
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

American Journal of Infection Control 42 (2014) 1261-5

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

State of the Science Review

# Middle East respiratory syndrome coronavirus: Implications for health care facilities

Helena C. Maltezou MD, PhD [a,*], Sotirios Tsiodras MD, PhD [b]

[a] Department for Interventions in Health-Care Facilities, Hellenic Center for Disease Control and Prevention, Athens, Greece
[b] Fourth Department of Internal Medicine, University of Athens Medical School, Attikon University Hospital, Athens, Greece

*Key Words:*
Middle East respiratory syndrome coronavirus
Middle East respiratory syndrome
Hospital
Health care associated
Outbreak
Health care workers

***Background:*** Middle East respiratory syndrome coronavirus (MERS-CoV) is a novel coronavirus that causes a severe respiratory disease with high case fatality rate. Starting in March 2014, a dramatic increase of cases has occurred in the Arabian Peninsula, many of which were acquired in health care settings. As of May 9, 2014, 536 laboratory-confirmed cases and 145 deaths have been reported globally.
***Methods:*** Review of publicly available data about MERS-CoV health care–associated transmission.
***Results:*** We identified 11 events of possible or confirmed health care–associated transmission with high morbidity and mortality, mainly among patients with comorbidities. Health care workers are also frequently affected; however, they tend to have milder symptoms and better prognosis. Gaps in infection control were noted in all events. Currently, health care–associated outbreaks are playing a pivotal role in the evolution of the MERS-CoV epidemic in countries in the Arabian Peninsula.
***Conclusion:*** There is a need to increase infection control capacity in affected areas and areas at increased risk of being affected to prevent transmission in health care settings. Vaccines and antiviral agents are urgently needed. Overall, our knowledge about the epidemiologic characteristics of MERS-CoV that impact health care transmission is very limited. As the MERS-CoV epidemic continues to evolve, issues concerning best infection control measures will arise, and studies to better define their effectiveness in real life are needed.


Middle East respiratory syndrome coronavirus (MERS-CoV) is a novel betacoronavirus of the *Coronaviridae* family that causes a severe respiratory disease with a high case fatality rate.[1-4] The virus was isolated for the first time in September 2012 from a 60-year-old patient with fatal pneumonia in Saudi Arabia.[5] However, the earliest identified human cases were traced back to March 2012, to a cluster of severe respiratory infections in a hospital in Jordan.[6] Up until now, all MERS-CoV infected cases are directly or indirectly linked to the Middle East; therefore, the name MERS-CoV was established.[4] Over the first 2 years after the emergence of MERS-CoV, the World Health Organization (WHO) has been notified of 191 laboratory-confirmed cases, of which 82 were fatal.[7] However, starting in mid- to late March 2014, a dramatic increase of cases has been recorded, many which were acquired in health care settings and concerned health care workers (HCWs).[8] As of May 9, 2014, 536 laboratory-confirmed cases and 145 deaths have been reported to the WHO globally.[8] As a result, concerns have been expressed about the possibility of a virus genetic change conferring increased transmissibility, and the novel virus received media attention globally. In the context of uncertainties about its epidemiology, the high case fatality rate, the urgent need for a specific antiviral treatment, and the unavailability of a vaccine, MERS-CoV has been a major public health concern of global dimensions. Given the current local epidemiologic trends of MERS-CoV[8] and the large numbers of travelers that fly out of the Arabian Peninsula,[9] it is almost certain that an increasing number of cases will be exported to other countries; these cases, especially when that patient is seriously ill, will require medical attention and hospitalization. Herein, we review publicly available data about MERS-CoV focusing on health care–associated transmission. Aspects relevant to infection control are also discussed.

* Address correspondence to Helena C. Maltezou, MD, PhD, Department for Interventions in Health-Care Facilities, Hellenic Center for Disease Control and Prevention, 3-5 Agrafon St, Athens, 15123 Greece.
*E-mail address:* helen-maltezou@ath.forthnet.gr (H.C. Maltezou).
The opinions presented in this article are those of the authors and do not necessarily represent those of their institutions.
Conflicts of interest: None to report.

0196-6553/$36.00 - Copyright © 2014 by the Association for Professionals in Infection Control and Epidemiology, Inc. Published by Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.ajic.2014.06.019

## SEARCH STRATEGY

We searched PubMed from September 2012 through June 19, 2014, using the terms *Middle East respiratory syndrome*, *MERS*, and *novel coronavirus*. The abstracts of articles identified through the first PubMed search were screened, and articles presenting original data on health care–associated infections and outbreaks were included. The reference lists of these articles were also reviewed as were any relevant review articles. In addition, we searched the Web sites of the WHO, United States Centers for Disease Control and Prevention (CDC), and European Centre for Disease Prevention and Control (ECDC). In total, we reviewed 252 articles on MERS-CoV and identified 10 articles presenting original data about 11 possible or confirmed health care–associated transmission events. Details about the health care–associated transmission ranged widely among these articles. To the best of our efforts, we avoided presenting duplicated data. In addition, we selected 30 original and review articles. All articles were studied by both authors independently.

### *Epidemiology and clinical aspects*

MERS-CoV infection so far has been described in 10 countries in the Middle East (Saudi Arabia, United Arab Emirates, Qatar, Jordan, Oman, Kuwait, Egypt, Yemen, Lebanon, Iran), 6 countries in Europe (United Kingdom, Germany, France, Italy, Greece, the Netherlands), 2 country in Africa (Tunisia, Algeria), 2 countries in Asia (Malaysia, the Philippines), and 1 county in the Americas (United States).[10]

Molecular analyses of MERS-CoV or similar viruses from bats and camels suggest that these 2 species are the natural reservoirs of the virus.[11,12] Whole genome sequencing showed that human and camel viruses from Saudi Arabia are indistinguishable.[12] Multiple transmission routes are suspected; however, their exact contribution has not been elucidated so far. A phylogenetic study of 21 MERS-CoV genomes from Saudi Arabia suggested that both human-to-human transmission and sporadic zoonotic events occur.[13] The stability of the virus for prolonged periods in camel milk suggests the potential of excretion of the virus into camel milk and spread through consuming raw milk.[14]

The upsurge of cases since mid-March in the Arabian Peninsula (mainly in Saudi Arabia) is possibly attributed to an increase in the number of primary cases and hospital-acquired cases, some as a part of mainly small (1-2 cases), but in a few instances large, outbreaks.[8] A change in the transmissibility pattern of the virus and increased efficacy for sustained transmission could facilitate in-hospital transmission; however, epidemiologic and molecular data to this effect do not exist. Family clusters of MERS-CoV have been recorded.[15] The secondary attack rate in families was 1.35% in Saudi Arabia in 2014.[8] Among imported travel-associated cases, very few instances of person-to-person transmission have been verified.[16-18] Recent phylogenetic analysis using human sequences from Jeddah suggests that the virus has not changed from previous strains.[8] Overall, it seems unlikely that the virus has increased its transmissibility or patterns of transmission. The basic reproductive number has been estimated to be $<1$ using real-time data until June and August 2013, respectively,[19,20] even though the upper range of estimates exceeded 1 in a scenario where infection control was not implemented.[20] These findings indicate no pandemic potential for MERS-CoV so far. Recently, a committee appointed by the WHO concluded that the conditions for a public health emergency of international concern have not yet been met. Moreover, increased testing rates of less ill or asymptomatic cases may have contributed to the upsurge of detected cases.

Regarding characteristics of affected patients, most are men (male-to-female ratio: 2:1), with a median age of 49 years (range, 9 months-94 years).[8] The spectrum of MERS-CoV infections ranges from asymptomatic infection to very severe pneumonia with acute respiratory distress syndrome, septic shock, and multiorgan failure resulting in death. In an analysis of 144 confirmed and 17 possible cases, symptomatic patients typically had fever and cough, chills, sore throat, myalgia, and arthralgia, whereas vomiting and diarrhea were present in at least one third of patients.[21] In the same study, 63.4% of patients developed severe respiratory disease. It appears that severe disease predominantly occurs in patients with comorbidities; 76% of the patients in this report had at least 1.[21] The overall case fatality with the latest WHO figures is 27%.[8]

### *MERS-CoV in health care facilities*

From the very first events of the MERS-CoV epidemic, the virus showed its health care–associated dynamic.[6] Apart of sporadic community cases and family clusters, health care–associated transmission has been reported on several occasions during the last 2 years, indicating human-to-human, although inconsistent, transmission (Table 1).[2,3,6,8,22-27] Gaps in infection control were the common denominator in the events of health care associated–transmission.[2,3,6,8,22,24] During the largest so far–published outbreak of MERS-CoV that occurred in Al-Hasa, Saudi Arabia, in 2013, 4 health care facilities were affected through transfer of patients but also possibly because of repeated introductions of cases from the community.[3] The outbreak extended for almost 2 months and involved 34 cases, including 2 HCWs. Most cases were confined in the hemodialysis unit with rapid transmission and high attack rates.[3] This outbreak gave the opportunity to elucidate several epidemiologic parameters of secondary MERS-CoV infection, such as the incubation period (5.2 days; 95% confidence interval, 1.92-14.7 days), serial interval (7.6 days; 95% confidence interval, 2.5-23.1 days), and heterogeneity in transmission, with many infected patients not transmitting the infection at all and 1 infected patient transmitting the infection to 7 others.[3] Moreover, this outbreak raised the possibility of transmission through direct or indirect contact and between rooms in the same ward.[3] A recent study showed that MERS-CoV remained viable for up to 48 hours under specific environmental conditions, which mimic the hospital environment (20°C with 40% relative humidity), whereas its stability was not reduced during aerosolization.[28] These data show that MERS-CoV has the potential to spread through contact or fomites caused by prolonged survival. A model-based study found that the virus structural characteristics render it very likely to remain viable in the environment for a long period and support fecal-oral transmission.[29]

Vomiting and diarrhea are common in patients with MERS-CoV[1,22,27] and may contribute to transmission. The MERS-CoV case imported in France shared his bathroom with the secondary hospital-acquired case, which raises the possibility of spread through stools.[22] MERS-CoV is predominantly shed through respiratory secretions during cough. MERS-CoV has been detected through polymerase chain reaction for up to 16 days in respiratory specimens and stools and up to 13 days in urine.[22,30,31] Our knowledge about virus shedding and viral load kinetics throughout the clinical course of ill patients is scarce and therefore can provide limited guidance about the duration of implementation of infection control measures.[31] The possibility of prolonged shedding under an immunocompromised status should also be investigated and considered for infection control purposes.

Health care–associated MERS-CoV infections and outbreaks have been associated with high morbidity, high rates and prolonged use of mechanical ventilation, and fatality rates up to 65%.[2,3,23] Given the fact that health care services are often used by older people with comorbidities and in association with the severe course

**Table 1**
Published events of possible or confirmed health care–associated transmission of MERS-CoV globally

| Author/country/year | Setting | Number of cases (laboratory confirmed/ probable) | Number of HCWs (% of total cases) | Nurses (% of HCWs) | Median age of cases, years (range) | Median age of HCWs, years (range) | Fatal cases (% of total) | Fatalities in HCWs (% of HCWs) | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Hijawi et al[6] and Al-Abdallat et al[26]/Jordan/2012 | ICU, CCU, medical and emergency wards | 13 (8/5)* | 10 (76.9) | 8 (80) | 33 (25-65) | 31.5 (25-47.5) | 2 (15.4) | 1 (10) | Biphasic outbreak; no use of PPE apart from gloves; HCW at work while symptomatic; retrospective investigation and testing |
| Arabi et al[2]/Saudi Arabia/ 2012-2013 | 2 medical-surgical ICUs, 1 cardiac ICU | 15 (14/1) | 4 (26.7) | 4 (100) | 59 (36-83)† | 36 (1 HCW with data) | 7 (46.6) | 3 HCWs survived; no data about the critically ill HCW | 2 hospitals; 11 critically ill patients and 4 HCWs (1 severe course, 1 mild symptoms, 2 asymptomatic); 3 cases in patients and 3 in HCWs were health care associated; the 3 HCWs did not use PPE |
| Assiri et al[3]/Saudi Arabia/2013 | Hemodialysis unit, ICUs, medical wards | 34 (23/11) | 2 (5.9) | 1 (50) | 56 (24-94) | 43.5 (42-45) | 15 (65) | 0 (0) | 2-month outbreak in 4 health care facilities; high attack rate in hemodialysis unit; transfer of patients important for spread; gaps in infection control |
| Memish et al[24]/Saudi Arabia/ 2012-2013 | NR | 7 (7/0) | 7 (100) | 6 (86) | n/a | 42 (28-59) | n/a | 0 (0) | 7 HCWs from 6 hospitals, 2 asymptomatic, 5 with mild symptoms; 4 of 7 with <1 hour exposure; gaps in infection control; 1 PCR positive for 8 days |
| Guery et al[22]/France/2013 | Medical ward | 2 (2/0) | 0 (0) | n/a | 57.5 (51-64) | n/a | 1 (50) | n/a | Second patient was identified through contact tracing; patients had common room and bathroom; gaps in infection control |
| Omrani et al[23]/Saudi Arabia/2013 | Emergency department/ rooms | 3 (2/1) | 0 (0) | n/a | 40 (39-51) | n/a | 2 (66.7) | n/a | Family cluster most likely health care acquired |
| Tsiodras et al[27]/Greece/2014 | Extensive contact with the health care environment in Jeddah | 1 (1/0) | 0 (0) | n/a | 69 | n/a | 0 (0) | n/a | Imported case; most likely health care associated transmission |
| WHO[8]/Saudi Arabia/2014 | NR | 128 (128/0) | 39 (30.4) | NR | 48.5 (NR) | Younger than non-HCW cases | NR | NR | 14 hospitals in Jeddah; >60% of cases were hospital acquired; HCWs more likely to be younger, women, and exhibit mild or no symptoms; 15% of HCWs had severe disease or died; gaps in infection control |
| WHO[8]/Saudi Arabia/2014 | NR | 127 (127/0) | 26 (20.4) | NR | NR | NR | NR | NR | From Tabuk, Riyadh, and Medina |
| WHO[8]/United Arab Emirates/2014 | NR | 37 (37/0) | (67) | NR | 41 (4-73) | NR | NR | NR | 28 of 37 cases were identified in a hospital cluster; 1 HCW with severe disease; the remaining HCWs mild or no symptoms |
| Bialek et al[25]/United States/2014 | NR | 2 (3/0) | 2 (100) | NR | NR | NR | 0 (0) | 0 (0) | 2 imported MERS-CoV cases in HCWs in Saudi Arabia |

*CCU*, coronary care unit; *HCW*, health care worker; *ICU*, intensive care unit; *MERS-CoV*, Middle East respiratory syndrome coronavirus; *n/a*, nonapplicable; *NR*, not reported; *PCR*, polymerase chain reaction; *PPE*, personal protective equipment; *WHO*, World Health Organization.

*Data about laboratory confirmation were obtained from Al-Abdallat et al[26]; the remaining data were obtained from Hijawi et al.[6]

†Median age and range concerns the 12 critically ill patients out of the 15 MERS-CoV infected cases.

of MERS-CoV among these groups,[2] it is not surprising that patients with comorbidities are overrepresented in such outbreaks.[3] Beyond the considerable morbidity and mortality, such outbreaks are costly because of the high-level health care required, need for strict infection control measures, and extensive contact tracing among hundreds of patients, family members, and HCWs.[3,16,17,22,27,32-34] Regarding frequency of secondary transmission to HCWs in health care settings, Memish et al[32] presented data from 5,065 contacts in Saudi Arabia during a 12-month period (October 1, 2012-September 30, 2013). Of 1,695 HCW contacts of laboratory-confirmed MERS-CoV cases, 19 (1.12%) tested positive, less than the 3.4% (17 of 462) rate of infection among family contacts. These findings indicate a rather small risk of transmission to HCWs and that the recommended infection control measures are adequate thus far.

In the description of demographics of secondary MERS-CoV cases, a drop of the median age from 59 to 43 years old compared with primary cases has been reported.[21] This depends on the conditions of each outbreak and may be affected by the preponderance of affected HCWs in each instance. For example, in the most recent WHO report,[8] the HCWs who tested positive for MERS-CoV in the 2014 Jeddah outbreaks were more likely to be younger, women, and to exhibit mild or no symptoms compared with primary cases. However, 15% of HCWs developed a severe disease, which resulted in admission to an intensive care unit or death.[8]

Unsuspected cases are the main source for the introduction of MERS-CoV virus from the community or another health care facility.[3] Although such patients may present with compatible symptoms, the diagnosis may not be considered early or symptoms may be mild.[2,24,33] In the hospital outbreak that occurred in Saudi Arabia in 2013, 3 patients exhibited no fever during initial presentation.[3] HCWs may acquire MERS-CoV infection either in the community or through occupational exposure.[2,3,32] Nurses are mostly affected, which is attributed to their prolonged, repeated, and closer physical contact with patients. HCWs may continue working despite being symptomatic.[6] An asymptomatic or mildly symptomatic course has been described in HCWs,[2,8,24] which raises the possibility of transmission of the infection to their vulnerable patients during an asymptomatic phase or early incubation. Patient-to-patient transmission has been noted as well.[3,22]

Currently, health care–associated outbreaks are playing a pivotal role in the evolution of the MERS-CoV epidemic.[8] In the recent mission report by the WHO authorities evaluating data on 128 laboratory-confirmed cases in 14 hospitals in Jeddah, Saudi Arabia, with onset of symptoms between February 17 and April 26, 2014, one-third of the cases were considered to be primary cases (some of the investigations are still ongoing), whereas >60% of the cases (including 39 HCWs) were classified as hospital acquired.[8] In the rest of Saudi Arabia, 26 out of 127 (20.5%) recent cases were identified in HCWs.[8] Overall, 65 of the 290 (22.4%) cases reported from Saudi Arabia from March 27 to May 9, 2014, were HCWs.[23] In Mecca, another large outbreak in a hospital was described with 28 laboratory-confirmed cases, including 27 HCWs.[8] Both outbreaks were larger than the originally described outbreak in Saudi Arabia.[3] In the United Arab Emirates, HCWs accounted for more than two-thirds of 37 cases reported during the same period.[8] Although the WHO points to infection control gaps for the recent propagation of MERS-CoV within health care facilities in Saudi Arabia and the United Arab Emirates, we do not know if this concerns the use of personal protective equipment, hand hygiene, procedures, environmental cleaning, or triage.

### *Infection control in health care facilities*

Given that no vaccines or specific antiviral prophylaxis against MERS-CoV are available,[35,36] the prevention and control of transmission of MERS-CoV within health care facilities relies solely on early detection, isolation, and strict implementation of infection control measures. Rapid and accurate diagnosis is crucial to trigger contact tracing in the hospital and the community and should be ordered as soon as possible in the context of a relevant epidemiologic profile but also in the event of a health care–associated cluster of severe respiratory illness cases.

Patients with confirmed or suspected MERS-CoV infection should be cared under contact and droplet precautions until testing results. In accordance with WHO guidelines, a high protection mask (eg, N95 respirator) along with eye goggles, gowns, and gloves should be used during aerosol-generating procedures; the latter should be performed in an adequately ventilated room (minimum of 6-12 air changes per hour) (airborne infection isolation room).[37] For consistency with the recommendations during the 2009 H1N1 pandemic, the United States CDC recommends the use of N95 respirators in all contacts with a laboratory-confirmed or suspected MERS-CoV infected case.[38] The rationale for this recommendation relies on the gaps of knowledge about the potential for airborne transmission of the novel coronavirus. However, N95 respirators are less tolerated by HCWs and are more expensive.[39] The United States CDC also recommends that patients with confirmed or suspected MERS-CoV infection are placed in an airborne infection isolation room.[38] HCWs with MERS-CoV infection should be strictly excluded from patient care, even with mild symptoms. The role of asymptomatic HCWs is under question. Overall, there is a need to increase infection control capacity in affected areas and areas at increased risk of being affected to prevent transmission in health care settings.

## UNANSWERED QUESTIONS

Our knowledge about the epidemiologic characteristics of MERS-CoV that impact health care transmission is very limited. To interrupt in-hospital transmission, routes of efficient exposure and virus shedding should be well studied. The contribution of primary cases to the so-called hospital-acquired cases in the recent upsurge of detected cases in the Arabian Peninsula is still unclear, and further epidemiologic data and analyses are necessary. In 1 analysis, 60 of 95 (63.2%) cases with evidence of secondary transmission acquired the infection in the hospital environment; nevertheless, 49 of them had additionally reported exposure to animals, therefore not eliminating an alternative source of infection.[21]

The stability of the proportion of asymptomatic versus symptomatic cases is an argument against increasing testing as a possible explanation for either primary or secondary cases.[10] On the other hand, a reverse scenario could be that additional cases are missed because cases at the early incubation period or with low viral loads may be missed with molecular testing. A transmission event under similar circumstances has been described in the community for the first imported MERS-CoV case in the United States that tested negative by molecular assays but subsequently tested positive by serology.[25,40]

### *Research for the future*

Active surveillance and testing are of outmost importance to provide answers about the epidemiology of MERS-CoV and evolution of the current epidemic. Case-control, serologic studies in exposed HCWs are needed to better define the effectiveness of infection control measures. Transmission of the virus via asymptomatic shedding in feces or other routes (eg, fomites, environment) is another topic for investigation. Studies of viral kinetics in affected patients with molecular analyses of samples from various body sites will provide answers for infection control as well.

A vaccine against MERS-CoV should be developed along with specific antiviral agents.

## CONCLUSIONS

There is no doubt that MERS-CoV remains a serious threat and has exhibited a significant public health impact in the affected countries. Currently, health care–associated transmission plays a pivotal role in the evolution of the MERS-CoV epidemic in countries in the Arabian Peninsula. A significant cost has been encountered in terms of personnel and time required for contact tracing and means of implementing infection control and prevention measures in health care settings. So far, there is no evidence of sustained human-to-human transmission. However, significant concerns exist in terms of the increased number of health care–associated cases, gaps in knowledge regarding transmission routes, and limited infection control capacity in affected countries. As the MERS-CoV epidemic continues to evolve, vaccine and specific antiviral agents against MERS-CoV are urgently needed. Studies about the effectiveness of infection control measures will provide answers and eventually promote safety in health care facilities both for patients and HCWs.

## References


1. Assiri A, Al-Tawfiq JA, Al-Rabeeah AA, Al-Rabiah FA, Al-Hajjar S, Al-Barrak A, et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. Lancet Infect Dis 2013;13:752-61.
2. Arabi YM, Arifi AA, Balkhy HH, Najm H, Aldawood AS, Ghabashi A, et al. Clinical course and outcomes of critically ill patients with Middle East respiratory syndrome coronavirus infection. Ann Intern Med 2014;160:389-97.
3. Assiri A, McGeer A, Perl TM, Price CS, Al Rabeeah AA, Cummings DA, et al. Hospital outbreak of Middle East respiratory syndrome coronavirus. N Engl J Med 2013;369:407-16.
4. de Groot RJ, Baker SC, Baric RS, Brown CS, Drosten C, Enjuanes L, et al. Middle East respiratory syndrome coronavirus (MERS-CoV): announcement of the Coronavirus Study Group. J Virol 2013;87:7790-2.
5. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med 2012;367:1814-20.
6. Hijawi B, Abdallat M, Sayaydeh A, Alqasrawi S, Haddadin A, Jaarour N, et al. Novel coronavirus infections in Jordan, April 2012: epidemiological findings from a retrospective investigation. East Mediterr Health J 2013;19(Suppl 1):S12-8.
7. World Health Organization. Middle East respiratory syndrome coronavirus (MERS-CoV) – update. Available from: http://www.who.int/csr/don/2014_03_17/en/. Accessed May 17, 2014.
8. World Health Organization. Middle East respiratory syndrome coronavirus (MERS-CoV) summary and literature update–as of 9 May 2014. Available from: http://www.who.int/csr/disease/coronavirus_infections/MERS_CoV_Update_09_May_2014.pdf?ua=1. Accessed May 17, 2014.
9. Khan K, Sears J, Hu VW, Brownstein JS, Hay S, Kossowsky D, et al. Potential for the international spread of Middle East respiratory syndrome in association with mass gatherings in Saudi Arabia. PLoS Curr 2013;5.
10. European Centre for Disease Prevention and Control. Epidemiological update: Middle East respiratory syndrome coronavirus (MERS-CoV). Available from: http://www.ecdc.europa.eu/en/press/news/_layouts/forms/News_DispForm.aspx?List=8db7286c-fe2d-476c-9133-18ff4cb1b568&ID=1016. Accessed June 5, 2014.
11. Memish ZA, Mishra N, Olival KJ, Fagbo SF, Kapoor V, Epstein JH, et al. Middle East respiratory syndrome coronavirus in bats, Saudi Arabia. Emerg Infect Dis 2013;19:1819-23.
12. Briese T, Mishra N, Jain K, Zalmout IS, Jabado OJ, Karesh WB, et al. Middle East respiratory syndrome coronavirus quasispecies that include homologues of human isolates revealed through whole-genome analysis and virus cultured from dromedary camels in Saudi Arabia. MBio 2014;5:e01146-14.
13. Cotten M, Watson SJ, Kellam P, Al-Rabeeah AA, Makhdoom HQ, Assiri A, et al. Transmission and evolution of the Middle East respiratory syndrome coronavirus in Saudi Arabia: a descriptive genomic study. Lancet 2013;382:1993-2002.
14. Van Doremalen N, Bushmaker T, Karesh WB, Munster VJ. Stability of Middle East respiratory syndrome coronavirus in milk [letter]. Available from: http://wwwnc.cdc.gov/eid/article/20/7/14-0500_article.htm. Accessed May 17, 2014.
15. Memish ZA, Zumla AI, Al-Hakeem RF, Al-Rabeeah AA, Stephens GM. Family cluster of Middle East respiratory syndrome coronavirus infections. N Engl J Med 2013;368:2487-94.
16. Puzelli S, Azzi A, Santini MG, Di Martino A, Facchini M, Castrucci MR, et al. Investigation of an imported case of Middle East respiratory syndrome coronavirus (MERS-CoV) infection in Florence, Italy, May to June 2013. Euro Surveill 2013;18:20564.
17. Health Protection Agency (HPA) UK Novel Coronavirus Investigation team. Evidence of person-to-person transmission within a family cluster of novel coronavirus infections, United Kingdom, February 2013. Euro Surveill 2013;18:20427.
18. European Centre for Disease Prevention and Control. Severe respiratory disease associated with Middle East respiratory syndrome coronavirus (MERS-CoV). Ninth update, 24 April 2014. Available from: http://www.ecdc.europa.eu/en/publications/Publications/Middle-East-respiratory-syndrome-coronavirus-risk-assessment-25-April-2014.pdf. Accessed May 17, 2014.
19. Breban R, Riou J, Fontanet A. Interhuman transmissibility of Middle East respiratory syndrome coronavirus: estimation of pandemic risk. Lancet 2013;382:694-9.
20. Cauchemez S, Fraser C, Van Kerkhove MD, Donnelly CA, Riley S, Rambaut A, et al. Middle East respiratory syndrome coronavirus: quantification of the extent of the epidemic, surveillance biases, and transmissibility. Lancet Infect Dis 2014;14:50-6.
21. The WHO Mers-Cov Research Group. State of knowledge and data gaps of Middle East respiratory syndrome coronavirus (MERS-CoV) in humans. PLoS Curr 2013;5.
22. Guery B, Poissy J, el Mansouf L, Séjourné C, Ettahar N, Lemaire X, et al. Clinical features and viral diagnosis of two cases of infection with Middle East respiratory syndrome coronavirus: a report of nosocomial transmission. Lancet 2013;381:2265-72.
23. Omrani AS, Matin MA, Haddad Q, Al-Nakhli D, Memish ZA, Albarrak AM. A family cluster of Middle East respiratory syndrome coronavirus infections related to a likely unrecognized asymptomatic or mild case. Int J Infect Dis 2013;17:e668-72.
24. Memish ZA, Zumla AI, Assiri A. Middle East respiratory syndrome coronavirus infections in health care workers. N Engl J Med 2013;369:884-6.
25. Bialek SR, Allen D, Alvarado-Ramy F, Arthur R, Balajee A, Bell D, et al. First confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection in the United States, updated information on the epidemiology of MERS-CoV infection, and guidance for the public, clinicians, and public health authorities - May 2014. MMWR Morb Mortal Wkly Rep 2014;63:431-6.
26. Al-Abdallat MM, Payne DC, Alqasrawi S, Rha B, Tohme RA, Abedi GR, et al. Hospital-associated outbreak of Middle East Respiratory Syndrome coronavirus: a serologic, epidemiologic, and clinical description. Clin Infect Dis 2014;59:1225-33.
27. Tsiodras S, Baka A, Mentis A, Iliopoulos D, Dedoukou X, Papamavrou G, et al. A case of imported Middle East respiratory syndrome coronavirus infection and public health response, Greece, April 2014. Euro Surveill 2014;19:20782.
28. van Doremalen N, Bushmaker T, Munster VJ. Stability of Middle East respiratory syndrome coronavirus (MERS-CoV) under different environmental conditions. Euro Surveill 2013;18:20590.
29. Goh GK, Dunker AK, Uversky V. Prediction of intrinsic disorder in MERS-CoV/HCoV-EMC supports a high oral-fecal transmission. PLoS Curr 2013;5.
30. Bermingham A, Chand MA, Brown CS, Aarons E, Tong C, Langrish C, et al. Severe respiratory illness caused by a novel coronavirus, in a patient transferred to the United Kingdom from the Middle East, September 2012. Euro Surveill 2012;17:20290.
31. Drosten C, Seilmaier M, Corman VM, Hartmann W, Scheible G, Sack S, et al. Clinical features and virological analysis of a case of Middle East respiratory syndrome coronavirus infection. Lancet Infect Dis 2013;13:745-51.
32. Memish ZA, Al-Tawfiq JA, Makhdoom HQ, Al-Rabeeah AA, Assiri A, Alhakeem RF, et al. Screening for Middle East respiratory syndrome coronavirus infection in hospital patients and their healthcare worker and family contacts: a prospective descriptive study. Clin Microbiol Infect 2014;20:469-74.
33. Buchholz U, Müller MA, Nitsche A, Sanewski A, Wevering N, Bauer-Balci T, et al. Contact investigation of a case of human novel coronavirus infection treated in a German hospital, October-November 2012. Euro Surveill 2013;18:20406.
34. Pebody RG, Chand MA, Thomas HL, Green HK, Boddington NL, Carvalho C, et al. The United Kingdom public health response to an imported laboratory confirmed case of a novel coronavirus in September 2012. Euro Surveill 2012;17:20292.
35. Zhang N, Jiang S, Du L. Current advancements and potential strategies in the development of MERS-CoV vaccines. Exert Rev Vaccines 2014;13:761-74.
36. Chan JF, Chan KH, Kao RY, To KK, Zheng BJ, Li CP, et al. Broad-spectrum antivirals for the emerging Middle East respiratory syndrome coronavirus. J Infect 2013;67:606-16.
37. World Health Organization. Infection prevention and control during health care for probable or confirmed cases of novel coronavirus (nCoV) infection. Available from: http://www.who.int/csr/disease/coronavirus_infections/IPCnCoVguidance_06May13.pdf?ua=1. Accessed May 17, 2014.
38. Centers for Disease Control and Prevention. Middle east respiratory syndrome (MERS). Interim infection prevention and control recommendations for hospitalized patients with Middle East respiratory syndrome coronavirus (MERS-CoV). Available from: http://www.cdc.gov/coronavirus/mers/infection-prevention-control.html. Accessed May 17, 2014.
39. Mermel KA. Preventing the spread of influenza A H1N1 2009 to health-care workers. Lancet Infect Dis 2009;9:723-4.
40. Centers for Disease Control and Prevention. Illinois resident who had contact with Indiana MERS patient tests positive for MERS coronavirus. Available from: http://www.cdc.gov/media/releases/2014/p0517-mers.html. Accessed May 17, 2014.