

EDUCATIONAL OBJECTIVES

After participating in this activity pharmacists and pharmacy technicians will be able to:

- Describe the difference between SARS-CoV-2 (the virus) and COVID-19 (the viral infection).
- Describe the pandemic's origins of the current pandemic.
- List signs, symptoms, and concerns related to infection.
- Describe various approaches to help patients and customers implement protective measures.



The University of Connecticut School of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Pharmacists and pharmacy technicians are eligible to participate in this knowledge-based activity and will receive up to 0.2 CEU (2 contact hours) for completing the activity, passing the quiz with a grade of 70% or better, and completing an online evaluation. Statements of credit are available via the CPE Monitor online system and your participation will be recorded with CPE Monitor within 72 hours of submission

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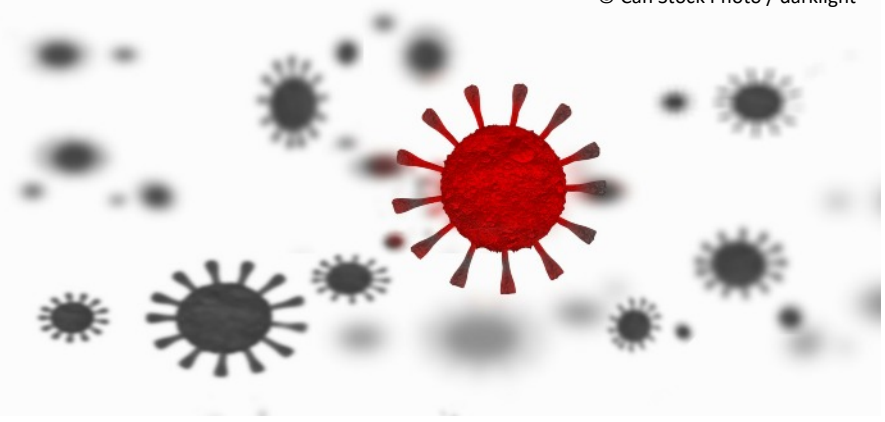
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Use your NABP E-profile ID and the **session code 20YC36-TXF88 for pharmacists or**

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For questions concerning the online CPE activities, email joanne.nault@uconn.edu.



SARS-CoV-2 and COVID-19: A Primer for Pharmacists and Technicians

ABSTRACT: UConn faculty assembled this homestudy in response for a high demand to reliable education on coronavirus. It answers questions proposed by our learners.

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INTRODUCTION

On March 10, 2020, we (the UConn School of Pharmacy) asked our listserv members if they thought a continuing education (CE) activity on the novel coronavirus would be helpful. Within seconds of sending the message, the first answer arrived. Within hours, more than 600 people responded, with 96% of respondents indicating they would like to see a CE. In 24 hours, we exceeded 800 respondents. Almost 60% asked for a written homestudy, so here it is. We've used your questions and comments to fashion what we think you need. We thank you for helping us understand what you face in your workplaces, and allowing us to commiserate. We also hope you'll appreciate some levity, as we will share some amusing anecdotes. Please note that completing this homestudy requires neither facemasks nor hand sanitizer!

The best predictor of a future event is a past event. This is true for many situations and illnesses, and it is true for viral infections that cause serious illnesses. This outbreak is unique in many ways, but it is also similar to several other coronavirus outbreaks and viral epidemics. We can take comfort that we understand viruses better than ever before, and we have seen outbreaks similar to this in various parts of the world. At the same time, we need to respect the fact that this virus is different and we are still learning about its peculiarities.

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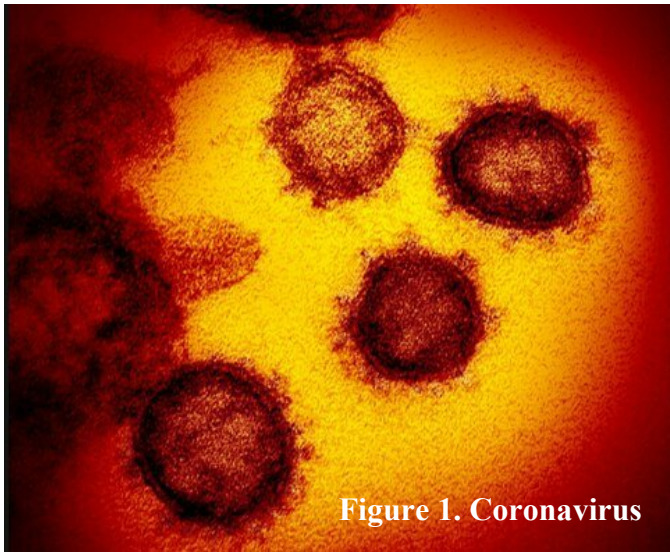


Figure 1. Coronavirus

It's Only Been Weeks since It Started

In December 2019, Chinese health officials reported a cluster of severe pneumonia cases of unknown cause in Wuhan, Hubei province, China. In early 2020, the World Health Organization (WHO) identified the causative virus, and raised the alert that it can be fatal. As is often the case with new diseases and epidemics, the nomenclature can be confusing. The WHO developed viral naming guidelines in 2015 that ensure names for emerging viral diseases do not refer to a geographical location, an animal, or an individual or group of people. This reduces stigma associated with names. It also looks for names that are pronounceable and related to the disease. According to the WHO and the International Committee on Taxonomy of Viruses, the virus and the disease it causes have different names:

- The virus's name is **severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)**
- The name for the disease it causes is **Corona Virus Disease-19 (COVID-19)**

The outbreak spread from China around the world quickly. On January 30, 2020, WHO declared that the SARS-CoV-2 outbreak is a Public Health Emergency of International Concern. By February 28, 2020, public health officials had reported more than 80,000 confirmed cases worldwide. On March 10, 2020, the WHO reported 113,702 confirmed cases globally and 4,012 deaths; of these, 80,9924 case were in China (but only 20 new cases had been reported in the last 24 hours), and 3,140 deaths occurred there.¹ The WHO updated the status to Global Pandemic on March 11, 2020. More cases of COVID-19 are likely to be identified in the United States in the next days and weeks. The WHO's Director-General now indicates this virus is pandemic; this pandemic is different than previous pandemics for one unique reason: it is the first pandemic in history that can be controlled.

What is COVID-2019?

To understand COVID-19, one needs to have a little background. Coronaviruses (CoV) are a large and well-known family of viruses initially identified in the 1960s. The name emanates from the virions' characteristic appearance under electron microscopy; they have a fringe of large, bulging surface projections that appear crown-like, and the Latin word for crown is "corona." Coronavirus often infects the nose, sinuses, or upper throat, and generally leads to an annoying cold or upper respiratory infection. That is, they aren't as a rule dangerous. They tend to spread most rapidly in the late autumn, winter, or cooler spring months when humidity is low.² They thrive in cold, dry weather. To date, researchers have associated four human coronaviruses with the common cold. SARS-CoV-2 is a novel coronavirus, previously unidentified in humans.

One respondent to our survey noted that no true microscopic image of a virus has ever been taken. This is somewhat true. One cannot see viruses under a regular (light) microscope, but electron microscopes work. Researchers at the NIH released pictures of the corona virus from an infected American on February 21, 2020 (see Figure 1, which has been colorized to emphasize its structure).

Occasionally, viruses in the coronavirus family can cause severe diseases. Scientists identified two such viruses in the past: Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). MERS-CoV caused outbreaks in 2012, 2015, and 2018, and SARS was epidemic in Asia in 2003, but has disappeared since. SARS-CoV-2 infection can cause a similar illness, COVID-19. The Centers for Disease Control and Prevention indicates that SARS-CoV-2 virus is a betacoronavirus (see Sidebar), as are MERS-CoV and SARS-CoV. All three of these viruses (SARS-CoV, MERS-CoV, and SARS-CoV-2) originated in bats, and the CDC says that it is highly likely that SARS-CoV-2 emerged from an animal reservoir very recently.

SARS-CoV-2 seems to be more similar to SARS-CoV than to MERS-CoV. Both SARS-CoV and SARS-CoV-2 use angiotensin-converting enzyme 2 (ACE2) as a receptor when they bind to human cells. MERS-CoV uses dipeptidyl peptidase 4 (DPP4). Interestingly, SARS-CoV and SARS-CoV-2 both raised their ugly heads in cold, dry winter conditions. Researchers indicate that under these conditions, blood supply to the nasal mucosa is diminished, and fewer immune cells are available to confront viral particles. Low humidity decreases the ability of the cilia to clear viral particles and secrete mucous. This impairs innate immunity.³ Based on previous epidemics of similar viruses, it seems that low humidity is more important than cold temperature, but both are factors.²

PAUSE AND PONDER: How much do you know about zoonotic disease? Is zoonotic disease becoming more of a threat to human health?

SIDEBAR: Is Coronavirus New?

Pharmacists and pharmacy technicians often find the history behind diseases interesting. RNA viruses cause most emerging infectious diseases because they mutate often and well, have short generation times, and occur in large populations. Combined, those factors spur rapid evolution. Scientists use molecular clock dating to trace viruses' origins, and they know quite a bit about the coronavirus family. Coronaviruses, which are positive sense single stranded RNA viruses, have a most recent common ancestor (MRCA) from around 8000 BCE—that's approximately 10,000 years ago.

Four genus diverged from the MRCA. They are designated the alphacoronavirus, betacoronavirus, deltacoronavirus, and gammacoronavirus lines. It appears that the alphacoronavirus line diverged from its parent virus in about 2400 BCE, with the betacoronavirus, gammacoronavirus, and deltacoronavirus lines emerging at about 3300 BCE, 2800 BCE and 3000 BCE respectively.

Warm-blooded flying vertebrates (bats and birds) are ideal hosts for the coronavirus gene source. Researchers suspect that this particular outbreak came from a bat that passed the virus to an intermediary animal.

SOURCE: Reference 4



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Coronaviruses: Zoonotic Disease

Coronaviruses are zoonotic, meaning they originate as animal diseases and are somehow transmitted to people. Here, we can learn from history. Several known coronaviruses that have not yet infected humans are circulating in animals. The earliest identified human-infecting coronaviruses—those we now associate with the common cold—came from chickens.⁵ Detailed investigations found that SARS-CoV was transmitted from civet cats (a small, lean, mostly nocturnal mammal native to tropical Asia and Africa) to humans and MERS-CoV from dromedary camels to humans.²

Public health officials linked the initial cluster of SARS-CoV-2 epidemiologically to a seafood and live animal wholesale market in Wuhan, but ultimately could not make the connection between many of the initial 41 cases and exposure to the market. This suggests the virus initially came from an animal, but spread person-to-person. In a very short period, some international locations reported community spread, meaning people have been infected and it is unclear how or where they were exposed. This is the main point that answers one common question (How did people who had no contact with infected others contract SARS-CoV-2?)²:

- The initial SARS-CoV-2 probably came from a bat or avian carrier.
- The initial human infection probably came from an animal that was infected with SARS-CoV-2.
- Early transmission was person-to-person, and person-to-person spread is still possible.
- Eventually, community spread occurred. Think of it this way: Have you ever contracted a cold and had no idea where you picked it up? That's community transmission.

One question that many scientists have (as did our respondents) is how could people who had no contact with infected people develop this infection? Many infected individuals were in geographically distinct areas. This is a question for which we have no answers currently, but will in the future.

Why is the worldwide response so extreme?

Let's repeat what the WHO's Director-General stated on March 8, 2020: This epidemic (now a pandemic) is different than previous pandemics for one unique reason: if it develops, this will be the first pandemic in history that can be controlled. The emphasis here is preparation and planning. Unfortunately, people who are uneducated about topics may misunderstand and panic. We certainly see this with unanticipated weather disasters.⁶⁻⁸

When the world learned of the epidemic in China, it only took weeks for the topic to go "viral" on social media (pun intended). Much of the information was misleading, speculative, and false. Misinformation leads to fear and distrust. We won't review many of the myths and conspiracy theories that are rampant; we

Table 1. World Health Organization’s Strategic Objectives for SARS-CoV-21

WHO’s strategic objectives for this response are to:

- Interrupt human-to-human transmission including reducing secondary infections among close contacts and health care workers, preventing transmission amplification events, and preventing further international spread*;
- Identify, isolate and care for patients early, including providing optimized care for infected patients;
- Identify and reduce transmission from the animal source;
- Address crucial unknowns regarding clinical severity, extent of transmission and infection, treatment options, and accelerate the development of diagnostics, therapeutics and vaccines;
- Communicate critical risk and event information to all communities and counter misinformation;
- Minimize social and economic impact through multisectoral partnerships.

**This can be achieved through a combination of public health measures, such as rapid identification, diagnosis and management of cases, identification and follow up of contacts, infection prevention and control in healthcare settings, implementation of health measures for travelers, awareness-raising in the population and risk communication.*

know you have heard them and know, for example, that Corona beer has no connection whatsoever to coronavirus.⁶⁻⁸ The response that makes the most sense is to look at past epidemics and implement the measures that worked. **Table 1** is the WHO’s strategic objectives.

Pharmacy staff is accustomed to dealing with misinformation; we see and hear from people who don’t believe in vaccinations; think diabetes is no problem because they feel fine; or take supplements for their health benefits, when no such benefits exist. This situation is no different except for its size. The only solution is to offer reliable information. That includes saying, “I don’t know. I would like that information, too, and I am watching the professional literature and reliable organizations for more information.” Table 2 lists the areas where we desperately need more information to be able to answer questions honestly.

Some respondents asked us to address contradictions between advice promulgated by the WHO and advice from the CDC. In general, we found that these two bodies agree on the major recommendations. Different organizations can interpret things

slightly differently given their educated guesses about risks and because the situations in different countries are different. We will note that these organizations may differ in their reports of total cases, simply because they have slightly different sources for the data and different update procedures/lag times for updates.⁹

What are COVID-19’s signs and symptoms?

Based on data from the China CDC, COVID-19 patients most commonly had fever (~80%), dry cough (~40%), and fatigue (~30%). Headache, muscle aches, sore throat, chest tightness, chills, and other respiratory symptoms were also reported (less frequently) in patients. It appears that most COVID-19 illness is mild. The CDC indicates that in China, approximately 16% of cases were severe. Older people and people with severe underlying health conditions (e.g., heart disease, lung disease, diabetes) regardless of age seem to be at higher risk of for serious COVID-19 illness and/or death from the disease. Infection resulting in severe disease can cause pneumonia, severe acute respiratory syndrome, kidney failure, and possibly death.¹⁰

Table 2. Areas Requiring Additional COVID-19 Investigation

Area of Information Deficit	Implications
Incubation period and duration of virus shedding	Identification will specify the duration of quarantine and other mitigation measures
Relative importance of various modes of transmission (droplets, aerosols, and fomites*)	This information will help clarify infection control and prevention measures, including the use of personal protective equipment
Severity and case-fatality rate of COVID-19 among cases in the U.S. health care system, and a full description of the illness’s spectrum and risk factors for infection and severe disease	Knowing more about severe illness will help determine best treatment approaches
Role of asymptomatic infection in ongoing transmission	At this time, containment measures are unclear, so this information will help use understand testing and when it is necessary
Immunologic response to infection	This information will help researchers narrow down treatment options, vaccines, and therapeutics.

**A fomite is any inanimate object (such as a towel or money or clothing or dishes or books or toys etc.) that can transmit infectious agents from one person to another*

The clinical course of severe acute respiratory syndrome has had a typical pattern in the past. Stage 1 is a flulike prodrome that begins 2-7 days after incubation, lasts 3-7 days, and is characterized by the following^{10,11}:

- Fever (>100.4°F [38°C])
- Fatigue
- Headaches
- Chills
- Myalgias (muscle aches and pains)
- Malaise (a feeling that you are slightly sick, although you cannot say what exactly is wrong)
- Anorexia (lack of appetite)

Some patients may also have increased sputum production, sore throat, and coryza (an inflammation of the mucous membrane lining the nose usually associated with nasal discharge). Nausea and vomiting, dizziness, and diarrhea are also possible but rarely seen in this outbreak.

Stage 2 occurs when the infection migrates into the lower respiratory tract. Symptoms include the following^{10,11}:

- Dry cough
- Dyspnea (shortness of breath)
- Progressive hypoxemia (low blood oxygen levels) in many cases
- Respiratory failure that requires mechanical ventilation in some cases

Many of our respondents asked for exact mortality rates. This, too, is information that is difficult to pinpoint. Currently, the mortality rates for cases globally appears to be between 1% to 2%.¹² We discuss this in more detail below.

How is SARS-CoV-2 spread?

Studies to date suggest that the virus that causes COVID-19 is transmitted primarily through contact with respiratory droplets, similar to the way that colds and the flu are transmitted.

Standard recommendations to prevent infection spread include regular hand washing, and covering mouth and nose when coughing and sneezing. Avoid close contact with anyone showing symptoms of respiratory illness such as coughing and sneezing. Isolated reports indicate that traces of the virus have appeared in the feces of people who were infected.¹³ It is not clear if viral exposure via the fecal route could result in COVID-19 infection, but it is possible. However, data from the outbreak in China strongly suggests no epidemiologic evidence of fecal-oral transmission of COVID-19. If it does happen, it would be a very rare event. This would require fecal-oral contamination (see Sidebar). Fecal contamination from getting SARS-CoV-2 on a surface and then having someone touch that surface and touch their face/mucus membranes could expose them; surface contamination would be much more likely from respiratory droplet deposition. Cleaning surfaces, washing hands, substituting a wave or nod for a handshake, and keeping hands away from the face unless they were just scrubbed are reasonable precautions. Research continues to

SIDEBAR: What is fecal-oral contamination?

Fecal-oral transmission occurs when bacteria or viruses found in a person's or animal's feces find their way to another person's oral mucosa. This is especially common in group daycare settings, where fecal organisms may contaminate surfaces and care providers' hands. Usually, the contamination cannot be seen by the naked eye (if it could, responsible adults would wash their hands or the surface). Swimming pools and water parks can also be locations of fecal-oral transmission. If the water is not visibly contaminated and is adequately chlorinated, just getting the water in the mouth is usually not enough to cause an infection; swallowing greatly increases the risk.

Many healthcare providers do not understand fecal-oral contamination. They think, "This doesn't happen here. We wash our hands!" While fecal-oral contamination usually occurs in places where sanitation is poor, it can occur if

- water is treated insufficiently
- fecal matter sits in the open
- soil in the garden is contaminated and a person works there
- microscopic quantities of fecal matter transfer from a person who has just changed a baby's diaper or petted an animal
- flies visit a toilet or laundry basket and then land on food
- people swim in community swimming pools
- sex transfers minute quantities of feces

With some infections, such as rotavirus or norovirus, very few viral particles can cause an infection. These can spread directly through a group-care setting quite quickly, often spreading by fomites. Other infections, such as salmonella, require a larger number of organisms to establish an infection. In the absence of visible stool contamination, these infections often travel through infected food or beverages.

If SARS-CoV-2 is transmitted by the fecal-oral route (current evidence suggests that it may be possible but highly unlikely/rare), preventive mechanisms are the same: good hygiene.

be done to determine how long SARS-CoV-2 virus particles capable of infecting humans can survive on surfaces, but so far, it appears that the virus may persist on surfaces for a few hours or perhaps up to a few days.¹⁴

What are the risk factors for COVID-19?

The most significant risk factors appear to be advanced age or underlying chronic disease, especially pulmonary compromise.¹² At this time, public health officials have not been able to identify any other specific risk factors.

How contagious is SARS-CoV-2?

As evidenced by its rapid spread, it appears to be very contagious. Based on studies done so far, it appears to be more contagious than the flu.¹⁵ It infects two to three people for every one person infected as compared to the flu, which infects

slightly more than one person for every person infected. This is probably because we have no vaccine to bend the susceptibility curve, and because SARS-CoV-2 produces mild symptoms. People remain ambient in the community longer and can be infectious before they show notable symptoms.

What is the best way to access testing; can pharmacists assess people to triage for testing?

Testing availability depends on a number of things: kit availability and geographic region. The best place to find information about testing is through your state or local health department. In larger metropolitan areas, public health advisors have designated certain hospitals to receive patients with COVID-19 to reduce its spread to our most vulnerable citizens. Pharmacy staff can do the following to stay informed:

- Determine how your local health department is disseminating information about testing, and ask to be included
- Watch local news stations; they will often provide information
- Visit the CDC's web site regularly

One respondent noted that overseas they now have “drive-through” testing at some hospitals. Patients stay in their car. This respondent said this looks like a good way to prevent the spread! Depending on the virus's trajectory in the U.S., we may see this intervention in the future. In Connecticut, Hartford Hospital has already beta-tested this, and it will be up and running soon!

What is the incubation period for COVID-19?

As noted above, we need more information to determine SARS-CoV-2's true incubation period. We have some indicators, however^{13,16-19}:

- An early analysis in Chinese provinces outside Wuhan looked at 88 confirmed cases. These researchers examined travel data to estimate the exposure interval. They found that the mean incubation period was 6.4 days with a range of 2.1 to 11.1 days.
- Next, researchers analyzed 158 confirmed cases outside Wuhan and found a median incubation period of 5 days (range of 2 to 14 days).

These estimates align with estimates from 10 confirmed cases in China in which it appeared that the mean incubation period was 5.2 days and with a clinical report of COVID-19 in a familial cluster that identified an incubation period of 3 to 6 days after assumed exposure.

As noted, we have copious quantities of data in other human coronaviruses. These estimates for SARS-CoV-2 are similar to those of other known human coronaviruses.

Is hand washing, sneezing into a sleeve, and cleaning enough to prevent transmission?

In short, yes. All current evidence indicates that the same steps

we take to prevent colds and flu work for SARS-CoV-2, too. It will reduce your risk of getting—and spreading—the virus! Tell patients to:

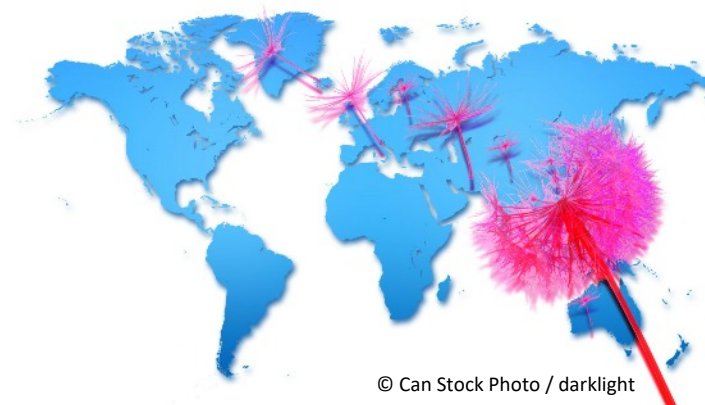
- Wash hands often with soap and water for at least 20 seconds.
 - One respondent said that they are telling people to wash their hands like they just chopped jalapeno peppers and need to remove their contact lenses. Thank you!
 - Antibacterial soap is unnecessary—any soap will do.
 - Use an alcohol-based hand sanitizer only if soap and water are not available.
- Avoid touching the eyes, nose, and mouth.
- Cover the mouth and nose with a tissue or sleeve (not hands) when coughing or sneezing.
- Clean and disinfect frequently touched objects and surfaces (see below).
- STAY HOME if you are sick, especially if you have symptoms of COVID-19.
- Get an annual flu shot to prevent co-infection with flu and SARS-CoV-2.
- Avoid contact with sick people as much as possible.
- Follow the CDC travel policy.

Can coronavirus survive on surfaces?

Researchers have not determined how long SARS-CoV-2 survives on surfaces, but preliminary evidence suggests it behaves like other coronaviruses. Most coronaviruses persist on surfaces for a few hours and up to several days depending on ambient conditions (e.g., surface type, temperature, humidity). Cleaning surfaces with simple disinfectant will kill the virus. **Table 3** lists tips for cleaning surfaces and objects.

In a controlled research environment designed to simulate the amount of virus in human respiratory secretions, the research team used a mechanism to aerosolize the virus into a test environment (a closed container called a “Goldberg drum”) at a 65% relative humidity.¹⁴ The SARS-CoV-2 virus remained viable in aerosols for the duration of the experiment (three hours), but it became considerably less viable as time progressed. The SARS-CoV-2 virus was most stable on plastic and stainless steel surfaces. At 24 hours, cardboard surfaces had no detectable SARS-CoV-2 virus.

These results are similar to those of the SARS-CoV-1 virus (from the SARS outbreak). The aerosolization test result, combined with some preliminary evidence that some patients may shed and transmit the virus while pre-symptomatic or asymptomatic, provides some support to the hypothesis that SARS-CoV-2 is capable of causing so-called “super-spreading” events (where one infected person can cause a large number of secondary cases).¹⁴



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Table 3. Household Cleaning to Prevent SARS-CoV-2 Transfer²⁰⁻²²

- Household members should practice good hygiene if a household member has SARS-CoV-2
- Remind patients to disinfect objects and surfaces such as telephones, computer keyboards, light switches, doorknobs, remote controls devices, toilets, sinks, and children’s toys
 - Advise cell phone users not to use window cleaner on cell phones; instead, moisten a cloth with a prepared mix of 60% water/40% isopropyl alcohol and wipe gently with a microfiber cloth or purchase a commercial cell phone cleaner
- Dispose of used tissues IMMEDIATELY in a covered trash receptacle
 - Empty trash frequently wearing gloves
- The U.S. Environmental Protection Agency only allows manufacturers to use words like “sanitize” or “disinfect” on products that have proven ability to kill germs; look for these products.
 - Coronaviruses are enveloped viruses, and one of the easiest viruses to kill with the appropriate disinfectant product
 - The most commonly used products are Pine Sol, Clorox, and Lysol. The EPA provides a list of cleaning products here: https://www.epa.gov/sites/production/files/2020-03/documents/sars-cov-2-list_03-03-2020.pdf
 - Lemon juice, lavender, and tea tree oil or natural products have disinfectant properties, but no guidance indicates how much to use
 - A mixture of 1/4 cup chlorine bleach to 1 gallon hot water will also disinfect
 - Vinegar has **no** disinfectant properties
- Consider using washing machine or the dishwasher to clean communal items; many items can be washed in these appliances, and using hot settings and soap can disinfect

What is the best symptomatic treatment for mild cases?

Let’s say this first, and put it behind us: this is a viral infection, so antibiotics are unnecessary unless the viral infection evolves into a bacterial infection.

At the moment, the best interventions are supportive. Patients may need antipyretics, analgesics, or cough suppressants. It’s generally similar to a cold or flu, and should be treated as such. In moderate to severe cases, patient will need supportive care in a hospital environment.

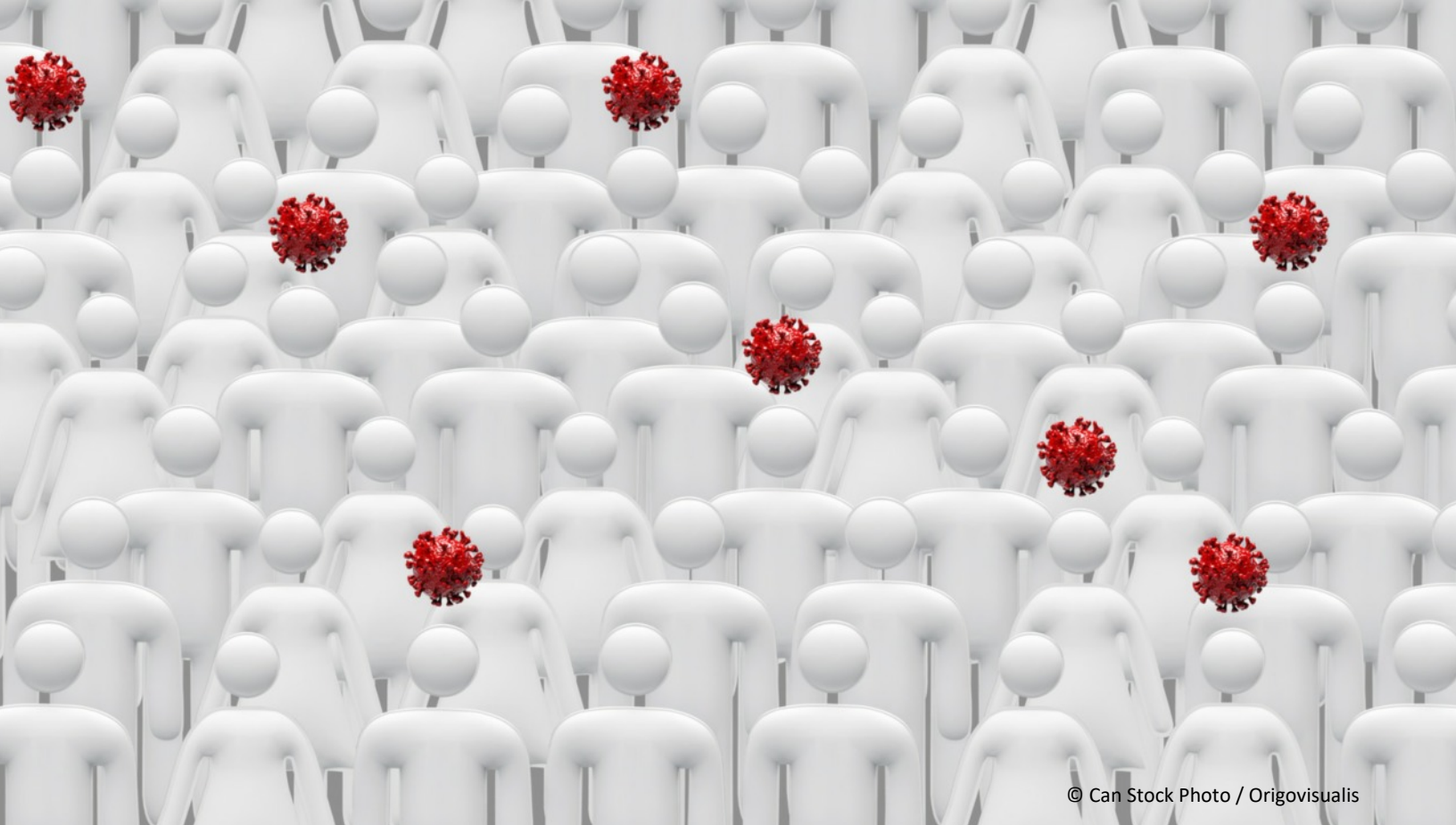
What is quarantine, and how is it accomplished?

Quarantine means staying at home and away from others until you are no longer contagious. Current recommendations are to self-quarantine for 14 days. This is for people who are not actively sick but were exposed and might become sick in the future. Most people exhibit symptoms by the fifth day and almost all people who were infected will show symptoms by the 14th day after exposure. However, rarely some people have exhibited symptoms after that 14-day time point.²³

Are there any current or possible antivirals that can treat SARS-CoV-2 infection?

Bringing new medications to market often takes years. Global spread of COVID-19 has been an impetus to find a treatment quickly. Researchers are relying on information they have gleaned from SARS-CoV and Ebola to bolster their search. The science behind this approach is this: SARS-CoV and SARS-CoV-2 share only 82% RNA “sequence identity,” but they share 96% “sequence identify” of their RNA-dependent RNA polymerase (RdRp). Drugs that target SARS-CoV’s viral RdRp proteins may work for SARS-CoV-2. Remdesivir is one such antiviral, and it has received the most attention. Other agents include 6’-fluorinatedaristeromycin analogs, acyclovir fleximer analogs favipiravir, galidesivir, ribavirin, and penciclovir.²⁴⁻²⁷

In the United States, the National Institutes of Health (NIH) is collaborating with pharmaceutical companies on possible vaccines and therapeutics for COVID-19. Chinese researchers have already initiated multiple clinical trials of investigational agents. Two trials using remdesivir, an investigational antiviral drug, have started.



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In addition, NIH has received approval to start randomized controlled clinical trials of investigational therapeutics for hospitalized COVID-19 patients in the U.S., and is beginning its study using remdesivir.

There were some reports from the first SARS epidemic indicating an anti-HIV medication (lopinavir/ritonavir) might have possible activity and clinical benefit in the treatment of the SARS-CoV-1 virus. It is too soon to say definitely whether this medication could provide some benefit in the treatment of COVID-19 patients; a small case series recently published didn't really provide convincing evidence to support it being possibly beneficial.²⁸ Lopinavir/ritonavir's manufacturer recently announced that they are "...collaborating with select health authorities and institutions globally to determine antiviral activity as well as efficacy and safety of lopinavir/ritonavir against COVID-19."²⁹

What's the best way to handle panicking individuals?

Many of our respondents asked this question, and asked for information on group dynamics in times of trouble. We have two approaches, and you may wish to create your own. One way to calm people is to remind them that this pandemic is neither Ebola nor the Black Plague, nor MERS (which had a very high case fatality rate). It is like having an extra flu season. Most people who contract COVID-19 will be sick for a while but will be just fine in a matter of 10 days to two weeks. The vast majority of people will be fine even if they contract it.

Our seniors and those with many baseline health issues are most at risk and very vulnerable. Children can be infected but based on information so far are not likely to become seriously ill or to die. The issue with children is their propensity to "share with the group"—they can spread infection.

The death rate being recorded/reported currently is likely to be much higher (and could end up being very much higher) than the TRUE death rate from all people with COVID-19 infection since we are unable to determine the true number of all cases definitively. Many cases are so mild that they go undetected.

A second approach is to remind people what the world's health leader has said repeatedly: this is the first time we have the ability to control a pandemic. We (pharmacy staff and healthcare providers) must emphasize the WE (residents in our communities) in that statement. We need to model good, calm behavior, and WE need to use proven preventive and protective measures (discussed above).

If you get it once can you get it again?

Like influenza, infected individuals who recover should be immune (although it is always possible that the virus can mutate and individuals may not be completely immune to that variant). In addition, it is not known if immunity is a long-term immunity or something that would wane over time (years). There is some evidence that it could be possible to get the infection more than once, but much more investigation is needed. People with severe immune compromise might be able to contract it again but there is no evidence that this is true yet for COVID-19.³⁰

What are some of the lasting side effects of the virus post infection? Can it live in the host and re-infect the host at a later date?

Long-term complications among survivors of SARS-CoV-2 infection are not yet available. No evidence yet suggests that SARS-CoV-1 or SARS-CoV-2 can lie dormant in someone's body (e.g., in their blood, lungs, nerves, muscles) after their infectious syndrome has gone away and "re-activate" to cause another infection.

Can you (and should you) compare SARS-CoV-2 to influenza, and what can we learn from previous pandemics?

We've discussed comparisons with other outbreaks above. As noted throughout this CE activity, SARS-CoV-2 is new and somewhat different than other viruses. We need time to make good comparisons.

That said, researchers from Spain recently compared pandemic influenza in European ICUs in 2009 to what we know about SARS-CoV-2. Some of their observations include the following³¹:

- The mean age of onset for patients who have severe COVID-19 is 59.7; for influenza (H1N1)pdm2009 it was 50. Men are more likely to develop severe illness in both infections (with 65-67% of cases in men).
- It seems that some coronavirus patients with severe illness shed very large amounts of virus; that is an infrequent occurrence in influenza patients.
- Mortality rates look like they are higher for COVID-19 than for severe influenza, but the researchers admit the data may be skewed by small numbers of COVID-19 patients, and limited resources at the outbreak's start.
- COVID-19 seems to cause respiratory deterioration seven to 10 days after onset in vulnerable patients; in influenza, vulnerable patients tend to develop respiratory decline earlier at the three to five day mark.

As you read these statistics, be smart in your interpretation. These findings are based on preliminary observations and small numbers.

Will insurance allow patients to obtain prescription refills early due to the request for seniors to self-quarantine?

Unfortunately, we have no way of knowing. Insurance companies will make these decisions individually, and will rely on the best available information in specific geographic areas. The best source of information is the insurer's web site or help line.

What is the best way to educate patients who come in the pharmacy looking for hand sanitizer (which is out of stock), masks (also out of stock), and other personal protective equipment?

First, the absolute, undisputed, BEST way to protect oneself is by washing hands with soap and water often. Hand sanitizer is

no substitute.³² Many of you said that you have moved hand sanitizer behind the counter. When you provide it to patients, it's good to remind them that hand-washing is better.

But, there are times when people have no access to a sink, soap, and water. The Internet is full of suggestions, and many if not most of them are not valid. For example, using vodka to sanitize your hands is ineffective; it does not have enough alcohol. A number of recipes are available on the Internet, and many include tea tree oil, which has some antibacterial oils. People should never apply undiluted tea tree oil to their skin, as it can cause burn-like rashes. There is no way to verify that these recipes actually sanitize the hands. If people choose to make their own hand sanitizer, you can remind them that commercial products have an alcohol concentration of at least 60%. Any recipe they select should have at least 60% alcohol when it's mixed and bottled. One such recipe contains 2/3 cup isopropyl alcohol, 1/3 cup aloe vera gel, and 8 to 10 drops of essential oil. Again, hand washing with soap and ample water for 20 seconds is preferred.

The fact that television news, newspapers, and Internet media outlets constantly show pictures of people in masks leads people to believe they need masks. Most do not. Health advisory organizations consistently say that people do not generally need masks. Here's a primer on the two main types of mask²⁹:

- If you are healthy, surgical masks are only needed under the following conditions:
 - if you are taking care of a person with suspected SARS CoV-19 infection
 - if you are coughing or sneezing
 - if you use it in combination with frequent hand-cleaning with alcohol-based hand rub or soap and water
 - if you know how to use it and dispose of it properly
- N95 respirator masks block smaller particles than surgical masks do. No one will ever need N95 respirators for the coronavirus. An N95 respirator is designed for airborne diseases, not respiratory droplets. They aren't designed for diseases like COVID-19. They come in various sizes, and are so hard to wear properly that every health care worker has to undergo specialized, standardized "fit testing" annually.

Can natural remedies help?

This is unclear at this time. A mouse study suggested that black licorice could have antiviral effects versus SARS, but no researchers have studied its use against SARS-CoV-2.³³ In vitro, Lycoris radiata, also known as red spider lily, was the most effective inhibitor of the SARS virus.³⁴ While potentially effective against the common cold and influenza virus, Echinacea purpurea and Elderberry, respectively, have not been studied against coronaviruses. It is not clear whether colloidal silver is an effective antiviral product.

If patients want to try a natural product, explain the limitations in knowledge about their effectiveness and tell them not to

take more than is recommended. Suggest they preferentially use products that are USP, NSF, or ConsumerLabs certified to be free of contaminants and adulterants.³⁵

When is this pandemic likely to go away?

There is no highly accurate answer to this question at this time. It could dramatically slow through one of several factors all being explored simultaneously.

- 1) Once researchers find, test, and produce an effective vaccine in sufficient quantities to cause individual and herd protection of the masses (estimates are 14 to 20 months), it will go away. So the worst case scenario is two years.
- 2) The virus itself could mutate again and lose the ability to infect humans or at least do so with much less virulence. This can happen at any time.
- 3) Public health measures can suppress the spread of the virus to new communities and eventually it will be eradicated (or the numbers of new cases will decrease significantly). Worldwide, we are not in that place now because we have lacked rapid detection and response capabilities, but communities across the country are in a better place to detect and respond now. The evolution of COVID-19 infection in China (where, since 3/7/2020, the numbers of new reported cases have been fewer than 50 cases per day compared to a high of 15,000+ cases on 2/13/2020) and the infection prevention measures that they implemented are encouraging evidence that aggressive public health measures can have a very positive impact on eliminating the COVID-19 pandemic.
- 4) Once it spreads widely through the world's population and many people develop immunity, it should also spread much more slowly.

Are there other coronaviruses that can infect patients in the future?

Yes, in virology studies in mainland China bat populations, several other coronaviruses that have the potential to infect humans have been identified. Many just cause mild cold symptoms but others have more serious potential.³⁶ It may

be that, in the future, a coronavirus vaccine will need to be developed against those variants most likely to be harmful. This approach would be similar to how we address influenza now with three or four possible variants in one vaccine. Then if the circulating variant is not an exact match, partial protection is possible.

All pharmacy providers need to be prepared to remind people about these risks once this pandemic is over lest they forget. We could have made more progress in this regard after the SARS epidemic, but international interest waned after the immediate crises abated.

CONCLUSION

One respondent to our survey wrote, "People want predictions and we are not in that business." That sums up our situation pretty well. None of us has a crystal ball that can predict what's happening. Another wrote, "Sometimes you just have to respect people's concerns and not dismiss them." We agree.

Years ago, before memes were a thing, people use to copy a sign that said, "Your failure to plan doesn't constitute an emergency on our part," and post these signs in service locations. Unfortunately, failure to plan sometimes does constitute an emergency for healthcare providers.

Pharmacies might consider downloading some of the wonderful patient information sheets from the WHO or the CDC. Readers may also find comfort in reviewing the WHO's Coronavirus disease (COVID-2019) situation reports regularly. Find them here: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>. The report for March 9 through March 11 indicate that the number of reported cases and deaths in China is down to a handful, indicating they are coming out of the pandemic. This site provides a tremendous amount of other information as well.

Again, we appreciate your feedback in our recent survey, and hope you have found this material helpful. We will provide updates if necessary using our listserv.

And a Gentle Reminder: Empathy is the Order of the Day

Please remember that many of our patients have unique needs:

- People with obsessive compulsive disorder, anxiety disorders, and serious or stress-provoking health concerns may find casual conversation about the virus uniquely distressing. Ask people if it's okay with them before making small talk about the virus.
- Public health authorities and media personality constantly say that people with disabilities and chronic conditions are at serious risk. While reassurances that "only" elderly and chronically ill people are at serious risk may comfort the healthy, they are frightening to people with disabilities. Please remember that at-risk people can hear you.
- Every effort you make to conduct business remotely and accommodate people who can't leave their homes resonates deeply with your patients and customers. They are also accommodations that people with disabilities have asked for for years.
- Not touching your face has unique implications for people who use sign language.

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