

# Zero Transmission of Middle East Respiratory Syndrome: Lessons Learned From Thailand

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New emerging pathogens can quickly become a global health threat in this era. A number of Middle East respiratory syndrome (MERS) outbreaks have been linked to healthcare facilities. The healthcare-associated transmission of Middle East respiratory syndrome coronavirus (MERS-CoV) has been attributed to overcrowding, delayed diagnosis, and the breakdown of infection control systems. Strict infection control precautions and a well-prepared hospital system may have contributed to no nosocomial transmission occurring during the treatment of MERS-CoV infections imported to Thailand. The recent outbreaks of MERS and previous emerging infections provide valuable lessons to be learned. Continuous vigilance and strengthening of infection control systems will shape the capacity to prevent and control MERS-CoV or new emerging disease transmission.

**Keywords.** Middle East respiratory syndrome; MERS-CoV; transmission; lessons; Thailand.

The Middle East respiratory syndrome coronavirus (MERS-CoV) has recently become a serious global threat and has had momentous impact on the public health of affected countries. A number of nosocomial outbreaks of MERS-CoV have been reported [1–4]. The strategy to prevent and control healthcare-associated transmission is a crucial way to counter the threat of MERS-CoV. To date, Thailand has had 3 laboratory-confirmed cases of MERS-CoV infection [5–7]. All of them were hospitalized at our institute, the Bamrasnaradura Infectious Diseases Institute (BIDI), Department of Disease Control, Ministry of Public Health. No secondary cases of healthcare-associated MERS-CoV infection were reported to the World Health Organization (WHO), including transmission to healthcare workers (HCWs) [8, 9]. This article discusses the lessons we have learned from the MERS outbreaks and our response to MERS.

## THE WORLD HAS CHANGED: BE READY AND WELL-PREPARED

We are currently living in a remarkable era. Globalization makes the world a smaller place. International travel and ecological and human behavioral changes are considered to be factors responsible for the emergence of infectious diseases [10]. The ease of world travel has added layers of complexity to the containment of emerging infectious diseases (EIDs) within their areas of origin [11]. Severe acute respiratory syndrome (SARS) and the

recent 2009 H1N1 influenza are examples of an epidemic and a pandemic, respectively, that resulted from convenient international air travel. A MERS outbreak that occurred in South Korea was also begun by a single imported case [12, 13].

MERS-CoV was first reported in 2012 and still circulates in the Arabian Peninsula [14]. Thailand has almost 30 million tourists each year [15], including medical tourists from Middle Eastern countries. In addition, the pilgrimage to Mecca is common among Thai Muslims. For these reasons, BIDI has put itself on alert for a MERS threat since 2013. Hospital preparedness for a MERS response plan has been developed including clinical triage, using proper infrastructure to prevent transmission, strengthening the infection prevention and control system, accelerating laboratory capacity for early detection, and periodic education and training of HCWs on case management along with personal protective equipment, as well as environmental cleaning. Algorithms describing actions in response to a case or suspected case of MERS-CoV infection were developed. Simulation drill exercises have been conducted annually. Business continuity planning has also been created to ensure adequate supplies and effective response when the real situation occurs.

Continuous vigilance for EIDs is important in the globalized world. The hospital system should be prepared and functioning well before the arrival of any cases.

## INFECTION PREVENTION AND CONTROL INFRASTRUCTURES MUST BE DEVELOPED DESPITE LIMITED RESOURCES

Inadequate response capacity in a single country can endanger the public health security of national populations and in the rest of the world [16]. Although the development of healthcare

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capacities for the control of transmission of emerging diseases in low-resource settings is limited, it is not impossible. To enable the development of infrastructure prepared for EIDs, response in these areas needs support from public health authorities.

In 2003, our institute admitted a patient with laboratory-confirmed SARS. We were alerted to prepare to hospitalize the patient shortly prior to his arrival. Due to the lack of an airborne isolation room at that time, we had to modify a private room to be a special isolation unit. Personal protective equipment including N95 respirators was provided to HCWs who were involved with the patient as much as possible. With strict adherence to infection control measures, no secondary SARS transmission occurred in the institute [17]. However, SARS reminded us that our response system needed improvement. BIDI and the Ministry of Public Health of Thailand realized that a standard airborne isolation unit is essential in preparedness for future outbreaks of new EIDs. Development of the hospital infection control system was also accelerated. After this wake-up call, an airborne isolation unit with 5 negative pressure rooms was built with support from the Thai government. This unit is currently an important part of the environmental control for EIDs, including the MERS response of our institute.

In outbreak preparedness in resource-limited settings, investment in health systems is necessary, and the government must act on this issue. Lack of proper isolation room facilities can lead to failure in infection control and prevention in health-care settings. An airborne isolation unit is costly but necessary. However, the support of local health authorities is still limited in some developing countries. The development of infrastructures may need some contribution from the international community. Sufficiency of well-trained healthcare personnel, equipment, and supplies is also vital. The Ebola outbreak in western African countries may be another good lesson to learn in keeping a local outbreak from becoming a global threat.

### **EARLY RECOGNITION AND TIMELY DIAGNOSIS ARE CRUCIAL**

Effective administrative controls play the most important role in infection prevention and control strategies to prevent nosocomial MERS-CoV transmission. A single unrecognized case can spark a major MERS outbreak in South Korea [12, 18]. Thirteen HCWs who became infected with MERS-CoV after caring for a source case patient in Abu Dhabi were found to have been exposed to the MERS patient before the diagnosis of the patient [19]. These reports emphasize the importance of early identification and isolation of suspected MERS cases. Administrative controls are the first priority to set up prevention of MERS-CoV transmission. Control measures should be developed, including clinical triage, flow of the patient from the first point of contact until their placement in an isolation room, and training on the use of protective equipment.

In our institute, we have designed the entry point to the hospital as the triage area for patients with acute respiratory illness

(ARI). The HCWs at a screening desk use a screening template and have been trained on proper infection control practices. If a patient with ARI comes from the Middle East or a MERS outbreak country, they are brought to a designated pathway and receive an examination in the negative pressure isolation rooms with a rate of ventilation of 12 air changes per hour. Any suspected patient is placed separately until MERS-CoV infection can be ruled out. All specimens for MERS-CoV testing are carefully obtained and placed for transportation in leak-proof specimen bags. The clinical specimen examination is performed in a biosafety level 2 laboratory. All personnel who are involved with specimens are trained and adhere to infection control practices. The availability of the polymerase chain reaction assay for MERS-CoV testing is necessary; the utility of the test is not only for prompt diagnosis, but also for helping to determine the duration of the isolation of the patient.

In EID preparedness, hospitals must implement an appropriate screening system. The syndromic approach with a travel history gathered is very helpful for early detection and isolation. Rapid laboratory diagnostic testing of the emerging pathogen should be enhanced and integrated into the preparedness system.

### **INFECTION CONTROL WORKS**

Because there is still no definitive treatment against MERS-CoV infection, and no vaccine currently exists, infection control measures are vital to prevent the spreading of MERS-CoV in the healthcare setting. Human-to-human transmission has been well-established including transmission to HCWs [1, 2, 12, 20]. Two reports of MERS-CoV outbreaks have demonstrated that those cases were associated with exposure to healthcare facilities [21, 22]. Poor ventilation and suboptimal adherence to infection control standards were documented to have resulted in healthcare-associated transmission [23, 24].

Recommendations for the management of hospitalized patients with MERS-CoV infection from the WHO and the US Centers for Disease Control and Prevention (CDC) have some differences. Implementation of standard and contact precautions is recommended from both guidelines. However, the CDC includes airborne transmission precautions whereas the WHO has recommended the use of surgical masks when caring for MERS patients and particulate respirators for aerosol-generating procedures (Table 1) [25, 26]. Although spread of MERS-CoV is more likely to occur via droplets and contact [28], the CDC recommendations are based on an expert review that contends that maximum precautions are required due to the high case fatality rate associated with MERS [29]. This discordance in recommendations may lead to confusion among healthcare providers. Nonetheless, we may never be able to know what kind of protective gear against MERS-CoV is the best in practice because conducting any randomized control trial would be unethical [30]. BIDI has opted for implementation of the maximum precautions

**Table 1. Comparison of Recommendations of Personal Protective Equipment and Patient Placement to Healthcare Workers Caring for Hospitalized Patients With Middle East Respiratory Syndrome Coronavirus Infection**

Recommendation	CDC [25]	WHO [26]	ECDC [27]
Patient placement	Negative-pressure single rooms (airborne isolation room)	Adequately ventilated single rooms or airborne precaution rooms if possible	- Negative-pressure single rooms - If negative-pressure room is not available, a single room with en suite facilities can be used
Respiratory protection	At least as protective as a fit-tested NIOSH-certified disposable N95 filtering face-piece respirator	- Medical mask when in close contact - Particulate respirators (N95 or equivalent) when performing aerosol-generating procedures	- If airborne exposure cannot be ruled out, use filters with a specification of FFP2 or FFP3 - If only droplet exposure is expected and respirators are not available, a surgical or medical procedure mask can be considered
Eye protection	Recommended	Recommended	Recommended
Gowns	Recommended (disposable gown)	Recommended (long-sleeved gown)	Recommended
Gloves	Recommended	Recommended	Recommended

Abbreviations: CDC, Centers for Disease Control and Prevention; ECDC, European Centre for Disease Prevention and Control; FFP, filtering facepieces; NIOSH, National Institute for Occupational Safety and Health; WHO, World Health Organization.

stipulated in CDC guidance due to the gaps of present knowledge about the potential for airborne transmission of the novel coronavirus. In our institute, rapid isolation was done upon receiving laboratory-confirmed cases of MERS-CoV infection. We placed the patients in an airborne infection isolation room, and precautions to prevent airborne and contact transmission were strictly implemented. HCWs who were working with any MERS patient and/or their body fluids were protected by using an N95 respirator that had been fit tested, a gown, disposable gloves, eye protection, and a disposable cap. Hand hygiene was performed before entering and after leaving patients' rooms or after examining their specimens. We identified no transmission from any of our MERS patients to any of our HCWs [9].

**Table 2. Comparison of the Hospital Preparedness of Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome Coronavirus—Bamrasnaradura Infectious Diseases Institute, Thailand**

Characteristic	SARS	MERS
First reported case [28, 35]	November 2002	September 2012
Pathogen [28, 35]	SARS coronavirus	MERS coronavirus
Transmitting pathway [28, 35]	Respiratory droplets	Respiratory droplets
Airborne transmission [28, 35]	Possible	Uncertain
First case in Thailand [36]	March 2003	June 2015
Total confirmed cases in Thailand [36]	1	3
Total confirmed cases in BIDI	1	3
Hospital preparedness and response plan	Not developed	Developed
Triage system	Not well established	Well established
No. of airborne isolation rooms	None	5
PPE including N95 respirators and hand hygiene supplies	Adequate	Adequate
Molecular diagnostics in the institute	Not available	Available
Environmental cleaning procedures	Implemented	Implemented
Infectious waste management	Implemented	Implemented
Business continuity plan	Not developed	Developed

Abbreviations: BIDI, Bamrasnaradura Infectious Diseases Institute; MERS, Middle East respiratory syndrome; PPE, personal protective equipment; SARS, severe acute respiratory syndrome.

In a time of evolving knowledge on the transmission of MERS-CoV, an infection control committee must choose the optimal control measures for their healthcare institute. A clear-cut policy and protocols from the administrative level will result in adequate supplies, confidence among personnel, and effective transmission prevention while caring for the MERS-CoV-infected patient. The reported nosocomial transmissions of MERS warn us to realize the basics of infection control. The infection control system in healthcare facilities should thus be further strengthened.

### ENVIRONMENTAL CONTAMINATION SHOULD NOT BE NEGLECTED

The modes of human-to-human MERS-CoV spread are incompletely understood [31]. Spread was assumed largely to occur via large droplets and contact; however, the possibility of airborne or fomite transmission has not been excluded [28]. During the SARS outbreak of 2002–2004, a report from Taiwan found SARS coronavirus RNA from inanimate objects. Environmental contamination may have led to infection among HCWs without contact with SARS patients [32]. In a MERS outbreak in South Korea, a number of those infected by the index MERS case of South Korea resided in the same hospital but in different wards or on different floors, making fomite transmission possible [33]. A recent study demonstrates that MERS-CoV remained viable for up to 48 hours under low temperature and low humidity conditions [34]. We have thus placed importance on environmental factors during the hospitalization of MERS patients. Environmental cleaning has been included in the MERS preparedness protocol of our institute. Room floors were wiped with sodium hypochlorite solution daily. Other surfaces were cleaned with 70% alcohol-based disinfectants twice daily.

The duration of viral shedding and environmental contamination in MERS-CoV requires further investigation. Strict infection control precaution is the key to prevent nosocomial spread of emerging diseases. However, the possibility of environmental and fomite contamination should not be discounted.

## CONCLUSIONS

The world is currently vulnerable to the threat of EIDs. New pathogens will continue to emerge and challenge. Continued vigilance is necessary for early case detection. Development of healthcare capacities and strengthening of infection control systems will be the keys to prevent disease transmission and to protect HCWs as well as others.

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