UPDATED RAPID RISK ASSESSMENT

Severe respiratory disease associated with Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

18 June 2013

New in this update

- Updated epidemiological situation including cases in new EU country
- Guidance on aircraft contact tracing
- Incubation period extended to 14 days
- Guidance to travellers to the Middle East.

Summary and conclusions

- As of 17 June 2013, 64 cases of MERS-CoV had been reported worldwide, including 38 deaths. All cases remain associated (including indirect association following secondary person-to-person transmission in the UK, Italy, Tunisia and France) with transmission in the Middle East. The age of cases ranges from two years to 94 years (N=60 cases, information on age not available for four cases), with a median of 56 years. Overall 70% (43/61) of cases are males.
- The reports of new infections in Saudi Arabia over the past few weeks indicate that there is an ongoing source of infection and low risk of transmission to humans in the Middle East.
- The first French case raises the possibility that presentations may not initially include respiratory symptoms, especially in those with immunosuppression or underlying chronic conditions. This also needs to be taken into account when revising case detection strategies.
- The confirmed infection in France of a patient who shared a hospital room with an index patient returning from the United Arab Emirates corroborates the risk of nosocomial transmission. The incubation period for this patient is calculated to have been 9—12 days, which is longer than previously estimated. One case in the Jordan cluster has an incubation period of 13 days. Therefore until further evidence emerges, the incubation period is being extended from 10 to 14 days, in accordance with the WHO decision.
- These conclusions should be viewed in the light of the many uncertainties surrounding the investigation of cases in the Middle East. It is unusual to have such a degree of uncertainty at this stage in an outbreak.

Recommendations

Travel

ECDC supports the WHO travel advice which imposes no travel or trade restrictions in relation to MERS-CoV. However, EU citizens travelling to the Middle East need to be aware of the presence of MERS-CoV in this geographical area and the small risk of infection. Member States may consider increasing the amount of information available for travellers to areas most at risk. In view of forthcoming religious pilgrimages to the region, specific advice should be drawn up and circulated through travel and religious organisations where appropriate

- Although the source of the virus and the mechanism of transmission are unknown, it would be prudent to try to reduce the general risk of infection while travelling by:
  - Avoiding close contact with people suffering from acute respiratory infections.
  - Frequent hand-washing, especially after direct contact with people who are ill or their environment.
  - Adhering to food safety and hygiene rules, such as avoiding undercooked meats, raw fruits and vegetables unless they have been peeled, or unsafe water.
- Avoiding close contact with animals or their waste products. Travellers to the Middle East who develop symptoms either during travel or up to 14 days after their return are encouraged to seek medical attention and to share their history of travel. People with symptoms of acute respiratory infection should practice cough etiquette (maintain distance, cover coughs and sneezes with disposable tissues or clothing, and wash hands) and delay travelling until they are no longer symptomatic, to reduce any exposure to other passengers.

Import of cases

- Patients with chronic underlying conditions who develop symptoms of infection (not just respiratory infections) should also be investigated rapidly for MERS-CoV if they have been in the Middle East in the preceding 14 days.
- Healthcare workers in the EU should be vigilant in identifying patients that may require further investigation.
- Any patients developing severe respiratory infections who have been in the Middle East in the preceding 14 days should be investigated rapidly. Special attention should be given to medical evacuated patients from the Middle East.
- Companies undertaking medical evacuations from the Middle East should be reminded of the risk of transferring infections across borders and of their obligations to protect staff engaged in the transfer; the same applies to the staff of institutions receiving patients.

Contact tracing

- Close contacts of confirmed cases must be monitored for symptoms for 14 days after the last exposure. They should be tested with polymerase chain reaction (PCR) using appropriate sampling and by serology at baseline and 21 days post-baseline. They should be informed of what to do should they become ill [Guidance PHE, UK].
- Countries should trace contacts of confirmed MERS-CoV cases on aircraft, as a priority those passengers in the same row and the three rows in front and behind a symptomatic case. Considering the uncertainties in determining the transmission efficiency of the MERS-CoV, where feasible public health authorities may consider contact tracing all passengers on the aircraft, following the RAGIDA guidance on SARS. At this stage this recommendation applies to all flights, irrespective of the flight time.

Sampling/microbiology

- Increasing evidence suggests that nasopharyngeal (NP) swabs are not as sensitive as lower respiratory specimens for detecting MERS-CoV infections. NP swabs have been negative in patients who were close contacts of confirmed cases and who developed pneumonia following contact. In addition, a number of cases have now had negative tests on NP swabs but positive tests of lower respiratory track specimens.
- As demonstrated, cases with dual influenza and MERS-CoV infections or streptococcal pneumonia and MERS-CoV infections, there is a possibility of co-infection and this should be taken into consideration by healthcare personnel. Identification of one causative agent should not exclude testing for MERS-CoV if indicated.
- ECDC does not currently consider that there is a need to screen individual patients with unexplained pneumonias or other respiratory symptoms unless they fall into one of the above categories.

Infection control

- Healthcare workers caring for patients under investigation for MERS-CoV or confirmed cases should exercise standard precautions (including hand hygiene) and use personal protective equipment (PPE) including a well-

fitted, single-use filtering face-piece respirator, gloves, eye protection and gown. Further information on infection control can be obtained from national and international WHO guidance.
- Healthcare workers caring for confirmed cases should be monitored for early symptoms of infection and are advised to immediately self-isolate if they become unwell and thereafter seek testing.
- Clusters of severe acute respiratory infections in the community or in healthcare settings, either among patients or healthcare workers, should always be reported rapidly and investigated for pathogens, regardless of where in the world these infections occur.
- Medical procedures, particularly aerosol-generating procedures and all airway management, such as tracheal intubation, broncho-alveolar lavage, other diagnostic airway procedures and manual ventilation, require specific protection measures. The number of persons in the room should be limited to a minimum during such procedures and all those 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 collect or transport clinical specimens should adhere rigorously to standard precautions to minimise the possibility of exposure to pathogens. Additional references are from WHO and the European Committee for Standardisation.

Reporting

- Any probable or confirmed case being diagnosed in the EU/EEA should be reported to national authorities through the Early Warning and Response System (EWRS) and to WHO under the International Health Regulations (2005). Only probable cases which cannot be confirmed should be reported (as for the Tunisian index case). Reporting through 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 the outcome of such testing exercises should be shared with ECDC.

Source and date of request

ECDC internal decision, 7 June 2013.

Public health issue

This fifth update of the rapid risk assessment on severe respiratory disease associated with a novel coronavirus (MERS-CoV) was produced in relation to additional cases of laboratory-confirmed infections reported during the last month. The aim of this updated risk assessment is to review changes since the May update and assess the implications for ECDC's recommendations to EU/EEA countries.

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It should be noted that opinions expressed by individual experts do not necessarily represent the opinion of their institutions.

Background information

On 17 May 2013, the date of the last ECDC rapid risk assessment, 38 cases of MERS-CoV had been confirmed worldwide.

The first confirmed case was reported in a 60-year-old male who lived in Saudi Arabia. He died from severe pneumonia complicated by renal failure in Jeddah on 24 June 2012. The genome of the new coronavirus was

isolated from this case, sequenced and the genetic code put in the public domain [1]. 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 [2]. 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 (EWRS) 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 [3] and a second imported case to Europe (from Qatar to Germany) reported on 23 November.

Two fatal cases were confirmed retrospectively in Jordan. Both cases came from a cluster of 11 people with severe lower respiratory infections associated with a hospital in April 2012. Although the other nine persons also matched the WHO definition for probable novel coronavirus infections, the cases were less severe than the two confirmed cases. It has not yet been possible to undertake confirmatory virological or serological testing for these probable cases.

Three additional cases were diagnosed in February 2013 in the UK in a family cluster associated with an index case with a travel history to Saudi Arabia and Pakistan. These cases included the first two transmissions in Europe [4] and resulted in the 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 United Arab Emirates. 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 2013 [5].

At the beginning of May 2013, twenty-two cases, including 10 deaths, were reported by Saudi Arabia. All cases belonged to a cluster in Al-Ahsa in the Eastern Province of Saudi Arabia, which may be linked to a single healthcare facility [6].

The first case reported by France on 7 May 2013 was in a French resident with a history of travel to Dubai and the United Arab Emirates 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 2013. 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 2013 [7]. On 12 May, France informed ECDC of an additional laboratory-confirmed case. The case was 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 123 contacts of the index case, or among the 39 contacts of the secondary case, during the 10-day follow-up period [7].

Recent developments

Since 17 May 2013, 26 additional confirmed cases of MERS-CoV have been reported worldwide, totalling 64 cases including 38 fatalities.

On 21 May 2013, three cases were reported by the Ministry of Health in Tunisia. The probable index case, who died on 10 May 2013, was a 66-year-old man with underlying health conditions and a recent travel history to Qatar and Saudi Arabia. Infection with MERS-CoV was not confirmed and an autopsy was not done. The two laboratory-confirmed secondary cases, a 34-year-old man and a 35-year-old woman, are a sibling and a child of the index case. Both had mild respiratory illness and neither required hospitalisation.

On 1 June 2013, Italy reported an imported case, a 45-year-old man who had recently travelled to Jordan. This is the first time a patient was diagnosed with MERS-CoV in Italy. He returned to Italy on 25 May 2013 and was hospitalised on 28 May 2013. Italy reported two secondary cases on 2 June, a two-year-old niece and a 42-year-old female co-worker of the index case. All three patients are reported to be in a stable condition.

An additional 19 cases have been reported from Saudi Arabia since 17 May 2013.

On 15 June 2013, three additional cases were reported through WHO:

- a 45-year-old man with underlying medical conditions from Al-Taif Governorate who became ill at the end of May 2013 and was reported as deceased on 16 June 2013;

- a 68-year-old woman with underlying medical conditions from Al-Taif Governorate who became ill on 6 June 2013 and was reported as deceased on 16 June 2013;
- a 46-year-old man from Wadi Al-Dawaser who became ill on 29 May 2013, was admitted to hospital on 8 June 2013 and has died.

On 16 June 2013, the Ministry of Health of Saudi Arabia reported three additional cases:

- a 42-year-old Saudi citizen in the Eastern region suffering from chronic asthma who had been hospitalised;
- a 63-year-old Saudi female in Riyadh Region suffering from chronic disease, still in ICU;
- a two-year-old child in Jeddah suffering from chronic pulmonary disease, still in ICU.

Epidemiological summary

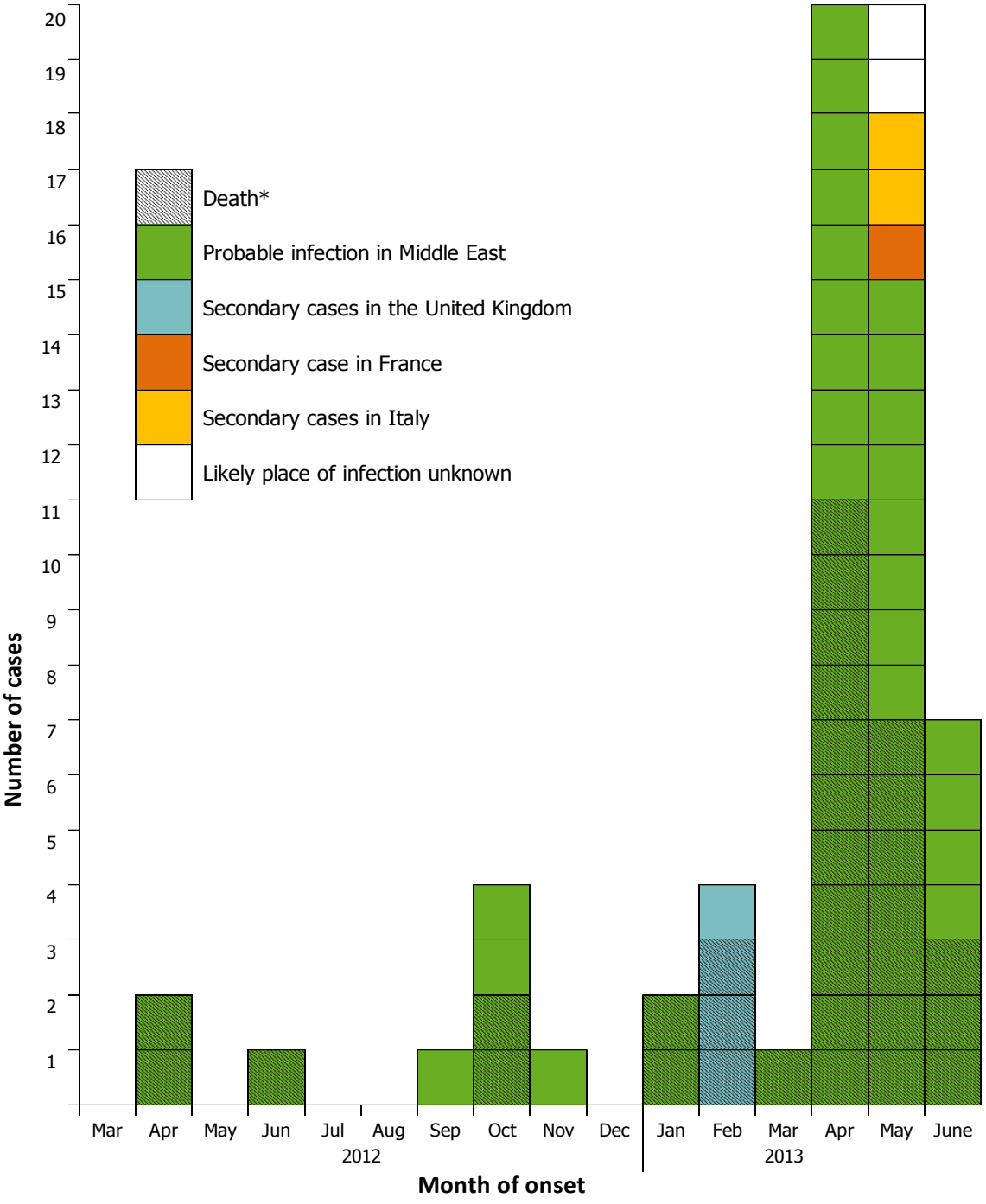
As of 17 June, 64 confirmed cases have been reported worldwide, including 38 deaths, yielding a case-fatality ratio of 59%.

An epicurve of reported cases by month of onset, clinical outcome and probable place of infection is shown in Figure 1.

All 64 confirmed cases worldwide remain associated (including indirect association following secondary person-to-person transmission in the UK, Italy and France) with transmission in the Middle East, the majority associated with Saudi Arabia.

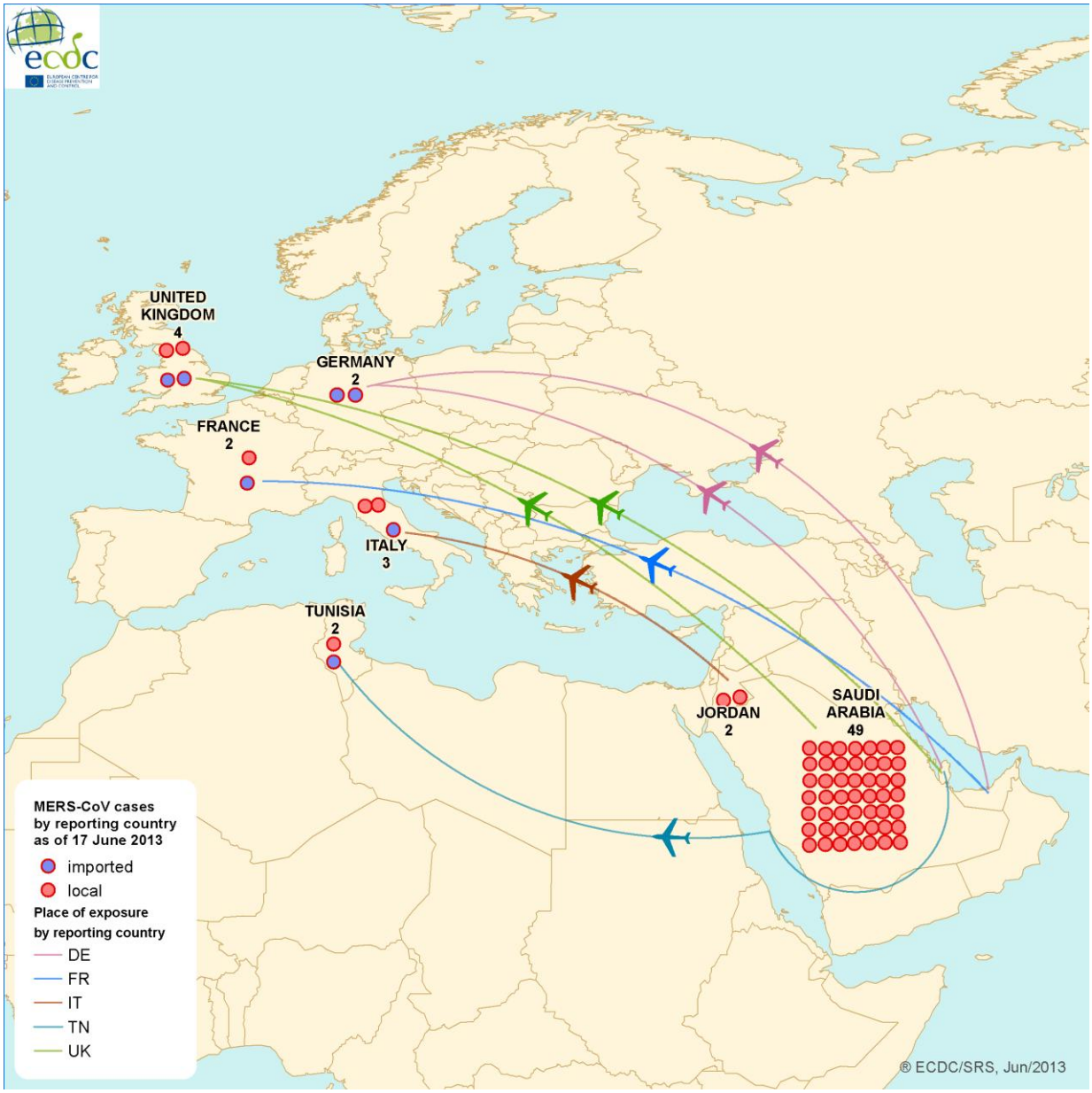
Eleven cases were initially identified and diagnosed in four European countries: three came to Europe as a result of medical transfers, three developed illness after returning from the Middle East, and five secondary cases were the result of limited, non-sustained person-to-person transmission in Europe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

Figure 1. Distribution of confirmed cases of MERS-CoV reported worldwide, by month of disease onset, outcome and place of infection, April 2012 – 17 June 2013 (N=63, one case with missing month of onset)



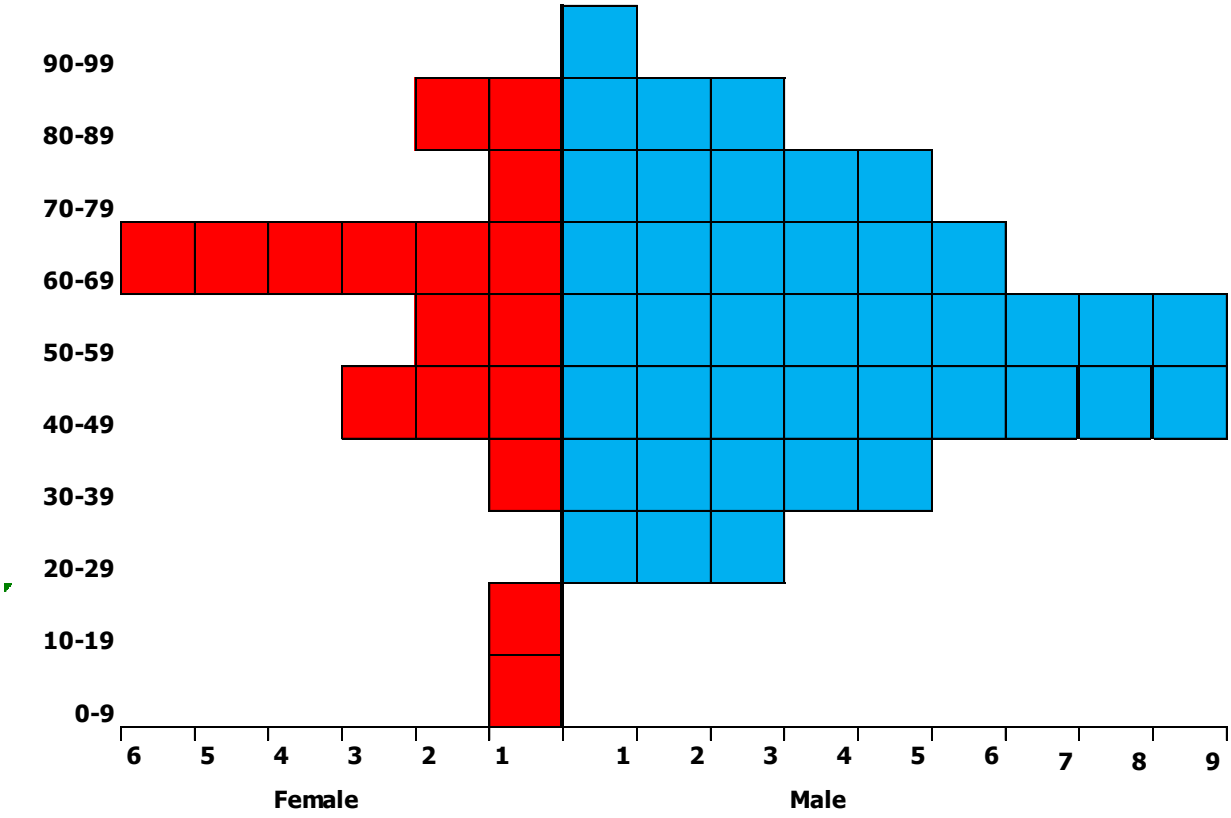
*The month of onset for 5 deaths is missing.

Figure 2. Distribution of confirmed MERS-CoV cases by place of reporting and place of exposure, April 2012 to 17 June 2013 (n=64)



The majority of reported cases continue to be associated with severe disease (lower respiratory tract infection such as pneumonia and/or renal failure). The majority of cases with more detailed information have reported a history of underlying disease or immunosuppression. Five cases (8%) with unknown immune status have presented with mild influenza-like symptoms. Thirty-eight of the 64 cases are reported to have died, resulting in a case-fatality ratio of 59%. The age of cases ranges from two years to 94 years (n=60 cases, information not available for four cases), with a median of 56 years. Overall, 70% of cases (43/61, three with sex unknown) are males (Figure 3).

Figure 3: Distribution of MERS-CoV cases by gender and age, April 2012 – 17 June 2013 (N=58) [Three cases with missing age and/or sex information]



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 [8].

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 [9]. 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) [10]. Cyclosporin A has been shown to be 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 [11].

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 [12-15] and on the University of Bonn website.

Since routine microbiological sampling through nasopharyngeal swabs may give initial negative results in persons later shown to be infected with the coronavirus, 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 recently been developed and validated with a limited number of specimens [16]. 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 [17].

Following the identification and analysis of the viruses obtained from the first cases, the flow of viruses to specialised laboratories, especially from the Middle East cases, is partial, limiting the possibility of determining 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 Qatari patient with travel history to Saudi Arabia [18], one genome sequence from an imported case into Germany from the United Arab Emirates and four genome sequences from viruses involved in the hospital outbreak in Al-Ahsa. Together with earlier published data, this opens up the possibility for comparative genomic studies of the 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) [14-15].
- Further analysis of genomic information on a larger sample of strains will probably shed light on the evolutionary rates of the virus and the most recent common ancestor as well as enabling the testing of alternative hypotheses on the transmission events underlying the emergence of MERS-CoV human infections.

Epidemiological surveillance

On 19 February 2013, WHO re-published its earlier case definition for the novel coronavirus in humans, along with its interim surveillance recommendations for human infection of December 2012 [19]. This publication also includes a category for 'patient under investigation'. A confirmed case is a case in which novel coronavirus has been identified in a biological sample from the patient.

The French case raises the possibility that presentations may not initially include respiratory symptoms, especially in those with immunosuppression or other underlying chronic conditions and, as a result, delay the detection and implementation of measures. The secondary French case showed that the estimated incubation period could be as long as 12 days. Furthermore, a case in Jordan is estimated to have had an incubation period of up to 13 days (unpublished data). Therefore, CDC published an update of the situation on 7 June 2013 recommending the extension of the period from a probable exposure to onset of symptoms to 14 days. This extension was subsequently agreed during an EU Health Security Committee meeting and endorsed by WHO (technical consultation).

The number of cases with immunosuppression or other underlying conditions, and the transmission to and from them, as in the two French cases, suggests that such persons may be at increased risk of acquiring or transmitting infections.

Protocols on the standardisation of influenza seroepidemiology have already been published [18, 20]. Drawing on these and in-country protocols, the UK has published a protocol specifically for the purpose of investigating cases of MERS-CoV infections. This protocol is suitable for use in other EU countries [21]. Most recently, 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 [22].

The epidemiological pattern of the infections is unusual, with an excess of male cases and cases presenting with co-morbidities, as well as an underrepresentation of children [23]. This is different from SARS, where there was a small female excess, co-morbidities were less marked, and cases were younger.

Applied epidemiological and laboratory studies will be of assistance here, 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 placed on capturing the results of case detection 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 provide information on the true geographical extent of these infections [13, 18].

Possible sources and routes of transmission

The retrospective finding of two cases in Jordan raised the issue of whether this is a new infection in humans or one that has been occurring for some time. Since similar animal coronaviruses can be found in bats in all regions of the world [8-9, 24-27], it is possible that these infections are to be found sporadically in many countries. This makes a strong case for further studies of animal coronaviruses and prospective and retrospective searches for cases in other regions, as was already pointed out in ECDC's risk assessment in February 2013. The testing of people with respiratory tract infections among those who came to Europe between September and November 2012 did not reveal any additional infections to the three already mentioned [2, 13, 22].

No reservoir or source of infection for MERS-CoV has been identified so far in the Middle East, including Saudi Arabia, the country reporting most indigenous cases to date. The routes of transmission to humans have not yet been determined. For a number of cases, contact with animals, in particular camels in herds or in camel markets,

has been mentioned but there is no firm evidence to support this link. However, this information is not available for many of the primary cases.

This is a common issue with emerging zoonoses where there are often simultaneous possibilities, including environmental, animal and human exposures. There is very little information in the public domain, which contrasts with the situation during the SARS outbreak ten years ago [28-31].

In Germany and the UK, a follow-up screening exercise has been completed for nearly 200 personal contacts and healthcare workers who were exposed to the first two imported, confirmed cases. No evidence of human-to-human transmission was found. Although some contacts in Germany and the UK developed mild respiratory infections, virological and serological investigations did not link these infections to MERS-CoV [2, 27]. In France, the epidemiological investigation and contact identification was performed [7].

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 from an imported case to a healthy relative paying a hospital visit [4]. Person-to-person transmission also took place in the most recent French cases and the two secondary cases in Italy.

Aircraft contact tracing

Countries should trace contacts of confirmed MERS-CoV cases on aircrafts according to the guidelines for SARS contact tracing in RAGIDA. This should be irrespective of 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 the respiratory secretions of the index case; and
- passengers living in the same household as the index case.

Depending on the clinical presentation of the case during the flight and feasibility, Member State officials may consider extending contact tracing beyond three rows, possibly including all passengers and crew members. If there is no firm evidence of on-board MERS-CoV transmission, all 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 all passengers cannot be contacted, contact tracing efforts should at least concentrate on all passengers seated in the area where 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. Contact passengers should provide to the health authorities their identification and valid contact addresses for 14 days after the flight (locator cards) in order to facilitate contact tracing, if needed. Captains should radio ahead to the airport of destination informing of a suspected MERS-CoV case on board (International Health Regulation 2005, Article 28 (available from http://whqlibdoc.who.int/publications/2008/9789241580410_eng.pdf).

Threat assessment for the EU

Information on many of the basic epidemiological indicators required for determining effective control measures is still missing for most cases (e.g. reservoir of infection, risk groups, incubation period, period of infectivity, mode of transmission, settings where infection has occurred), despite the requirements formulated in Article 6.2 of the 2005 International Health Regulations. In particular, information from the earlier clusters in private homes, from hospitals in the Middle East, and from the recent cases in Saudi Arabia is insufficient, which makes it difficult to comment on the routes of transmission or the underlying pattern of infection and disease. Consequently, it is not possible to estimate the disease risk with any degree of accuracy. As a result, ECDC has to consider a number of underlying scenarios that are compatible with the information available. At this stage, it is not possible to exclude a future SARS-like scenario, especially in the light of the hospital-related outbreaks in Jordan and Al-Ahsa, Saudi Arabia.

The additional cases reported by the Saudi Arabian authorities in the past few weeks and the imported cases reported by Germany (related to medical evacuation), Italy (travel-related), France (travel-related) and Tunisia (travel-related) indicate that an ongoing source of human infection remains present in the Middle East and that more cases may be identified in the EU in the immediate future.

Medical evacuations represent a particularly high risk for the introduction of cases into European Member States. The number of transfers may increase as concern grows among clinicians and the public in the Middle East that there is a risk of MERS-CoV infection associated with hospitals in the area.

The five person-to-person transmissions that have been documented in Europe, two of which are nosocomial, indicate that the risk of onward transmissions in Europe is significant, in particular in healthcare settings.

In those primary cases from the Arabian Peninsula in which more detailed information is available, the majority have a history of underlying disease and/or immunosuppression. However, given a median age of 56 years, this may be normal for these age groups [23]. It is therefore necessary to investigate whether older adults may be at increased risk of acquiring MERS-CoV infection and/or transmitting it.

The reason for the strong male predominance among the cases is unexplained. This is different from SARS, and investigation is needed to ascertain whether this represents a difference in care-seeking behaviour or care receiving in the Middle East [23].

Despite extensive contact tracing amongst previous contacts, only five secondary cases have been detected to date in the EU. It is therefore quite possible that more mild cases could be present in exposed populations in the Middle East.

Further work to document the spectrum of illness and the route of transmission is still needed. A seroepidemiological approach might be useful once the tests available have been validated in the Middle East [18].

The imported cases reported by the UK, Germany, France and Italy following medical evacuation and travel suggest that more imported cases may be expected in the EU in the future.

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 the South East and Pacific Asia.

The number of visitors to Saudi Arabia is expected to increase significantly in the coming months, when Ramadan begins. This is one of the peak times for Umra, the pilgrimage to Mecca in Saudi Arabia. Ramadan in 2013 will start on Tuesday 9 July and will continue for 30 days until Wednesday 7 August. Another important pilgrimage event is the Hajj which is between 13 and 18 October 2013. Around four 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 European Union [32-33]. For a few years now, quotas have been implemented by country for the number of pilgrims that can attend Hajj. Each Muslim country can send 1 000 pilgrims per million Muslim population. However, there is no current quota system for Umra. Up to six million people are reported to have performed Umra in 2012 and the numbers are expected to increase by 10—20% per year. Therefore specific advice should be drawn up (also 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 & Umra) for 1434 (2013) [34].

Conclusions

- As of 17 June 2013, 64 cases of MERS-CoV had been reported worldwide, including 38 deaths. All cases remain associated (including indirect association following secondary person-to-person transmission in the UK, Italy, Tunisia and France) with transmission in the Middle East. The age of cases ranges from two years to 94 years (N=60 cases, information not available for four cases), with a median of 56 years. Overall, 70% (43/61) of cases are males.
- The reports of new infections in Saudi Arabia over the past few weeks indicate that there is an ongoing source of infection and low risk of transmission to humans in the Middle East.
- The first French case raises the possibility that presentations may not initially include respiratory symptoms, especially in those with immunosuppression or underlying chronic conditions. This also needs to be taken into account when revising case detection strategies.
- The confirmed infection in France of a patient who shared a hospital room with an index patient returning from the United Arab Emirates corroborates the risk of nosocomial transmission. The incubation period for this patient is calculated to have been 9—12 days, which is longer than previously estimated. One case in the Jordan cluster had an incubation period of 13 days. Therefore until further evidence emerges, the incubation period is being extended from 10 to 14 days in accordance with the WHO decision.
- These conclusions should be viewed in the light of the many uncertainties that remain with the investigation of cases in the Middle East. It is unusual to have such a degree of uncertainty at this stage in an outbreak.

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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
- Saudi Arabia – Ministry of Health: click here
- Novel coronaviruses: click here