Has Hajj-associated Middle East Respiratory Syndrome Coronavirus transmission occurred? The case for effective post-Hajj surveillance for infection

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The 2013 Muslim Hajj pilgrimage was completed in October. Thankfully there have been, as of yet, no confirmed cases of Hajj-associated Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Saudi Arabia or abroad. Screening PCR (E gene) for the virus was positive in three samples from a 61-year-old woman who returned to Spain from the 2013 Hajj pilgrimage on I November and one of her contacts who was accompanying her on the Hajj journey who developed symptoms on the same day and was suspected to have acquired the infection from the first case [1]. The first patient, who had no pre-existing medical condition, attended Hajj during October in Saudi Arabia. She became symptomatic 3 days before departure and attended a hospital in Makkah where pneumonia was confirmed by chest X-ray. In-flight to Spain she needed oxygen and was hospitalized on arrival in Madrid. However, sequencing for MERS-CoV has, to date, been unsuccessful and definitive confirmatory tests were negative [1]. If positive, this could be the first European case of post-Hajj-associated MERS-CoV with a second case among very close contacts.

In addition, multiple media reports about cases have related to Hajj, including one suspected MERS-CoV death in Egypt that was confirmed negative by testing by the Egyptian health authority, and an Omani man who died from confirmed MERS-CoV infection following presumed contact with a son-in-law who had returned from Hajj (although the returning pilgrim was negative on testing, so this is unlikely to be a Hajj-associated case). Two additional case reports from India appear to be false and a product of media hype [2,3]. Indeed, many of these cases are likely to be flu [4].

These reports raise several issues regarding returning pilgrims in Europe and elsewhere, including the importance of high-quality post-Hajj surveillance with rapid reliable testing.

In October 2013, about 2 million pilgrims from all parts of the world attended Hajj pilgrimage in Saudi Arabia. Almost all left Saudi Arabia by the end of November. As of I December 2013, 160 confirmed MERS cases have been reported worldwide, of whom 68 (42.5%) have died (Fig. I) [5]. Only nine cases (not including these Spanish cases) have been recorded outside the Middle East: three in Tunisia, of which one was 'imported' (i.e. brought in from the Middle East but not diagnosed in country of origin), and six in Europe [5]. Although much about the virus remains uncertain, compared with severe acute respiratory syndrome (SARS), it appears to have a higher mortality rate (42% versus 10%), human-to-human spread is much slower and it causes especially severe disease in those with a pre-existing medical illness [6].

In 2012, MERS-CoV was actively searched for among a cohort of French pilgrims during the Hajj but no case was found [7]. A syndromic survey among Australian pilgrims was also conducted among Hajjis in 2012 and no probable case was identified [8].

Intense crowding, shared accommodation and exposure to environmental dust and pollutants provide the ecology for transmission of respiratory infections among pilgrims; at least one-third of them are elderly and/or have pre-existing chronic medical conditions. High attack rates of respiratory infections, including influenza, pertussis and tuberculosis, have in the past been reported at Hajj and there has been intercontinental spread of potentially air-borne infections, e.g. the meningococcal W135 outbreaks in 2000 and 2001 [9,10].

Pilgrims are likely to have had direct or indirect contact with animals harbouring MERS-CoV. Sacrificing four-footed animals, including a small proportion of camels, is part of the Hajj rituals, and between I and 2 million animals are sacrificed at designated abattoirs located within walking distance of pilgrims' tents (Fig. 2). Although official slaughtering is now performed by proxy by professional abattoir workers, the meat is consumed by pilgrims, many of whom also enjoy camel rides or photographs during their stay in Makkah. In recent studies, a very high prevalence of neutralizing antibodies against MERS-CoV has been found in Arabian camels of the Middle East and Egypt [11,12]. Also, a camel in Jeddah has been

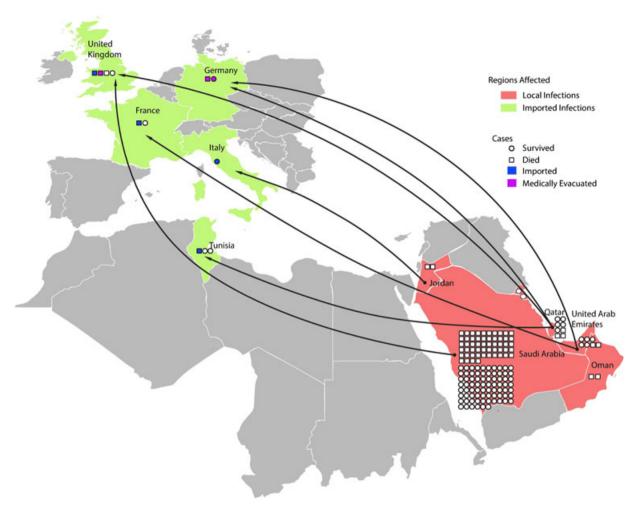


FIG. I. Map of reported Middle East respiratory syndrome cases.



FIG. 2. Herd of camels at the Hajj site in Mina, Makkah.

reported to have an active infection (i.e. PCR positive), whose owner was also infected [13]. Bats have been suspected as a possible source for the MERS-CoV with part of the genome

identified in a faecal sample from an Egyptian tomb bat captured in the living vicinity of a patient from Bisha, Saudi Arabia [14]. Human contact with fruit bat excreta/secretions, by consuming unwashed fruits, especially dates which are a Hajj delicacy, might increase the risk of MERS-CoV.

In most Muslim communities worldwide, it is a tradition for friends and relatives to warmly welcome returned pilgrims, who also meet and visit their friends and neighbours in the mosques and community centres. This involves close contact, particularly hugging. Those who are unwell are especially looked after and visited more frequently. A recent report suggests the possibility of transmission of MERS-CoV from unrecognized asymptomatic or mild cases [15]. Also, in countries that do not routinely test for MERS-CoV, unrecognized cases might not be able to be linked definitively to Hajj despite heightened post-Hajj surveillance.

Observational studies conducted during the SARS epidemic of 2003 demonstrated the importance of hand washing in healthcare workers. This was shown to be effective if performed a minimum of 11 times daily and used with other

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personal protective measures (e.g. facemasks, gowns and goggles) while caring for the sick [16]. Hand hygiene, especially after sneezing, yawning and cleaning the nose, is important, and complements Muslims' daily ablutions, which are performed at least five times before prayers [17]. A recent survey conducted among French pilgrims has shown that these measures are acceptable to pilgrims [18]. As individuals with co-morbidities are at particularly high risk of infection and severe disease [6], protection of pilgrims and their households is achieved by vaccination against influenza, pneumococcal disease, measles and pertussis (if not already up to date), the control of pre-existing diseases like bronchial asthma and diabetes, and smoking cessation.

The French survey also showed that about 35% of pilgrims were not aware of the MERS situation in Saudi Arabia [18], and indicated the importance of awareness and educational campaigns with the help of mass media. Misleading media reports should be rapidly corrected. Healthcare workers who look after the pilgrims also need education about the disease, its prevention, diagnosis and reporting. Diagnostic tests should be readily available to front-line medical staff. Any returned Hajj pilgrim presenting with symptoms suggestive of respiratory infection, particularly pneumonia, should be suspected of having MERS-CoV, and contact tracing of confirmed cases is essential.

Careful and systematic post-Hajj surveillance is required with international cooperation from health systems, airlines and airport authorities who should have a proper understanding of its purpose. Targeted research to identify the source(s) of MERS-CoV, modes of transmission, therapeutic options, vaccine development and other preventive actions are all a priority. With respect to prevention, we embarked on a large trial to assess the efficacy of facemasks against respiratory viruses including MERS-CoV and influenza at this year's Hajj and this will continue next year. We hope the trial will determine if facemasks are effective in preventing viral respiratory infection such as MERS-CoV and influenza.

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References

- European Centre for Disease Prevention and Control. Rapid Risk Assessment: Severe respiratory disease associated with Middle East respiratory syndrome coronavirus (MERS-CoV). Available at: http:// ecdc.europa.eu/en/publications/Publications/mers-cov-risk-assessment-6-November-2013.pdf (last accessed 30 November 2013).
- Times of Oman. Omani man dies of MERS-CoV. Available at: http:// www.timesofoman.com/News/Article-25446.aspx (last accessed 30 November 2013).
- The Hindu. MERS coronavirus: no need to panic, say doctors. Available at: http://www.thehindu.com/news/cities/bangalore/mers-coronavirusno-need-to-panic-say-doctors/article5340095.ece (last accessed 30 November, 2013).
- 4. Raoult D, Charrel R, Gautret P, Parola P. From the Hajj: it's the flu, idiot. Clin Microbiol Infect 2014; 20: O1.
- World Health Organization. Middle East respiratory syndrome coronavirus (MERS-CoV) update. Available at: http://www.who.int/csr/don/2013_I1_26/en/index.html (last accessed I December, 2013).
- Assiri A, Al-Tawfiq JA, Al-Rabeeah AA 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: 752–761.
- Gautret P, Charrel R, Belhouchat K et al. Lack of nasal carriage of novel corona virus (HCoV-EMC) in French Hajj pilgrims returning from the Hajj 2012, despite a high rate of respiratory symptoms. Clin Microbiol Infect 2013; 19: E315–E317.
- Rashid H, Barasheed O, Booy R. Acute febrile respiratory infection symptoms in Australian Hajjis at risk of exposure to Middle East respiratory syndrome coronavirus. Med J Aust 2013; 199: 453.
- Haworth E, Barasheed O, Memish ZA, Rashid H, Booy R. Prevention of influenza at Hajj: applications for mass gatherings. J R Soc Med 2013; 106: 215–223.
- Booy R, El Bashir H, Rashid H, Shingadia D, Haworth E. Influenza and meningococcal disease: lessons for travellers and government from 2 epidemic diseases. *Travel Med Infect Dis* 2009; 7: 253–256
- 11. Perera RA, Wang P, Gomaa MR et al. Seroepidemiology for MERS coronavirus using microneutralisation and pseudoparticle virus neutralisation assays reveal a high prevalence of antibody in dromedary camels in Egypt, June 2013. Euro Surveill 2013; 18: pii=20574.
- Reusken CB, Haagmans BL, Müller MA et al. Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: a comparative serological study. Lancet Infect Dis 2013; 13: 859– 866.
- Centre for Infectious Disease Research and Policy (CIDRAP). Camel with MERS-CoV had signs of illness. Available at: http://www.cidrap. umn.edu/news-perspective/2013/11/camel-mers-cov-had-signs-illness (last accessed 30 November, 2013).
- Memish ZA, Mishra N, Olival KJ et al. Middle East respiratory syndrome coronavirus in bats, Saudi Arabia. Emerg Infect Dis 2013; 19: 1819–1823.

- 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–e672.
- Jefferson T, Del Mar CB, Dooley L et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database Syst Rev 2011; 7: CD006207.
- Ahmed QA, Memish ZA, Allegranzi B, Pittet D; WHO Global Patient Safety Challenge. Muslim health-care workers and alcohol-based handrubs. Lancet 2006; 367: 1025–1027.
- Gautret P, Benkouiten S, Salaheddine I et al. Hajj pilgrims knowledge about Middle East respiratory syndrome coronavirus, August to September 2013. Euro Surveill 2013; 18: pii=20604.