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Middle East respiratory syndrome: An emerging coronavirus infection tracked by the crowd



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ABSTRACT

In 2012 in Jordan, infection by a novel coronavirus (CoV) caused the first known cases of Middle East respiratory syndrome (MERS). MERS-CoV sequences have since been found in a bat and the virus appears to be enzootic among dromedary camels across the Arabian Peninsula and in parts of Africa. The majority of human cases have occurred in the Kingdom of Saudi Arabia (KSA). In humans, the etiologic agent, MERS-CoV, has been detected in severe, mild and influenza-like illness and in those without any obvious signs or symptoms of disease. MERS is often a lower respiratory tract disease associated with fever, cough, breathing difficulties, pneumonia that can progress to acute respiratory distress syndrome, multiorgan failure and death among more than a third of those infected. Severe disease is usually found in older males and comorbidities are frequently present in cases of MERS. Compared to SARS, MERS progresses more rapidly to respiratory failure and acute kidney injury, is more often observed as severe disease in patients with underlying illnesses and is more often fatal. MERS-CoV has a broader tropism than SARS-CoV, rapidly triggers cellular damage, employs a different receptor and induces a delayed proinflammatory response in cells. Most human cases have been linked to lapses in infection prevention and control in healthcare settings, with a fifth of virus detections reported among healthcare workers. This review sets out what is currently known about MERS and the MERS-CoV, summarises the new phenomenon of crowd-sourced epidemiology and lists some of the many questions that remain unanswered, nearly three years after the first reported case.

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1. Brief history of the localised epidemic.

The world was made aware of a newly discovered coronavirus *via* an email from Dr. Ali Mohamed Zaki, an Egyptian virologist working at the Dr. Soliman Fakeeh Hospital in Jeddah in The Kingdom of Saudi Arabia (KSA). The email was published on the website of the professional emerging diseases (ProMED) network on 20-September-2014 (ProMED, 2014). That first case was a 60 year old man from Bisha in the KSA and, thanks to the email, the rapid discovery of a second case of the virus, this time in an ill patient from Qatar, was transferred to the United Kingdom for care (Fig. 1) (Bermingham et al., 2012). As of 20th January 2015, there have been 969 detections of viral RNA or virus-specific antibodies reported publicly, 955 confirmed by the World Health Organization (WHO), with over a third of the positive people dying

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(n=351, 37%); data from public sources including the WHO and Ministries of Health). First known as novel coronavirus (nCoV), the following two to three years were a slow discovery process revealing a virus that appears well established among dromedary camels (DC; Camelus dromedarius) across the Arabian Peninsula and parts of Africa. From infected DCs, the virus is thought to infrequently infect exposed humans. Concern was raised early on that patenting of the first viral isolate would lead to restricted access to the virus and to viral diagnostics (Sciencemag, 2014). However, sensitive, validated reverse transcriptase real-time polymerase chain reaction (RT-rtPCR)-based diagnostics were available (Abdel-Moneim, 2014) almost immediately. Virus was also made freely available subject to routine biosafety considerations, supporting many of the research findings described herein. In search of an animal host, bats were implicated in August 2013 (Memish et al., 2013a) but in that same month a DC link was reported (Reusken et al., 2013c) and that link has matured into a verifiable association. In humans, overt disease was finally given the name Middle East respiratory syndrome and the acronym MERS. From these animal-to-human spillover events, the MERS coronavirus (MERS-CoV; see Section 3 for variation in naming) spread sporadically among people, causing

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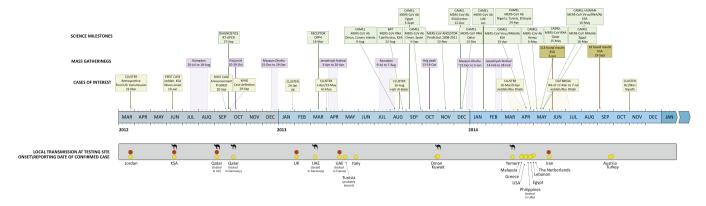


Fig. 1. A timeline of key scientific milestones, cases of interest and mass gatherings of relevance to the potential spread of MERS-CoV among humans and from animals to humans. A yellow circle indicates when a country reported a laboratory confirmed detection and an orange circle denotes ensuing local transmission. Mention of DC contact prior to disease is marked by a black camel icon.

more severe disease among older males with underlying diseases. The proportion of infected people who are confirmed to have died from MERS-CoV infection is much higher than for severe acute respiratory syndrome (SARS)-CoV, influenza virus or many other pathogens. The spread of MERS-CoV among humans has often been associated with outbreaks in hospitals, which in 2012-2014 usually commenced in March (Mackay, 2014; Maltezou and Tsiodras, 2014). This spread may be linked to some seasonal environmental changes, change in host animal behaviour, or perhaps simple coincidence between season and successive hospital outbreaks. Approximately a fifth of all cases to date have involved healthcare workers (HCWs), spiking alongside periods of increased total case numbers. Social media, blogs and the mainstream media have kept close tabs on the spread of MERS-CoV to 23 countries in Europe, Asia and the United States of America (USA; Fig. 2), mostly with an origin in the KSA from where 88% of viral detections have occurred. Twitter in particular has provided a global forum through or فنوروك# specific hashtags like #MERS and the Arabic hashtag #Coruna. An engaged world has helped understand how the virus has affected the KSA and its neighbouring countries and allowed outsiders to view science musings take shape, collaborations form, local news and commentary trend and new results be discussed in real time. Social media provides new avenues for scientists to express experienced opinion, to more widely communicate their

research and to engage with public health entities, the public themselves and the mainstream media. This degree of engagement was not possible in 2002/2003 when the SARS global outbreak began its rise to 8100 human cases including 770 deaths (proportion of fatal cases, or PFC, of 9.5%). The ubiquity of social media appears to have changed what the public expects from a State when it communicates about new or existing infectious disease outbreaks and epidemics, and how quickly they expect that to occur.

2. Middle East respiratory syndrome (MERS)

Patients with MERS often present themselves to a hospital with systemic and lower respiratory tract (LRT) signs and symptoms of disease which usually include fever, chills or rigors, dry or productive cough, shortness of breath (dyspnea) and one or more comorbidities including diabetes (prevalent in the KSA), chronic kidney disease including renal failure, chronic heart disease and heart failure, recent surgery, hypertension, chronic lung disease, asthma, obesity, smoking, malignant disease or steroid use (Arabi et al., 2014; Assiri et al., 2013a; Hijawi et al., 2013; Zaki et al., 2012). MERS-CoV may be identified in patients with severe hypoxaemic respiratory failure and extrapulmonary organ dysfunction which can precede death in over a third of infections (Arabi et al., 2014; Assiri et al., 2013a; Hijawi et al., 2013; Zaki et al., 2012).

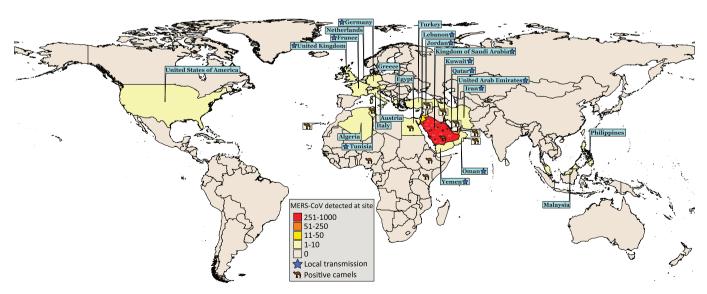


Fig. 2. The 23 countries in which MERS-CoV has been identified and a guide as to the number of cases at each location. Local transmission is highlighted (blue star) as are countries with DCs that contain antibodies reactive with MERS-CoV, viral RNA or infectious virus (camel icon). Correct as of the 20th January, 2015.

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