Coronavirus Infections: SARS, MERS, and COVID-19

Purpose

The purpose of this course is to provide current information about coronaviruses, including SARS, MERS, and Wuhan (2019-nCoV), including 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.

Introduction

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.

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 Wuhan coronavirus (2019-nCoV).

**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 or 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 modes 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.
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)

On December 31, 2019, 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.

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 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, Chinas 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. As of this writing (March 16, 2020), China has had 80,880 cases of COVID-19 with 3213 deaths, the most of any country to date. Current new cases in China have fallen to double-digits and daily deaths under 20.

Korea also experienced a significant outbreak with 28 cases on February 15 increasing to 8326 by March 16 with 75 deaths. 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.

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.

In the United States, 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 16, 27 deaths have been 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 (March 16, 2020):

The COVID-19 virus is now (March 16) present in 49 states (West Virginia has not yet identified any cases). Cases are beginning to soar: 4598 confirmed cases and 86 deaths. The cases literally increase hourly. Identification of active cases has been hampered by problems with testing in the United States. While Europe is using a test developed in Germany and distributed through the WHO, the United States declined use of the test and
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 continues to be) woefully inadequate.

Despite the growing threat in the United States, Europe is ahead of the United States in the spread of COVID-19. Italy, for example has almost 27,980 cases with 2158 deaths and its medical facilities have been overwhelmed with patients needing care and ventilators, resulting in the necessity of triaging patients so that those most likely to survive are placed on ventilators.

Iran has 14,991 cases and 853 deaths; Spain, 9428 cases and 853 deaths; Germany 7174 cases and 14 deaths, France 5423 cases and 127 deaths; Switzerland 2353 cases and 18 deaths; the UK, 1543 cases and 36 deaths.

In response to the severity of the pandemic, countries have begun to enforce stringent restrictions. For example, virtually all schools and businesses except banks, grocery stores, and pharmacies are closed in Italy and Spain. People are restricted to their homes.

In the United States, the federal government has been slow in making recommendations and has not established mandatory restrictions but is currently recommending the following:
- Home school
- Avoid gatherings of more than 10 people.
- Avoid 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

Individual states, cities, and counties have implemented further restrictions. For example, California has asked all individuals in the state age 65 and older to self-isolate. San Francisco and surrounding counties have asked all but essential workers to shelter in place. Many states have closed all schools, bars, and restaurants and limited gatherings of people.

It’s important to note that while most patients are older adults, especially those with underlying health problems, 2.1% of victims in China’s were under 20 years although no deaths were reported under age 10. Deaths have otherwise occurred in people in all different ages.

**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.
**Signs and symptoms**
Presentation is similar to SARS with most presenting with fever (77–98%), cough (46%–82%), myalgia or fatigue (11–52%), and shortness of breath (3–31%) at illness onset, but patients may progress to bilateral interstitial pneumonia. 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. Children tend to have milder symptoms than adults.

**Complications**
At present the most common complication is pneumonia. Symptoms of pneumonia 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. Other complications may include cardiac injury, arrhythmia, septic shock, liver dysfunction, acute kidney injury, and multi-organ failure.

**Diagnosis**
Testing is guided by the CDC, which recommends multiple specimens from upper and lower respiratory tract for PCR assay and serologic testing. Tests were originally available only from the CDC but some medical facilities and companies have now developed testing so opportunities for testing have expanded although testing is still limited. Additionally, x-rays and CTs may identify the typical pneumonia presentation.

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

**Transmission and prevention**
COVID-19 appears to spread through droplets and is more contagious than the flu. 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. Close contact for this coronavirus is 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. Some authorities suggest that COVID-19 may remain viable in the air for up to 3 hours, but this has not been substantiated as yet.

**Treatment**
As with SARS and MERS, treatment is primarily supportive because no specific treatment has been found to be effective. About 20 to 30% of those hospitalized for pneumonia require intensive care treatment. Treatment may include high flow oxygen, intubation and ventilation, ECMO. The CDC has not yet recommended drug therapy although a variety of antivirals have been used in China and Korea, including remdesivir (an experimental antiviral drug) and Kaletra (lopinavir/ritonavir), which is an antiretroviral medication.

**Fatality rate**
The death rate varies widely, ranging from <1% to 6% or more, and the reason for this is not clear but may reflect widespread testing identifying more asymptomatic cases in some countries. China reported a fatality rate of 2.3%. The WHO declared an overall fatality rate of 3.4%. Italy currently has a fatality rate of almost 7.7%.

**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.

References


