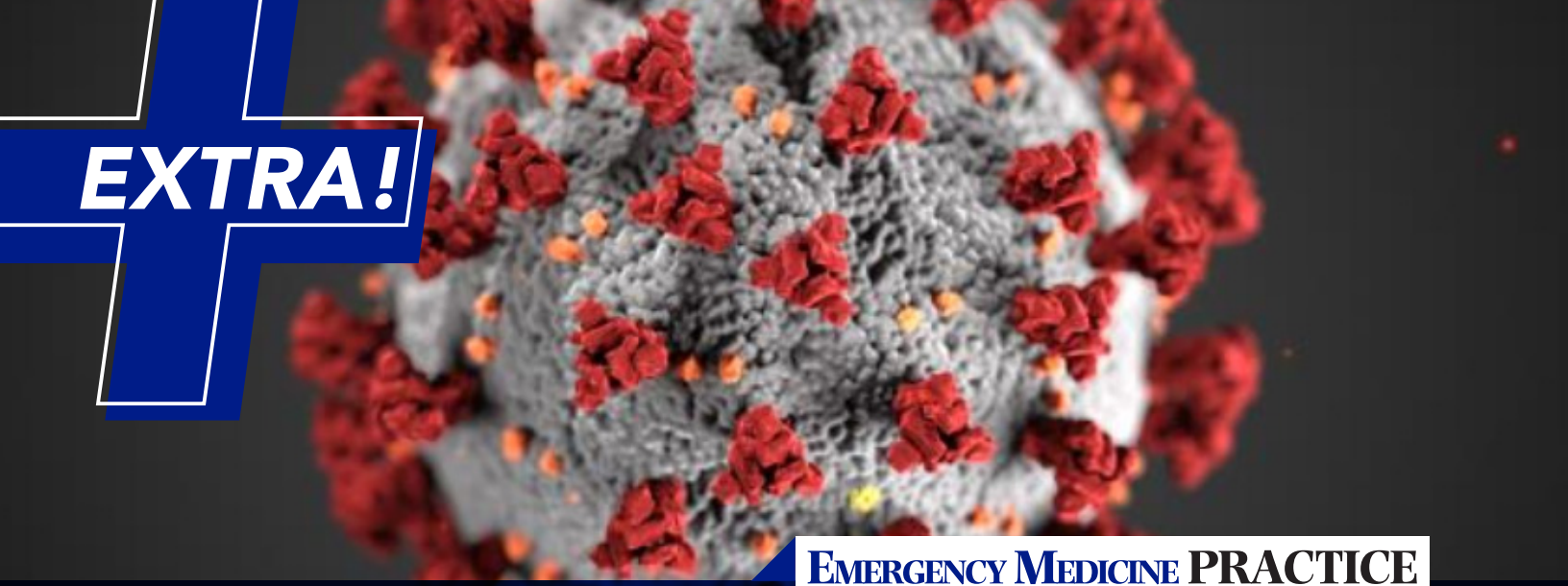

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SPECIAL REPORT :: COVID-19
FEBRUARY 2020

Novel Coronavirus COVID-19:
An Overview for Emergency Clinicians

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KEY POINTS

- The mortality rate of COVID-19 appears to be between 2% to 4%. This would make the COVID-19 the least deadly of the 3 most pathogenic human coronaviruses.
- The relatively lower mortality rate of COVID-19 may be outweighed by its virulence.
- 29% of the confirmed NCIP patients were active health professionals, and 12.3% were hospitalized patients, suggesting an alarming 41% rate of nosocomial spread.

Save this supplement as your trusted reference on COVID-19, with the relevant links, major studies, authoritative websites, and useful resources you need.

A 42-year-old man presents to your ED triage area with a high-grade fever (39.6°C [103.3°F]), cough, and fatigue for 1 week. He said that the week prior he was at a conference in Shanghai and took a city bus tour with some people who were coughing excessively, and not all were wearing masks. The triage nurses immediately recognize the risk, place a mask on the patient, place him in a negative pressure room, and inform you that the patient is ready to be seen. You wonder what to do with the other 10 patients who were sitting near the patient while he was waiting to be triaged and what you should do next...

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Introduction

Coronaviruses earn their name from the characteristic crown-like viral particles (virions) that dot their surface. This family of viruses infects a wide range of vertebrates, most notably mammals and birds, and are considered to be a major cause of viral respiratory infections worldwide.[1,2] With the recent detection of the 2019 novel coronavirus (COVID-19), there are now a total of 7 coronaviruses known to infect humans:

1. Human coronavirus 229E (HCoV-229E)
2. Human coronavirus OC43 (HCoV-OC43)
3. Human coronavirus NL63 (HCoV-NL63)
4. Human coronavirus HKU1
5. Severe acute respiratory syndrome-related coronavirus (SARS-CoV)
6. Middle East respiratory syndrome-related coronavirus (MERS-CoV)
7. Novel coronavirus (COVID-19, also known informally as Wuhan coronavirus)[3]

Prior to the global outbreak of SARS-CoV in 2003, HCoV-229E and HCoV-OC43 were the only coronaviruses known to infect humans. Following the SARS outbreak, 5 additional coronaviruses have been discovered in humans, most recently the novel coronavirus COVID-19, believed to have originated in Wuhan, Hubei Province, China. SARS-CoV and MERS-CoV are particularly pathogenic in humans and are associated with high mortality. In this review, the epidemiology, pathophysiology, and management of the recently discovered COVID-19 are reviewed, with a focus on best practices and the public health implications.

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Critical Appraisal of the Literature

PubMed, ISI Web of Knowledge, and the Cochrane Database of Systematic Reviews resources from 2012 to 2020 were accessed using the keywords *emergency department, epidemic, pandemic, coronavirus,* and *COVID-19*. The United States Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) websites were also accessed.

Epidemiology

As of February 20, 2020, there have been 78,771 cases of COVID-19 globally, with 76,936 of those in mainland China; there have been 2461 confirmed deaths.[4] Confirmed cases span 32 countries across North America, Europe, Asia, and Australia, prompting the WHO to declare COVID-19 a global health emergency. Of the 2461 deaths, all but 17 have occurred in China, with the majority occurring in the Hubei province of China, the capital of which is Wuhan. This amounts to a current global mortality rate of 3.12%; however, this number is subject to change as the number of cases and affected patient populations grow and change respectively. With the outbreak of COVID-19 coinciding with the celebration of the Chinese Lunar New Year in late January 2020 and an associated approximate 15 million visits to Wuhan City, the challenges in containing the outbreak are and will continue to be difficult to estimate. Initial reports from affected patient populations in hospitals in China indicate that the majority of those infected with severe disease and poor outcomes (as measured by intensive care unit [ICU]-level care and mortality) tend to be patients with comorbid conditions such as asthma, chronic obstructive pulmonary disease, or advanced age.[5,6]

In late January 2020, the first data detailing the clinical features, course, and prognosis from infection with COVID-19 relative to the previous 2 deadly coronavirus outbreaks (MERS-CoV and SARS-CoV) were published in *The Lancet.*[7,8] **(See Table 1, page 4.)** In the time since the publication of these data, the global disease burden of COVID-19 has come to drastically outpace that of the previous 2 novel coronavirus outbreaks. With the aforementioned 78,771 cases and 2461 deaths as of February 23, 2020, COVID-19 is the deadliest of the novel coronaviruses in absolute magnitude while approximating the mortality rate found in this early study.[4,7,8]

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Table 1. Early Demographic and Clinical Characteristics of COVID-19 Relative to Outbreaks of Previously Novel Coronaviruses, MERS-CoV and SARS-CoV[4,8]

Clinical Characteristics	COVID-19	MERS-CoV	SARS-CoV
Epidemiologic Statistics[a]			
Cases	78,771	2494	8096
Deaths	2461	858	744
Mortality	3.12%	37%	10%
Demographic Statistics[b]			
Date	December 2019	June 2012	November 2002
Location of first detection	Wuhan, China	Jeddah, Saudi Arabia	Guangdong, China
Age, years (range)	49 (21-76)	56 (14-94)	40 (1-91)
Male:female ratio	2.7:1	3.3:1	1:1.25
Symptoms (%)[b]			
Fever	98	98	99-100
Dry cough	76	47	29-75
Dyspnea	55	72	40-42
Diarrhea	3	26	20-25
Sore throat	0	21	13-25
Ventilatory support	9.8	80	14-20

[a]Epidemiologic statistics on COVID-19 as of February 23, 2020.[4]
[b]Demographic and symptom statistics for COVID-19 are based on early epidemiologic data from the first 41 patients reported by Chaolin Huang, et al (admitted before January 2, 2020).[8] Further data will be needed to detail clinical symptomatology and demographics in the > 70,000 cases now confirmed. Data are n, or n% unless otherwise stated.

Of note, though findings are quite early and the actual prevalence of the virus is far greater than the numbers listed in **Table 1**, the mortality rate appears to be relatively consistent with current trends, between 2.5% and 3.5%. This would make the COVID-19 the least deadly of the 3 most pathogenic human coronaviruses. Nonetheless, this relatively lower mortality rate may be outweighed by the virulence of COVID-19. With more than 75,000 cases and 2400 deaths, the total death toll from COVID-19 has exceeded that of both the MERS-CoV and SARS-CoV combined.[4]

In epidemiology, the R_0 value (pronounced "R-naught") is known as the basic reproduction number and can be thought of as the expected number of cases generated directly by 1 case in a population, where all individuals are susceptible to infection. Early epidemiologic studies in the case of COVID-19 estimate an R_0 value of 2.2 (90% high density interval: 1.4-3.8), a value similar to SARS-CoV and pandemic influenza, suggesting the potential for sustained human-to-human transmission and a global pandemic.[9]

Given the early timeframe of these calculations, the recent spate of case clusters outside of China with untraceable origins, and the first confirmed case in Africa (Egypt), where the primary and public health-

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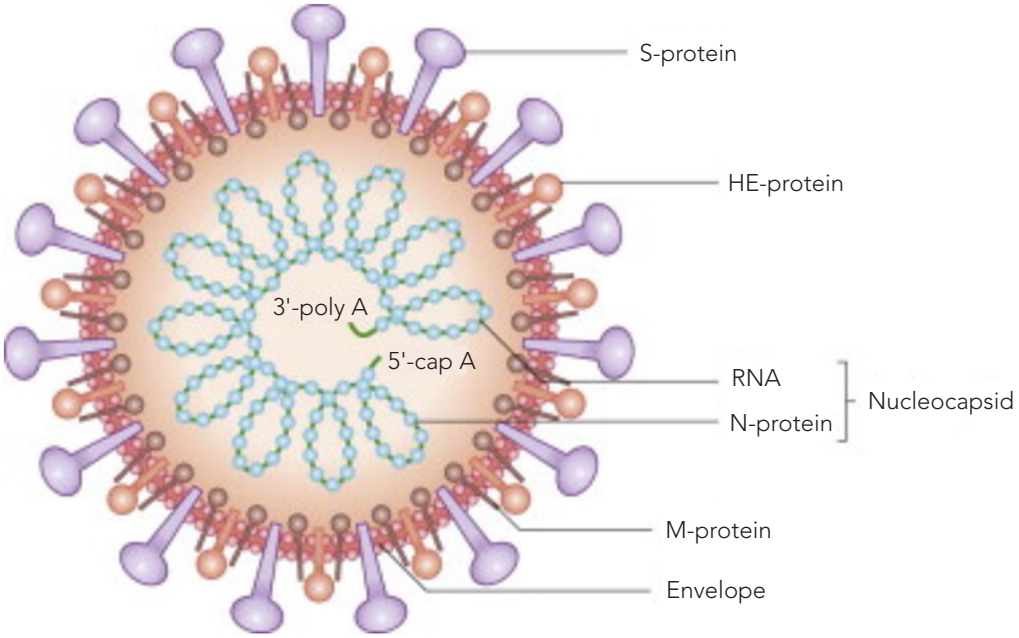
care systems are less equipped to contain viral spread, fears of COVID-19 becoming a pandemic are mounting.[10,11]

Virology

Coronaviruses are in the order Nidovirales, in the family Coronaviridae, and subfamily Orthocoronavirinae. Coronaviruses are enveloped with positive-sense single-stranded RNA, and possess the largest genome of all RNA viruses. Two-thirds of the coronavirus genome at the 5′ terminus encodes viral proteins involved in transcribing viral RNA and replication, while one-third at the 3′ terminus encodes viral structural and group-specific accessory proteins.[2] The major proteins in coronaviruses are named S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins. These biomarkers play a central role not just in how we diagnose the disease, but how we will come to understand its pathogenicity profile, and ultimately any options for a vaccine and/or direct antiviral treatment targeted to dismantle the viral life cycle. **(See Figure 1.)**

Figure 1. Coronavirus With Major Proteins Labeled



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The SARS-CoV and MERS-CoV viruses were both believed to have resulted from zoonotic spread from the bat population.[12] While coronaviruses likely evolved over thousands of years remaining confined to bat populations, intermediate mammalian hosts, such as civet cats in the case of SARS-CoV, and dromedary camels in the case of MERS-CoV, have been implicated and likely play a role in the ultimate transmission of these novel coronaviruses

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to humans.[13,14] The outbreak of COVID-19 is suspected to have originated in the Huanan Seafood Wholesale Market in Wuhan City; however, other researchers have suggested that this market may not be the original source of viral transmission to humans.[7,15] Bats are rare in markets in China, but they are hunted and sold directly to restaurants for food.[16]

Pathophysiology

Coronaviruses primarily infect the upper respiratory and gastrointestinal tracts of birds and mammals. The surface spike glycoprotein (S-protein) is a key factor in the virulence of coronaviruses, as it is believed to enable it to attach to host cells. In SARS-CoV, human angiotensin-converting enzyme 2 (ACE2) is the primary cellular receptor, and is believed to have played a role in the ability of SARS-CoV to produce infections of both the upper and lower respiratory tracts, contributing to its lethality.[17] Similarly, MERS-CoV has been shown to bind to dipeptidyl-peptidase 4 (DPP4), a protein that has been conserved across species known to harbor this strain of coronavirus. While most respiratory viruses infect ciliated cells, DPP4 is expressed in nonciliated cells in human airways, which is believed to be an important factor in its zoonotic transmission and high mortality rate.[18]

Prevention

Based on the transmission specifications of coronaviruses as a class and documented transmission patterns of the SARS-CoV and MERS-CoV outbreaks, the transmission of COVID-19 is presumed to be primarily through droplets and fomites. The WHO and the CDC recommendations for infection control and transmission prevention differ slightly from each other.

- **WHO recommendations:** Standard, contact, and droplet precautions with eye or face protection. Airborne precautions are recommended in cases where the patient is undergoing aerosol-generating procedures, such as tracheal intubation, noninvasive ventilation, tracheotomy, cardiopulmonary resuscitation, manual ventilation (eg, prior to intubation), and bronchoscopy.[19] This is especially important in the context of preliminary data from an initial cohort of 138 COVID-19-infected patients, which showed a rate of nosocomial infection as high as 41%.[6]

- **CDC recommendations:** Standard, contact, and airborne precautions, with eye protection. If an airborne infection isolation room is unavailable, the patient should wear a mask and be placed in a private room with the door closed. All personnel interacting with the patient should wear the appropriate personal protective equipment in accordance with the precautions delineated above.[20]

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Both the WHO and CDC guidelines similarly emphasize the importance of strict hand hygiene in curtailing COVID-19 transmission. This stems from the uncertainty surrounding the transmission vectors aboard the quarantined *Diamond Princess* cruise ship off the coastal waters of Japan, as well as increasing reports from around the world of COVID-19 appearing in people who have not had direct contact with a known or suspected carrier or a traveler to China.[21,22] Given the recent reports from the Chinese CDC of COVID-19 virus being found in the feces of seropositive patients, the likelihood of fecal-oral and, hence, hand transmission is very high.[23] Healthcare professionals and patients should follow standard hand-washing techniques: wash hands with soap and water for at least 20 seconds, especially after going to the bathroom; before and after eating; and after blowing the nose, coughing, or sneezing. If soap and water are not available, one should use an alcohol-based sanitizer with at least 60% alcohol.[3] While in vitro survival rates of COVID-19 on surfaces remains to be studied, past data on HCoV-229E suggest the capability for strains of coronavirus to survive outside of the host for multiple days, under the right conditions.[24,25]

Additional guidelines for those with close contacts and suspicious exposures include "strong recommendations" (based on high-quality evidence) for immediate medical attention, an observation period of 14 days, wearing N95 masks, prioritizing private transportation over public, prenotification of the hospital prior to patient arrival, and cleansing of the transport vehicle with 500 mg/L chlorine-containing disinfectant, with open ventilation.[26] Note that the recommended observation period may soon be modified, given recent case reports and studies suggesting incubation periods of 0 to 24 days.[27,28]

Evaluation and Diagnosis in the Emergency Department

Although we are approaching the end of the winter season, with its abundance of influenza and influenza-like illnesses, reports from the CDC and WHO suggest COVID-19 may persist well past the winter season. Emergency department (ED) staff need to maintain a high index of suspicion when evaluating a patient with fever, cough, dyspnea, or signs of a lower respiratory tract illness who have had recent travel or contact with a recent traveler to endemic areas. The CDC had initially focused their travel warnings and epidemiological risks on those with recent travel or contact with a traveler to Wuhan City, Hubei province, China; however, with people in the United States, Egypt, Iran, Italy, Canada, and other non-Asian countries contracting COVID-19 and potentially spreading it to others, the connection to China will increasingly diminish. **See Table 2, page 8** for the CDC's clinical features and epidemiological risks for the evaluations of persons suspected of having COVID-19.

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Table 2. Clinical Features and Epidemiological Risks of COVID-19

Clinical Features	AND	Epidemiologic Risk
Fever* **or** signs/symptoms of lower respiratory illness (eg, cough or shortness of breath)	AND	Any person, including healthcare workers, who has had close contact* with a laboratory-confirmed* 2019-nCoV patient* within 14 days of symptom onset
Fever* **and** signs/symptoms of a lower respiratory illness (eg, cough or shortness of breath)	AND	A history of travel from Hubei Province, China* within 14 days of symptom onset
Fever* **and** signs/symptoms of a lower respiratory illness (eg, cough or shortness of breath) requiring hospitalization	AND	A history of travel from mainland China* within 14 days of symptom onset

*For explanation of use of the terms, *fever, close contact, laboratory-confirmed, 2019-nCoV patient,* and *China,* view the source at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fclinical-criteria.html#foot1

An early, retrospective, single-center case series of 138 consecutively hospitalized patients with confirmed novel coronavirus-infected pneumonia (NCIP) provides valuable information on the clinical presentation and laboratory trends for patients infected with this virus. The findings from this study are summarized in the article published in *JAMA*, which can be accessed in full at: https://jamanetwork.com/journals/jama/fullarticle/2761044. According to Table 1 in the *JAMA* article, notable demographics include a median age of 56 years, with interquartile range of 42 to 68 years, with ICU patients strongly favoring those more advanced in age. Of note, 40 (29%) of the confirmed NCIP patients were active health professionals, and 17 (12.3%) were hospitalized patients, suggesting an alarming 41% rate of nosocomial spread. Infected patients requiring ICU-level care were more likely to have underlying comorbidities.[6]

According to Table 2 in the *JAMA* article, notable laboratory findings in this population include lymphopenia in 97 patients (70.3%), prolonged prothrombin time (13.0 seconds [interquartile range,12.3-13.7 seconds]) in 80 patients (58%), and elevated lactate dehydrogenase (261 U/L [interquartile range, 182-403 U/L]) in 55 patients (39.9%). Patients requiring ICU-level care tended to have higher white blood cell counts, with a $P = .03$, and higher lactate dehydrogenase levels ($P < .001$).

Findings on chest imaging in COVID-19 have been similar to findings seen in previous years from the SARS-CoV and MERS-CoV outbreaks. A recent cohort analysis of 41 patients infected with COVID-19 found all but 1 with bilateral lung involvement.[8] A study of computed tomography (CT) scans of 21 patients with COVID-19 infection showed 3 (21%) with normal CT scans; 12 (57%) with ground-glass opacity only; 6 (29%) with ground-glass opacity and consolidation at presentation; and interestingly, 3 (14%) with

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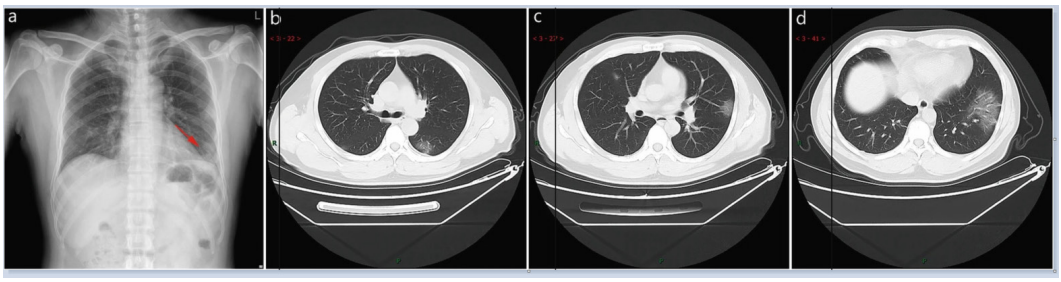
normal scans at diagnosis. Fifteen patients (71%) had 2 or more lobes involved, and 16 (76%) had bilateral disease.[29] Of the 18 patients with positive findings on chest CT, all had the presence of ground glass opacities, with 12 of the 18 having concomitant lobar consolidations.[29]

The article, "A Rapid Advice Guideline for the Diagnosis and Treatment of 2019 Novel Coronavirus (2019-nCoV)-Infected Pneumonia (standard version)," published in the journal, *Military Medical Research*, provided rapid advice guidelines and diagnostic imaging of several cases. **Figure 2** presents a typical x-ray and CT images of a patient with COVID-19.

Figure 2. X-Ray and Computed Tomography Imaging of COVID-19 Pneumonia



Typical CT /X-ray imaging manifestation (case 2). A 51-year-old male with general muscle ache and fatigue for 1 week, fever for 1 day (39.1°C), anemia. Laboratory tests: normal white blood cells (9.24×10^9/L), lymphocytes percentage (5.1%), decreased lymphocytes (0.47×10^9/ L), decreased eosinophil count (0×10^9/L), increased C-reaction protein (170.91 mg/L), increased procalcitonin (0.45 ng/mL), increased erythrocyte sedimentation rate (48 mm/hr). Imaging examination: **(a)** shows patchy shadows in the outer region of the left lower lobe; **(b)** shows large ground-glass opacity in the left lower lobe; **(c)** shows subpleural patchy ground-glass opacity in posterior part of right upper lobe and lower tongue of left upper lobe; and **(d)** shows large ground-glass opacity in the basal segment of the left lower lobe.
Available at: https://doi.org/10.1186/s40779-020-0233-6
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The article, "Evolution of CT Manifestations in a Patient Recovered from 2019 Novel Coronavirus (2019-nCoV) Pneumonia in Wuhan, China," published in the journal *Radiology*, published 6 images of the evolution of chest imaging of a 42-year-old male patient infected with COVID-19 who recovered over 31 days.[30] These images can be viewed at: https://doi.org/10.1148/radiol.2020200269

Within a month of initial reports detailing the COVID-19 outbreak, the CDC developed a real-time reverse transcription-polymerase chain reaction (rRT-PCR) test that diagnoses COVID-19. While diagnostic testing in the United States was available initially only through the CDC, this assay is now being made available at the state level with the use of the International Reagent Resource (IRR). The IRR was initially established by the CDC for the study and detection of influenza, but it has been expanded to include newly discovered influenza and coronaviruses.[31] International,

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state, and local public health departments utilize this standard reagent in order to monitor and ensure quality control and standardized results. The reagent is expected to be available at the state and local levels by the end of the first quarter of 2020.[32] It should be noted that widely available respiratory viral panels test only for the earlier forms of human coronavirus, namely human coronaviruses 229E, NL63, OC43, and HKU1.[33] The SARS-CoV, MERS-CoV, and COVID-19 strains require more specialized assays that are not as widely available.

Management

In the case of infection with any of the coronavirus strains, there is no known directed treatment specific to the virus. Many patients with confirmed NCIP in the *JAMA* study received broad-spectrum antibacterial therapy (moxifloxacin, 89 [64.4%]; ceftriaxone, 34 [24.6%]; azithromycin, 25 [18.1%]) and most received antiviral therapy (oseltamivir, 124 [89.9%]), with some additionally receiving steroids (glucocorticoid therapy, 62 [44.9%]).[6]

Considering the lack of direct evidence with regard to treatment of COVID-19, recently proposed guidelines have been built largely on treatment guidelines for SARS-CoV, MERS-CoV, and influenza. Currently, there are weak recommendations for alpha-interferon atomization inhalation twice/day, and lopinavir/ritonavir orally twice/day; however, evidence supporting these in reducing the incidence and mortality of acute respiratory distress syndrome (ARDS) in patients infected with SARS-CoV and MERS-CoV are limited to case series and case reports.[26] A recent systematic review showed that lopinavir/ritonavir's anticoronavirus effect was seen mainly in its early application, and no significant effect was seen in late application of therapy.[34] At this time, the use of combined antivirals in the treatment of COVID-19 is controversial, as there are currently no randomized controlled trials in humans to support their use.[35,36]

In a systematic review in the Chinese literature of treatments for SARS-CoV, 14 studies were identified in which steroids were used. Twelve studies were inconclusive and 2 showed potential harm. One study reported diabetes onset associated with methylprednisolone treatment.[37] Another uncontrolled, retrospective study of 40 SARS patients reported avascular necrosis and osteoporosis among corticosteroid-treated SARS patients.[38] A randomized, double-blind, placebo-controlled trial measured SARS-CoV plasma viral load across time after fever onset and found corticosteroid use within the first week of illness was associated with delayed viral clearance.[39] Yet another case-controlled study found that patients who developed psychosis while on steroids received higher cumulative doses of steroids than patients without psychosis (10,975 mg vs 6780 mg; $P = .017$).[40]

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In patients who deteriorate and require ICU-level care, treatment should consider noninvasive ventilation, mechanical ventilation, or extracorporeal life support if necessary.[26] In patients with poor outcomes, development of ARDS and respiratory decompensation plays a central role in pathogenesis. In this sense, the following treatment principles are key in managing COVID-19 patients:

- Hemodynamic management, with vasopressor support if necessary
- Nutritional support
- Blood glucose control
- Expeditious evaluation and treatment of nosocomial or superinfective pneumonia
- Prophylaxis against deep vein thrombosis and gastrointestinal bleeding
- Proper patient positioning to aid oxygenation and ventilation

Looking to the Future

The future is unpredictable regarding the outbreak of COVID-19. Given case reports of transmission of COVID-19 from asymptomatic carriers,[27] its spread and containment will face unprecedented challenges. Daily information (and misinformation) have added to the challenges to the general public as well as the medical community. *The Lancet* published an online editorial (https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2930379-2), which appeals to the medical community to seek verified information through the CDC or WHO and avoid social media and other unverified sources for information. Many worried well patients will show up in the ED, taxing our already overburdened systems. This is an opportunity for hospital leadership to develop and/or expand their telehealth options to be used during such an outbreak, to minimize the numbers of worried well or low-risk patients with mild symptoms bombarding local EDs.

There has been funding directed at producing a vaccine for MERS-CoV, which is notorious for its high mortality, and the effort has met with significant advances as well as continued challenges. There is currently a DNA vaccine candidate that has entered into human clinical trials, while 2 vector-based candidates will soon begin human trials; protein-based vaccines are still at the preclinical stage.[41] Challenges to successful vaccine development include incomplete understanding of viral transmission, pathogenesis, and immune response; lack of optimal animal challenge models and standardized immunological assays; as well as insufficient sustainable funding.

Remdesivir has recently been recognized as a promising antiviral drug against a wide array of RNA viruses, including SARS-CoV and MERS-CoV infection in vitro and in nonhuman primate models.[42] Furthermore, recent

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in vitro studies conducted on COVID-19 have found that remdesivir and chloroquine inhibit viral infection of cells with low micromolar concentration with a high selectivity index.[41]

Hospital Management

With several media and public health agencies warning of a continued global outbreak and possible pandemic, there is a high probability United States hospitals will see a large influx of cases of COVID-19, which will overwhelm many health systems. The CDC has issued guidance to all healthcare institutions, stating:

All United States hospitals should be prepared for the possible arrival of patients with COVID-19. All hospitals should ensure their staff are trained, equipped, and capable of practices needed to:

- Prevent the spread of respiratory diseases, including COVID-19, within the facility
- Promptly identify and isolate patients with possible COVID-19 and inform the correct facility staff and public health authorities
- Care for a limited number of patients with confirmed or suspected COVID-19 as part of routine operations
- Potentially care for a larger number of patients in the context of an escalating outbreak
- Monitor and manage any healthcare personnel that might be exposed to COVID-19
- Communicate effectively within the facility and plan for appropriate external communication related to COVID-19[43]

Additionally, the CDC has released a checklist for hospital preparedness, which can be found at: **https://www.cdc.gov/coronavirus/2019-ncov/downloads/hospital-preparedness-checklist.pdf**

In the event of a mass influx of patients with exposure to or symptoms concerning for COVID-19, immediate isolation is required. If 1 infected person presents to a busy ED triage area without a mask and touches objects, there is a high likelihood of spreading the virus and potentially contaminating others. The CDC recommends placing ample supplies of touchless hand sanitizer stations and easy-dispense boxes of face masks at entrances to the ED and hospital. They also recommend placing signs that advise anyone entering the facility to "immediately put on a mask and keep it on during their assessment; cover their mouth/nose when coughing or sneezing; use and dispose of tissues; and perform hand hygiene after contact with respiratory secretions."[43] The CDC also advises patients with fever or symptoms of respiratory infection and recent travel outside the United States, specifically to China, to immediately notify triage per-

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sonnel, so appropriate precautions can be put in place.[43] However, travel history is becoming increasingly vague as more cases outside of China, and without a connection to China, become prevalent.

Clearly, each hospital will have differing capabilities to put appropriate precautions in place, as this could require dedicated isolation areas for perhaps a handful of patients to potentially several dozen (or more). The mere potential magnitude of cases presenting to EDs across the United States is staggering and should raise a heightened sense of urgency to emergency management and infectious disease prevention specialists to ensure their hospitals have enough isolation areas and supplies for patients and staff. It is unlikely that the United States has the capability to build several-thousand-square-foot dedicated isolation (quarantine) hospitals in the span of days to cope with the potential outbreaks in each metropolitan area, as was done in China. However, with the assistance of the federal government, agencies such as the Federal Emergency Management Agency (FEMA) and the Department of Defense (DoD) could be mobilized to bring portable emergency hospitals to areas that may have local hospitals that are overwhelmed. Hospital leadership should be coordinating with FEMA and the DoD pre-emptively, and not during an outbreak. Lastly, emergency medical services (EMS) medical directors should develop or establish protocols for paramedics or emergency medical technicians (EMTs) to render aid to those at home who are not sick enough to require hospital services.

Case Conclusion

You recalled your recent training on recognizing infectious diseases and the need for immediate and proper donning of personal protective equipment. You and a nurse put on your complete PPE and obtained the patient's vital signs, which confirmed a temperature of 39.6°C [103.3°F], pulse of 106 beats/min, respirations of 22 breaths/min, blood pressure 102/68 mm Hg, and pulse oximetry 89% on room air. His exam was notable mostly for rhonchi bilaterally to all lung fields. You started him immediately on supplemental oxygen and confirmed his travel history and possible contacts with people who may have been exposed to COVID-19. You contacted your hospital infectious disease and infection prevention team, who directed you to also contact your local department of public health, who sent a representative to find out all of his possible contacts. The patient was eventually admitted to an isolation room after bilateral patchy infiltrates were noted on his chest x-ray. You started empirical coverage for bacterial pneumonia, consulted the CDC and WHO for up-to-date guidance on additional treatment recommendations, and remembered to avoid steroids.

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Table 3. Helpful Resources for COVID-19

Organization	Link
United States Centers for Disease Control and Prevention	https://www.cdc.gov/coronavirus/2019-ncov/index.html
World Health Organization	https://www.who.int/emergencies/diseases/novel-coronavirus-2019
Johns Hopkins University COVID-19 Global Case Tracker	https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6
United States Department of Labor, Occupational Safety and Health Administration	https://www.cdc.gov/coronavirus/2019-ncov/index.html
American College of Emergency Physicians COVID-19 Clinical Alert	https://www.acep.org/by-medical-focus/infectious-diseases/coronavirus/
The Lancet COVID-19 Resource Centre	https://www.thelancet.com/coronavirus?dgcid=kr_pop-up_tlcoronavirus20

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study will be included in bold type following the references, where available.

1. Yip CC, Lam CS, Luk HK, et al. A six-year descriptive epidemiological study of human coronavirus infections in hospitalized patients in Hong Kong. *Virol Sin.* 2016;31(1):41-48. **(Epidemiologic surveillance study) DOI: https://doi.org/10.1007/s12250-016-3714-8**
2. Shi ZL, Guo D, Rottier PJ. Coronavirus: epidemiology, genome replication and the interactions with their hosts. *Virol Sin.* 2016;31(1):1-2. **(Epidemiologic editorial) DOI: https://doi.org/10.1007/s12250-016-3746-0**
3. United States Centers for Disease Control and Prevention. 2019 novel coronavirus (COVID-19). Available at: **https://www.cdc.gov/coronavirus/2019-ncov/index.html**. Accessed February 15, 2020. **(CDC website)**
4. Johns Hopkins University Center for Systems Science and Engineering. Coronavirus COVID-19 Global Cases by Johns Hopkins CSSE. Available at: **https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6**. Accessed February 15, 2020. **(Johns Hopkins epidemiologic tracking website)**

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5. 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. *Lancet.* 2020;395(10223):507-513. **(Retrospective single-center descriptive study; 99 patients)** **DOI: https://doi.org/10.1016/S0140-6736(20)30211-7**
6. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA.* Published online February 7, 2020. **(Retrospective, single-center case series; 138 patients)** **DOI: https://doi.org/10.1001/jama.2020.1585**
7. Wang C, Horby PW, Hayden FG, et al. A novel coronavirus outbreak of global health concern. *Lancet.* 2020;395(10223):470-473. **(Epidemiologic review) DOI: https://doi.org/10.1016/S0140-6736(20)30185-9**
8. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497-506. **(Retrospective epidemiologic review; 41patients)** **DOI: https://doi.org/10.1016/S0140-6736(20)30183-5**
9. Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. *Eurosurveillance.* 2020;25(4):2000058. **(Epidemiologic surveillance and simulation study)** **DOI: https://doi.org/10.2807/1560-7917.ES.2020.25.4.2000058**
10. Farge E, Nebehay S. "WHO Says Man With Coronavirus in Egypt is Recovering, No Longer a Carrier." Reuters World News. Available at: **https://www.reuters.com/article/us-china-health-egypt/who-says-man-with-coronavirus-in-egypt-is-recovering-no-longer-a-carrier-idUSKBN20D284**. Accessed February 20, 2020. **(News article)**
11. No author listed. "COVID-19: Fighting Panic with Information." *The Lancet.* 395(10224).537. Available at: **https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30379-2/fulltext#articleInformation**. Accessed February 22, 2020. **(Editorial article)**
12. Wang N, Li SY, Yang XL, et al. Serological evidence of bat SARS-related coronavirus infection in humans, China. *Virol Sin.* 2018;33(1):104-107. **(Epidemiologic surveillance study [serologic])** **DOI: https://doi.org/10.1007/s12250-018-0012-7**
13. Hui DSC, Zumla A. Severe acute respiratory syndrome: historical, epidemiologic, and clinical features. *Infect Dis Clin North Am.* 2019;33(4):869-889. **(Systematic review of epidemiology and clinical features of SARS) DOI: https://doi.org/10.1016/j.idc.2019.07.001**
14. Hejase H. Review of dromedary camels and the transmission of Middle East respiratory syndrome coronavirus (MERS-CoV). *Publons.* 2018. Available at: **https://publons.com/publon/878949/#review-2686681**. Accessed February 15, 2020. **(Epidemiologic history)**

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15. Cohen J. "Wuhan Seafood Market May Not Be Source of Novel Virus Spreading Globally." Science. 2020. Available at: **https://www.sciencemag.org/news/2020/01/wuhan-seafood-market-may-not-be-source-novel-virus-spreading-globally**. Accessed February 15, 2020. **(Online magazine article)**
16. Li H, Mendelsohn E, Zong C, et al. Human-animal interactions and bat coronavirus spillover potential among rural residents in Southern China. *Biosafety and Health.* 2019;1(2):84-90. **(Prospective epidemiologic surveillance study; 1597 patients)**
DOI: https://doi.org/10.1016/j.bsheal.2019.10.004
17. Lam C-Y. *Comparative molecular analysis of the binding between severe acute respiratory syndrome coronavirus (SARS-COV) spike protein and angiotensin converting enzyme 2 (ACE2).* Open Dissertation Press; 2007. **(Dissertation)**
18. Kleine-Weber H, Schroeder S, Krüger N, et al. Polymorphisms in dipeptidyl peptidase 4 reduce host cell entry of Middle East respiratory syndrome coronavirus. *Emerging Microbes & Infections.* 2020;9(1):155-168. **(Basic science research)**
DOI: https://doi.org/10.1080/22221751.2020.1713705
19. World Health Organization. Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected. Published January 25, 2020. Available at: **https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125**. Accessed February 15, 2020. **(Guidelines)**
20. United States Centers for Disease Control and Prevention. "What Healthcare Personnel Should Know About Caring for Patients With Confirmed or Possible 2019-nCoV Infection." Available at: **https://www.cdc.gov/coronavirus/2019-ncov/hcp/caring-for-patients.html**. Accessed February 20, 2020. **(CDC website)**
21. Lesney MS. "WHO Urges That 'Window of Opportunity' on Containing Novel Coronavirus Not Be Missed." Medscape Medical News. Available at: **https://www.medscape.com/viewarticle/925561?nlid=134099_3901&src=wnl_newsalrt_200221_MSCPEDIT&uac=19371DT&impID=2286918&faf=1**. Accessed February 20, 2020. **(Medical news site)**
22. CNBC Live. World Health Organization holds a news converence on the coronavirus outbreak, 2/21/20. Available at: **https://www.youtube.com/watch?v=KAPKonW_CNk**. **(Press conference video)**
23. Zhang Y, Chen C, Zhu S, et al. Isolation of 2019-nCoV from a stool specimen of a laboratory-confirmed case of the coronavirus disease 2019 (COVID-19). *China CDC Weekly*. 2020;2(8):123-124. Available at: **http://weekly.chinacdc.cn/en/article/id/ffa97a96-db2a-4715-9dfb-ef662660e89d**. Accessed February 20, 2020. **(China CDC website; translated)**

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24. Ijaz MK, Brunner AH, Sattar SA, et al. Survival characteristics of airborne human coronavirus 229E. *J Gen Virol*. 1985;Dec; 66 (Pt 12):2743-2748. **(Basic science research)**
DOI: https://doi.org/10.1099/0022-1317-66-12-2743
25. Geller C, Varbanov M, Duval RE. Human coronaviruses: insights into environmental resistance and its influence on the development of new antiseptic strategies. *Viruses*. 2012;4(11):3044-3068. **(Basic science review) DOI: https://doi.org/10.3390/v4113044**
26. Jin Y-H, Cai L, Cheng Z-S, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res*. 2020;7(1):4. **(Clinical practice guidelines – United States)**
DOI: https://doi.org/10.1186/s40779-020-0233-6
27. Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. *JAMA*. Published online February 21, 2020. Available at: **https://jamanetwork.com/journals/jama/fullarticle/2762028**. Accessed February 20, 2020. **(Case report)**
28. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of 2019 novel coronavirus infection in China. *medRxiv*. Published online February 9, 2020. Available at: **https://www.medrxiv.org/content/10.1101/2020.02.06.20020974v1**. Accessed February 20, 2020. **(Preprint article website)**
29. Chung M, Bernheim A, Mei X, et al. CT imaging features of 2019 novel coronavirus (2019-nCoV). *Radiology*. Published online February 4, 2020. **(Retrospective study; 21 patients)**
DOI: https://doi.org/10.1148/radiol.2020200230
30. Shi H, Han X, Zheng C. Evolution of CT manifestations in a patient recovered from 2019 novel coronavirus (2019-nCoV) pneumonia in Wuhan, China. *Radiology*. Published online February 7, 2020. **(Case report) DOI: https://doi.org/10.1148/radiol.2020200269**
31. United States Centers for Disease Control and Prevention. IRR (International Reagent Resource). Available at: **https://www.internationalreagentresource.org/About/IRR.aspx**. Accessed February 20, 2020. **(CDC website)**
32. United States Centers for Disease Control and Prevention. CDC Tests for COVID-19. Available at: **https://www.cdc.gov/coronavirus/2019-ncov/about/testing.html**. Accessed February 20, 2020. **(CDC website)**
33. Legacy Health. Respiratory Panel by PCR. Available at: **https://www.legacyhealth.org/for-health-professionals/refer-a-patient/laboratory-services/test-table/respiratory-virus-panel-by-pcr.aspx**. Accessed February 20, 2020. **(Healthcare provider website)**
34. Jiang H, Deng H, Wang Y, et al. The possibility of using Lopinave/Litonawe (LPV/r) as treatment for novel coronavirus COVID-19 pneumonia: a quick systematic review based on earlier coronavirus clinical

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studies. *Zhonghua Jizhen Yixue Zazhi.* 220;29(2):182-186. **(Systematic review of Chinese literature on antivirals in SARS-CoV and MERS-CoV) DOI: https://tinyurl.com/tkbefz3**

35. Khan P, Nousheen B, Maryam N, et al. Middle East respiratory syndrome (MERS): a systematic review. *International Journal of Pharmaceutical Sciences and Research.* 2018;9(7):2616-2625. Available at: **https://ijpsr.com/bft-article/middle-east-respiratory-syndrome-mers-a-systematic-review/?view=fulltext.** Accessed February 15, 2020. **(Systematic review)**
36. Falzarano D, de Wit E, Rasmussen AL, et al. Treatment with interferon-alpha2b and ribavirin improves outcome in MERS-CoV-infected rhesus macaques. *Nat Med.* 2013;19(10):1313-1317. **(Randomized controlled trial with 6 subjects) DOI: https://doi.org/10.1038/nm.3362**
37. Xiao JZ, Ma L, Gao J, et al. [Glucocorticoid-induced diabetes in severe acute respiratory syndrome: the impact of high dosage and duration of methylprednisolone therapy]. *Zhonghua Nei Ke Za Zhi.* 2004;43(3):179-182. **(Retrospective study; 133 patients)**
38. Li YM, Wang SX, Gao HS, et al. [Factors of avascular necrosis of femoral head and osteoporosis in SARS patients' convalescence]. *Zhonghua Yi Xue Za Zhi.* 2004;84(16):1348-1353. **(Retrospective study; 40 patients)**
39. Lee N, Allen Chan KC, Hui DS, et al. Effects of early corticosteroid treatment on plasma SARS-associated coronavirus RNA concentrations in adult patients. *J Clin Virol.* 2004;31(4):304-309. **(Randomized double-blinded placebo-controlled prospective trial; 16 patients) DOI: https://doi.org/10.1016/j.jcv.2004.07.006**
40. Lee DT, Wing YK, Leung HC, et al. Factors associated with psychosis among patients with severe acute respiratory syndrome: a case-control study. *Clin Infect Dis.* 2004;39(8):1247-1249. **(Retrospective case-control study; 15 cases, 30 controls) DOI: https://doi.org/10.1086/424016**
41. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res.* 2020 Feb 4 [Epub ahead of print]. **(Basic science/microbiology research) DOI: https://doi.org/10.1038/s41422-020-0282-0**
42. Sims A. The small molecule nucleoside prodrug GS-5734 exhibits broad antiviral activity against pathogenic human coronaviruses and related zoonotic strains. *Clinical Microbiology: Open Access.* 2016;5(5 Suppl). **(Basic science/microbiology research)**
43. United States Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19) hospital preparedness assessment tool. Available at: **https://www.cdc.gov/coronavirus/2019-ncov/hcp/hcp-hospital-checklist.html**. Accessed February 20, 2020. **(CDC website)**

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Practice Questions

1. **Which of the following is most accurate regarding the epidemiology of COVID-19?**
   a. It affects mostly children under the age of 12
   b. Early data suggests COVID-19 is much more clinically severe than MERS-CoV or SARS-CoV
   c. Early data suggests a mortality rate of approximately 3%
   d. It predominantly causes a severe viral pneumonia in a single lung

2. **What is the most common clinical symptom in patients found to be infected with COVID-19?**
   a. Cough
   b. Diarrhea
   c. Fever
   d. Vomiting

3. **Which animal is thought to have harbored coronaviruses during its evolution, prior to zoonotic transmission to humans?**
   a. Cats
   b. Bats
   c. Gnats
   d. Camels

Answer Key is on page 20.

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Answer Key

1. Which of the following is most accurate regarding the epidemiology of COVID-19?

Answer: C, Early data suggest a mortality rate of approximately 3% from COVID-19. See Table 1, page 4. According to the early findings, the mortality of COVID-19 is 3.12%. The age range is 21 years to 76 years. In the "Evaluation and Diagnosis in the Emergency Department" section on pages 8 and 9, the early findings on chest imaging in COVID-19 have shown typically bilateral lung involvement.

2. What is the most common clinical symptom in patients found to be infected with COVID-19?

Answer: C, Fever. See Table 1, page 4. Early findings show that fever is present in 98% of patients with COVID-19. Also see Table 2, page 8 for the CDC's recent findings that fever is the most common clinical symptom in patients with COVID-19.

3. Which animal is thought to have harbored coronaviruses during its evolution prior, to zoonotic transmission to humans?

Answer: B, Bats. See the "Virology" section, page 5. Although the origin has not been confirmed, serologic evidence has shown that those coronaviruses are believed to have resulted from zoonotic spread from the bat population, with an intermediate mammalian host (civet cats for SARS-CoV and dromedary camels in the case of MERS-CoV).

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