## Reply to Oh

To the Editor—We thank Dr Oh for his interest in our work and for his thoughtful observations.

Although the mode of human-to-human transmission of Middle East

respiratory syndrome coronavirus (MERS-CoV) is not completely understood, this virus has frequently caused healthcare-associated outbreaks at hospitals in Saudi Arabia and Korea [1–3]. Since the first MERS-CoV outbreak in South Korea on 20 May 2015, a total of 186 confirmed cases of MERS-CoV infection have been reported in 16 hospitals, which is the largest outbreak outside the Middle East. In about 44% of the cases, patients were exposed in hospitals, with 32.8% being caregivers and 13.4% being healthcare personnel [4]. Although exported cases of MERS-CoV infection have been reported in 18 countries [3], in most cases only a few additional healthcare workers were infected, unlike the outbreak in South Korea. Recently, the World Health Organization and coinvestigators of the Ministry of Health of South Korea reported that the initial spread of MERS-CoV was expanded in several hospital clusters due to overcrowding in emergency rooms and medical wards, as well as poor infection control measures in hospitals during the early period of the outbreak [5, 6]. Widespread contamination of the hospital environment was suspected as a cause of the rapid transmission, although direct evidence is limited. In our study, MERS-CoV was detected in specimens taken from various hospital environments, especially in patient isolation rooms as well as in the respiratory specimens from MERS-CoV–infected patients [7]. A concern was raised by Dr Oh with regard to our data showing that although the MERS-CoV was detected and isolated from a respiratory specimen from patient 3 on day 25 after disease onset, we failed to detect or isolate the virus on day 27 [7]. Dr Oh commented that such a rapid disappearance of MERS-CoV viruses in respiratory specimens is unusual, considering that most virus-positive specimens contained $>10^7$ copies/mL and virus isolation was unsuccessful in later stages of infection based on a previous Saudi Arabian study [8]. In this study, Muth et al reported that the proportion of successful isolation was 66.7% at RNA concentrations $>10^7$ copies/mL, but only 5.9% below this value [8]. In our study, real-time polymerase chain reaction (PCR) was not used to calculate the viral RNA concentration, so the virus copy number could not be calculated in the specimens; however, we did directly inoculate the specimens into cells within 1 hour, without storage at −80°C, to improve the virus isolation efficacy. Actually, Muth et al indicated that 5.9% of viruses were still recovered from the specimens $<10^7$ copies/mL [8]. Furthermore, in our study, we defined virus isolation as "only cultures positive for MERS-CoV by both RT-PCR and sequencing" during the 12 days of cell culture with cytopathic effects monitoring (see Materials and Methods) [7]. Recently we have finished full-length genomic sequencing and are preparing a separate manuscript containing these data. In brief, we used cytopathogenic effect-positive cell culture samples of each specimen and the viruses were isolated from the environmental and late stage of MERS-CoV–infected patients' specimens. Regarding patient 3, she was a 76-year-old woman with diabetes mellitus and left femur fracture [7]. These conditions may have attenuated the patient's immune status and influenced the virus shedding period. Therefore, we hypothesized that the attenuated immune status of the patient and the prompt inoculation of respiratory specimens into proper cell lines possibly contributed to prolonged period of virus isolation in our study.

## Notes

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