentrate on all passengers seating in the area the crew member was working during the flight as well as the other members of the crew.

During the flight, if a passenger is suspected of having MERS-CoV – as with any other respiratory infection – the potentially infectious passenger should, if possible, be isolated and provided with a surgical face mask. The flight attendant should follow the IATA guidelines for infection control. Captains should radio ahead to the destination airport informing it of a suspected MERS-CoV case on board according to article 28 in the International Health Regulation 2005 [3]. Contact passengers should provide identification- and contact details (locator cards) to the health authorities within 14 days after the flight (in order to facilitate contact tracing, if needed.

Infection control

In accordance with international WHO guidance, the prevention and control of transmission in healthcare settings requires the implementation of control measures, organised hierarchically according to their effectiveness in administrative measures, engineering/environmental measures and the use of personal protective equipment (PPE).

Possible and confirmed cases requiring admission should be admitted directly to negative-pressure single rooms, if available. If this is not possible then a single room with en-suite facilities should be used.

Healthcare workers caring for patients under investigation for MERS-CoV or confirmed cases should exercise standard precautions (including hand hygiene) as well as contact and airborne precautions. This entails the use of personal protective equipment (PPE) consisting of a well-fitted single use FFP2 or FFP3 respirator, gloves, eye protection and gown. It should be noted that the EU recommendation about the standard of mask to be used when caring for patients under investigation (FFP2 or FFP3) differs from the WHO recommendation (medical/surgical mask). Further information on infection control can be obtained from national and international WHO guidance.

Medical procedures, particularly aerosol-generating procedures and all airway management, such a tracheal intubation, broncho-alveolar lavage, other diagnostic airway procedures and manual ventilation, require particular protection measures. The number of persons in the room should be limited to a minimum during such procedures and all present should wear:

- A well-fitted FFP3 respirator;
- Tight-fitting eye protection;
- Gloves and long-sleeved impermeable protective gowns.

All specimens collected for laboratory investigation should be regarded as potentially infectious, and healthcare workers who transport clinical specimens should adhere rigorously to Standard Precautions to minimize the possibility of exposure to pathogens. Additional references are available from WHO and the European Committee for Standardisation.

Reporting

All cases diagnosed in the EU/EEA should be reported by the national authorities to the Early Warning and Response System (EWRS) and to WHO under the International Health Regulations (IHR) (2005). Reporting in EWRS qualifies as IHR notification and avoids double reporting. Patients still under investigation do not need to be reported internationally while awaiting confirmation, but information on outcome of such testing exercises should be shared with ECDC.

Source and date of request

ECDC Internal Decision, 8 July 2013.

Public health issue

This 6th update of the rapid risk assessment of the MERS-CoV outbreak reviews information that has become available since the 17 June update and its implications for EU/EEA countries.

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Event background information

The first confirmed case was reported in a 60-year-old male who died from severe pneumonia and renal failure in Jeddah, Saudi Arabia on 24 June 2012. The genome of the novel coronavirus isolated from this case was sequenced and the genetic code placed in the public domain [4] . In September 2012, a 49-year-old male living in Qatar presented with symptoms similar to the first case. He was transferred to Europe for further care [5]. A virus was isolated from this case, sequenced and the genetic code put in the public domain by the UK authorities. It was found to be almost identical to the virus from the case in Saudi Arabia. The emergence of a novel coronavirus causing severe respiratory disease in two separate parts of the Middle East led to notifications through the International Health Regulations (IHR) and the EU Early Warning and Response System on 22 September 2012.

In November 2012, four additional cases with similar symptomatology were diagnosed in Saudi Arabia, including a family cluster of three confirmed cases, one probable case [6] and a second imported case to Europe (from Qatar to Germany) reported on 23 November.

In November 2012, two fatal cases from Jordan were confirmed retrospectively. Both cases came from a cluster of 13 cases of respiratory disease in April 2012 linked to a hospital in Zarqha City near Amman. The 11 non-fatal cases had symptoms of varying severity, from mild disease to severe pneumonia [7] but their diagnosis could not be laboratory confirmed. Serum samples from altogether 124 contacts of the two confirmed cases have later been tested with newly developed, not yet validated, serological tests for MERS-CoV and these preliminary results indicate that an additional eight contacts have serologic evidence of infection[8]. One of the contacts with positive serology reporting not having any symptoms.

Three additional cases were diagnosed in February 2013 in the UK in a family cluster associated with an index case who had a travel history to Saudi Arabia and Pakistan. These cases included the first two transmissions in Europe [9]. These cases resulted in four cases identified and reported by the UK to date.

At the end of March, a second imported case to Germany was reported: a person seeking medical care arriving from the UAE. The patient, a 73-year-old male with underlying clinical conditions, had been hospitalised in United Arab Emirates and was transferred for clinical care to a hospital in Germany where the diagnosis of MERS-CoV infection was confirmed. Despite intensive-care treatment, the patient died on 26 March [10].

In the beginning of May, twenty-two cases including ten deaths were reported by Saudi Arabia. All cases belonged to a cluster in Al-Ahsa in the Eastern Province of Saudi Arabia, which were linked to transmission in four healthcare facilities [11].

The first case reported by France on 7 May 2013 was in a French resident with a history of travel to Dubai, UAE in the two weeks prior to onset of illness in France (9–17 April). The 65-year-old man had a history of renal impairment and had sought medical care in France for fever, diarrhoea and lumbar pain on 23 April. Though he did not initially present with respiratory symptoms, pneumonia was subsequently diagnosed and laboratory tests were undertaken for novel coronavirus infection, as recommended by national and ECDC guidance. A naso-pharyngeal specimen was negative for MERS-CoV on 3 May. A bronchoalveolar lavage (BAL) specimen taken on 26 April arrived at the Reference Laboratory on 7 May and tested positive for MERS-CoV. He died on 28 May [7].

On 12 May, France informed ECDC of an additional laboratory-confirmed case. The case is an immunosuppressed male in his fifties who, from 27 to 29 April 2013, shared a hospital room with the first laboratory-confirmed patient in France. This secondary case was identified as part of the epidemiological investigation initiated by the French authorities, following laboratory confirmation of the first case on 7 May 2013. The patient is currently hospitalised. An epidemiological investigation and contact identification was performed. No other cases of MERS-CoV infection were identified among the index case's 123 contacts, or among 39 contacts of the secondary case, during the 10-day follow-up period [12].

Epidemiological summary

As of 18 July 2013, 88 confirmed cases of MERS-CoV infections have been reported worldwide of which 45 have been fatal. The age ranges from 2 to 94 years.

The following developments are noteworthy:

- The median age has decreased from 56 years in June to 51 years in July.
- The case sex ratio has become less skewed; as of 18 July, 62% of the cases have been male. The proportion of males in the 25–64 years age groups is around 57% in Saudi Arabia [13].
- The cumulative case–fatality rate (CFR) decreased from 59% in June to 51% in July.

The proportion of asymptomatic to symptomatic confirmed cases is increasing. Eight asymptomatic cases were reported in June compared to none in April or May despite similar number of confirmed cases in the three months, and two asymptomatic cases have been reported in July.

All the cases have either occurred in the Middle East or have had direct links to a primary case infected in the Middle East. Saudi Arabia has reported 68 cases including 38 deaths, Jordan two cases including two deaths, and UAE five cases. Thirteen cases have been reported from outside of the Middle East in: UK (4), Italy (3), France (2), Germany (2) and Tunisia (2). These 13 cases resulted from seven separate chains of transmission. The primary case for each chain was infected in the Middle East and local secondary transmission following importation was reported from four countries: UK, France, Italy and Tunisia. The primary case for the cluster in Tunisia remains a probable case and does not appear in the list of confirmed cases. Ten asymptomatic cases have been reported among contacts of which six have been healthcare workers.

Eleven cases were initially identified and diagnosed in four European countries: three came to Europe as a result of medical transfers, three developed illness after returning from the Middle East, and five secondary cases were the result of limited non-sustained person-to-person transmission in Europe, two of these due to a nosocomial transmission (Figure 2).

Since April 2013, a ten-fold increase of new cases per month was observed in Saudi Arabia compared to previous months.

As in any emerging disease outbreak, including MERS-CoV, raised awareness, increased clinical suspicion, improved diagnostic capacity, and more effective contact tracing will often result in more cases being detected even when the true transmission rate remains stable. Higher case detection rate often leads to a larger proportion of the cases being reported as mild or asymptomatic as result of cases that would otherwise not present for healthcare being detected. It is not clear to what extent the increase observed in recent months reflects a true increase in transmission or is the result of improved case finding, or a combination of both.

Recent developments, including a decreasing CFR, a more balanced sex ratio, a less skewed age distribution and the recognition of more mild and asymptomatic cases are all supporting a contribution of improved case-finding in the increase of cases noted lately.

Figure 1. Distribution of confirmed cases of MERS-CoV reported worldwide, by month of disease onset and probable place of infection, March 2012 – 19 July 2013

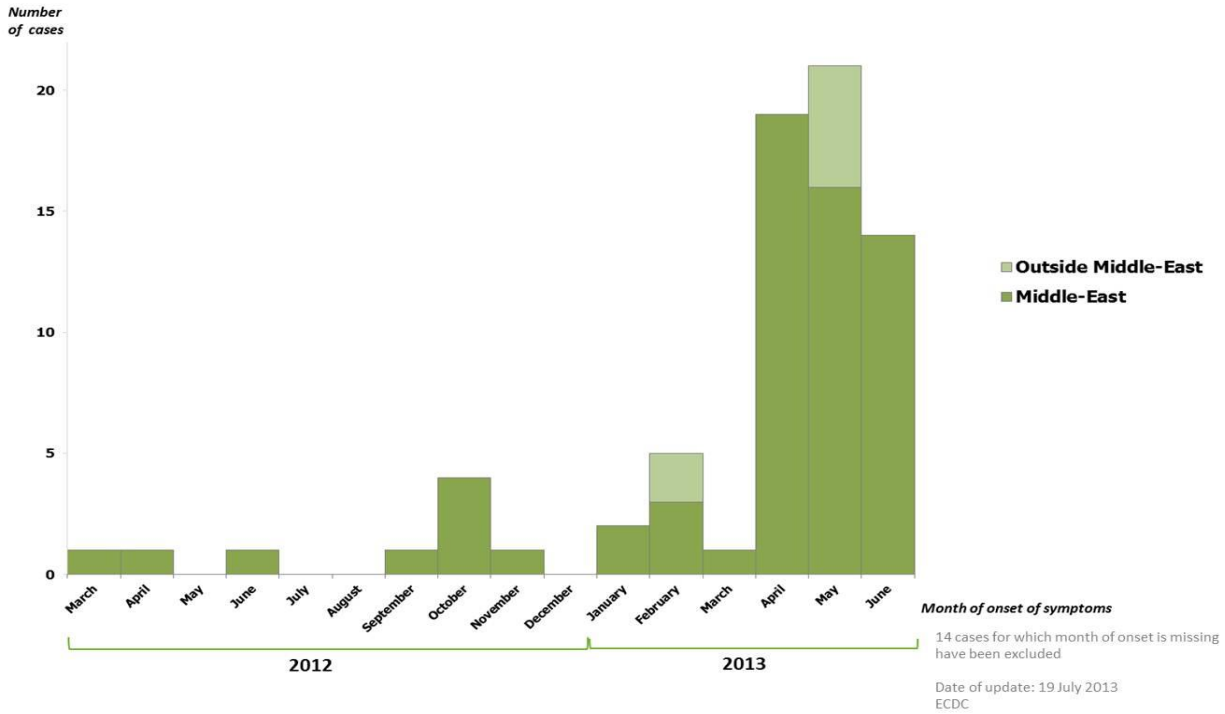
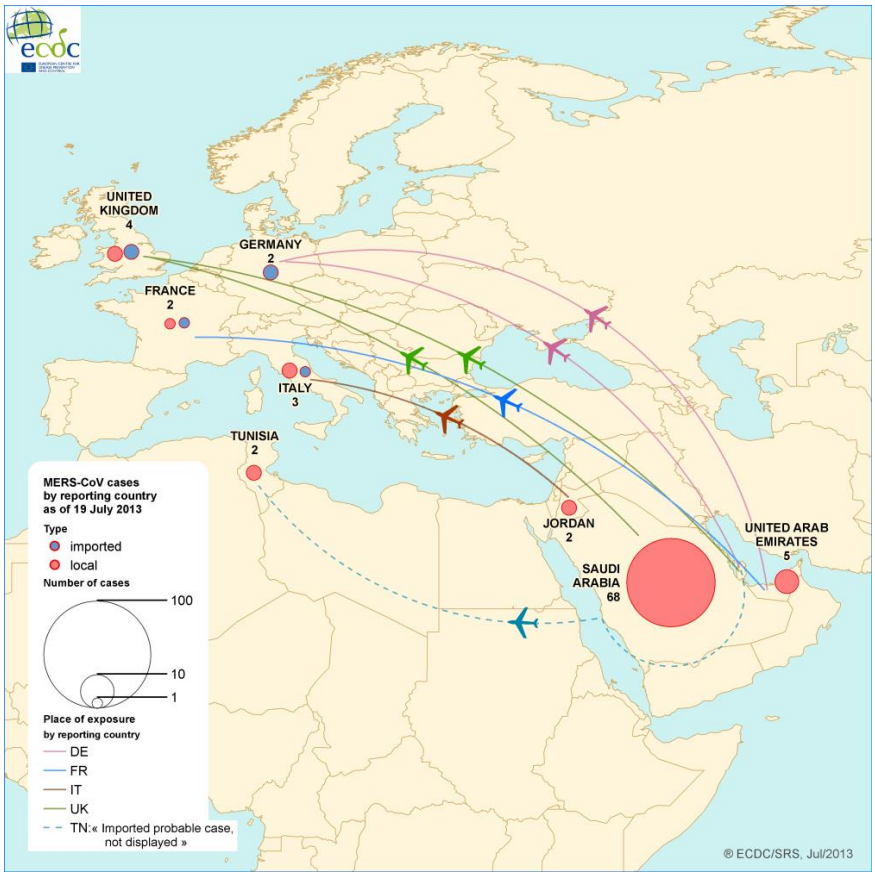


Figure 2. Distribution of confirmed cases of MERS-CoV by place of reporting and place of exposure, April 2012 – 19 July 2013



Virological information

MERS-CoV is distinct from the coronavirus which caused the SARS outbreaks in 2003, and distinct from the endemic human coronaviruses (HCoV) OC43, 229E, HKU1, and NL63. It belongs to lineage C within the *Betacoronavirus* genus (*Coronavirinae* subfamily) along with several viruses detected in bats in Europe and China [8].

No animal reservoir or mode of zoonotic transmission has yet been identified for MERS-CoV although the similarities to bat coronaviruses make bats a likely source, specifically insectivorous species such as *Pipistrellus*. However, experience with SARS indicates that the exposure need not be directly from bats, but may result from environmental contamination or via intermediary animal hosts [14].

Analysis of virus tropism indicates that these viruses can infect a variety of cell lines, including human cells via surface receptors distinct from SARS coronavirus receptors [15]. MERS-CoV seems to be fully able to penetrate human bronchial epithelia cultures. At the same time, like SARS-CoV, it appears to be sensitive to treatment with interferons (types I and III) [16]]. Cyclosporin A has been shown as an inhibitor of MERS-CoV replication in cell culture and MERS-CoV was found to be 50 to 100 times more sensitive to interferon-alpha (IFN-α) treatment than SARS-CoV [17]].

Interim laboratory testing guidance for screening and confirmation of MERS-CoV infection was issued by WHO in December 2012. More information about diagnostic procedures can be found in other articles [18-21] and on the University of Bonn website.

Viral loads are higher in lower respiratory tract specimens and low in nasopharyngeal samples [22]. Consequently, routine microbiological sampling through nasopharyngeal swabs may give negative results in persons later shown to be infected with the coronavirus and tests should be repeated on deeper respiratory samples if a person meets the criteria for investigation, especially if their condition is worsening.

Serological tools for the detection of specific MERS-CoV IgM and IgG antibodies based on protein microarray technology have been recently developed and validated with a limited number of specimens [23]. These assays, presently in the hands of some specialised laboratories, can be used to aid diagnosis in individual patients, for confirmatory testing of positive tests and for (large-scale) contact studies. These tests will need to be validated for use in the Middle East [24].

Following the identification and analysis of the viruses obtained from the first identified cases, the flow of viruses to specialised laboratories, especially from the Middle East cases, is partial, limiting the possibility to determine the full virological picture and making it difficult to assess whether the viruses are evolving.

In total, six strains are available in GenBank. The complete genome sequence of a MERS-CoV from a patient from Qatar with travel history to Saudi Arabia [25], one genome sequence from an imported case into Germany from the United Arab Emirates as well as four genome sequences from viruses from the hospital outbreak in Al-Ahsa. Together with earlier published data, this opens-up the possibility of comparative genomic studies of MERS-CoV.

Preliminary conclusions from this recent development are:

- The viral strain genome sequences reported to date do not indicate sequence variability that should interfere with molecular diagnostic assays for MERS-CoV screening and confirmation in clinical samples (C. Drosten, personal communication) [18,19].
- Further analysis of genomic information on a larger sample of strains will likely shed light on evolutionary rates of the virus and on the time of most recent common ancestor and allow testing alternative hypotheses on the transmission events underlying the emergence of MERS-CoV human infections.

Epidemiological surveillance

On 27 June, WHO published updated Interim surveillance recommendations for human infection with Middle East respiratory syndrome coronavirus. The new guideline makes stronger recommendations for collecting specimens from the lower respiratory tract, where the viral load is higher, rather than from naso-pharynx.

On 3 July 2013, WHO published 'Revised interim case definition for reporting to WHO – Middle East respiratory syndrome coronavirus (MERS-CoV)'. A confirmed case is a laboratory-confirmed case as defined in 'Laboratory testing for novel coronavirus: Interim recommendations'. The revised case definition identifies four categories of probable cases based on clinical presentation, exposure and level of testing.

The period of observation for contacts of cases has been extended to 14 days following an EU Health Security Committee meeting decision endorsed by a WHO technical consultation.

Protocols on the standardisation of influenza seroepidemiology have been published [25,26]. Drawing on these and in-country protocols, the UK has published a protocol for investigating cases of MERS-CoV infections which is suitable for use in other EU countries [27]. The CONSISE group has published specific coronavirus protocols [20]. Seroepidemiological studies of close contacts are being undertaken in France, similar to studies already performed in Germany [28].

Applied epidemiological and laboratory studies will be of assistance, and opportunistic and retrospective case-finding will be invaluable, focusing on severe cases for which there are suitable samples as defined by the WHO laboratory guidance of 12 December 2012. Particular emphasis should be on capturing the results of case finding operations, negative as well as positive and on testing convalescent sera. The ECDC-WHO laboratory survey could serve as an example, as it helped to inform about the true geographical extent of these infections [20,25].

Possible sources and routes of transmission

No reservoir or source of infection for MERS-CoV has been identified so far in Saudi Arabia or the Middle East. The transmission pattern in Saudi Arabia, with many sporadic cases distributed over a large geographical area, points to infrequent introductions of the virus from a continuous non-human source. Contact with animals, in particular camels, has been reported for several cases but this is anecdotal evidence which needs to be validated in case-control studies. Unrecognized circulation among humans with sporadic symptomatic cases, particularly in patients with underlying conditions or immunosuppression remains a possibility. Finding the source of the virus is key to formulating advice on how to reduce the risk of exposure.

There is clear evidence that person-to-person transmission occurs but whether the transmission is through respiratory droplets and fomites, as is the case with other coronaviruses including SARS-CoV, remains to be confirmed. The potential for airborne transmission of the virus is still unclear.

In Germany and the UK, a follow-up screening exercise of nearly 200 personal contacts and healthcare workers who were exposed to two imported confirmed cases found no evidence of human-to-human transmission.

There have been at least six instances in Europe where person-to-person transmission is certain to have taken place. Two of these transmissions were in a small family cluster of three cases in the UK. One transmission took place when the contact visited a hospitalised case on mechanical ventilation [9]. Person-to-person transmission also took place in France where a patient on immunosuppressive treatment shared a room and toilet with a patient who was later confirmed to have MERS-CoV infection, and to two secondary cases in Italy.

A healthcare-associated outbreak of MERS-CoV infection has been documented in the Al-Ahsa region of the Kingdom of Saudi Arabia [11]. During this outbreak that involved 4 healthcare facilities, 23 confirmed and 11

probable cases were reported. The majority of the cases were patients, but five family members and two healthcare workers were also affected. The hemodialysis unit was the most heavily affected with nine confirmed cases linked to it, but transmission also occurred in the intensive care unit and the medical ward. One of the patients in the hemodialysis unit transmitted the infection to seven persons, one patient transmitted the infection to three persons, and four patients transmitted the infection to two persons each.

The epidemiologic and phylogenetic analysis of the data in this study provides additional evidence for human-to-human transmission. However, it was not possible to determine whether transmission occurred through contact and respiratory droplets alone. Transmission also apparently occurred between rooms of the same ward. Although airborne transmission of MERS-CoV cannot be excluded based on the currently available data, there is no indication that it plays an important role in the transmission of the virus.

Based on information on the first 77 cases, the basic reproduction number of the infection (R0) has been estimated to be 0.69 (95% CI 0.50–0.92)[29], indicating a low pandemic potential[30]. For comparison, the R0 was estimated to be 0.80 (95% CI 0.54–1.13) for SARS-CoV, using the same methodology. However, the small number of confirmed cases, the detection of asymptomatic cases and potential evolution of the virus should be taken into account when interpreting these results [2].

ECDC threat assessment for the EU

Although it is not clear to what extent the increased number of cases reported since April 2013 reflects a true increase in transmission or is the result of improved case finding, or a combination of both, it is clear that transmission continues in Saudi Arabia. In any emerging disease outbreak, it is anticipated that raised awareness, increased clinical suspicion, improved diagnostic capacity, and more effective contact tracing will result in more cases being identified even if the actual transmission remains stable. Higher case detection rate should increase the proportion of mild and asymptomatic cases among new cases and this is currently observed in the MERS-CoV outbreak.

There is no evidence of a change in infectiousness of the MERS-CoV. The number of secondary cases remains low and modelling of transmission estimated the basic reproduction number to be well below 1. However, the fact that the virus transmits from person to person and in healthcare setting is of concern for the risk of transmission in the EU. The highest risk of transmission in the EU is likely to be from undiagnosed imported cases and efforts to rapidly identify cases in need of investigation are critical to the prevention of disease.

The risk of transmission to travellers to Saudi Arabia is difficult to estimate in the absence of more information about the source of infection, routes of transmission, and behavioural risk factors. However, the risk of importation of MERS-CoV cases to the EU is also determined by the number of EU visitors to Saudi Arabia and their length of stay. In 2007, Saudi Arabia received around 46 000 visitors from EU Member States. A more recent estimate is not available but the number of EU visitors to Saudi Arabia is assumed to remain similar today or to have increased.

Medical evacuations represent a particularly high risk for importation of cases to the EU. The number of transfers may increase as concerns arise among clinicians and the public in the Middle East that there is a risk of MERS-CoV infection associated within hospitals in the area.

The reason for the strong male predominance in the beginning of the outbreak remains unexplained. However, there are indications that the sex distribution is becoming more balanced over time as contact tracing improves and more mild and asymptomatic cases are being detected. It is important to note that there are more men than women in the Saudi population (M:F 1.21) and that this skewed sex distribution is most accentuated in 25–54 year age group (M:F 1.36). It is possible that gender based care-seeking and care-receiving behaviour in the Middle East plays a role [31].

Due to the large number of guest workers in the Middle East attention must also be drawn to the possible importation of MERS-CoV to South East Asia and Pacific Asia.

The number of visitors to Saudi Arabia is expected to increase significantly in the coming month, when Ramadan begins. This is one of the peak times for Umrah, the pilgrimage to Mecca in Saudi Arabia. Ramadan in 2013 started on Tuesday 9 July and will continue for 30 days until Wednesday 7 August. Another important event for pilgrimage is the Hajj which this year is between 13 and 18 October. Around 4 million pilgrims from 180 countries are reported to have performed Hajj in 2012. Of these over 50% arrive from outside Saudi Arabia and around 45 000 from the EU [32,33]. There is now a quota for the number of pilgrims from each country that can attend the Hajj. Each Muslim country can send 1 000 pilgrims per million Muslim populations. However, there is no current quota system for Umrah, with up to 6 million people reported to have performed Umrah in 2012 and numbers anticipated to increase 10–20% per year. Therefore specific advice should be drawn-up, including in regional languages, and circulated through travel and religious organisations where appropriate. The Ministry of Health in Saudi Arabia has issued health recommendations for travellers to Saudi Arabia for the pilgrimage to Mecca (Hajj and Umrah) [34].

Conclusions

The risk of importation of MERS-CoV to the EU is unchanged and the sporadic importation of cases is expected to continue. The precise risk of importation is difficult to estimate as long as the source of the virus is unknown and behavioural risk factors that are critical for transmission in the Middle East have not been established. It is possible that the risk of importation will increase as a result of increasing transmission in Saudi Arabia and increasing number of visitors from the EU to Saudi Arabia during Ramadan and the Hajj.

The risk of secondary transmission in the EU remains low and could be reduced further through screening for exposure among patients presenting with respiratory symptoms, and strict implementation of infection prevention and control measures for patients under investigation.

Person-to-person transmission has occurred in several clusters, both among household contacts and within healthcare facilities. However, with the exception of the health facility associated cluster in Al-Ahsa, the number of confirmed secondary cases per cluster has remained low and there is no convincing evidence of the virus becoming more infective over time.

MERS-CoV has been transmitted in healthcare settings, both in Europe and in the Middle East. The Al-Ahsa outbreak with 23 confirmed cases in four facilities, the transmission in France between two people who shared a room and toilet, and the transmission in London from an intubated case to a visiting relative are the best documented occasions and indicate a significant risk for nosocomial transmission.

The pandemic potential of MERS-CoV remains low. A modelling study published in Lancet on 5 July 2013 estimated the basic reproduction number (R0) to be 0.69, lower than for pre-pandemic SARS-CoV (0.80) and well below the epidemic threshold.

The Al-Ahsa cluster is a significant event, an 'outlier' that breaks the established pattern of transmission in the outbreak. This cluster could have been caused by lack of appropriate infection prevention measures in the health facilities but also raises concerns about the possibility of super-spreaders, a phenomenon that played an important role for the spread of the SARS-CoV pandemic.

The virus reservoir remains unknown. The transmission pattern in Saudi Arabia, with many sporadic cases distributed over a large geographical area, points to infrequent introductions of the virus from a continuous non-human source, but unrecognised circulation among humans should not be ruled out. Finding the source of the virus is key to formulating advice on how to reduce the risk of exposure.

References

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Sources of additional information and further resources

- WHO source page novel coronaviruses: click here
- Public Health England (previously Health Protection Agency – coronaviruses source page: click here
- Robert Koch Institute – coronaviruses source page (in German): click here
- University of Bonn – Diagnosis: click here
- ECDC Coronaviruses – source page: click here and here
- CONSISE website: click here; CONSISE protocols: click here
- Protocols for novel coronaviruses: click here
- ISARIC and WHO SARI and natural history protocols: click here
- Kingdom of Saudi Arabia – Ministry of Health: click here
- Novel coronaviruses: click here