

Coronavirus Infections: SARS, MERS, and COVID-19

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Purpose

The purpose of this course is to provide current information about coronaviruses, including SARS, MERS, and COVID-19 as well as the history of the recent COVID-19 pandemic and the signs and symptoms, complications, transmission precautions, diagnosis, and treatment.

Goals

Upon completion of this course, the nurse should be able to

- Describe the coronavirus, including appearance.
- Discuss the history of severe coronavirus infections.
- Describe the role that wet markets have in spreading zoonotic diseases to humans.
- Describe typical signs and symptoms of the two stages of SARS.
- Explain the 3 types of transmission prevention required for SARS and other severe coronavirus infections.
- Discuss transmission of MERS.
- Discuss diagnosis and treatment options for MERS and SARS.
- Explain the history of COVID-19.
- Discuss transmission concerns for COVID-19.
- Discuss at least 10 common symptoms of COVID-19.
- Describe at least 5 major complications of COVID-19.
- Discuss treatment options for COVID-19.
- Discuss at least 2 medications that may be used for COVID-19
- Discuss prevention measures for COVID-19

Introduction



The news about coronavirus remains grim even though the worst seems to be easing—at least for now.

During the peak of the current outbreak, healthcare providers were exhausted and at high risk of infection. Hospitals were overwhelmed and out of

ventilators and PPE. Convention centers were being converted to hospitals. Field hospitals were being set up in parks. Navy hospital ships were anchored at New York City and Los Angeles. Refrigerator trucks stood outside of hospitals to hold the dead. Stores were boarded up, and streets are vacant. People were—and still are--out of work and afraid.

Coronaviruses are not new. They have been around for aeons, infecting humans with mild upper respiratory infections, such as the common cold. Animals infected with coronaviruses may develop respiratory, gastrointestinal, liver and neurologic disease. Therefore, when these viruses jump from animal species to humans, severe illness and the risk of pandemics can result.

Coronaviruses are a group of viruses and are so named because of their shape, which is round with a halo of proteins spiking from the surface.



Coronaviruses are composed of RNA, and each variety can be very distinct from others. There are four primary type of coronaviruses: alpha, beta, delta, and gamma. Alpha and beta types are able to infect human beings. Four varieties (229E, NL63, OC43, and HKU1) cause up to 30% of

common colds.

Coronaviruses first came to the attention of the public in 2002. In November 2002, the first case of a new type of coronavirus infection occurred in Guangdong Province, China, resulting in the death of the patient, followed by more infections, but the Chinese government failed to report the outbreak to the WHO or to acknowledge that an outbreak was occurring,

even though the WHO requested information in December based on internet reports of a “flu outbreak.” When, several months later, the WHO was able to take action, 500 people had died and over 2000 cases had occurred worldwide.

This new coronavirus infection was referred to as severe acute respiratory syndrome (SARS) and was a documented instance of a coronavirus jumping from wildlife to humans. By April, the CDC was able to publish the sequence of the virus.

The CDC issued a number of travel alerts (Toronto, Singapore, Toronto, China, Taiwan, Hong Kong (areas with outbreaks) in order to reduce risk to the United States. By July 2003, the outbreak was contained, but SARS had spread to 17 countries with 8096 identified cases and 774 deaths, a 9.6% mortality rate. Only 8 people in the United States became infected and all survived. It is estimated that the SARS outbreak cost the world about \$40 billion dollars.

Subsequently, SARS has been followed by outbreaks of MERS and the COVID-19, the coronavirus infection now ravaging the world.

How are wet markets implicated in transmission of coronaviruses in China?

Coronaviruses are zoonotic diseases (those that spread between animals and humans). In China, both SARS and the Wuhan coronavirus have been linked to wet markets that sell fruits, vegetables, spices, live animals (pigs, chicken, ducks, civets, rats, beavers, porcupines) butchered meat, dogs, rabbits, fish, shellfish and snakes. The Chinese, especially, like to purchase



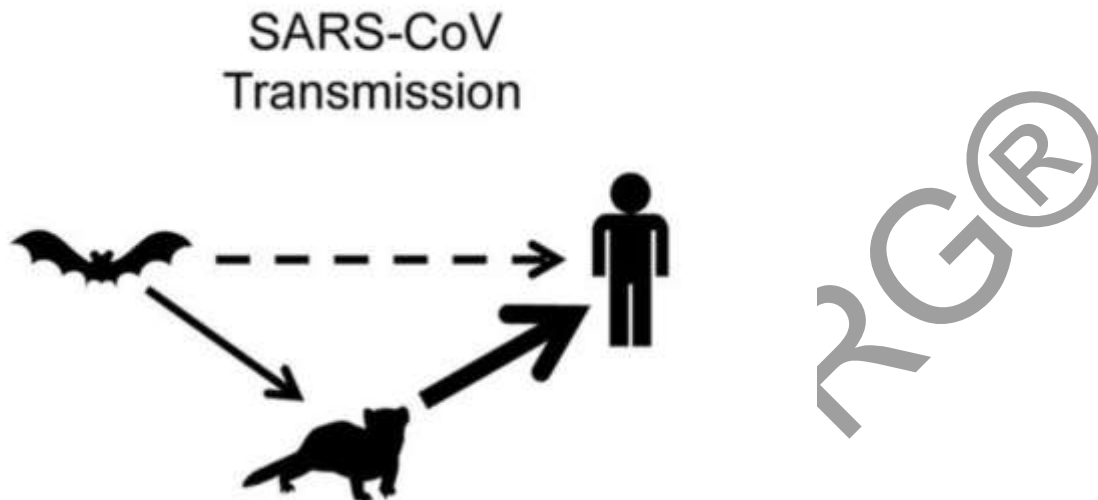
live animals and have a penchant for wild animals, which many believe can cure disease and improve male potency.

The markets that sell this wide range of food products are called wet markets because workers slosh water about the floor to wash away the inevitable feces and urine,

resulting in a literal soup of pathogens. Whether people become infected from contact with the animals or ingestion is not always clear. The SARS

coronavirus infection was finally traced to civets (cat-like mammals), which had become infected from bats.

Severe Acute Respiratory Syndrome (SARS-CoV)



The public became generally aware of the SARS outbreak in February 2003, when an American (Johnny Chen) traveling from China to Singapore became seriously ill on the plane and was hospitalized in Hanoi, Vietnam, where he died. Subsequently, a number of staff members at the hospital became ill despite using standard precautions in caring for Chen. In response to the severity of the illnesses, the WHO issued a global alert in March 2003 and the CDC issued a health alert. However, the disease continued to spread.

The SARS-associated coronavirus (SARS-CoV) is from the Coronaviridae family and is spread through close contact with an infected animal or person. Civets infected by bats are thought to have initially spread the disease to a human. Person-to-person transmission is primarily through respiratory droplets (sneeze, cough), usually no more than a 3-foot distance. However, the disease can also spread through contact with contaminated surfaces or exchange of body fluids. SARS appears to be easily transmitted with close contact. It is also possible that fecal-oral transmission can occur.

The incubation period for SARS is generally 2 to 7 days although this may extend to 10 to 14 days in rare cases. People with the infection are contagious when they are symptomatic.

Signs and symptoms

SARS typically begins with mild to moderate flu-like symptoms, but some patients progress to pneumonia and respiratory failure. Some may be asymptomatic as well.

Stage 1	This upper-respiratory stage usually lasts from 3 to 7 days during which the patient may have fever (>100.4°F/38°C), chills, headaches, fatigue, general malaise, myalgias, anorexia. Some may complain of sore throat, nausea and vomiting, dizziness, diarrhea (occurs in 10 to 20%), coryza, and increased sputum production. Delirium may occur in older adults.
Stage 2:	This lower respiratory stage is characterized by dry, non-productive cough, increasing dyspnea and hypoxemia, and respiratory failure requiring mechanical ventilation (10 to 20%) in severe cases. The patient's condition may worsen rapidly.

Complications

Between about 25% and 70% of those infected develop hepatitis, resulting in worse outcomes. Some patients may develop a severe neurological syndrome. Most patients develop pneumonia, and pneumonia is the most common cause of death associated with SARS.

Diagnosis

If a patient enters stage 2, the chest x-ray may appear normal for the first 7 days or more but eventually patchy interstitial infiltrates appear if the patient develops pneumonia. SARS pneumonia results in diffuse alveolar damage.

Various tests are typically carried out, including blood cultures, sputum Gram stain, viral respiratory pathogen tests, antibody tests, PCR, and viral culture/isolation tests. CDC provides guidance regarding confirming diagnosis. Laboratory findings associated with SARS include elevation in creatinine kinase, lactate dehydrogenase, alanine aminotransferase, and hepatic transaminase. Patients may exhibit mild hyponatremia and hypokalemia as well as mild lymphopenia, leukopenia, and thrombocytopenia.



Transmission and prevention

Healthcare providers and those in contact with infected patients should utilize contact, droplet, and airborne precautions with N95 respirators. Patients are advised to avoid contact with others and to remain at home until 10 days after the fever is resolved and no respiratory symptoms are present. SARS does not appear to be contagious during the incubation period. Gloves should be applied for any direct

touching of a patient with SARS, and patients and those in contact with the patients should wear face masks.

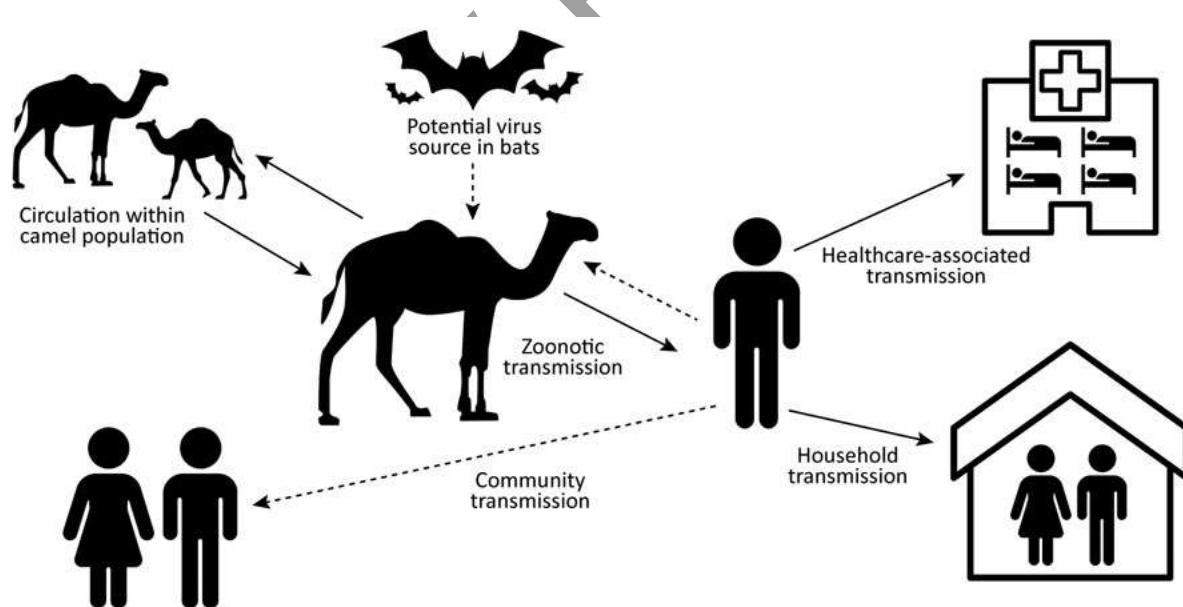
The basic reproductive rate of SARS (the number of cases of the disease that typically result from exposure to an infected person) is 2 to 4 although instituting effective precautions can lower this rate considerably.

Treatment

There is no definitive treatment protocol for SARS, so treatment is usually carried out with consultation from state public health officials and the CDC. Antibiotics are not recommended because they are ineffective for viral infections. Various treatments have been tried, including steroids, which may reduce lung injury but increase risk of mortality.

Treatment has often included an antiviral agent (typically with a steroid) although ribavirin (the most commonly used) appears to have no effect. A high-affinity human monoclonal antibody (huMab) has shown promise in animal studies. While vaccines are being studied, none are available at this time.

Middle East Respiratory Syndrome (MERS)



MERS was first reported in Saudi Arabia in 2012 but has subsequently been found in 27 countries, including the United States with 2 imported cases in 2014 (Indiana and Florida). Both patients had traveled from Saudi Arabia to

the United States and both recovered. MERS is believed to have spread from live camels, which had become infected by bats, to humans through association rather than ingestion.

By November 2019, 2494 cases of MERS worldwide had been confirmed with 780 deaths, a death rate of 34.4%. Outbreaks associated with healthcare have occurred in Saudi Arabia, United Arab Emirates, and South Korea.

The incubation period is typically 5 to 6 days although it can range from 2 to 14 days. Median time from onset of symptoms to hospitalization is 4 days and median time from onset of severe symptoms to admission to ICU is 5 days. Death usually occurs within 12 days.

Signs and symptoms

Some patient may be asymptomatic while others may exhibit a range of respiratory symptoms. Mild fever, nonproductive cough, headache, and dyspnea are common as is pneumonia, which can result in the need for mechanical ventilation. Some may develop diarrhea. Severe disease is most common in those with immunocompromise, chronic disease, and older age.

Complications

The most common complications are acute respiratory failure, ARDS, refractory hypoxemia and extrapulmonary disorders, such as acute kidney injury, hypotension, hepatitis, and septic shock.

Diagnosis

Patients should be evaluated for MERS if they have signs and symptoms associated with the disease and a history of travel in or near the Arabian Peninsula within 14 days of onset of symptoms, close contact with a symptomatic traveler from that area, or a history of being in a healthcare facility in or near the Arabian Peninsula within 14 days, or close contact with a confirmed MERS patient.

Testing is guided by the CDC, which recommends multiple specimens from upper and lower respiratory tract for MERS rRT-PCR assay and serologic testing. Imaging may show unilateral/bilateral patches of densities or opacities, interstitial infiltrates, consolidation, and pleural effusions.

Transmission and prevention

Dromedary camels have been found to harbor the same coronavirus as that infecting humans, suggesting that animal-to-human transmission can occur. Additionally, human-to-human transmission can occur with close contact. Healthcare providers and those in close contact with infected patients should adhere to standard, contact, and airborne precautions.

Currently, most cases occur in the Middle East (80% in Saudi Arabia) or with travelers who were infected in the Middle East. Preventive measures include avoiding contact with camels, drinking of raw camel milk/urine, or eating meat that has not been properly cooked.

Treatment

No specific treatment is currently available, so supportive care (hydration, analgesics, antipyretics) is recommended. Antibiotics are ineffective unless a superinfection, such as sepsis, occurs. Antiviral medications do not appear to be effective. Other treatment may depend on the severity of illness but may include mechanical ventilation, renal replacement therapy, and vasopressors.

2019 novel coronavirus, (COVID-19)

As of November, 25, 2020, more than 60 million cases of COVID-19 have occurred worldwide, resulting in over 1.4 million deaths. In the United States alone, almost 13 million cases have occurred and over 266,000 deaths.

History

It began on December 31, 2019, when the Chinese authorities notified the WHO that several cases of pneumonia from an unknown virus had occurred in Wuhan (first cases in early December) and that several of the infected had been employed at the Huanan Seafood Wholesale Market (a wet market), which was closed down on January 1 although the animal implicated is not yet certain, but the virus is believed to have originally derived from a bat.

By January 7, a new coronavirus, then dubbed the 2019 novel coronavirus (2019-nCoV) or Wuhan coronavirus was identified. On January 22, Wuhan authorities banned the trade of live animals at wet markets. The first reported death occurred on January 9, but as of January 27, 81 people had died with the death toll increasing daily and 2800 cases recorded. Up until then, all deaths occurred in China.

On January 13, the first case outside of China occurred in Thailand in a woman who had come from Wuhan. While most cases occurred in China, by the end of January 2020, almost 10,000 cases of the coronavirus infection had been reported in 21 countries, including Australia, Cambodia, Canada, France, Japan, Malaysia, Nepal, Singapore, South Korea, Sri Lanka, Taiwan, Vietnam, and the United States. The first case in the United States was reported on January 20 in Snohomish County, Washington in a man who had returned from Wuhan.

In an effort to curb spread of the disease, China blockaded a large area of the country, using the military to seal off the area, and travel advisories were in place from the CDC regarding travel to and from China. People in China were advised to wear face masks and to avoid unnecessary contact with others. Eventually, those infected in China were forced into quarantine centers, but the death rate continued to rise until late in February when it began to level out, suggesting that the drastic methods used to control the disease were having a positive effect.

On February 11, 2020, the WHO dubbed the novel coronavirus COVID-19 to discourage use of "Wuhan coronavirus" and identifying the coronavirus with China. The virus is also sometimes referred to as SARS-CoV-2.

As of March 30, 2020, China had 81,470 cases of COVID-19 with 3304 deaths (4% death rate), but China was surpassed by the United States, Italy, and Spain. As of August 31, 2020, China has reported a total of 85,379 infections and 4634 deaths, suggesting that the stringent lockdown was effective.

South Korea also experienced a significant outbreak with 28 cases on February 15 increasing to 9661 by March 16 with 158 deaths (1.6% death rate). Korea instituted massive testing and isolation of those infected, and many authorities credit this with the fact that the death rate in Korea has been lower than in other countries. As of August 31, 2020, South Korea has reported a total of 19,947 total infection and 324 deaths.

Another cause for concern was an outbreak that occurred on the *Diamond Princess*, a cruise ship. On January 20, a passenger on the cruise ship disembarked in Hong Kong and was hospitalized with infection. By February 4 in Japan, an additional 10 passengers were diagnosed with coronavirus infection, and the Japanese placed the ship in quarantine with passengers confined on the ship.

Eventually, the passengers were evacuated to home countries or to hospital facilities in Japan, but by March 5, 696 passengers and crew (out of 3711) had become infected, and 7 died. This resulted in warnings about the danger of the infection spreading on cruise ships. As of March 30, the number infected has increased to 712 (19%) and 3 additional people have died for a total of 10 (1.4% death rate).

On January 26, 2020, the United States had confirmed 5 cases of COVID-19 from travelers. Subsequently, on January 31 the United States suspended

entry of foreign nationals who had traveled in China in the past 15 days. The first death outside of China occurred in the Philippines on February 2.

But it wasn't until February 29 that the United States recorded its first death from a patient near Seattle. The first deaths from COVID-19 were associated with the LifeCare Center nursing facility in Kirkland, Washington, and were also the first cases identified as resulting from community spread. At that time, 52 patients and staff were also showing symptoms. (As of March 21, 35 deaths were linked to that facility alone.)

On March 11, the WHO formally declared the COVID-19 outbreak a pandemic with 114 countries (at that date) recording infections. Current worldwide expansion of the infection (May 25, 2020):



By March 30, COVID-19 virus was present in 50 states. Cases were beginning to soar: on March 16 there were 4598 confirmed cases and 86 deaths. As of March 30, 2020, the United States had 163,470 cases and 3148 deaths (1.9% death rate), but the cases were literally increasing hourly. By August 31, 2020, over 6 million cases have occurred and over 185,000 deaths.

The United States has had the most cases and the highest death count of any other country in the world, and the reasons for that (inadequate response, conflicting messages, confusion, distrust of authorities, conspiracy theories) will likely be debated for many years.

Identification of active cases has been hampered by problems with testing in the United States. While Europe used a test developed in Germany and distributed through the WHO, the United States decided the CDC should develop its own test, but the original tests that were shipped were defective,

and the supply of tests has been (and often continues to be) inadequate and unevenly distributed.

In response to the severity of the pandemic, individual states, cities, and counties have implemented restrictions, including self-isolation/stay at home. Schools closed across most of the United States in March and April and all but essential businesses closed on most states. Stay at home orders have been the norm and people are urged to maintain distance from others and to wear facemasks when in public.

Now, even though the death rate is a concern, states are starting to phase in opening. Increasingly, people who have been untouched by the coronavirus are appearing in public in groups and without masks, increasing concern that the death rate will begin to spiral out of control. Subsequent increases in caseload have caused some states to retrench and reimpose lockdowns, especially of high risk venues such as bars and restaurants. Schools in many areas remain closed to in-person classes.

It's important to note that while most patients who die are older adults, especially those with underlying health problems, people of all ages are at risk. Children, who were thought essentially exempt, are developing severe illness, and some have died.

The death rate varies widely from one country to another, and the reason for that is not yet totally clear but may have to do with testing capabilities and availability of ICU beds and ventilators as well as the age of the patients. South Korea, for example, had a high rate of infections in younger adults while Italy had a high rate of infections in older adults.

Another factor is that death usually occurs 2 to 4 weeks after the onset of symptom, so the number of deaths continues even if the rate of infection slows.

Incubation

Much is still not known about the disease, but the incubation period appears to be about 10 to 14 days with many showing symptoms by day 5. Many are infected but asymptomatic, and this poses a serious problem for transmission.

Signs and symptoms

Much information about Covid-19 still comes from journalists and is anecdotal rather than from medical researchers because of the newness of the virus, but new information is appearing almost daily.

Presentation is similar to SARS with most presenting at onset with:

- Fever (77–98%):
- Cough (46%–82%)
- Myalgia or fatigue (11–52%)
- Shortness of breath (3–31%)
- Chills

Other common symptoms include:

- Loss of taste and smell (an early symptom).
- Hemoptysis
- Nausea
- Diarrhea
- “Red eyes,” conjunctivitis.
- Hallucinations (associated with fever)
- Confusion
- Rash, hives.

Some patients, such as the very young, very old, and immunocompromised may not exhibit fever. Others may develop sore throat, headache, sputum production, hemoptysis, nausea, and diarrhea. Healthcare workers are reporting that diarrhea is common, with or without respiratory symptoms. A study in the UK indicates that an early sign of COVID-19 infection is a sudden loss of taste and smell even though no other signs may be initially present.

Some present with only GI symptoms, nausea and diarrhea. Patients can progress to severe bilateral interstitial pneumonia, the most common cause of death. Additionally, patients who seem to have mild disease may take a sudden turn for the worse, and patients who have been ill and then show improvement may rapidly decompensate within hours.

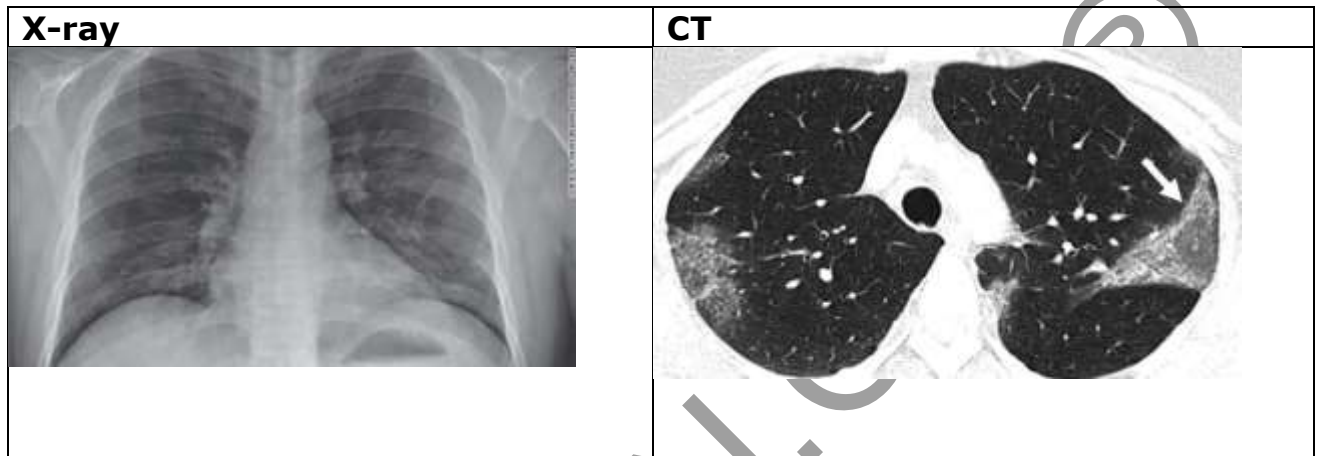
Patients may test negative even with symptoms and then later convert to positive. Some patients who tested negative after having COVID-19 infection later test positive again. Reports of reinfection were primarily anecdotal; but in August, four cases (including one in Nevada) were documented. The patient in Nevada was found to be infected with a different strain of the virus than with the initial infection.

Children tend to have milder symptoms than adults although one study suggests that infants and young children are at increased risk of developing pneumonia.

Pneumonia: At present the most common complication is pneumonia, bilateral interstitial pneumonia. Patients may present with pneumonia or

may have milder symptoms that progress. Patients may develop severe respiratory distress very rapidly, within hours.

Symptoms of pneumonia typically develop about 8 to 9 days (5-13) days after onset. Up to 29% of hospitalized patients develop acute respiratory distress syndrome. About half of those with critical illness die.



The CT and x-ray show ground glass opacities. The CT is more sensitive and may detect abnormalities earlier. Post-mortem exams show these areas fill with mucous that prevents oxygen exchange and accounts for the increasing dyspnea.

Other complications may include cardiac injury, arrhythmia, septic shock, liver dysfunction, acute kidney injury, and multi-organ failure.

COVID toe:



Some patients have reported a rash, and others have developed hives, but increasing numbers of patients in the United States and Europe have

developed painful red inflammation of the toes, similar to the chilblains found with cold exposure. Most patients have been children and young adults, those who are otherwise healthy.

The toes may become edematous and appear red at first and then purple. Some may develop petechial macular lesions. The lesions may appear on a few toes or all toes on both feet. The lesions may be easily overlooked on dark-skinned patients.

There is a report of one patient with finger lesions. Although the lesions are painful and may itch or burn, generally the lesions resolve with no problem over time. Some people report that they take diphenhydramine to relieve the itching.

Cardiac injury: Studies indicate that about 20% of patients with COVID-19 have indications of heart injury, even if they don't have respiratory symptoms. It appears that COVID causes generalized inflammation, referred to as a cytokine storm, that can affect many organs, including the heart. Additionally, some of the drugs that have been studied, such as hydrochloroquine and remdesivir, may cause cardiac damage. Patients may develop myocarditis and heart failure. The virus may also directly infect cardiovascular muscles.

A cardiologist interviewed on CNN reported that patients who now have or have had COVID-19 infection are presenting with symptoms that mimic those of a heart attack (chest pain, pressure, shortness of breath) and that ECG changes are similar. The physician suggested that all patients presenting with signs of a heart attack should be checked for COVID-19.

Kidney failure: Studies show that up to 30% of patients hospitalized for COVID-19 in New York and China and other places as well have shown signs of kidney failure with some requiring dialysis, posing a problem for hospitals lacking adequate dialysis equipment and staff training. It's unclear exactly what mechanism is involved in damage to the kidneys, but it could be from direct infection, hypoxemia, cytokine storm, or blood clots.

It's still not clear whether patients will regain kidney function if they recover from COVID-19 infection.

Blood clots: Patients with COVID-19 are at greater risk of developing blood clots, often multiple, than other hospitalized or bedridden patients, with studies in Europe indicating that 20% to 30% of critically ill patients develop clots. Even young people are developing and sometimes dying from COVID-

associated strokes, and anticoagulants have not been reliably effective in preventing clots.

Patients with high levels of D-dimer have a high risk of mortality from blood clots. Autopsies have shown that capillaries in some patients were clogged with small clots. This may be the reason that some patients exhibit very low levels of oxygen and do not respond to mechanical ventilation. The reason for the formation of blood clots is not yet clear, but it may be related to the cytokine storm that can occur with COVID-19.

Multisystem inflammatory syndrome in children (MIS-C): While children were believed to suffer only mild disease initially, there have been scattered cases of children who became seriously ill, primarily with pneumonia. Recently, however, it has become clear that not only infants and children but also adolescents and young adults can develop a syndrome now referred to as multisystem inflammatory syndrome in children (MIS-C).

Symptoms are similar to those of Kawasaki disease (which typically only affects Asian children under 5 years) and toxic shock syndrome. Symptoms include high fever, GI upset, cardiac dysfunction (which can lead to cardiac failure). Criteria for diagnosis (CDC) include:

- Age <21 with fever, laboratory evidence of inflammation, and evidence of severe illness with multisystem organ involvement requiring hospitalization AND
- No alternative plausible diagnosis AND
- Positive findings of current or recent COVID-19 infection or positive antigen test or COVID-19 exposure within preceding 4 weeks.

The children affected by MIS-C have been infected with COVID-19 or have antibodies, suggesting an earlier infection that in many cases was asymptomatic. As of August 20, 2020, 694 confirmed cases, resulting in 11 deaths have occurred in the United States with cases reported in 42 states and Washington, DC. Most cases have been in ages 1 through 14 although the range is 1 to 20.

The true numbers of this complication are not yet clear as it has been so recently identified. Cases have been reported in other countries, including the UK, Italy, and Spain. Symptoms typically develop 2 to 4 weeks after infection with COVID-19.

Diagnosis of COVID-19

Testing is guided by the CDC, which initially recommended multiple specimens from upper and lower respiratory tract for PCR assay and serologic testing. Tests were originally available only from the CDC but many

medical facilities, states, and companies have now developed testing so opportunities for testing have expanded although testing, including antibody testing, is still limited in many areas—resulting in numbers of infected that are far from reliable because often only the sickest patients are tested. A point-of-care test that requires only 5 to 15 minutes to results has been developed and is available commercially but has about a 15% error rate.

Multiple other tests and imaging may be ordered depending on the patient's symptoms.

Transmission and prevention

COVID-19 appears to spread primarily through droplets (although airborne transmission can also occur) and is more contagious than the flu. The reproduction number or R_0 (pronounced R-nought) is the number of people that one infected person will in turn infect. The R_0 for flu is 1.3, and a JAMA review (2020, February 28) estimates that the R_0 of COVID-19 is 2 to 3.

COVID-19 infects the body by attaching to angiotensin converting enzyme 2 (ACE 2) receptors, which are expressed by epithelial cells in the nares, oral cavity, lungs, intestines, heart, kidneys, and blood vessels, which can account for the variety of different symptoms that patients exhibit.

An early report out of Washington increased concerns about airborne transmission: A group of 60 people gathered for chorale practice on March 10. They used hand sanitizers, avoided sharing music sheets, and avoided any contact, maintaining social distancing. Despite that, 45 out of the 60 have subsequently tested positive and 2 have died.

There is increasing evidence that COVID-19 is, in fact, airborne, and cases are generally treated accordingly in healthcare facilities, with patients placed in negative pressure rooms as long as they are available although appropriate PPE and infection control procedures are often not available. Studies have shown that the coronavirus may remain in the air for up to 3 hours. A recent study suggests that the virus can travel up to 19 feet if the person coughs and up to 26 feet with a sneeze.

The infection is contagious even in those who are asymptomatic and patients may remain infectious even after symptoms subside. This is a distinct difference from SARS and MERS and increases the risk of transmission. Recent studies suggest that about 40% of those who are infected are asymptomatic. However, it has been reported that even asymptomatic patients may show changes on chest x-rays, suggesting that asymptomatic infections may not be as benign as some believe.



Close contact is generally defined for this coronavirus as within 6 feet or within the room or care area for a prolonged period without appropriate PPE, including N95 respirator. Healthcare providers and those in close contact with infected patients should adhere to standard, contact, and airborne precautions.

A study by the CDC found that COVID-19 survived on the *Diamond Princess* cruise ship for up to 17 days, but researchers are unsure if transmission occurred as the result of surface contamination.

Because most people (but not all) exhibit fever, checking temperatures is one of the main tools used now to identify people who may be infected. The CDC recommends that those who have been exposed check their temperatures twice daily and contact a physician if the temperature exceeds 100.4° F. Typically, only those sick enough to be hospitalized are now being tested in most places because testing capability is still low.

In the United States, the federal government was slow in making recommendations and left it to the states to issue mandatory guidelines, which have included

- Stay at home.
- Home school
- Avoid gatherings of more than 10 people.
- Close restaurants, bars, food courts, gyms, and other venues.
- Avoid travel.
- Stay away from others if underlying health condition or sickness.
- Practice good hygiene and frequent handwashing

Most states issued some form of stay-at-home order, but not all. In some cases, restrictions apply to only part of a state. Most states have closed restaurants and bars except for take-out and delivery, but restaurants and bars remain open in in some states. Cities tend to have more restrictions than rural areas. Currently, most states are phasing in opening but this varies from one region and state and even county to another.

Initially, the WHO and CDC did not recommend that the public use face masks although China and South Korea stressed the importance of face masks in reducing transmission.

Now, however, it is recommended that everyone except children under 2 years wear facemasks in public and maintain a social distance of at least 6 feet, stressing that the masks prevent others from becoming infected



although there is some protection from the wearer as well. This suggests that the primary reason that masks were not recommended is that the supply was too low rather than that they were not helpful. One study reported that face masks cut transmission by 50%. N95 masks, which are more effective, are in short supply even in hospitals.

In an ideal world, healthcare providers would be outfitted in hazmat suits and N95 masks, but at the moment, this is not an ideal world. Most guidelines regarding the use of face masks in hospitals have been loosened by the CDC to allow reuse of masks and the CDC has even suggested use of a bandana tied about the face if no masks are available. Healthcare workers have become infected and many have died.

Treatment

As with SARS and MERS, treatment is primarily supportive because no specific treatment has been found to be effective. In response to demands for treatment approval, on March 29, 2020, the FDA approved the use of chloroquine and hydroxychloroquine (anti-malarial drugs) for teenagers and adults if no clinical trial was available although the evidence for use was primarily anecdotal and slim at best.

A study in China found that hydroxychloroquine was no more effective than standard supportive treatment. However, a study in France with only with 20 patients was more positive. Fourteen patients received hydroxychloroquine alone and half got better. However, the small sample sized precluded making a conclusive determination of effectiveness.

Despite the weakness of evidence and adverse effects (including cardiac damage) associated with the drug, hydrochloroquine was touted by President Trump (who later claimed he was taking it for preventive purposes), leading to a rush to prescribe the drug. Subsequent research indicates that hydrochloroquine does not shorten the course of the disease, and those treated with the drug have a higher rate of mortality.

Remdesivir, another drug being studied, has been shown to shorten the course of the disease, but the mortality rate of severely ill patients remains high. Clinical trials are evaluating the efficacy of many different drugs.

About 20 to 30% of those hospitalized for pneumonia require intensive care treatment. Treatment may include high flow oxygen, intubation and

ventilation, and ECMO₂. Many patients require dialysis. Patients are often positioned on their abdomens for at least part of each day in order to facilitate expansion of their lungs.

Children and young adults with PMIS-C are treated as for Kawasaki disease with IV immunoglobulin, corticosteroids, aspirin, and supportive care, depending on the severity of symptoms.

Supportive treatments include:

- Acetaminophen, ibuprofen for fever and discomfort.
- Albuterol for shortness of breath.

Current (August 31, 2020) treatment guidelines (NIH)

- Recommendations AGAINST the use of
 - chloroquine and hydroxychloroquine.
 - sarilumab, tocilizumab, or siltuximab except in clinical trials.
 - Ivermectin except in clinical trials.
 - Interferons except in clinical trials
- Recommendations FOR the use of
 - Dexamethasone 6 mg/day for up to 10 days or until hospital discharge, for patients who are mechanically ventilated or require supplemental oxygen.
 - Note: prednisone, methylprednisolone, or hydrocortisone may be used if dexamethasone is not available.
- Note: these guidelines do not include remdesivir although some studies suggest it may shorten the duration of symptoms.

Recommendations regarding plasma therapy have varied from day to day with the FDA recommending the treatment and then softening the recommendations. While a recent study of 35,000 patients indicates that plasma therapy reduces morbidity and mortality, because there was no placebo group for comparison, the overall value of the treatment is difficult to determine. However, the FDA has authorized the treatment since so few medications are available to treat the virus

Mortality rate

The reported mortality rate varies widely, ranging from <1% to almost 12%, and the reason for this is not clear but may reflect widespread testing identifying more asymptomatic cases in some countries, the age of the

patients, smoking rates, or other variables. China originally reported a fatality rate of 2.3%. The WHO declared an overall fatality rate of 3.4%, but this is a moving target, and the actual mortality rate is very difficult to determine at this time because much early testing was only of symptomatic and/or hospitalized patients and excluded those who were infected but asymptomatic.

While China and Europe (primarily the UK, Italy, France, and Spain) were originally ahead of the United States in cases and mortality rates, the United States now has the most cases and most deaths of any country in the world even though cases are now coming down. Currently, Brasil is another hotspot in the Western hemisphere with over 23,000 deaths, and cases in Mexico are on the rise.

Conclusion

For years, public health officials have warned that another pandemic could sweep the world and result in millions of deaths, such as the 1919 Spanish flu that killed about 50 million people and HIV/AIDS that killed 25 million. While antibiotic resistant bacteria certainly are a concern, viruses have posed the greatest threats, including Ebola virus outbreaks in Africa and the coronavirus outbreaks in China and the Middle East.

It is increasingly difficult to confine an outbreak to a small area because of international travel and commerce. When one outbreak, such as SARS, subsides, another one appears, such as MERS and the more recent coronavirus—COVID-19. COVID-19 has become a pandemic that has killed thousands of people throughout the world and continues to pose a serious health threat.

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