
Southeast Asian Foot-and-Mouth Disease Viruses in Eastern Asia

**Nick J. Knowles, JiJun He, Youjun Shang,
Jemma Wadsworth, Begoña Valdazo-González,
Hiroyuki Onosato, Katsuhiko Fukai,
Kazuki Morioka, Kazuo Yoshida, In-Soo Cho,
Su-Mi Kim, Jong-Hyeon Park, Kwang-Nyeong Lee,
Geraldine Luk, Vladimir Borisov,
Alexey Scherbakov, Anna Timina,
Dashzeveg Bold, Tung Nguyen, David J. Paton,
Jef M. Hammond, Xiangtao Liu,
and Donald P. King**

Foot-and-mouth disease (FMD) outbreaks recently affected 2 countries (Japan and South Korea) in eastern Asia that were free of FMD without vaccination. Analysis of viral protein 1 nucleotide sequences indicated that FMD serotype A and O viruses that caused these outbreaks originated in mainland Southeast Asia to which these viruses are endemic.

Foot-and-mouth disease (FMD) is a highly contagious transboundary disease that affects domesticated animals and wildlife in Africa, Asia and parts of South America. Outbreaks of FMD in these disease-endemic regions continuously threaten livestock industries in countries that are free of FMD (with or without vaccination). The causative agent, FMD virus (FMDV), is a small, nonenveloped, picornavirus (genus *Aphthovirus*) that has 7 serotypes. This virus is easily transmitted by movement of infected livestock or animal products, contaminated persons, objects, and aerosols.

Author affiliations: Institute for Animal Health, Pirbright, UK (N.J. Knowles, J. Wadsworth, B. Valdazo-González, D.J. Paton, J.M. Hammond, D.P. King); Lanzhou Veterinary Research Institute, Gansu, China (J. He, Y. Shang, X. Liu); National Institute of Animal Health, Tokyo, Japan (H. Onosato, K. Fukai, K. Morioka, K. Yoshida); National Veterinary Research and Quarantine Service, Gyeonggi Do, South Korea (I.-S. Cho, S.-M. Kim, J.-H. Park, K.-N. Lee); Tai Lung Veterinary Laboratory, Hong Kong, China (G. Luk); Federal Centre for Animal Health, Vladimir, Russia (V. Borisov, A. Scherbakov, A. Timina); State Central Veterinary Laboratory, Ulaanbaatar, Mongolia (D. Bold); and National Centre for Veterinary Diagnostics, Hanoi, Vietnam (T. Nguyen)

DOI: <http://dx.doi.org/10.3201/eid1803.110908>

FMDV serotypes O, A, and Asia 1 are endemic to countries in mainland Southeast Asia (Cambodia, Laos, peninsula Malaysia, Myanmar, Thailand, and Vietnam) where regular outbreaks of FMD have been reported (1,2). Viral protein 1 (VP1) nucleotide sequence data are widely used for phylogenetic analyses (2,3) and have been used to characterize different FMDV lineages in Southeast Asia and track transboundary movements of the virus. Studies have shown close epidemiologic links between field outbreaks in countries in Southeast Asia (4–6).

During 2009–2010, the geographic range of 2 FMDV lineages endemic to Southeast Asia (serotypes A and O) expanded into eastern Asia and caused outbreaks in 6 countries in the region. Although outbreaks of FMD caused by serotype Asia 1 have been recently reported (2005–2009) (7), there have been no reported outbreaks caused by serotype A in eastern Asia since 1973.

Furthermore, serotype O strains from Southeast Asia have not been detected in countries in eastern Asia since 2004 when samples were sent to the Federal Centre for Animal Health (Vladimir, Russia) from Mongolia (GenBank accession no. JQ070317) (online Appendix Figure, wwwnc.cdc.gov/EID/article/18/3/11-0908-FA1.htm). In 1999–2002, extensive outbreaks caused by the PanAsia strain of serotype O were reported in Japan, South Korea, China, Taiwan, and Russia (8–10). The purpose of this study was to determine the origins of recent FMD outbreaks in eastern Asia.

The Study

FMDVs characterized by antigen ELISA as serotype A were isolated from samples collected from FMD field outbreaks in Hubei Province, China, and in Gyeonggi-do Province, South Korea. Before FMD cases appeared in China in January 2009, serotype A infections had not occurred in that country since 1964 (11), and until serotype A appeared in South Korea in January 2010, that country had been free of FMD without vaccination (for all FMDV serotypes) since 2002.

Phylogenetic analysis (12) showed that VP1 sequences obtained at Lanzhou Veterinary Research Institute (Gansu, China), the National Veterinary Research and Quarantine Service (Gyeonggi Do, South Korea), and the Institute of Animal Health (Pirbright, UK) were genetically similar to sequences obtained during 2008–2009 in Southeast Asia (Thailand and Malaysia), which belonged to the A/ASIA/Sea-97 lineage (online Appendix Figure, panel A) (6). Additional FMD outbreaks caused by the same serotype that affected mainly cattle were reported in 6 provinces in China (Shanghai, Jiangsu, Guangxi, Guizhou, Shandong, and Xinjiang) in 2009; in Beijing in January 2010 (online Appendix Figure, panel A); and in Gyeonggi-do Province, South Korea, in January–March 2010 (6 cases).

Similar outbreaks occurred during 2010 that were caused by an FMD lineage of serotype O that is endemic to Southeast Asia (online Appendix Figure, panel B). As of 2011, outbreaks caused by this serotype continue to occur across a wide region (online Appendix Figure, panel B) and have affected China (including Hong Kong), South Korea, Japan, Mongolia, Russia, and North Korea.

Many FMD outbreaks ($n = 292$) were reported in Miyazaki Prefecture, Japan (April–June 2010). Fewer outbreaks ($n = 18$) were reported in China (in Guangdong, Gansu, Shaanxi, Jiangxi, and Guizhou Provinces; and in the autonomous regions of Ningxia, Xinjiang, Uyghur, and Tibet). Three outbreaks were reported in Hong Kong (February–March 2010); thirteen in South Korea (April 2010); nine, including 1 ongoing, in Mongolia (April 2010), and 2 in Russia (July and August 2010).

Japan had been free of FMD (without vaccination) since 2000, and Mongolia and Russia had not reported FMD outbreaks caused by serotype O since 2003 and 2004, respectively. These outbreaks have affected domesticated pigs, cattle, and small ruminants, and have spread to (gazelles, as represented by isolate O/MOG/9/2010) in Domod Province, Mongolia. A new increase in cases of FMD caused by serotype O has recently been reported in South Korea during December 2010 (>100 outbreaks) and in North Korea, and this serotype continues to pose a threat to livestock industries in the region.

VPI sequences generated in the United Kingdom, China, Japan, South Korea, and Russia and those available in GenBank were analyzed by using MEGA5 (12). Analysis showed that FMDVs causing serotype O outbreaks form 2 genetic clusters related to viruses within the Southeast Asia topotype (O/SEA/Mya-98 lineage), which are usually restricted to mainland Southeast Asia (online Appendix Figure, panel B). There was $>97.3\%$ sequence relationship between sequences for FMDVs from China and those from outbreaks in Hong Kong, South Korea, and Japan.

Sequences for viruses collected in Mongolia were distinct (differing by 11.9% nt identity) and more closely related to other viruses collected during 2009 and 2010 in Southeast Asia (Thailand, Vietnam and Malaysia) (6). The 2 outbreaks in Russia (July and August 2010), which were caused by viruses from 2 of these sublineages, were located close to the borders with China and Mongolia and separated by ≈ 250 km. These outbreaks represent 2 distinct introductions of FMD into Russia.

Conclusions

Sequence data implicate regions of mainland Southeast Asia to which FMD is endemic as the source of serotype O and A FMDVs that have caused recent outbreaks in eastern Asia. These events are not unprecedented; a

previous instance of spread of FMDV from Southeast Asia into China (Yunnan Province) in 2006 involved the Asia 1 serotype. Furthermore, FMDV O/SEA topotype (Mya-98) was also detected in China in 2003 and in Mongolia in 2004. These findings provide evidence for the porous nature of borders between mainland Southeast Asia and neighboring countries and highlight the continued threat posed by FMD as a transboundary disease in the region. The extent to which viruses have spread into countries that were previously free of FMD (without vaccination) is a cause for concern.

Although VPI sequence data can be used to characterize the viruses that are causing these outbreaks, further coordination and sharing of sequence data are now urgently required to formally identify transboundary transmission links between affected countries in the region. Complete FMDV genome sequence analyses from these field cases and additional material may provide a suitable approach to reconstruct high-resolution transmission trees and connect clusters of outbreaks (13,14).

This report describes recent incursion of FMDVs from Southeast Asia into eastern Asia. In vitro vaccine matching data (from the Institute of Animal Health) indicate that currently available vaccine strains (A/May/97 and O/Manisa) should protect against representative isolates of these 2 serotypes. However, close monitoring of antigenicity and of the spread of these lineages from Southeast Asia is essential to ensure that risks for further and continued outbreaks can be mitigated.

Acknowledgments

We thank researchers in Southeast Asia for providing data and samples, and Wilai Linchongsabongkoch and colleagues at the Regional Reference Laboratory in Pakchong, Thailand for assistance. Nucleotide alignments used for phylogenetic analyses are available by request from the corresponding author.

This study was supported by the Department for Environment, Food and Rural Affairs (SE2939), the Food and Agriculture Organization (PR 41764), and the Network of Excellence for Epizootic Disease Diagnosis and Control IC4.7 projects (contract no. FOOD-CT-2006-016236).

Mr Knowles is a molecular virologist at the Institute for Animal Health in Pirbright, UK. His research interests are the molecular epidemiology and evolution of picornaviruses of animals, particularly foot-and-mouth disease virus.

References

- Gleeson LJ. A review of the status of foot-and-mouth disease in South-East Asia and approaches to control and eradication. *Rev Sci Tech.* 2002;21:465–75.

2. Rweyemamu M, Roeder P, Mackay D, Sumption K, Brownlie J, Le-forban Y, et al. Epidemiological pattern of foot-and-mouth disease worldwide. *Transbound Emerg Dis.* 2008;55:57–72. <http://dx.doi.org/10.1111/j.1865-1682.2007.01013.x>
3. Knowles NJ, Samuel AR. Molecular epidemiology of foot-and-mouth disease virus. *Virus Res.* 2003;91:65–80. [http://dx.doi.org/10.1016/S0168-1702\(02\)00260-5](http://dx.doi.org/10.1016/S0168-1702(02)00260-5)
4. Le VP, Nguyen T, Lee K-N, Ko Y-J, Lee H-S, Nguyen VC, et al. Molecular characterization of serotype A foot-and-mouth disease virus circulating in Vietnam in 2009. *Vet Microbiol.* 2010;144:58–66. <http://dx.doi.org/10.1016/j.vetmic.2009.12.033>
5. Le VP, Nguyen T, Park J-H, Kim S-M, Ko Y-J, Lee H-S, et al. Heterogeneity and genetic variations of serotypes O and Asia 1 foot and mouth disease viruses isolated in Vietnam. *Vet Microbiol.* 2010;145:220–9. <http://dx.doi.org/10.1016/j.vetmic.2010.04.005>
6. Abdul-Hamid NF, Hussein NM, Wadsworth J, Radford AD, Knowles NJ, King DP. Phylogeography of foot-and-mouth disease virus types O and A in Malaysia and surrounding countries. *Infect Genet Evol.* 2011;11:320–8. <http://dx.doi.org/10.1016/j.meegid.2010.11.003>
7. Valarcher J-F, Knowles NJ, Zakharov V, Scherbakov A, Zhang Z, Shang Y-J, et al. Multiple origins of foot-and-mouth virus serotype Asia 1 outbreaks, 2003–2007. *Emerg Infect Dis.* 2009;15:1046–51. <http://dx.doi.org/10.3201/eid1507.081621>
8. Knowles NJ, Samuel AR, Davies PR, Midgley RJ, Valarcher JF. Pandemic strains of foot-and-mouth disease virus serotype O. *Emerg Infect Dis.* 2005;11:1887–93.
9. Sakamoto K, Kanno T, Yamakawa M, Yoshida K, Yamazoe R, Murakami Y. Isolation of foot-and-mouth disease virus from Japanese black cattle in Miyazaki Prefecture, Japan 2000. *J Vet Med Sci.* 2002;64:91–4. <http://dx.doi.org/10.1292/jvms.64.91>
10. Wee S-H, Park J-Y, Joo Y-S, Lee J-H, An S-H. Control measures implemented during the 2002 foot-and-mouth disease outbreak in the Republic of Korea. *Vet Rec.* 2004;154:598–600. <http://dx.doi.org/10.1136/vr.154.19.598>
11. Liu Z, Zhao Q, Liu W, Zhou P, Zhu C, Chang H, et al. Analysis of VP1-coding nucleotide sequences of six strains of foot-and-mouth disease virus type A. *Chin J Virol.* 1998;14:60–7.
12. Tamura K, Peterson D, Peterson N, Stecher G, Nei M, Kumar S. MEGA5: molecular evolutionary genetics analysis using maximum likelihood, evolutionary distance, and maximum parsimony Methods. *Mol Biol Evol.* 2011;28:2731–9. <http://dx.doi.org/10.1093/molbev/msr121>
13. Cottam EM, Haydon DT, Paton DJ, Gloster J, Wilesmith JW, Ferris NP, et al. Molecular epidemiology of foot-and-mouth disease virus outbreak in the United Kingdom. *J Virol.* 2006;80:11274–82. <http://dx.doi.org/10.1128/JVI.01236-06>
14. Cottam EM, Wadsworth J, Shaw AE, Rowlands RJ, Goatley L, Maan S, et al. Transmission pathways of foot-and-mouth disease virus in the United Kingdom in 2007. *PLoS Pathog.* 2008;4:e1000050. <http://dx.doi.org/10.1371/journal.ppat.1000050>

Address for correspondence: Donald P. King, Institute for Animal Health, Ash Rd, Pirbright, Surrey, GU24 0NF, UK; email: donald.king@iah.ac.uk

The opinions expressed by authors contributing to this journal do not necessarily reflect the opinions of the Centers for Disease Control and Prevention or the institutions with which the authors are affiliated.



Centers for Disease
Control and Prevention
National Center for Emerging and
Zoonotic Infectious Diseases



Yellow Fever Vaccine: Information for Health Care Professionals Advising Travelers

CDC's Travelers' Health Branch has created this online course for healthcare providers who want to learn more about yellow fever disease and yellow fever vaccine.

Lesson 1: Yellow Fever: History, Epidemiology, and Vaccine Information

Lesson 2: The Pre-travel Consultation and Best Practices for Yellow Fever Vaccine Providers and Clinics

COURSE OBJECTIVES:

- Understand yellow fever history and epidemiology
- Learn about the recommendations and requirements for yellow fever vaccination
- Identify the precautions and contraindications to yellow fever vaccination
- Recognize the common and rare adverse events associated with yellow fever vaccination
- Gain proficiency in conducting a thorough pre-travel consultation
- Learn best practices for yellow fever vaccine providers and clinics

CONTINUING EDUCATION (CE): Credit will be available for physicians, nurses, pharmacists, and health educators who complete both lessons of the course.

COST: Free!

TIME: Approximately 2 hours

HOW TO GET STARTED: Visit www.cdc.gov/travel to register for the course