ADULT INFECTIOUS DISEASES NOTES

10 years later...

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On November 16, 2002, in the city of Foshan in the province of Guangdong (China), a 45-year-old man developed a severe atypical pneumonia and further infected four relatives. This was the first case of severe acute respiratory syndrome (SARS), as demonstrated by epidemiological investigations (1). Almost exactly 10 years later, on November 8, 2012, the first report of a mortal case of acute pneumonia associated with renal failure due to a novel coronavirus in a businesswoman from Bisha, Saudi Arabia, was published (2). In retrospect, we now know that the first confirmed human cases arose in a cluster of 13 individuals with respiratory symptoms in a hospital in Zanqa, Jordan, in April 2012 (3,4).

Middle East respiratory syndrome coronavirus (MERS-CoV) belongs to the Coronaviridae family, a group of large, enveloped, single-stranded RNA viruses. Similar to most RNA viruses, they are known for their genomic plasticity, and infect mammalian and avian hosts. It is the fourth identified beta coronavirus with the ability to infect humans (the others are SARS-CoV, human CoV-HKU1 and human CoV-OC43). It belongs to lineage C, shares similarities with viruses identified in the Pipistrellus species of bats (HKU4 and HKU5) and has been demonstrated to replicate in various bat cell lines (4). Consequently, a bat origin for MERS-CoV has been suggested. However, no clear and repetitive exposure to bats has been reported in epidemiological studies, and the search for an intermediate host has led researchers to identify dromedary camels as potential suspects (5). The identification of MERS-CoV-neutralizing antibodies in camels from Oman and the Canary Islands, where no human case has been reported, raises more questions than answers.

It must be recognized that new information is being reported constantly and that the data presented in the present report may soon be outdated. As of October 18, 2013, 139 laboratory-confirmed cases of MERS-CoV have been reported, including 60 deaths, representing a case fatality rate of 43%. All cases have been directly or indirectly associated with renal failure due to a novel coronavirus in a businesswoman from Bisha, Saudi Arabia, was published (2). As of October 18, 2013, 139 laboratory-confirmed cases of MERS-CoV were circulating within 14 days of onset (5). The incubation period of MERS-CoV was measured using data from a well-defined hospital outbreak in Al-Hasa in Eastern Saudi Arabia, and estimated to be 5.2 days (95% CI 2.2 to 12.4 days) (12). This is similar to SARS-CoV, which has an average incubation period of four days (95% CI 1.8 to 10.6 days) (13). The serial interval time is the period of time between analogous phases of an infectious illness in successive cases of a chain of infection that is spread from person to person. In the same report, this was defined as 7.6 days for MERS-CoV (versus 8.4 days for SARS) (12,14).

Well-described clusters have been published. Despite several close family contacts with index cases, only a small number of secondary cases have been identified (12,15). The reproduction number (R0), defined as the number of cases generated by one infected individual on average in a fully susceptible population, is a very important epidemiological measure. When R0 is <1, the infection will usually die out over time, and when R0 is >1, there is a clear risk of spreading in the population. Breban et al (16) calculated the MERS-CoV R0 to be 0.69 (95% CI 0.5 to 0.92) in the worst-case scenario. Comparatively, they estimated the R0 for SARS during the preparedic stage in Southern Asia to be 0.80 (95% CI 0.54 to 1.13). It is expected that R0 will be updated as more data are reported because it may change seasonally according to school calendars and yearly gatherings, such as the Hajj pilgrimage, and if the virus evolves. Recent molecular data support the hypothesis of multiple introductions to explain the origin of cases linked in the same hospital outbreak (17). These data have a clear impact on R0 estimation, which will probably revolve R0 downward.

At this time, the main mechanism of transmission is not well defined. In some reports, secondarily infected patients were >1 m from the index case, which supports potential airborne transmission (12). For the moment, standard, contact and airborne precautions are recommended by the Centers for Disease Control and Prevention (Georgia, USA) and by Health Canada for health care workers involved in the management of suspected MERS-CoV cases or close contacts of confirmed cases (within 14 days of onset). These recommendations are consistent with those of SARS and were influenced by the high rate of morbidity and mortality in infected patients, unknown modes of transmission, potential human-to-human transmission, and lack of vaccine or chemoprophylaxis (18,19).

Assiri et al (20) recently reported a clinical comparison between patients infected with MERS-CoV and those infected with SARS. It is important to specify that this analysis is preliminary because it was performed on a limited number of subjects (n=47) and, consequently, is subject to change. General data were updated from other sources (Table 1). As with preliminary reports of SARS patients, data from cohorts described initially may strongly differ from larger, later cohorts. With SARS, the initial published cohorts included several health care workers (>50%) who were younger and healthier than the hospital
population. With MERS-CoV, several cases in early reports included patients attending the hemodialysis unit. Ongoing evaluation is required to assess whether chronic renal disease is a true risk factor for the development of MERS-CoV infection.

Although there is an ever-increasing body of evidence being reported, there are many knowledge gaps that need to be addressed (20). The origin and the natural reservoir for MERS-CoV remain obscure. The overall incidence and risk factors for acquisition of symptomatic disease and adverse outcome are not well defined. Our limited knowledge and lack of diagnostic tools challenge our ability to define optimal infection prevention and control procedures. We do not know whether there are any specific therapies beyond supportive treatments that will improve outcome.

Only the future will define whether MERS-CoV will be a limited regional phenomenon or whether a pandemic will ensue. While we cannot be certain of the future of MERS-CoV, we believe that the next decade(s) will inevitably witness the emergence of other novel respiratory viruses that, along with SARS and MERS-CoV, will have a profound influence on the global community.

REFERENCES
