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The threat to global health security from emerging and re-emerging respiratory tract infections will be ever present because of the genetic adaptability of microbes, and their ability to resist clinical interventions and public health measures aimed at their elimination. Although much has been learned from previous outbreaks, present surveillance systems have their inherent weaknesses, and recent experiences with MERS-CoV¹⁴ show that pandemic preparedness still faces major political and scientific challenges.¹⁵ An important priority for control of infectious disease is to ensure that scientific and technological advances in molecular diagnostics and bioinformatics are well integrated into public health. More effective and wider partnerships based on equity and best ethical practice, across governments, health care, academia, industry, and with the public, are essential to effectively galvanise economic, political and scientific measures required to develop core capacities, including legislation, national focal points, and pandemic planning to reduce risk of global spread and reduce the burden of respiratory tract infectious diseases. An urgent need exists to establish trusting and effective meaningful collaborations between countries to tackle new emerging microbial threats. This will facilitate early and rapid detection of potential pandemic infectious diseases through public health actions within the framework of the International Health Regulations.¹⁶

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- 1 Zumla A, Yew WW, Hui DS. Emerging respiratory infections in the 21st century. Preface. *Infect Dis Clin North Am* 2010; **24**: 13–16.
- 2 *The Lancet Infectious Diseases* Commission on antibiotic resistance. *Lancet* 2013. **384**: 53–63.
- 3 Fauci AS, Morens DM. The perpetual challenge of infectious diseases. *N Engl J Med* 2012; **366**: 454–61.
- 4 World Bank: World Development report 1993: Investing in health: world development indicators. Oxford University press, Oxford, UK. 1–346. <http://elibrary.worldbank.org/doi/pdf/10.1596/0-1952-0890-0> (accessed Aug 13, 2014).
- 5 Murray CJ, Lopez AD. Measuring the global burden of diseases. *N Engl J Med* 2013; **369**: 448–457.
- 6 Morens DM, Folkers GK, Fauci AS. Emerging infections: a perpetual challenge. *Lancet Infect Dis* 2008; **8**: 710–19.
- 7 Hui DS, Memish ZA, Zumla A. Severe acute respiratory syndrome vs. the Middle East respiratory syndrome. *Curr Opin Pulm Med* 2014; **20**: 233–41.
- 8 Hon KL. Severe respiratory syndromes: travel history matters. *Travel Med Infect Dis* 2013; **11**: 285–87.
- 9 Al-Tawfiq JA, Zumla A, Gautret P, et al. Surveillance for emerging respiratory viruses. *Lancet Infect Dis* 2014; published online Sept 2. [http://dx.doi.org/10.1016/S1473-3099\(14\)70840-0](http://dx.doi.org/10.1016/S1473-3099(14)70840-0).
- 10 McCloskey B, Dar O, Zumla A, Heymann DL. Emerging infectious diseases and pandemic potential: status quo and reducing risk of global spread. *Lancet Infect Dis* 2014; published online Sept 2. [http://dx.doi.org/10.1016/S1473-3099\(14\)70846-1](http://dx.doi.org/10.1016/S1473-3099(14)70846-1).
- 11 Gautret P, Gray GC, Charrel RN, et al. Emerging viral respiratory tract infections—environmental risk factors and transmission. *Lancet Infect Dis* 2014; published online Sept 2. [http://dx.doi.org/10.1016/S1473-3099\(14\)70831-X](http://dx.doi.org/10.1016/S1473-3099(14)70831-X).
- 12 Zumla A, Al-Tawfiq JA, Enne V, et al. Rapid point of care diagnostic tests for viral and bacterial respiratory tract infections—needs, advances, and future prospects. *Lancet Infect Dis* 2014; published online Sept 2. [http://dx.doi.org/10.1016/S1473-3099\(14\)70827-8](http://dx.doi.org/10.1016/S1473-3099(14)70827-8).
- 13 Zumla A, Memish ZA, Maeurer M, et al. Emerging novel and antimicrobial-resistant respiratory tract infections: new drug development and therapeutic options. *Lancet Infect Dis* 2014; published online Sept 2. [http://dx.doi.org/10.1016/S1473-3099\(14\)70828-X](http://dx.doi.org/10.1016/S1473-3099(14)70828-X).
- 14 C Raina MacIntyre. The discrepant epidemiology of Middle East respiratory syndrome coronavirus (MERS-CoV). *Environment Systems and Decisions* 2014; published online July 25. DOI:10.1007/s10669-014-9506-5.
- 15 McNabb SJ, Shaikh AT, Nuzzo JB, Zumla AI, Heymann DL. Triumphs, trials, and tribulations of the global response to MERS coronavirus. *Lancet Respir Med* 2014; **2**: 436–37.
- 16 Gostin LO, Sridhar D. global health and the Law. *N Engl J Med* 2014; **370**: 1732–40.

Case definition and management of patients with MERS coronavirus in Saudi Arabia



Exponential increases in the number of cases of the Middle East respiratory syndrome coronavirus (MERS-CoV) in Saudi Arabia in March, 2014,¹ led to the appointment of Adel Fakeih as acting Minister of Health

on April 21, 2014. He made the control of the MERS outbreak a top priority in the country's health agenda. An advisory council was set up to urgently develop scientific evidence-based plans to control the MERS

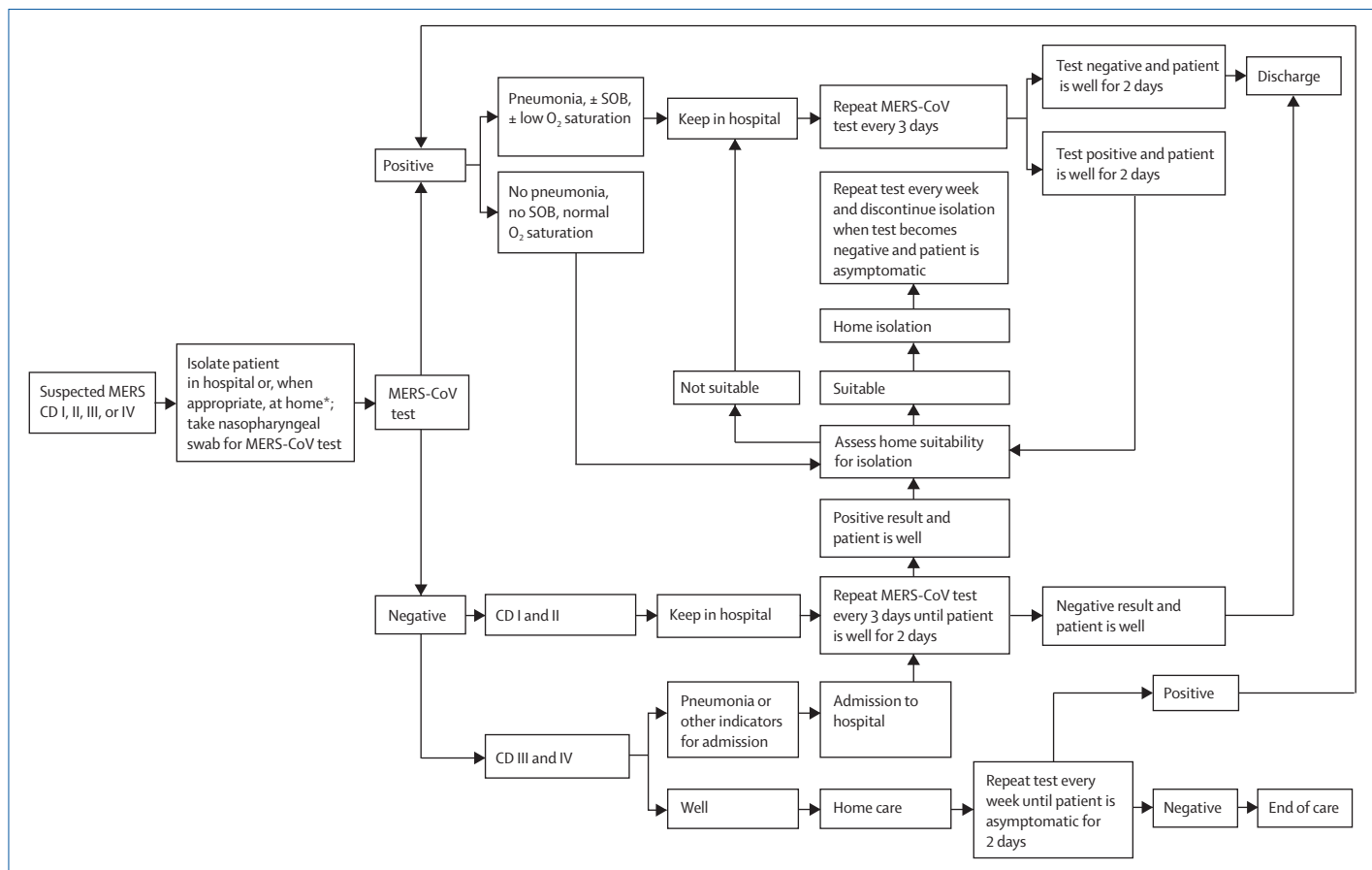


Figure: Management algorithm for patients suspected of MERS coronavirus infection
 CD=case definition. SOB=shortness of breath. *Patients with suspected MERS-CoV infection who do not have shortness of breath, hypoxaemia, or evidence of pneumonia can be cared for and isolated in their home (if suitable).

outbreak and prevent human-to-human and animal-to-human transmission; an appropriate management algorithm, including best-practice guidelines for accurate diagnosis, infection control, intensive care, emergency medicine, and treatment; prioritise research related to the MERS-CoV outbreak such as case-control and cohort studies, seroprevalence studies, and clinical trials; and to effectively monitor outbreak control activities.

A continuously operating command and control centre was established in the minister's office. In addition to the advisory council, nine further platforms were established: interministerial to coordinate efforts between the Ministry of Health (MOH) and other concerned ministries; capacity-building to recruit and mobilise qualified staff to work in hospitals treating patients with MERS-CoV, increase the number of beds in intensive care units,

and provide state-of-the-art machines such as extracorporeal membrane oxygenation to treat patients with respiratory failure refractory to conventional ventilation; public relations to communicate relevant information to the public, health-care workers, and local and international media; clinical operation to coordinate management of patients and transfers between hospitals; public health to collect data related to patients and their contacts; data analysis to enter and analyse data; epidemiological to provide consultations on data analysis and interpretation; laboratory to ensure fast and reliable diagnostic testing; and, infection control to oversee infection control practice and staff training activities.

A MERS referral hospital run by well trained staff was designated in Riyadh, Jeddah, and Dammam to receive and manage all patients infected with MERS-CoV. The MOH enforced strict infection prevention

and control measures in health-care facilities including King Fahd General Hospital, Jeddah, where substantial health-care-associated transmission of MERS-CoV between patients and staff happened, mainly due to overcrowding of patients by about four to five times its maximum capacity in the emergency room. Overflow patients in the emergency room were relocated to other hospitals in Jeddah to reduce the risk of further transmission of the virus. Intensive education and training of staff about essential infection control measures were done to abort transmission of MERS-CoV in health-care settings. The MOH has also invited experts from WHO and the US Centers for Disease Control and Prevention (CDC) to assess the outbreak. The advisory council, in collaboration with the CDC, has initiated case-control studies to identify risk factors for acquisition of MERS-CoV infection in primary and secondary cases.

As new clinical information became available, a revision of the MERS-CoV case definition seemed appropriate.² The new case definition (appendix) was developed based on reported health-care-associated MERS-CoV pneumonia (added as category 2 in the new case definition) and non-respiratory characteristics of patients with confirmed infection who first presented with acute febrile dengue-like illness with body aches, leucopenia, and thrombocytopenia (added as category 3). The new case definition added a fourth category for contacts of people with MERS-CoV who present with not only lower respiratory tract but also isolated upper respiratory tract features. This definition classified the status of patients into three categories of suspect, probable, or confirmed infection. The new MERS-CoV case definition was revised and approved by the advisory council after seeking external CDC expert opinion.

An algorithm for MERS-CoV case management was developed (figure). According to this algorithm, patients with confirmed MERS-CoV who have no evidence of pneumonia or who recover from pneumonia but remain positive for MERS-CoV, can be isolated at home after careful assessment of the home situation and suitability for isolation by the treating physician, highly trained social workers, or other health-care professionals by telephone or home visits. The CDC has released recommendations on how to assess the home situation and the advice to be given to patients on home isolation and his or her caregivers and household members,³ and also released guidance for the public, clinicians, and public-health authorities in the USA on control of the MERS-CoV infection.⁴

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I declare no competing interests. I thank Adel Fakeih for his moral and logistic support, Esam I Azhar, Basem Alraddadi, Abdulhakeem Althaqafi, Alimuddin Zumla, John Watson, John Jernigan, Ali Khan, Tim Uyeki, and Ray Arthur for their critical review of the case definition and the MERS-CoV case management algorithm, and Fadwa Mushtaq for her secretarial assistance.

- 1 World Health Organization. WHO experts probe Middle-Eastern respiratory syndrome coronavirus (MERS-CoV) in Jeddah, Saudi Arabia. <http://www.who.int/features/2014/saudi-arabia-coronavirus/en/> (accessed May 24, 2014).
- 2 World Health Organization. WHO Revised interim case definition for reporting to WHO—Middle East respiratory syndrome coronavirus (MERS-CoV): as of July 3, 2013. http://www.who.int/csr/disease/coronavirus_infections/case_definition/en/ (accessed May 24, 2014).
- 3 US Centers for Disease Control and prevention. Interim infection prevention and control recommendations for hospitalized patients with Middle East respiratory syndrome coronavirus (MERS-CoV). <http://www.cdc.gov/coronavirus/mers/infection-prevention-control.html> (accessed May 24, 2014).
- 4 Bialek SR, Allen D, Alvarado-Ramy F, 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**: 431–36.

See Online for appendix

Regulatory obstacles affecting ecological studies in the ICU

Health-care-associated bacterial infections are an important cause of morbidity and mortality in critically ill patients, especially patients needing mechanical ventilation. Decolonisation with topical antibiotics, such as selective digestive tract decontamination (SDD) or selective oropharyngeal decontamination (SOD), eradicates potentially pathogenic bacteria, preventing

ventilator-associated pneumonia and bacteraemia. In two Dutch studies,^{1,2} SDD and SOD reduced mortality, intensive-care unit (ICU) length of stay, ICU-acquired bacteraemia, and carriage with antibiotic-resistant bacteria. Accordingly, both measures were deemed cost effective.³ Only studies that assessed the unit-wide implementation of SDD or SOD provide evidence of a