

Middle East respiratory syndrome (MERS)

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The severe acute respiratory syndrome (SARS) pandemic that occurred in 2002–2003 was caused by a coronavirus (SARS-CoV). The name coronavirus (Latin *corona*, meaning crown or a halo appearance) comes from the shape of the virus when it is observed using an electron microscope. Coronaviruses typically infect mammals and birds. Only a handful of coronaviruses cause disease in humans, with the most publicized being the SARS-CoV. The SARS-CoV caused a contagious and sometimes fatal pneumonia that spread throughout the world after its first appearance in China in November 2002. There have been no known cases of SARS since 2004. However, in 2012, another new human coronavirus emerged in Saudi Arabia. This new coronavirus is responsible for a viral disease known as Middle East respiratory syndrome (MERS).

Reporting of a new human virus

In September 2012, Ali Mohamed Zaki, a virologist at the Dr. Soliman Fakeeh Hospital in Jeddah, Saudi Arabia, announced the discovery of a new human virus on ProMED-mail (an online disease reporting system). He isolated the virus from a sample of sputum (mucus coughed up from a patient's lungs) taken from a 60-year-old male patient who died in June 2012 from atypical pneumonia and kidney failure. The term “atypical” is applied when diagnostic tests for known expected pathogens are negative. After isolating the virus, Zaki shipped the genetic material (RNA) of the virus to Ron Fouchier, a virologist at the National Influenza Center and Department of Virology, Erasmus Medical Center, located in Rotterdam, the Netherlands, for identification and sequencing.

Laboratory investigation

Fouchier's research team focuses on the identification and characterization of newly discovered viruses, including the human metapneumovirus, new human coronaviruses [such as the SARS-CoV and a human coronavirus isolated from hospitalized Dutch children (hCoV-NL)], and a new influenza A virus (H16N3) isolated from black-headed gulls found in urban city parks in the Netherlands. Asking for Fouchier's expertise was a logical action for Zaki to take. Fouchier's team confirmed that Zaki's isolated virus was a new human coronavirus.

Public awareness of a new virus threat

Zaki's ProMED-mail report caught the attention of doctors in a London hospital who were puzzled by the case of a 49-year-old man from Qatar suffering from atypical pneumonia. Eight days prior to Zaki's initial post, the Qatari man had been airlifted to the London hospital. The patient's symptoms began while he was in Qatar, but he had

visited Saudi Arabia in August 2012. While trying to solve the Qatari man's case, a physician and a scientist independently noticed the ProMED-mail announcement of the newly discovered virus. Immediately, they decided to test for the new virus and subsequently determined that the man had been infected with a human coronavirus. Within a day, the viral genome was sequenced and confirmed to be nearly identical to the new corona-virus discovered by Zaki.

Zaki's post ignited a global response and alert. By 2012, laboratories around the world had been equipped with the means to diagnose new cases of severe respiratory illnesses. Therefore, the world was much more prepared than it had been in 2002. When the SARS outbreak occurred in 2002, the outbreak came first and the SARS-CoV was discovered later. In 2012, the reverse situation occurred. The novel coronavirus was discovered first, and virologists and health-care workers watched and waited for any possible epidemic.

Epidemiology of MERS

As of May 2014, 571 confirmed cases from 18 different countries, including 171 deaths (34%), had been reported to the World Health Organization (WHO). The initial cases originated in Jordan, Qatar, Saudi Arabia, and the United Arab Emirates. Therefore, the new coronavirus was named the Middle East respiratory syndrome coronavirus (MERS-CoV). The average age of the laboratory-confirmed cases was 60 years. Forty-two (21%) of the cases were health-care workers (**Fig. 1**). Despite this evidence of person-to-person transmission, the number of contacts infected by persons with laboratory-confirmed infections has been very low. The WHO was confident enough in the global response to MERS that no travel restrictions were imposed on pilgrims traveling to Saudi Arabia for the Hajj, which begins during mid-October of each year. The Hajj is one of the largest mass gatherings of Muslim people in the world (**Fig. 2**).

Investigations have continued to search for an animal reservoir of the MERS-CoV. The MERS outbreak was different from the SARS outbreak, which was associated with live-animal marketplaces in China. So far, researchers have found that the MERS-CoV could replicate in various bat cell lines. In addition, seven teams of researchers have collaborated to collect blood samples from camels (**Fig. 3**), goats, sheep, and cattle in the Middle East (Oman), Spain, the Netherlands, and Chile. They discovered that 100% (50 of 50) of the blood samples from camels in Oman and 14% (15 of 105) of the blood samples from Spanish camels contained neutralizing antibodies against the MERS-CoV, indicating infection with or exposure to the new virus. Blood samples from European sheep, goats, and cattle did not contain antibodies. Additional studies have found antibodies against the MERS-CoV in camels in Egypt, Jordan, Saudi Arabia, and the Canary Islands. These results suggest that the MERS-CoV or a related virus has infected the camel populations, making them a possible animal reservoir of the virus. Of the 203 human cases of MERS, 7 had confirmed contact with camels.

A more recent study on archived camel blood samples originally collected from 1992 to 2010 in Saudi Arabia has determined that the MERS coronaviruses have been circulating in camels countrywide since at least 1992. The research team also screened blood samples from sheep and goats, but found no evidence of MERS-CoV infections

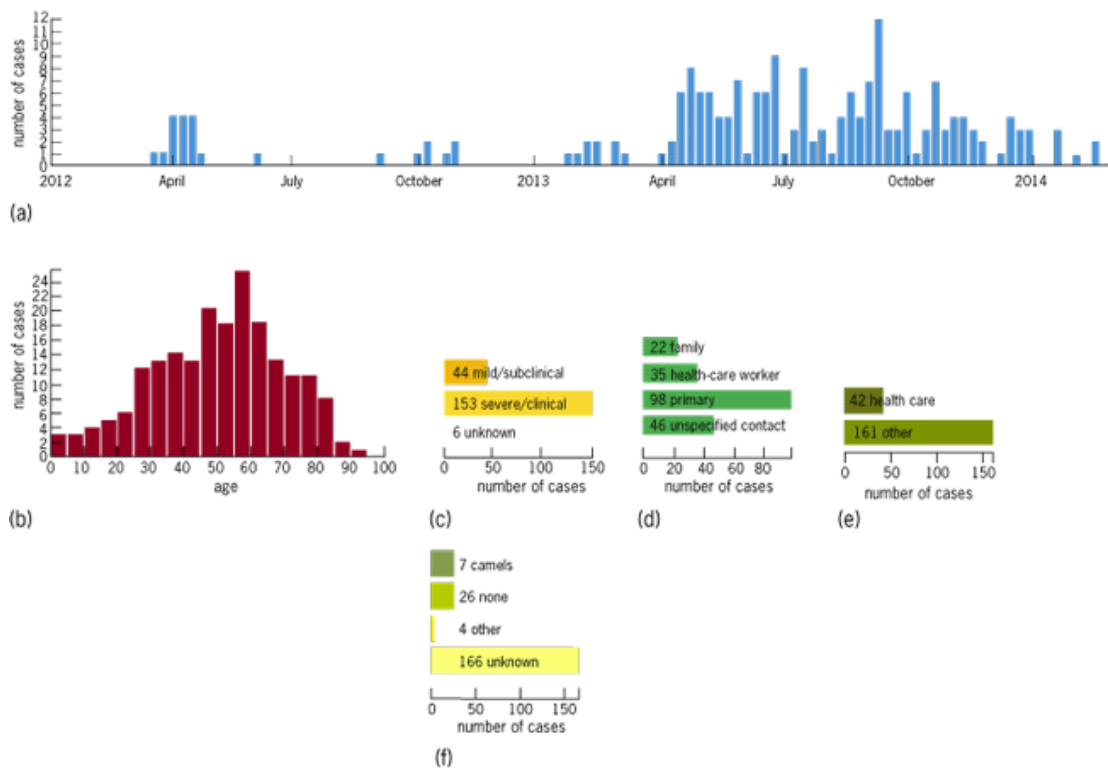


Fig. 1 Epidemiology of the MERS epidemic. (a) Timeline of human MERS cases: January 2012 to February 2014. (b) Age of human cases. (c) Cases categorized by severity of illness. (d) Cases categorized by contact with other sick individuals. (e) Cases categorized by occupation. (f) Cases categorized by contact with animals. (Adapted from *Epidemic: Molecular Epidemiology and Evolution of Viral Pathogens—Coronaviruses*; Andrew Rambaut, Institute of Evolutionary Biology, University of Edinburgh; http://epidemic.bio.ed.ac.uk/coronavirus_background)

in these animals. It is not known whether human infections with the MERS-CoV occurred before 2012 because diagnostic tests were not yet available. The only way to answer this question would be to screen archived samples of human blood to determine when a cross-species zoonotic transmission from camels to humans occurred.

Controversy over the rights to the MERS-CoV

The growth of the MERS epidemic has been slow, but it has not been without controversy. When Zaki provided the coronavirus (which was isolated in the laboratory in Saudi Arabia) to Fouchier for testing, he handed over the sovereign and intellectual property rights to the first diagnostic tests or treatments based on the viral sequencing results to the Erasmus Medical Center in the Netherlands. The Erasmus Medical Center thus had control over requests by researchers to access samples of the virus through material transfer agreements (MTAs) related to patent applications. This created tensions among Zaki, the Saudi Ministry of Health authorities, and other researchers. The hospital authorities terminated Zaki's contract, and he left to work as a microbiologist in Cairo, Egypt. Dutch researchers have fulfilled the MTA requests by other laboratories, but they have placed certain



Fig. 2 The Hajj is an Islamic pilgrimage to Mecca that has been going on for centuries. It is the largest gathering of Muslim people in the world every year. This photograph depicts people praying at al-Masjid al-Haram, the holiest site of Islam, during the Hajj in 1889. Today, the crowds are much larger, posing an even greater risk for human-to-human transmission of infectious diseases. (Image courtesy of the Library of Congress; <http://www.loc.gov/pictures/item/2013646214/>)

restrictions on experiments with and applications of the new coronavirus. Unfortunately, this controversy has led to conflicts of political and commercial interests that may hamper the global community in its quest to develop a suitable vaccine or treatment.

Outlook

Regardless of the legal controversy involving the MERS-CoV, the main goal of scientists has been to stop the spread of the MERS illness. So far, the disease has been confined to areas of the Arabian Peninsula. A few travel-associated cases occurred in Europe and the United States. Most recently, two health-care workers who traveled to Indiana (April 2014) and Florida (May 2014) from Saudi Arabia became ill. A health-care worker taking care of the patient with MERS in the Florida hospital also became ill. Coordinated efforts were in place to identify



Fig. 3 A camel relaxing. The MERS-CoV is posited to be a zoonosis (a disease transmitted from animals to humans). Recent studies suggest that contact with camels may play a role in the transmission of the MERS-CoV. (Image courtesy of Alex Langmuir, Centers for Disease Control and Prevention, Atlanta, GA)

contacts and prevent the spread of MERS. After the hospital worker in Florida became ill, the WHO held an emergency meeting on MERS to discuss public health response efforts.

See also: CAMEL; CLINICAL MICROBIOLOGY; DISEASE ECOLOGY; EPIDEMIC; EPIDEMIOLOGY; INFECTIOUS DISEASE; RESPIRATORY SYSTEM; RESPIRATORY SYSTEM DISORDERS; VIRUS; VIRUS CLASSIFICATION; ZOONOSES.

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Keywords

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Additional Readings

CDC: Middle East Respiratory Syndrome (MERS)

Epidemic: Molecular Epidemiology and Evolution of Viral Pathogens—Coronaviruses

Middle East Respiratory Syndrome Coronavirus (MERS-CoV)