Acknowledgments

References

1. Ma C, An Z, Hao L, Cairns KL, Zhang Y, Ma J, et al. Progress toward measles elimination in the People's Republic of China, 2000–2009. J Infect Dis. 2011;204(Suppl 1):S447–54. http://dx.doi.org/10.1093/infdis/jir103
2. Ma C, Su QR, Hao LX, Wen N, Fan CX, Cao L, et al. Measles epidemiology characteristics and progress toward measles elimination in China, 2012–2013. Chinese Journal of Vaccines and Immunization. 2014;20:193–209.
3. National Health and Family Planning Commission of the People's Republic of China [cited 2015 Jul 30]. http://www.nhfpc.gov.cn/jkj/s3578/201502/847c041a3bac4c3e84 4f17309be0cabd.shtml
4. Ma C, He LX, Su QR, Ma J, Zhang Y, Cao L, et al. Measles epidemiology and progress toward measles elimination in China, 2011. Chinese Journal of Vaccines and Immunization. 2012;18:193–9.
5. Ma C, Li F, Zheng X, Zhang H, Duan M, Yang Y, et al. Measles vaccine cover-age estimates in an outbreak three years after the nation-wide campaign in China: implications for measles elimination, 2013. BMC Infect Dis. 2015;15:23. http://dx.doi.org/10.1186/s12879-015-0752-z
6. World Health Organization. Global measles and rubella strategic plan 2012–2020 [cited 2015 Jul 22]. http://www.who.int/immunization/newsroom/Measles_Rubella_StrategicPlan_2012_2020.pdf
7. World Health Organization. Global vaccine action plan 2011–2020 [cited 2015 Sept 9]. http://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/
8. McCarthy M. Measles outbreak linked to Disney theme parks reaches five states and Mexico. BMJ. 2015;350:h436. http://dx.doi.org/10.1136/bmj.h436
9. Najjar Z, Hope K, Clark P, Nguyen O, Rosewell A, Conaty S. Sustained outbreak of measles in New South Wales, 2012: risks for measles elimination in Australia. Western Pac Surveill Response J. 2014;5:14–20. http://dx.doi.org/10.5365/wpsar.2013.4.4.001
10. Hagmann SHF, Christenson JC. Measles and the risk posed by international travelers at the time of elimination or post-elimination. Travel Med Infect Dis. 2015;13:1–2. http://dx.doi.org/10.1016/j.tmaid.2014.12.017

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Objective Determination of End of MERS Outbreak, South Korea, 2015

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To the Editor: After not finding any additional cases of Middle East respiratory syndrome (MERS) for several weeks in South Korea, in July 2015, the South Korean government and the World Health Organization (WHO) discussed the appropriate time to declare the end of the outbreak in July 2015 (*1*). This declaration would enable allocation of human resources to healthcare facilities to return to normal and would help restore international travel to the country. A widely acknowledged criteria of WHO to determine the end of an epidemic has been twice the length of the incubation period since the most recently diagnosed case (*2*). For MERS, the longest incubation period is 14 days. Thus, adopting 28 days as the waiting period, and counting days from diagnosis of the most recent case on July 4, 2015, the earliest date the South Korean government could have declared the end of outbreak was August 2 if it adhered to WHO criteria (*1*). However, to emphasize safety to the nation and to international travelers at an earlier time, the South Korean government originally decided to announce the end of the MERS outbreak on July 27, the date the last quarantined MERS patient was released from movement restriction. Because we are concerned about the validity of strict adherence to the WHO criteria, we objectively calculated the probability of observing additional cases at a given time and compared that probability with the WHO criteria.

To clearly define the end of the outbreak, we excluded reintroduction of imported cases and cases of MERS coronavirus infection resulting from a zoonotic reservoir. We defined the end of the outbreak as the end of continued chains of transmission. The probability of observing additional cases was derived by using the serial interval; that is, the time from illness onset in the primary case-patient to illness onset in a secondary case-patient, and the transmissibility of MERS (online Technical Appendix, http://wwwnc.cdc.gov/EID/article/22/1/15-1383-Techapp1.pdf). Both of these epidemiologic variables were estimated by using case data in South Korea (*3*,*4*). As practiced in the determination of the length of quarantine (*5*), the end of outbreak can be declared if that probability is <5%, a threshold value.

Our analysis showed that the first date on which the posterior median probability decreased to <5% was July 21 (Figure, panel A). The first date on which the posterior median decreased to 1% was July 23. Compared with August 2 as calculated from the WHO criteria, the end of the outbreak could have been declared 11 and 9 days earlier, respectively. Because the choice of 5% or 1% as the threshold probability is arbitrary (as practiced in determining the p value in any hypothesis testing) and because of the need to account for parameter uncertainties, we also measured the sensitivity of the first date on which the South Korean government could declare the end of the outbreak to a variety of threshold values (Figure, panel B). Examination of the probability of observing additional cases in the range of 0.5% to 10% indicated the end of the outbreak could have been declared from July 21 to July 24 (i.e., 9–12 days earlier than August 2).

Our proposed method does not account for missing undiagnosed or mild cases, and underdiagnosis would considerably extend the time to declare the end of an outbreak (and thus the proposed method is not directly applicable to, for example, Ebola virus disease in West Africa, for which we are currently developing an alternative method). All possible contact with diagnosed case-patients in the late phase of the MERS outbreak in South Korea were traced (6,7); thus, we believe it was appropriate to ignore ascertainment bias in this specific setting. Although our proposed approach is simplistic, adopting the WHO criteria could have added >1 week to the elevated state of tension, and the use of the incubation period distribution would be fully supported only when the exact times of infection were known for exposed potential contacts. Although it is a posteriori reasoning, the original decision made by the South Korean government at an earlier date was ironically supported by our proposed method. Rather than adopting the use of "twice" and the "incubation period," which has not been theoretically justified, an objective decision of the end of an outbreak should explicitly rest on the risk of observing at least 1 more case on or after a specified date.

Figure. Estimated probability of observing additional cases of Middle East respiratory syndrome coronavirus infection, South Korea, 2015. A) Estimated probability of observing additional cases on each calendar date, given that no illness onset has been observed by the specified date. Circles represent posterior median values; whiskers extend to upper and lower 95% credible intervals. Horizontal dashed line represents 5%, a threshold level. Vertical line indicates August 2, 2015, on which the end of the outbreak might be declared if World Health Organization criteria were followed. B) Calendar date to declare the end of outbreak for different threshold probabilities and percentile points of posterior distribution. Horizontal axis corresponds to the probability of observing additional cases. Vertical axis shows the date of declaration which is calculated as 1 day plus the date at which the probability of observing additional cases lowered the specified threshold probability.

References

1. The Chosunilbo. Official end to MERS outbreak expected next month [cited 2015 Jul 18]. http://english.chosun.com/site/data/html_dir/2015/07/13/2015071301669.html
2. World Health Organization. Criteria for declaring the end of the Ebola outbreak in Guinea, Liberia or Sierra Leone [cited 2015 Jul 18]. http://www.who.int/csr/disease/ebola/declaration-ebola-end/en/
3. Cowling BJ, Park M, Fang VJ, Wu P, Leung GM, Wu JT. Preliminary epidemiological assessment of MERS-CoV outbreak in South Korea, May to June 2015. Euro Surveill. 2015;20:7–13.
4. Nishiura H, Miyamatsu Y, Chowell G, Saitoh M. Assessing the risk of observing multiple generations of Middle East respiratory syndrome (MERS) cases given an imported case. Euro Surveill. 2015;20:pii:21181.
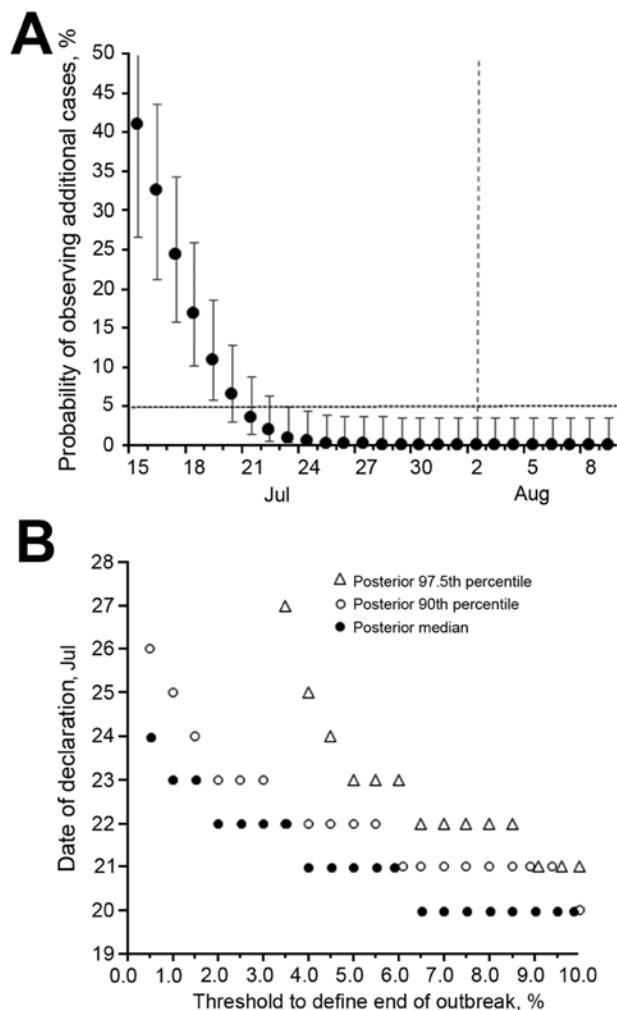
5. Nishiura H. Determination of the appropriate quarantine period following smallpox exposure: an objective approach using the incubation period distribution. Int J Hyg Environ Health. 2009;212:97–104. http://dx.doi.org/10.1016/j.ijheh.2007.10.003

6. Mizumoto K, Endo A, Chowell G, Miyamatsu Y, Saitoh M, Nishiura H. Real-time characterization of risks of death associated with the Middle East respiratory syndrome (MERS) in the Republic of Korea, 2015. BMC Med. 2015;13:228. http://dx.doi.org/10.1186/s12916-015-0468-3

7. Mizumoto K, Saitoh M, Chowell G, Miyamatsu Y, Nishiura H. Estimating the risk of Middle East respiratory syndrome (MERS) death during the course of the outbreak in the Republic of Korea, 2015. Int J Infect Dis. 2015;39:7–9. http://dx.doi.org/10.1016/j.ijid.2015.08.005

Surveillance for Coronaviruses in Bats, Lebanon and Egypt, 2013–2015

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To the Editor: Coronaviruses (CoVs) in bats are genetically diverse, and evidence suggests they are ancestors of Middle East respiratory virus CoV (MERS-CoV), severe acute respiratory syndrome CoV, and human CoVs 229E and NL63 (*1–4*). We tested several bat species in Lebanon and Egypt to understand the diversity of bat CoVs there.

Samples were collected during February 2013–April 2015. A total of 821 bats were captured live in their caves; sampled (oral swab, rectal swab, serum); and released, except for 72 bats that died or were euthanized upon capture. Lungs and livers of euthanized bats were harvested and homogenized. Caves were in proximity to human-inhabited area but not in proximity to camels.

In Egypt, we sampled 3 bat species (online Technical Appendix 1, http://wwwnc.cdc.gov/EID/article/22/1/15-1397-Techapp1.pdf). Eighty-two Egyptian tomb bats (*Taphozous perforatus*) tested negative for CoV. We also sampled 31 desert pipistrelle bats (*Pipistrellus deserti*) and detected an HKU9-like betacoronavirus (b-CoV) in the liver of 1 bat (prevalence 3.2%). From 257 specimens from Egyptian fruit bats (*Rousettus aegyptiacus*), we detected b-CoV in 18 samples from 18 different bats (prevalence 7%). A murine hepatitis virus–like CoV was detected in the lung of 1 bat. HKU9-like viruses were detected in 5 oral, 2 lung, 5 liver, and 5 rectal samples. Overall, 5.1% of the bats tested positive.

In Lebanon, we sampled 4 bat species. Four *Rhinolophus hipposideros* bats and 6 *Miniopterus schribersii* bats tested negative. One of 3 *Rhinolophus ferrumequinum* bats sampled was positive. We sampled 438 *Rousettus aegyptiacus* bats from 10 different locations and detected HKU9-like viruses in 24 rectal swab specimens (prevalence 5.5%). Overall, 5.5% of the bats tested positive.

A subset of the samples (696 samples: 516 from Egypt, 180 from Lebanon) were tested for MERS-CoV by using the specific upstream of E quantitative reverse transcription PCR; all tested negative. Serum samples from 814 bats tested negative for MERS-CoV antibodies.

Phylogenetic analysis revealed that the RNA-dependent RNA polymerase (*RdRp*) genes of viruses detected in *R. aegyptiacus* bats in Lebanon and Egypt were closely related to the *RdRp* gene of HKU9 CoV (Figure). Our viruses clustered in 3 groups: A, B, and C. Group A viruses were closely related to HKU9-10-2 virus and included viruses from Egypt. Group B included viruses from both countries and were closely related to HKU9-1 and HKU9-4 viruses. Group C also included viruses from both countries that were related to HKU9-3 and HKU9-5 viruses. The *RdRp* fragments sequenced had <90% nt similarity among groups A, B, and C. Within-group nucleotide similarity was >90%, and amino acid variability was 2%–4% (online Technical Appendix 2, http://wwwnc.cdc.gov/EID/article/22/1/15-1397-Techapp2.xlsx). The phylogenetic tree of the N gene also showed proximity of the viruses detected in our study to HKU9 viruses (online Technical Appendix 1). Viruses from Lebanon clustered together as did the viruses from Egypt.

Most of the positive samples were detected in Egyptian fruit bats. These are cave-dwelling species that inhabit regions of East Africa, Egypt, the Eastern Mediterranean, Cyprus, and Turkey (*5*). This species is a reservoir for several viruses, including Marburg, Kasokero, and Sosuga