Three Emerging Coronaviruses in Two Decades

The Story of SARS, MERS, and Now COVID-19

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In the past two decades, the world has seen three coronaviruses emerge and cause outbreaks that have caused considerable global health consternation. Coronaviruses are enveloped, nonsegmented, single-stranded, positive-sense RNA viruses that have a characteristic appearance on electron microscopy negative staining **Image 1**. As a matter of fact, the characteristic electron microscopy appearance was the clue to amplify and sequence nucleic acids from Dr Urbani's (one of the health care providers who died of severe acute respiratory syndrome [SARS] in 2003) respiratory specimen using a consensus coronavirus primer.[1] The sequence of the virus was significantly different from other coronaviruses known to cause human disease at the time. The virus was ultimately named SARS-CoV, as febrile patients had severe acute respiratory syndrome and could present with pneumonia and lower respiratory symptoms such as cough and dyspnea.[2] The SARS-CoV outbreak started in Guangdong, China, and spread to many countries in Southeast Asia, North America, Europe, and South Africa. Transmission was primarily person to person through droplets that occurred during coughing or sneezing, through personal contact (shaking hands), or by touching contaminated surfaces. Of note, health professionals were particularly at risk of acquiring the disease, as transmission also occurred if isolation precautions were not followed and during certain procedures. The last case of SARS-CoV occurred in September 2003, after having infected over 8,000 persons and causing 774 deaths with a case fatality rate calculated at 9.5%.

Nine years later, a new coronavirus that causes respiratory disease appeared in the Middle East, thus the name of MERS-CoV. Symptoms of MERS-CoV are nonspecific, but many patients end up with severe acute respiratory distress. In these patients, travel history is imperative, as all cases have been linked to persons in or near the Arabian Peninsula. Similar to SARS-CoV, health professionals are at higher risk of acquiring the disease, as demonstrated in the outbreak in South Korea.[3] However, in comparison with SARS-CoV, MERS-CoV is still circulating, and the case fatality rate is much higher (around 35%). What has allowed control of MERS-CoV is a low R_0 (approximately 1), meaning each person with the disease transmits it to only one other person (the SARS-CoV R_0 was of approximately 4).

In December 30, 2019, a cluster of patients with pneumonia of unknown etiology was observed in Wuhan, China, and reported to the World Health Organization (WHO) China bureau in Beijing. A week later, January 7, 2020, a new coronavirus (SARS-CoV-2) was isolated from these patients. This virus was initially referred to as novel coronavirus 2019 (2019-nCoV) but was given the official name of COVID-19 by the WHO on February 11, 2020. This new virus has infected more people than either of its two predecessors. Several factors have allowed the rapid spread of this virus: Wuhan is the capital of China's Hubei province, with over 11,000,000 inhabitants, and it is a major transportation hub, which increases person-to-person contact and adds to the possibility of exporting cases to other locations. At this point, the R_0 is calculated between 2 and 3.5, indicating that one patient can transmit the disease to two to three other people. Patients with the COVID-19 infection proven by polymerase chain reaction have been an average age of 55 years (cases in children seem to be rare).[4] They present with fever, dry cough, and shortness of breath and, in the most severe cases, have pneumonia. The case fatality rate is around 2%

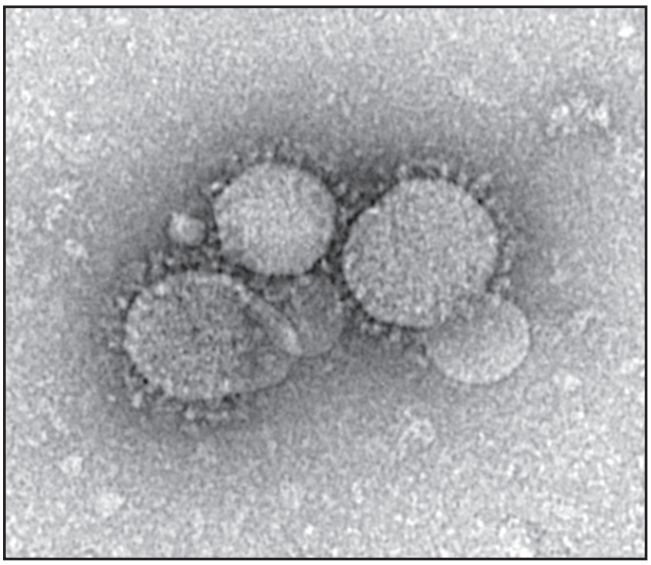

Image 1 Electron microscopy photograph of negative stain of a coronavirus (image from the Public Health Image Library).

to 3%. SARS-CoV-2 will cause many more deaths than its predecessors, even though the mortality rate is lower than MERS-CoV infections, because there have been so many more cases. Chinese authorities have taken the global threat very seriously, and the containment measures have been unprecedented (closing airports, train stations, and roads to Wuhan; building hospitals in record time). However, cases with SARS-CoV-2 are already being reported in many countries, including the United States.

The question of how to approach these patients for diagnosis and treatment is pressing. For patients in the United States, the Centers for Disease Control and Prevention (CDC) is continuously updating information and has instructions on who to test and the workflow to follow regarding specimen handling.[5] In brief, testing for SARS-CoV-2 needs to be sent to the state laboratory after consultation with it regarding patient clinical characteristics, the specimens it will receive, and packaging of the sample using shipping regulations for category B agents. Other tests, such as CBC count, chemistries, and microbiology (including molecular testing for other respiratory viruses), can be handled using universal precautions (face protection, gloves, and disposable gowns) in hospital laboratories, so as not to delay other necessary treatment. It should be noted that although some multiplex molecular panels include primers for SARS-CoV, MERS-CoV, and other coronaviruses responsible for upper respiratory infections (HcoV 229E, NL63, OC43, and HKU1), they do not detect COVID-19. The CDC is advising not to perform viral cultures in patients under investigation for either MERS-CoV or SARS-CoV-2. The WHO also has a webpage with guidance regarding multiple aspects, including surveillance, patient management, and laboratory testing specific for SARS-CoV-2.[6] Once a patient has been defined as infected with SARS-CoV-2, he or she should be treated, taking into consideration airborne and contact precautions. Most of the measures are symptomatic, although some antiviral medications have been used.

Last, at this point, reports of autopsies or lung tissue samples of patients with SARS-CoV-2 have not been published. However, based on imaging studies and what we know of SARS-CoV and MERS-CoV, patients with the most severe disease will likely show diffuse alveolar damage with hyaline membrane formation, inflammation in the alveolar walls, desquamation of pneumocytes, and, if the case is complicated by a secondary bacterial pneumonia, intra-alveolar inflammatory infiltrate by neutrophils. Any other specific features, such as multinucleated cells or potential viral inclusions, remain to be discovered through pathologic studies of patients with this new virus.

In summary, the story of SARS-CoV-2 continues to evolve. Because SARS-CoV and MERS-CoV have had different behaviors, SARS-CoV-2 will likely have unique features of its own that we will learn as the outbreak progresses.

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References

1. Ksiazek TG, Erdman D, Goldsmith CS, et al; SARS Working Group. A novel coronavirus associated with severe acute respiratory syndrome. *N Engl J Med.* 2003;348:1953-1966.
2. Centers for Disease Control and Prevention. Severe acute respiratory syndrome (SARS). Last reviewed 2005. https://www.cdc.gov/sars/guidance/b-surveillance/app1.html. Accessed February 3, 2020.
3. Hui DS, Azhar EI, Kim YJ, et al. Middle East respiratory syndrome coronavirus: risk factors and determinants of primary, household, and nosocomial transmission. *Lancet Infect Dis.* 2018;18:e217-e227.
4. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study [published online January 30, 2020]. *Lancet*.
5. Centers for Disease Control and Prevention. Interim guidelines for collecting, handling, and testing clinical specimens from patients under investigation (PUIs) for 2019 novel coronavirus (2019-nCoV). 2020. https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html. Accessed February 3, 2020.
6. World Health Organization. Novel coronavirus (2019-nCoV) technical guidance. 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance. Accessed February 3, 2020.

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