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Corona Virus 101

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COVID-2019 emerged from China in late December of 2019. It follows 2 other coronavirus outbreaks, the SARS-CoV and the MERS-CoV. Coronaviruses usually circulate among animals but sometimes can jump to humans. These 3 strains have caused severe disease in humans and global transmission concerns. Symptoms of COVID-2019 include cough, fever, and shortness of breath. Related illnesses can range from mild to severe to fatal. Primary care providers must be alert to respiratory symptoms they encounter that are associated with pertinent travel history, be prepared to safely screen, examine, and possibly test and/or report suspicions to the health department for further evaluation.

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Epidemiology and Pathophysiology

For the most part, little is known about emerging pathogens before they appear, so frequently, viruses from zoonotic sources that are unrecognized present a unique challenge to science and medicine. A zoonosis is an infection caused by bacteria, viruses, parasites, or fungi transferred from a nonhuman animal to humans.¹ Zoonotic transmission may be due to a spillover event from an animal to a human, which is caused by a sustained or new close human contact or by climate changes that affect the distribution of disease vectors—for example, insects that have been previously restricted geographically through the effects of climate changes. Evolution of a pathogen that has been previously animal-restricted can cause a virus to emerge and become capable of using a human receptor or the cellular machinery to cause infection.² Coronaviruses (CoVs) are large, enveloped, positive-strand RNA viruses. These viruses fall into 4 genera: alpha, beta, delta, and gamma. The 2 CoV subtypes known to affect humans (HCoVs) are alpha and beta. Four HCoVs, including HCoV229E, NL63, OC43, and HKU1, account for 10%–30% of adult respiratory infections and are endemic globally. The ecologically diverse coronavirus occurs most prevalently in bats, which serve as a host reservoir.³ The mild types of CoVs in humans, which cause the common cold, gained little attention until 2002 when the virus emerged from Guangdong Province, China, causing cases of severe atypical pneumonia. This disease, which became known as SARS, or severe acute respiratory syndrome, caused worldwide concern when it spread to 37 countries.⁴ The causative agent was SARS-CoV and bats were determined to be the zoonotic reservoir. Subsequent transmission to humans transpired from civets (an Asian animal related to the mongoose and weasel), which had become infected by a bat.^{4,5} Globally, this virus affected more than 8,000 people and had a 10% fatality rate.⁶ After SARS, MERS-CoV emerged in 2012 from the Middle Eastern Arabian Peninsula. Like SARS, the origin host for

MERS-CoV is the bat, but the transmitting animal is typically the dromedary camel. The virus has infected 1,728 people since its emergence and has had a 35.6% mortality rate since August 2016.⁷

Recently, in December 2019, coronavirus reemerged, once again from China, with the initial outbreak in Wuhan, a city located in the country's Hubei Province. It has since been designated as SARS-CoV-2, and the resulting disease is called COVID-2019.⁸ As of this writing, more than 2 million cases have been reported globally, since its outbreak. The point of origin is considered to be a seafood/animal market in Wuhan that houses and sells fish, as well as exotic animals including hedgehogs, badgers, snakes, and birds (turtle-doves).^{8,9} This new virus, like the SARS and MERS coronaviruses, is also a beta subtype, and its exact animal host/reservoir has yet to be determined. However, the World Health Organization (WHO) has reported that environmental samples taken from the marketplace came back positive for COVID-2019. Its similarity to SARS is found in the predominant human receptor for the SARS S glycoprotein, human angiotensin-converting enzyme 2 (ACE2), which is found primarily in the lower respiratory tract, rather than in the upper airway.³ This may be a partial explanation for the severe respiratory symptoms and consequences of both diseases, including acute respiratory distress syndrome (ARDS). When cases were being confirmed in people who had not visited the Wuhan seafood market or been in its proximity, suspicions arose that the virus was being transmitted from person to person.¹⁰ A study published in the *New England Journal of Medicine* of the first 435 patients who were infected with the new virus in Wuhan found that the median age was 59 years old (range 15–89 years), 56% were male, and no children younger than 15 years had contracted the disease.¹¹ Since that study, however, a retrospective study at Wuhan University that was published in *JAMA* reported that 9 infants had contracted COVID-2019 ranging in age from 1 to 11 months of which 7 were female.¹² The first confirmed U.S. case of COVID-2019 was diagnosed in the state of Washington on January 30, 2020, resulting

from person-to-person contact, and was it determined to be caused through international travel to Wuhan, China.¹³ This is also the date that the rapidly spreading virus was declared a public health emergency of international concern (PHEIC) by the International Health Regulations emergency committee of the WHO. PHEIC is defined by the WHO as “an extraordinary event which is determined to constitute a public health risk to other States through the international spread of disease; and to potentially require a coordinated international response.” This definition implies a situation that “is serious, unusual, or unexpected; carries implications for public health beyond the affected State’s national border; and may require immediate international action.” Declaring a PHEIC expands the WHO’s authority to coordinate a response in various ways, including through the issuance of recommendations on whether countries should impose trade and travel restrictions.¹⁰ Five other diseases that have met the WHO criteria for this particular designation include Ebola (2019) in the Democratic Republic of Congo, Zika (2016), Ebola (2014) in West Africa, Polio (2014), and H1N1 (2009).¹⁴ Since January 30, the Centers for Disease Control and Prevention (CDC) has reported close to three quarters of a million confirmed cases of COVID-2019 in the United States in all 50 states, the District of Columbia, Puerto Rico, Guam, and the U.S. Virgin Islands. Among this number, there has been nearly 40,000 deaths.⁸ The hardest hit state thus far has been New York which reports about a quarter of a million cases and a staggering number of deaths both of which contributed to the U.S. replacing China as the epicenter of the virus. Confirmed cases in four European countries: Spain, Italy, France, and Germany rank that continent closely behind the U.S.¹⁰ A global pandemic stemming from the virus was officially declared by the WHO on March 11. According to the WHO, more than 2 million cases reported globally thus far account for viral spread to most regions of the world with greater than 150,000 resultant deaths. This number represents an infection rate of 7% that continues to climb. China, the origin of the virus, has confirmed more than 80,000 cases with a current 4% mortality rate.^{8,10} Global mortality rate for COVID-2019, to date, is at 8% a rate approaching the rate for the SARS virus but which is still much lower than that of MERS at this point in time. Daily updated statistics can be found at the CDC and WHO websites. Some cities, states, and countries have been forced to issue shelter in place orders in an effort to prevent further spread. COVID-2019 has not, as yet peaked, according to public health authorities, but the curve of its spread is showing signs of flattening with the ultimate scope and effects of the outbreak remaining to be seen. The number of worldwide confirmed cases for COVID-2019 has far surpassed those of both SARS and MERS combined, placing an astounding strain on health care systems. The CDC recommendations for international travel from the United States can be found on its website. Ultimately, international travel is not recommended if it is not essential, and postponement of any nonessential international travel should particularly be considered by older adults and those with chronic medical conditions (CDC Warning Level 3).⁸

Transmission

Although the origin of the COVID-2019 is zoonotic, current epidemiologic data demonstrate that human transmission is occurring.^{8,10,15} It is thought to spread through respiratory droplets resulting from a cough or sneeze of an infected person that reaches people who are in close contact (ie, people who are 6 feet or less apart). Transmission may occur through people who have contact with infected surfaces or objects and then touch their eyes, nose, or mouth, but this, as yet, has not been considered a frequent route of transmission for this particular coronavirus. The COVID-2019 virus appears to spread most commonly from a person who is at the peak

of symptoms. It is also presumed to spread from persons infected with the virus who are not yet exhibiting symptoms.⁸ The incubation period has been determined to be 2 to 14 days. Transmission of the disease remains easy and sustainable in Hubei Province and in other parts of China and now has a similar spread in many other countries. The CDC issued a statement on February 25, 2020, that spread was expected to occur in the United States, and this, indeed, has proved to be the case exponentially.⁸

Clinical stigmatization is a phenomenon that may occur with an infectious disease. In the case of COVID, people may associate it, in general, with the Chinese population. Stigmatization occurs, for example, when a Chinese American, living in the United States, is associated with the virus.⁸

Clinical Symptoms

Predominant clinical symptoms are fever, dry cough, and shortness of breath.^{5,8,10,15-18} Ten percent of patients have presented with nausea and diarrhea 1–2 days before development of fever and dyspnea in a retrospective study in a Wuhan, China, hospital. Upon imaging examination, 74 (75%) patients in this same cohort showed bilateral pneumonia.⁵ As with SARS and MERS, a large number of patients have exhibited symptoms of viral pneumonia, including fever, difficulty breathing, and, in the most severe cases, bilateral infiltrates.¹⁶ Patients admitted to the intensive care unit (ICU) have been older adults and those who had comorbid conditions, suggesting a poor outcome.⁵ Complications, in addition to pneumonia, included respiratory failure, ARDS, cardiac injury, shock, kidney injury, and fatal outcomes.^{5,17}

Pregnant women, because they are in an immunosuppressive state that causes adaptive changes such as diaphragm elevation, increased oxygen consumption, and edema of respiratory mucosa, are particularly susceptible to respiratory pathogens. Severe pneumonia can render these women intolerant to hypoxia,¹⁹ and this could characterize this population as high risk for COVID-2019. A retrospective study of 9 pregnant Chinese women from Wuhan who were in late pregnancy and who had contracted the virus (all of whom delivered during the course of their illness) demonstrated that there was nonvertical transmission of the disease.¹⁹ Typical symptoms of the virus were exhibited in these women, and none developed pneumonia or died. Zhu et al confirmed nonvertical transmission in a study of 8 neonates born to Chinese women who had COVID-2019.²⁰ A larger cohort of 38 pregnant women studied by Schwartz included the 9 women from Wuhan and others from areas surrounding the epicenter of the viral outbreak. Again, it was demonstrated that there were no cases of viral-related maternal pneumonia or death and no vertical transmission to the neonates.²¹

In children, so far, mostly the very young appear to become infected. For example, in 9 infants studied by Wei et al who tested positive for COVID-2019, some had fever, others exhibited mild respiratory symptoms, and others had no symptoms at all. The latter group had been exposed to family members and so had been tested. No infants developed complications.¹² A second study of children with COVID-2019 published at a later date and conducted by Dong et al had a much larger cohort of 2,143 children from China, demonstrating spread of the disease. Most of the cases in this study were mild and, compared with infected adults who had severe or critical disease in the same time frame (18.5 %),²² only 5.9% of children had a similar progression of the disease. Only 1 child in this study died. The reduced clinical severity of COVID-2019 in children is not understood but is thought to be related to both exposure and host factors. There is also speculation that children are less sensitive because the binding ability; in other words, the maturity and function of ACE2 (discussed earlier) may be lower in children in comparison to adults. Children under age 1 year were

the most affected, in this study (10.6 %), followed by those 1–5 years old (7.3%), suggesting that young children, particularly infants, are the most vulnerable to COVID-2019.²³

Diagnosis and Evaluation

Infection control measures should be implemented, when COVID-2019 is suspected, with immediate isolation. A focus should be made on early recognition. Persons presenting with fever and/or lower respiratory tract symptoms who have had recent travel to a heavily affected region within 14 days or those who have had close contact with a person either suspected of having the infection or having been confirmed as infected, should be considered potentially infected and be tested. According to the CDC, if an individual is severely ill and no etiology has been determined, even if there has been no known exposure COVID-2019, testing should be done.⁸ Collection of specimens to test for COVID-2019 virus from the upper respiratory tract (nasopharyngeal and oropharyngeal swab) should be obtained. Sputum, tracheal aspirate, or bronchioalveolar lavage specimens are recommended as well, if possible, from the lower tract. Additional specimens (eg, stool, urine) may also be collected.^{8,10} COVID-2019 virus is detected by polymerase chain reaction; in the United States, testing is performed by the CDC or a CDC-qualified lab.^{8,15} Specimen collection should be done by personnel wearing appropriate PPE including gown, gloves, eye protection, and a mask that is at least as protective as a fit-tested NIOSH-certified disposable N95 filtering facepiece respirator mask.⁸ Critical shortages of PPE are being acknowledged by hospitals worldwide at this time.

Treatment and Prevention

Treatment is primarily supportive to help relieve symptoms, such as analgesics for fever and oxygen for hypoxia, as well as infection control measures. If the disease is severe, measures should be taken to support vital organ function. The WHO recommends that corticosteroids should be avoided unless indicated for other reasons (eg, chronic obstructive pulmonary disease) due to the potential for prolonging viral replication as observed in MERS-CoV patients.^{10,24} The following 2 retrospective studies of patients hospitalized in Wuhan, China, with the COVID-2019 virus outline implemented treatment regimens. In a study by Chen et al, in addition to supportive measures, at the Jinyintan Hospital, some patients were given antibiotics, 13 patients received noninvasive mechanical ventilator treatment, and 4 required invasive ventilation treatment.⁵ At Zhongnan Hospital of Wuhan University, patients, according to the study by Huang et al, in addition to supportive care, patients received antiviral therapy (oseltamivir, 124 [89.9%]), and many received antibiotics. ICU patients received high-flow oxygen, or noninvasive ventilation. Invasive mechanical ventilation was required in 17 patients.¹⁷ For patients with mild infection, who can be adequately isolated in an outpatient setting, home management may be appropriate if they have no underlying chronic conditions (eg, heart or lung disease, renal failure, or immunocompromising conditions). Management of such patients should focus on prevention of transmission to others and monitoring for clinical deterioration, which should be reported immediately to public health officials and would prompt hospitalization.^{8,10} Remdesivir and chloroquine, both broad-spectrum antivirals, were tested recently *in vitro* by Wang et al for efficacy against COVID-2019. Both drugs showed an ability to control the virus.²⁵ Remdesivir was compassionately used in the first U.S. patient confirmed with COVID-2019 in Washington State due to this person's worsening clinical condition.¹³ Compassionate use of an unapproved drug can occur when a patient's condition is serious

and no other treatment options are available. Wang et al have recommended use of both chloroquine and Remdesivir in persons who have this virus. However, randomized controlled trials are needed to determine the safety and efficacy of these drugs in patients with this infection, in keeping with the WHO's recommendation for avoidance of their use.

Management of patients who test positive during pregnancy and have no symptoms is similar to the general population in that self-monitoring at home is recommended for 14 days. These patients, as well as those self-monitoring for mild illness from the disease, due to the potential risk of intrauterine growth restriction, should have fetal growth ultrasounds and Doppler assessments bimonthly. Pregnant women with COVID-2019-related pneumonia should be cared for in a tertiary care center by a multidisciplinary team.²⁶ Women who test positive for COVID-2019 at delivery may safely breastfeed their newborns.⁸

The best way to prevent illness from COVID-2019, because there is no current vaccine, is to avoid being exposed to it. The CDC recommends everyday preventive actions to help stop the spread of respiratory disease, including avoiding close contact with people who are sick; covering your cough or sneeze; avoidance of touching eyes, nose, and mouth; washing hands often with soap or alcohol-based hand sanitizers; and not wearing a face mask if you are well. Masks at the beginning of the outbreak were not recommended for healthy persons for protection from the disease unless there was known exposure. Significant viral spread and mortality in the United States has warranted a recommendation from public health officials that masks be worn in public places such as grocery stores and pharmacies.⁸

The Role of Primary Care Providers

Indispensable tools for the detection and monitoring of outbreaks and public health emergencies include strong epidemiology and surveillance systems; however, strong primary care systems can form the foundation of any emergency response. Member states of the WHO have shown a consistent commitment to training community-based health professionals, who then become capable of providing care across the spectrum of prevention, preparedness, response, and recovery, which further develops primary care. Often considered the "front door" of the health care system, primary care should be involved in planning and action for health emergency risk management.²⁷ It is important that there be close coordination between clinicians and public health authorities at the local, state, and federal levels. From a clinical perspective, when a patient presents with fever and respiratory symptoms (in particular, a dry cough), clinicians should obtain a detailed travel history. CDC guidelines for health care professionals for evaluating patients' epidemiological risks, in conjunction with the characteristic symptoms of COVID-2019, can be found on its website. When symptoms, travel history, and relevant illness exposure raises suspicion for COVID-2019, the state or local health department should be immediately notified. This individual becomes a person under investigation (PUI) and should be placed in isolation and infection control personnel, if applicable, for the facility should be notified immediately. Health care staff members who are in contact with the patient should use PPE precautions. If and when testing is done, testing personnel should wear an N95 respirator mask as discussed in the diagnosis/evaluation section. In severely ill individuals, testing can be considered, as previously mentioned, when another etiology has not been identified and exposure history is equivocal (eg, uncertain travel or exposure, or no known exposure). Slowing U.S. transmission of COVID-2019 is critical, and the fact that primary care providers play an important role has already become evident, since the December emergence of the virus. This has

been demonstrated by the detection of 8 of the first 11 U.S. cases by clinicians who then collaborated with public health officials to test persons at risk.²⁸ Both early recognition and an increased understanding of the virus by health care providers can reduce transmission.²⁷

Conclusion

The Wuhan emergence of the third coronavirus this century is a stark reminder of the continuing threat of zoonotic diseases to global health security. There is increasing international concern regarding its continued spread. The rapid identification and containment of this virus by China's public health authorities reflects the increasing global capacity to detect, identify, and define new outbreaks.²⁹ The disease has met all 3 criteria for a pandemic: (1) caused by an illness and fatalities related to this illness, (2) had sustained person-to-person spread, and, recently (3) worldwide spread.⁸ A concerted and collaborative global effort, based on sharing experiences from all geographic regions and all disciplines, should continue to be led and coordinated by the WHO with an emphasis placed on containment, surveillance, and prevention in addition to rapid dissemination of clinical information related to the care of patients with this infection.²⁷ This effort can start with early detection of the virus by primary health care providers through an awareness of COVID-2019 characteristics and recognition of possible cases, which is then followed by, if needed, coordination with public health systems. The perpetual challenge of emerging infections and the importance of sustained preparedness has been underscored by a novel coronavirus from which pathogens have caused a global human disease.

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