Middle East Respiratory Syndrome (MERS-CoV)

Epidemiology on the ground identifies and tracks a new respiratory virus.

Last year, the infectious disease and public health communities learned of a new severe acute respiratory infection in Saudi Arabia. The stunningly rapid identification of the causative organism, the development of a diagnostic assay, online and ahead-of-print publishing, and heightened global surveillance efforts have made it possible to track the slow emergence of this new, often deadly infection.

In September 2012, a post on ProMED-mail reported that a novel human coronavirus had been isolated from the sputum of a 60-year-old Saudi Arabian man with pneumonia. \(^1\) (ProMED-mail, found at www.promedmail.org, is a free, Internet-based global reporting system from the International Society for Infectious Diseases that rapidly disseminates information on outbreaks of infectious disease and toxin exposures.) The man died from acute respiratory distress syndrome and renal failure in June 2012. \(^2\)

A pan-coronavirus assay of postmortem lung tissue was positive. (Coronaviruses, named for the crown-like projections on their surfaces, are among the viruses that cause the common cold.) The virus was forwarded to a research lab in Rotterdam, the Netherlands, where it was further identified as a new human coronavirus closely related to two bat coronaviruses. \(^2\) This disease would later be named Middle East respiratory syndrome (MERS), and the organism would be named MERS-CoV.

Also in September 2012, a previously healthy 49-year-old man from Qatar (just east of Saudi Arabia) was hospitalized with severe respiratory symptoms and soon airlifted to a London ICU. With no diagnosis yet established, and because there were similarities between the Qatar case and the one described in ProMED-mail, the Qatari patient was tested for coronavirus. The pan-coronavirus assay was positive. The United Kingdom’s Health Protection Agency then contacted the virologists in Rotterdam, who subsequently confirmed a 99.5% match between the viruses of the two patients. \(^3\)

Remarkably, within a month, two real-time reverse-transcription–polymerase chain reaction assays for the novel coronavirus were devised. \(^4\) A test was essential not only for the confirmation of suspected cases, but to permit researchers to analyze the natural course of the infection—the body fluids into which the virus sheds, the duration and peak of viral shedding (indicating likely transmission periods), and the body’s response to treatment. In addition, asymptomatic contacts could now be tested, possibly yielding epidemiologic clues about how these infections spread.

When an emerging infection is first recognized, clinicians and epidemiologists focus on several key questions:

- Are there other cases?
- What is the clinical spectrum of illness?
- Where did the organism come from? What is its reservoir?
**CASE FINDING**

Because a case definition is essential to case finding, the World Health Organization (WHO) quickly developed one, drawing on the international experience with severe acute respiratory syndrome (SARS) in 2002 and 2003. SARS, too, was caused by a previously unknown coronavirus, and SARS and the new virus are the only coronaviruses known to cause severe disease in humans.

An estimate of the incubation period—the time from infection to symptoms—helps to shape a case definition. The usual SARS incubation period is up to 10 days; with little else yet to go on, the same incubation period was proposed for MERS.

Case definitions are generally refined as more clinical and epidemiologic information becomes available, and that has been the case with MERS-CoV infection as well. (See Table 1 for current Centers for Disease Control and Prevention [CDC] definitions.)

- How is infection transmitted?
- Is there human-to-human spread?
- What infection control measures might stop transmission?

Initially, a direct link to confirmed cases or to countries where there have been confirmed cases was an integral part of the MERS case definition. However, the types of exposures that could lead to infection with this virus remain unclear. Under the current WHO definition, MERS should be considered a possible diagnosis in any clusters of undiagnosed severe acute respiratory disease or in cases of severe acute respiratory disease in health care workers exposed to severely ill patients with respiratory disease.

Cases of MERS-CoV infection have been reported in France, Germany, Italy, Jordan, Qatar, Saudi Arabia, Tunisia, the United Arab Emirates, Oman, and the United Kingdom. Because there are no U.S. cases of MERS at this time, the CDC continues to consider a link to one of these countries integral to the definition of a suspected case. As always when infectious disease is suspected, a travel history is an important part of a nursing or medical assessment.

In any unexpected cluster of infections (whether an emerging infection is suspected, or infection is caused by a well-understood organism), case finding is retrospective as well as prospective. Have there been previously undiagnosed illnesses with a...
similar clinical picture? In the fall of 2012, MERS case-finding efforts led to the reinvestigation of an April 2012 cluster of infections in a Jordan hospital, where two people including an ICU nurse died of an undiagnosed respiratory infection. Retesting of stored sputum and sera from these individuals confirmed MERS-CoV infection. It’s not yet clear when MERS-CoV shedding peaks or which body fluids are most likely to yield enough virus to test positive. Therefore, the optimal time for testing—that is, the time during the course of infection when specimens will most reliably test positive—is not yet known. The CDC recommends that lower respiratory tract specimens (sputum, bronchoalveolar lavage fluid, or endotracheal aspirate) be tested for MERS-CoV when possible and that testing be repeated at different times during the patient’s illness to increase the likelihood that a diagnosis can be made.

Clinical findings. MERS usually presents as a rapidly progressive pneumonia, but various other clinical features have also been described. Fever, cough, shortness of breath, and progressively severe acute respiratory disease are key symptoms in most cases. Some cases of milder respiratory symptoms have also been documented, usually among close contacts of severe cases. There have also been other manifestations of MERS-CoV infection, including progressive renal impairment and gastrointestinal symptoms such as diarrhea, vomiting, abdominal pain, and anorexia.

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Although most coronaviruses in humans cause only mild illness, when zoonotic transmission occurs—that is, when a nonhuman virus jumps the species barrier—the virus can cause severe illness and death. Almost half of all people with confirmed MERS-CoV infections have died. Death rates from SARS, by contrast, were about 10%. When any emerging infection is first identified, severe cases and a high death rate aren’t always a true reflection of the full spectrum of disease. Severely ill patients are more likely to seek medical help; undiagnosed mild illness that resolves spontaneously is not likely to elicit further investigation. When enzyme-linked immunosorbent assay–based serologic testing for MERS-CoV becomes available, serosurveys of asymptomatic individuals from the communities where cases have occurred will tell us more about the continuum of disease caused by MERS-CoV.

Source and transmission. A source or reservoir for the MERS virus has yet to be identified. In Saudi Arabia more than 200 different animal species have been tested for the virus, and none has been positive for MERS-CoV. A recent study suggests that MERS-CoV or a similar virus has been circulating among camels, although camels don’t seem to play a central role in transmission; most people infected with MERS-CoV have had no direct contact with them.

Although MERS-CoV is closely related to certain bat coronaviruses, that doesn’t mean that contact with bats has been a source of human infection. Is another mammal or bird an intermediate host? The well-known coronaviruses are usually spread by contact with contaminated surfaces and infectious droplets. These modes of transmission call for contact and droplet isolation precautions. But in the case of SARS, there were instances in which spread might have been due to aerosolization of respiratory or fecal matter. With MERS-CoV, airborne transmission appears to be possible.

The largest cluster of MERS-CoV infections to date, with 23 confirmed cases and 15 deaths, involved hemodialysis units, ICUs, and general inpatient units at four hospitals in the eastern region of Saudi Arabia. Most of those cases were hospital-acquired infections, and all patient-to-patient spread occurred after exposure to infected patients before MERS had been diagnosed and, therefore, before those patients had been isolated.

Limited person-to-person spread of MERS has been documented, both among close household contacts and between patients and health care workers. No sustained chains of transmission have yet been evident. As any emerging virus begins to adapt to its human host, however, limited person-to-person spread may merely be a prelude to more efficient transmission. The large Saudi Arabian cluster mentioned above suggested the possibility of enhanced person-to-person transmission of MERS-CoV.
Ultimately, though, despite the extent of patient-to-patient transmission in that cluster, confirmed MERS-CoV infection developed in only three of 217 household contacts and two of more than 200 exposed health care workers.

**Infection control.** The CDC’s infection control recommendations for suspected or confirmed cases of MERS include the use of contact, droplet, and airborne precautions, along with full personal protective equipment—gown, gloves, mask, and eye protection (goggles or face shield). Patients should be placed in a negative-pressure room. If the room’s air is not exhausted directly to the outside, a high-efficiency particulate air filter unit should be placed in the room.³⁷

As with active tuberculosis, the patient should leave the negative-pressure room only for essential tasks and needs to wear a surgical mask at such times. (Surgical masks are designed to contain exhaled droplets; N-95 respirator masks filter inhaled particles.) As with any emerging infection—that is, any infection whose reservoirs and modes of transmission are not fully understood—the number of personnel entering the room of a patient with suspected or confirmed MERS should be limited.

This full spectrum of precautions is used because of uncertainty about possible modes of MERS transmission, the documented person-to-person transmission, and its apparently high mortality rate.¹¹ Note that, as with any type of isolation precautions, routine procedures are adequate for the cleaning and disinfection of environmental surfaces, equipment, laundry, and dishes and utensils. No special red bagging of items or separate processing is necessary.¹⁷,¹⁸

The WHO hasn’t yet classified MERS-CoV as a “public health emergency of international concern.”¹⁹ New cases of MERS-CoV infection continue to be identified, and this virus has taken the spotlight away from other emerging viral infections such as avian influenza A H1N1 and H7N9. These and other newly identified viruses percolate in many parts of the globe. Because viral mutations are unpredictable, it’s impossible to predict whether any of these viruses or yet another emerging virus will be the cause of a new pandemic.▼

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**REFERENCES**


