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<THE TOPIC OF THIS MONTH>

Middle East Respiratory Syndrome (MERS), as of November 2015

Middle East Respiratory Syndrome (MERS) is an acute respiratory infectious disease caused by MERS coronavirus (MERS-CoV) that was first detected in Saudi Arabia in 2012. MERS-CoV is classified in the family *Coronaviridae*, genus β -coronavirus, which includes Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) that appeared in China in 2003 (see p. 236 of this issue).

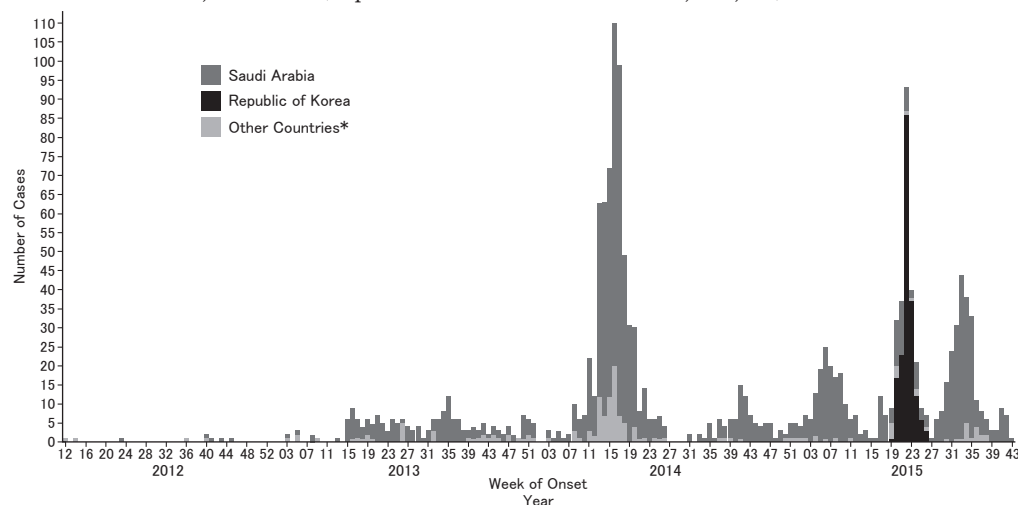
MERS-CoV is transmitted principally via droplet or contact. The incubation period is 2-14 days (median 5 days). Clinical manifestation is variable, ranging from mild upper respiratory infection to severe lower respiratory infection such as pneumonia, gastrointestinal syndromes such as diarrhea, to multiple organ failure. Asymptomatic infection is known. In severe cases, pneumonia exacerbates about 1 week after disease onset, which is accompanied by acute respiratory distress syndrome. The exacerbation may be followed by acute respiratory and/or multiple organ failure. The case fatality ratio among reported cases has been 20-40%. There are no specific therapeutics or vaccines, although they are currently under development.

Since September 2012, Ministry of Health, Labour and Welfare (MHLW) has been requesting the bureau of hygiene of prefectural governments to provide information on patients suspected of the new coronavirus infection. In July 2014, concerned by the increasing number of MERS-CoV patients in the Middle East and importations of MERS-CoV in various countries after April 2014, MHLW designated MERS as a “designated infectious disease” under the Infectious Diseases Control Law and a quarantinable infectious disease under the Quarantine Act. Accordingly, MHLW developed a legal framework for the quarantine and treatment of MERS patients. With further amendments to the Infectious Diseases Control Law in November 2014, MERS-CoV was classified as a Category II infectious disease (21 January 2015) (see p. 242 of this issue). Notification criteria are found in <http://www.nih.go.jp/niid/images/iasr/36/430/de4301.pdf>.

Reservoir of MERS-CoV

Dromedary camels are considered as the most likely reservoir of MERS-CoV, mainly because (i) a fatal case reported from Saudi Arabia in November 2013 had close contact with a MERS-CoV-infected camel, and (ii) a sero-prevalence study conducted in Saudi Arabia indicated that people who had contact with camels had higher anti-MERS-CoV antibody levels. In Middle East,

Figure. Epicurve of confirmed global cases of MERS-CoV in Republic of Korea, China, Saudi Arabia and other countries, 2012-2015 (Reported to WHO as of 13 Nov 2015, n=1,618)



*Other countries: Algeria, Austria, China, Egypt, France, Germany, Greece, Iran, Italy, Jordan, Kuwait, Lebanon, Malaysia, Netherlands, Oman, Philippines, Qatar, Thailand, Tunisia, Turkey, United Arab Emirates, United Kingdom, United States of America, Yemen

Source: <http://www.who.int/emergencies/mers-cov/en/>

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Table. Number of confirmed MERS-CoV cases, by reporting country, 2012-2015 (n=1,616 as of 13 October 2015)

Middle East	No.cases	Europe and Americas	No.cases	Asia	No.cases	Africa	No.cases
Saudi Arabia*	1,255	United Kingdom**	4	Republic of Korea**	185	Tunisia**	3
United Arab Emirates*	81	Germany	3	Philippines	3	Algeria	2
Jordan*	35	France**	2	China	1	Egypt	1
Qatar*	13	Netherlands	2	Malaysia	1		
Oman*	6	Austria	1	Thailand	1		
Iran*	6	Greece	1				
Kuwait*	4	Italy	1				
Lebanon	1	Turkey	1				
Yemen	1	United States of America	2				

Source: ECDC Rapid Risk Assessment on MERS-CoV, 21st update, 21 October 2015.

*cases with unknown exposure reported.

**person-to-person transmission from imported index case(s) reported.

dromedary camels are closely related to the daily life of the local population and are important not only as a source of meat but also for tourism and amusement (see p. 234 of this issue).

A survey of camels living in Japan indicated that none of the examined camels had MERS-CoV antibody or genetic material detected (see p. 238 of this issue).

Epidemiological situation of MERS

There were 1,618 laboratory-confirmed MERS-CoV cases reported from 26 countries to the World Health Organization (WHO) from 2012 to 13 November 2015, among whom 579 were fatal (case fatality ratio 36%) (Figure). More than 70% of the reported cases were from Saudi Arabia (Table). History of contact with camels was unknown for most of the cases. Person-to-person transmission was observed in several nosocomial outbreaks (see p. 233 of this issue).

Outside of Saudi Arabia, Republic of Korea (ROK) reported the largest number of MERS-CoV cases. In the ROK, majority of the transmissions was nosocomial, following a male index case who returned from the Middle East. Between May and July 2015, 186 cases were reported from 16 hospitals. The age of patients ranged from 16 to 87 years (median 55 years). Thirty-seven patients died (case fatality proportion 20%), among whom 33 (89%) were either elderly or had underlying disease, such as malignancy, heart disease, respiratory disease, renal disease, diabetes, or immunodeficiency. A total 39 cases (21% of the total patients) were medical workers but none of them developed fatal outcomes (see p. 235 of this issue).

Person-to-person transmission

Risk of person-to-person transmission of MERS-CoV in case of an importation to a non-endemic country was assessed by a mathematical model using the data of 36 events reported to WHO. The assessment suggested that secondary transmission was absent in most of the importation events, and the spreading potential of MERS-CoV was found to be modest, although the risk of an event with multiple generations as seen in ROK should be kept always in mind (see p. 244 of this issue).

Laboratory diagnosis of MERS-CoV (see p. 239 of this issue)

For laboratory diagnosis, detection of the viral genome(s) by real-time RT-PCR is used. On account of less virus materials in the upper respiratory tract, the lower respiratory tract specimens, such as sputa, tracheal aspirate, or bronchoalveolar lavage fluid, should be used. According to the WHO's criteria, detection of at least 2 different viral genomic regions is required for confirmatory diagnosis.

In Japan, prefectural and municipal public health institutes (PHIs), quarantine stations and the National Institute of Infectious Diseases (NIID) are prepared to conduct laboratory diagnosis. NIID has distributed the necessary diagnostic materials (e.g. upE primers, probes, positive control specimens) to PHIs and quarantine stations, and has also recently developed an RT-LAMP method that detects nucleocapsid protein region of MERS-CoV within 30 minutes.

Prevention and treatment

Contact with dromedary camels in MERS-CoV endemic countries should be avoided. Information on MERS-CoV, such as endemic countries and regions, notification criteria, response measures in case of MERS-CoV importation, is available on the MHLW home page [<http://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou/kekakaku-kansenshou19/mers.html> (in Japanese)]. NIID continuously assesses MERS risk in Japan using the best available epidemiological and virological information. The assessment is updated in a timely manner, according to the epidemiological situation abroad [<http://www.nih.go.jp/niid/ja/diseases/alphabet/mers.html> (in Japanese)].

For aspects regarding MERS treatment, a study group, "Investigation on clinical intervention of MERS and other emerging and re-emerging infections", was established in 2015 so as to collect information useful for treating MERS and to share the obtained information widely in Japan (see p. 241 of this issue).

The MERS outbreak in ROK reminded us of the importance of preparedness for infectious disease outbreaks, careful information collection of travel history of febrile patients, rapid contact investigation of suspected cases, and risk communication. It is important to ensure that these measures are well implemented in Japan.

The statistics in this report are based on 1) the data concerning patients and laboratory findings obtained by the National Epidemiological Surveillance of Infectious Diseases undertaken in compliance with the Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infections, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

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