

The Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Singapore

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As most of us would know, the newly emerged coronavirus which has been named the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) appeared first in Jordan in April 2012. It was not diagnosed at the time until a single case was identified in Saudi Arabia¹ (and subsequently confirmed and patented in the Netherlands) and another in the United Kingdom² in a medical tourist from Qatar. The virus was quickly characterised as a betacoronavirus belonging to the *Coronaviridae* family, which was somewhat related to the severe acute respiratory syndrome (SARS) coronavirus. That instantly triggered off alarm bells in particular in countries which were badly affected by the SARS crisis in 2003. The concern was raised higher when human-to-human transmission of MERS-CoV was documented first in the United Kingdom,³ then in Saudi Arabia⁴ and in France.⁵ While the initial clusters were small and limited to close contacts in the family or healthcare setting, the news of a large nosocomial outbreak in the Kingdom of Saudi Arabia at the beginning of this year⁶ caused a great deal of concern internationally. One of us was part of a joint Saudi-World Health Organization (WHO) mission that was sent to the Kingdom to help with the containment plans and protocols for this novel emerging pathogen.

The report of that mission has been published on the website of the WHO and there are several reassuring messages.⁷ The first is that the Saudis are testing widely and have as a result picked up more cases of MERS-CoV than any other country in the region and beyond. To date, there are to our knowledge, no published reports of large scale studies of unexplained respiratory illnesses looking for the presence of MERS-CoV in patients with severe pneumonias who were not travellers or contacts of patients with MERS-CoV. The tests are based on the widely available polymerase chain reaction and the WHO reiterated the recommendation to test individuals with unexplained severe respiratory illness and clusters of healthcare workers with respiratory illness regardless of travel histories. Indeed, it was the retrospective investigation of such a cluster in Jordan that yielded the first few cases of MERS-CoV

infection in humans.⁸

The second major point that emerged from the mission was the importance of infection control. It does appear that standard infection control precautions including contact and droplet precautions were effective in at least limiting if not containing the spread of MERS-CoV in healthcare facilities in Eastern Saudi Arabia.⁶ This is an important message and while controversy continues about the specific nature of personal protective equipment required to protect healthcare workers, patients and visitors from MERS-CoV, basic infection control measures including hand hygiene, prompt recognition and isolation of cases and droplet precautions appear to be effective as they were in the SARS epidemic 10 years ago.

Another reassuring point to note is that although there has been some limited transmission of the virus from infected patients to their close contacts, such as family members, fellow patients, or healthcare workers, there has thus far been no evidence of widespread person-to-person transmission of MERS-CoV.

Some areas of concern that remain include the fact that we do not have to date a reliable serologic test which would allow us to determine the full spectrum and extent of spread of the disease, including the likely presence of asymptomatic seroconverters. We are also no wiser about the origin of the virus and its definitive animal host although it has been found in bats in Africa and Europe⁹ (but interestingly, not widely in bats in the Middle East). There have also been unconfirmed reports of other animal hosts and more data from animals across the globe would be very helpful in understanding the animal reservoir without which it would be difficult to implement definitive source control measures to prevent repeated reintroductions into vulnerable human populations.

As a global city with a significant influx of tourists, including medical tourists, some of whom are from healthcare facilities in the Middle East, Singapore is certainly at risk for the introduction of MERS-CoV within our borders

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and into our healthcare facilities. Another concern is that the international mass gatherings in Saudi Arabia for the Hajj and Umrah pilgrimages may potentially increase the risk of exportation of the virus to all corners of the world,¹⁰ although a small joint surveillance programme in Saudi Arabia and France in 2012 showed no evidence of MERS-CoV carriage in returning pilgrims in France.¹¹

However, unlike with SARS, we are now far more prepared. We have a lot more information about the nature of the virus from published reports from Saudi Arabia and Europe. We are also well connected to a global network of health professionals and international public health organisations, which helps us to keep abreast of rapidly evolving disease situations.

Our national surveillance for the disease has been enhanced, and medical practitioners and healthcare institutions are on the alert for suspect cases. We have a diagnostic test which would allow us to rule in or rule out suspect cases rapidly. We have ramped up our isolation and intensive care unit (ICU) facilities and have backup plans in place should there be a need to further increase these capacities. Apart from measures in the healthcare sector, the Ministry of Health (MOH) has also worked with partner agencies to alert incoming and outgoing travellers to MERS-CoV and the precautionary measures to be undertaken when travelling to, or after returning from, affected areas. Additionally, MOH has worked closely with the Islamic Religious Council of Singapore (MUIS) to provide up-to-date health advisories to Umrah and Hajj pilgrims, which are aligned with travel advice issued to pilgrims by the Saudi government and the WHO.

In a way, our experience with the influenza A (H1N1-2009) pandemic helped a great deal. We rapidly put in place containment strategies and when it became apparent that the disease was less severe than initially feared, and community spread had become established, we stepped down to mitigation approaches that resulted in minimal disruption to the normal functioning of our healthcare system. Fortunately, the H1N1-2009 influenza outbreak was a mild one with no appreciable increase in influenza mortality or morbidity reported from Singapore.¹² Even pregnant women and immunocompromised patients did relatively well thanks to prompt recognition and early isolation and treatment.¹³ With MERS-CoV, the best treatment remains unclear. The numbers are too small right now for any meaningful analysis of the efficacy of the various treatment regimes that have been used. There are protocols that have been circulated among various networks for randomised clinical trials of agents including ribavirin and interferon which could hopefully get ethics approval before the first cases of MERS-CoV appear in many countries. Singapore was involved in one such network which published a

landmark study of the treatment of severe influenza.¹⁴ There is therefore a high likelihood that we will be ready to run high quality clinical trials on therapeutics for the virus, should we ever see MERS-CoV cases here.

One of the most important lessons learned from SARS was the importance of good and effective risk communication and social mobilisation. The WHO has learned these lessons too and has made most of its decisions and recommendations based on the available evidence rather than on fear which seemed to be the basis of some of the travel restrictions that were put in place during SARS. Singapore was very badly affected by some of these measures during SARS, perhaps even more than by the actual disease itself. Hopefully the world has learned its lesson, especially after our experience with the H1N1-2009 pandemic, and a more rational approach to disease control will be in place should MERS-CoV become widespread in more countries. The science is better now and global public health has been strengthened by the WHO's International Health Regulations and numerous collaborative networks. We are quietly confident that should the MERS-CoV reach our shores, we will be able to respond in a measured and evidence-based manner, balancing the need to minimise the spread of the disease against the desire to ensure that there is as little disruption to the lives of the people of Singapore as possible. The men and women who gave their lives to SARS did not die in vain.

REFERENCES

1. 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;367:1814-2.
2. 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.
3. 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.
4. Memish ZA, Zumla AI, Al-Hakeem RF, Al-Rabeeh AA, Stephens GM. Family cluster of Middle East respiratory syndrome coronavirus infections. *N Engl J Med* 2013;368:2487-94.
5. 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.
6. Assiri A, McGeer A, Perl TM, Price CS, Al Rabeeh AA, Cummings DA, et al. Hospital Outbreak of Middle East Respiratory Syndrome Coronavirus. *N Engl J Med* 2013 Jun 19 [Epub ahead of print].
7. Middle East respiratory syndrome coronavirus: Joint Kingdom of Saudi Arabia/WHO mission. Available at: www.emro.who.int/press-releases/2013/corona-virus-who-saudi-arabia-mission.html. Accessed 30 July 2013.
8. 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:S12-8.
9. Annan A, Baldwin HJ, Corman VM, Klose SM, Owusu M, Nkrumah EE, et al. Human betacoronavirus 2c EMC/2012-related viruses in bats, Ghana and Europe. *Emerg Infect Dis* 2013;19:456-9.
10. 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 Jul 17;5.
11. Gautret P, Charrel R, Belhouchat K, Drali T, Benkouiten S, Nougairede A, 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:E315-7.
12. Cutter JL, Ang LW, Lai FYL, Subramony H, Ma S, James L. Outbreak of pandemic influenza A (H1N1-2009) in Singapore, May to September 2009. *Ann Acad Med Singapore* 2010;39:273-10.
13. Lim ML, Chong CY, Tee WS, Lim WY, Chee JJ. Influenza A/H1N1 (2009) infection in pregnancy – an Asian perspective. *BJOG* 2010;117:551-6.
14. South East Asia Infectious Disease Clinical Research Network. Effect of double dose oseltamivir on clinical and virological outcomes in children and adults admitted to hospital with severe influenza: double blind randomised controlled trial. *BMJ* 2013;346:f3039.