Overview of COVID-19: Epidemiology, Clinical Presentation, and Transmission

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Epidemiology

The COVID-19 pandemic has exploded since cases were first reported in China in December 2019. As of July 9, 2020, more than 12 million cases of COVID-19—caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection—have been reported globally, including more than 550,000 deaths. Cases have been reported in more than 180 countries, including all 50 states of the United States.[1,2]

Individuals of all ages are at risk for infection and severe disease. However, the probability of serious COVID-19 disease is higher in people aged ≥60 years, those living in a nursing home or long-term care facility, and those with chronic medical conditions. In a recent analysis of more than 1.3 million laboratory-confirmed cases that were reported in the United States between January and May 2020, 14% of patients required hospitalization, 2% were admitted to the intensive care unit, and 5% died.[3] The percentage of patients who died was 12 times higher (19.5% vs. 1.6%) and the percentage of patients who were hospitalized was six times higher (45.4% vs. 7.6%) in those with reported medical conditions than in those without medical conditions. The mortality rate was highest in those aged >70 years, regardless of chronic medical conditions. Among those with available data on health conditions, 32% had cardiovascular disease, 30% had diabetes, and 18% had chronic lung disease. Other conditions that may lead to a high risk for severe COVID-19 include cancer, kidney disease, obesity, sickle cell disease, transplant recipients, and other immunocompromising conditions.[2,4-9]

Emerging data from the United States suggest that racial and ethnic minorities experience higher rates of COVID-19 and subsequent hospitalization and death.[10-14] However, surveillance data that include race and ethnicity are not available for most reported cases of COVID-19 in the United States.[2,15] Factors that contribute to the increased burden of COVID-19 in these populations may include over-representation in work environments that confer higher risks of exposure to COVID-19, economic inequality (which limits a person's ability to protect against COVID-19 exposure), neighborhood disadvantage,[16] and a lack of access to health care.[15] Structural inequalities in society contribute to health disparities for racial and ethnic minority groups, including higher rates of comorbid conditions (e.g., cardiac disease, diabetes, hypertension, obesity, pulmonary diseases), which further increases the risk for severe illness from COVID-19.[14]

Clinical Presentation

The estimated incubation period for COVID-19 is up to 14 days from the time of exposure, with a median incubation period of 4 to 5 days.[6,17,18] The spectrum of illness can range from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome (ARDS) and death. Among 72,314 persons with COVID-19 in China, 81% of cases were reported to be mild (defined in this study as no pneumonia or mild pneumonia), 14% were severe (defined as dyspnea, respiratory frequency ≥30 breaths/min, SpO_2 ≤93%, PaO_2/FiO_2 <300 mmHg, and/or lung infiltrates >50% within 24 to 48 hours), and 5% were critical (defined as respiratory failure, septic shock, and/or multiple organ dysfunction or failure).[19] In a report on more than 370,000 confirmed COVID-19 cases with reported symptoms in the United States, 70% of patients experienced fever, cough, or shortness of breath, 36% had muscle aches, and 34% reported headaches.[3] Other reported symptoms have included, but are not limited to, diarrhea, dizziness, rhinorrhea, anosmia, dysgeusia, sore throat, abdominal pain, anorexia, and vomiting.

The abnormalities seen in chest X-rays vary, but bilateral multi-focal opacities are the most common. The abnormalities seen in computed tomography (CT) of the chest also vary, but the most common are bilateral peripheral ground-glass opacities, with areas of consolidation developing later in the clinical course.[20] Imaging may be normal early in infection and can be abnormal in the absence of symptoms.[20]

Common laboratory findings of COVID-19 include leukopenia and lymphopenia. Other laboratory abnormalities have included elevated levels of aminotransferase, C-reactive protein, D-dimer, ferritin, and lactate dehydrogenase.

While COVID-19 is primarily a pulmonary disease, emerging data suggest that it also leads to cardiac,[21,22] dermatologic,[23] hematological,[24] hepatic,[25] neurological,[26,27] renal,[28,29] and other complications. Thromboembolic events also occur in patients with COVID-19, with the highest risk in critically ill patients.[30] The long-term sequelae of COVID-19 survivors are currently unknown.

Recently, SARS-CoV-2 has been associated with a potentially severe inflammatory syndrome in children (multisystem inflammatory syndrome in children or MIS-C).[31,32] Please see Special Considerations in Children for more information.

Routes of SARS-CoV-2 Transmission

Transmission of SARS-CoV-2 occurs primarily through respiratory secretions, and, to a lesser extent, contact with contaminated surfaces. Most transmissions are thought to occur through droplets; covering coughs and sneezes and maintaining a distance of six feet from others can reduce the risk of transmission. When consistent distancing is not possible, face coverings may further reduce the spread of droplets from infectious individuals to others. Frequent handwashing is also effective in reducing acquisition.[33] The onset and duration of viral shedding and the period of infectiousness are not completely defined. Viral RNA may be detected in upper respiratory specimens from asymptomatic or pre-symptomatic individuals with SARS-CoV-2.[34] An increasing number of studies have described cases where asymptomatic individuals have transmitted SARS-CoV-2.[35-37] The extent to which this occurs remains unknown, but this type of transmission may be contributing to a substantial amount of community transmission.

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Testing for SARS-CoV-2 Infection

Last Updated: June 11, 2020

Summary Recommendations
• The COVID-19 Treatment Guidelines Panel (the Panel) recommends that a molecular or antigen test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) should be used to diagnose acute SARS-CoV-2 infection **(AIII)**. • The Panel **recommends against** the use of serologic testing as the sole basis for diagnosis of acute SARS-CoV-2 infection **(AIII)**. • The Panel **recommends against** the use of serologic testing to determine whether a person is immune to SARS-CoV-2 infection **(AIII)**.
Rating of Recommendations: A = Strong; B = Moderate; C = Optional **Rating of Evidence:** I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies; III = Expert opinion

Virologic Testing for SARS-CoV-2 Infection

Virologic testing (i.e., using a molecular diagnostic or antigen test to detect SARS-CoV-2) should be done in all persons with a syndrome consistent with COVID-19 and in people with known high-risk exposures to SARS-CoV-2. Ideally, virologic testing should also be performed in people likely to be at repeated risk of exposure, such as health care workers and first responders. For more information, see the Centers for Disease Control and Prevention (CDC) COVID-19 website.

While initial diagnostic tests for SARS-CoV-2 infection have relied on reverse transcriptase polymerase chain reaction platforms, more recent tests have included a variety of additional platforms. A number of diagnostic tests for SARS-CoV-2 infection have received emergency use authorizations (EUAs) issued by the Food and Drug Administration (FDA).[1] Formal comparisons of the sensitivity and specificity of these tests are in progress.

The CDC recommends that nasopharynx samples be used to detect SARS-CoV-2. Nasal swabs or oropharyngeal swabs are acceptable alternatives.[2] Although lower respiratory tract samples have a higher yield than upper tract samples, they are often not obtained because of concerns about aerosolization of virus during sample collection procedures.

The CDC has established a priority system for diagnostic testing for SARS-CoV-2 infection based on the availability of tests;[3] the CDC testing guidance is updated periodically.

The following are the current CDC priorities for COVID-19 diagnostic testing:

High Priority:

- Hospitalized patients **with symptoms**
- Health care facility workers, workers in congregate living settings, and first responders **with symptoms**
- Residents in long-term care facilities or other congregate living settings, including prisons and shelters, **with symptoms**.

Priority:

- Persons **with symptoms** of potential COVID-19 infection, including fever, cough, shortness of breath, chills, muscle pain, new loss of taste or smell, vomiting or diarrhea, and/or sore throat
- Persons **without symptoms** who are prioritized by health departments or clinicians, for any reason, including but not limited to public health monitoring, sentinel surveillance, or screening of

other asymptomatic individuals according to state and local plans

Molecular diagnostic and antigen tests can yield false-negative results. In people with a high likelihood of infection based on exposure history and/or clinical presentation, a single negative test result does not completely exclude SARS-CoV-2 infection, and repeat testing should be considered. When a person who is strongly suspected to have SARS-CoV-2 infection has a negative result on an initial antigen test, repeat testing using a molecular diagnostic test may be warranted.

Serologic (or Antibody) Testing for Diagnosis of SARS-CoV-2 Infection

Unlike molecular diagnostic and antigen tests for SARS-CoV-2 that detect the presence of the virus, serologic tests are intended to identify persons with recent or prior SARS-CoV-2 infection. Because it may take 21 days or longer after symptom onset for seroconversion or detection of immunoglobulin M and/or immunoglobulin G antibodies to SARS-CoV-2,[4-9] the Panel does not recommend the use of serologic testing as the sole basis for diagnosing acute SARS-CoV-2 infection **(AIII)**. Given that molecular diagnostic tests and antigen tests for SARS-CoV-2 occasionally yield false-negative results, in some settings, serologic tests have been used as an additional diagnostic test in patients strongly suspected to have SARS-CoV-2 infection.

No serologic tests for SARS-CoV-2 are approved by the FDA and some, but not all, commercially available serologic tests for SARS-CoV-2 have received EUAs issued by the FDA. Several professional societies and federal agencies, including the Infectious Diseases Society of America, CDC, and FDA, provide guidance for clinicians regarding serologic testing for SARS-CoV-2.

Several factors should be considered when using these tests, including:

- Important performance characteristics, including the sensitivity and specificity (i.e., the rate of true positive and true negative results) of many of the commercially available serologic tests, have not been fully characterized. Serologic assays that have FDA EUAs are preferred for public health and clinical use. Formal comparisons of serologic tests are in progress.
- False-positive test results may occur due to cross-reactivity from pre-existing antibodies to other coronaviruses.

Serologic Testing and Immunity to SARS-CoV-2 Infection

The Panel **recommends against** the use of serologic testing to determine whether a person is immune to SARS-CoV-2 infection **(AIII)**. If serologic tests are performed and antibody is detected, results should be interpreted with caution for the following reasons:

- It is currently unknown how long antibodies persist following infection, *and*
- It is currently unknown whether the presence of antibody confers protective immunity against future infection.

In communities where the prevalence of SARS-CoV-2 infection is low, the proportion of positive tests that are false positives may be quite high. In these situations, confirmatory testing using a second independent antibody assay, ideally one that uses a different antigenic target (e.g., the nucleocapsid phosphoprotein if the first assay targeted the spike glycoprotein), can substantially improve the probability that persons with a positive test result are antibody positive.

Assuming the test is reliable, serologic tests to identify recent or prior SARS-CoV-2 infection may be used to:

- Determine who may be eligible to donate blood to manufacture convalescent plasma.
- Measure the immune response in SARS-CoV-2 vaccine studies.
- Estimate the proportion of the population exposed to SARS-CoV-2.

Lastly, serologic tests **should not be used** to:

- Make decisions about the grouping of persons residing in or being admitted to congregate settings (e.g., schools, dormitories, correctional facilities), *or*
- Determine whether persons should return to the workplace.

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Prevention and Prophylaxis of SARS-CoV-2 Infection

Last Updated: August 27, 2020

Summary Recommendations
• The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of any agents for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pre-exposure prophylaxis (PrEP), except in a clinical trial **(AIII)**. • The Panel **recommends against** the use of any agents for SARS-CoV-2 post-exposure prophylaxis (PEP), except in a clinical trial **(AIII)**.
Rating of Recommendations: A = Strong; B = Moderate; C = Optional **Rating of Evidence:** I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies; III = Expert opinion

General Prevention Measures

Most transmissions of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are thought to occur through respiratory droplets, and the risk of transmission can be reduced by covering coughs and sneezes and maintaining a distance of at least 6 feet from others. When consistent distancing is not possible, face coverings may further reduce the spread of infectious droplets from individuals with SARS-CoV-2 infection to others. Frequent handwashing is also effective in reducing the risk of infection.[1] Health care providers should follow the Centers for Disease Control and Prevention (CDC) recommendations for infection control and appropriate use of personal protective equipment.[2]

Vaccines

Vaccines for SARS-CoV-2 are aggressively being pursued. Vaccine development is typically a lengthy process, often requiring multiple candidates before one proves to be safe and effective. To address the current pandemic, several platforms are being used to develop candidate vaccines for Phase 1/2 trials; those that show promise are rapidly moving into Phase 3 trials. Several standard platforms, such as inactivated vaccines, live-attenuated vaccines, and protein subunit vaccines, are being pursued. Some novel approaches are being investigated, including DNA-based and RNA-based strategies and replicating and nonreplicating vector strategies, with the hope of identifying a safe and effective SARS-CoV-2 vaccine that can be used in the near future.[3,4]

Pre-Exposure Prophylaxis

- The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of any agents for SARS-CoV-2 pre-exposure prophylaxis (PrEP), except in a clinical trial **(AIII)**.

Rationale

At present, there is no known agent that can be administered before exposure to SARS-CoV-2 (i.e., as PrEP) to prevent infection. Clinical trials are investigating several agents, including emtricitabine plus tenofovir alafenamide or tenofovir disoproxil fumarate, hydroxychloroquine, and supplements such as zinc, vitamin C, and vitamin D. Studies of monoclonal antibodies that target SARS-CoV-2 are in development. Please check *ClinicalTrials.gov* for the latest information.

Post-Exposure Prophylaxis

- The Panel **recommends against** the use of any agents for SARS-CoV-2 post-exposure prophylaxis (PEP), except in a clinical trial **(AIII)**.

Rationale

At present, there is no known agent that can be administered after exposure to SARS-CoV-2 infection (i.e., as PEP) to prevent infection. Potential options for PEP that are currently under investigation include chloroquine, hydroxychloroquine, lopinavir/ritonavir, nitazoxanide, vitamin super B-complex, and vitamin D. Other post-exposure preventive strategies that are in development include the use of SARS-CoV-2 monoclonal antibodies and convalescent plasma. Please check *ClinicalTrials.gov* for the latest information.

Clinical Trial Data

Hydroxychloroquine

Both chloroquine and hydroxychloroquine have *in vitro* activity against SARS-CoV and SARS-CoV-2.[5,6] A small cohort study without a control group has suggested that hydroxychloroquine might reduce the risk of SARS-CoV-2 transmission to close contacts.[7]

Randomized, Double-Blind, Controlled Trial of High-Risk or Moderate-Risk Occupational or Household Exposures

A randomized, double-blind, controlled trial included 821 participants who self-enrolled in the study using an internet-based survey. Study participants had either high or moderate risk of occupational exposures (66% of participants) or household exposures (34% of participants). High-risk exposure was defined as being within 6 feet of an individual with confirmed SARS-CoV-2 infection for more than 10 minutes while not wearing a face mask or eye shield (87.6% of participants), and moderate-risk exposure was defined as the same distance and duration of exposure while wearing a face mask but no eye shield (12.4% of participants).[8]

Participants were randomized to receive placebo or hydroxychloroquine sulfate given once at a relatively high dose of 800 mg, followed by 600 mg 6 to 8 hours later, then 600 mg once daily for 4 additional days. Because enrollment was done online, study drugs were sent by overnight mail, resulting in more than 50% of participants initiating their first dose 3 to 4 days after exposure to SARS-CoV-2.[8]

A total of 107 participants developed the primary outcome of symptomatic illness, confirmed either by a SARS-CoV-2 positive molecular test or, if testing was not available, by a compatible, COVID-19-related syndrome based on CDC criteria. Due to limited access to molecular diagnostic testing, SARS-CoV-2 infection was confirmed in only 16 of the 107 participants (15%). There was no statistically significant difference in the incidence of the primary outcome (symptomatic illness) between the hydroxychloroquine group and the placebo group (11.8% vs. 14.3%, respectively; $P = 0.35$). There were more adverse events in the hydroxychloroquine group; mostly nausea, loose stools, and abdominal discomfort; with no serious adverse reactions or cardiac arrhythmias.[8]

This study had several important limitations, including:

- Initiation of therapy was delayed for at least 3 days after exposure to SARS-CoV-2 in most participants.
- Only 15% of participants who reached the primary outcome had SARS-CoV-2 infection confirmed by molecular diagnostics.
- The study population was young (with a median age of 40 years) and consisted of participants who had a relatively low risk of severe COVID-19.

It is notable that although high doses of hydroxychloroquine were associated with an increase in the frequency of adverse events, the reported adverse events were mostly mild, with no serious events reported.

Cluster-Randomized Trial of High-Risk Exposures in Spain

This study has not been peer reviewed.

An open-label, cluster-randomized trial included 2,314 asymptomatic contacts of 672 COVID-19 cases in Spain. Study participants were health care or nursing home workers (60.3%), household contacts (27.7%), or nursing home residents (12.7%) who were aged ≥18 years and documented to have spent >15 minutes within 2 meters of a polymerase chain reaction (PCR)-positive COVID-19 case during the 7 days prior to enrollment.[9]

Participants who were epidemiologically linked to a PCR-positive COVID-19 case were defined as study clusters (called rings). All contacts in a ring were simultaneously cluster-randomized 1:1 to either usual care (the control arm) or hydroxychloroquine 800 mg once daily for 1 day followed by 400 mg once daily for 6 days (the intervention arm). Participants were informed of their allocated study arm after being randomized to the intervention or control arm and signing a consent form. The primary outcome was onset of laboratory-confirmed COVID-19, defined as illness with at least one of the following symptoms: fever, cough, difficulty breathing, myalgia, headache, sore throat, new olfactory and taste disorders, or diarrhea; AND a positive SARS-CoV-2 PCR test. A secondary outcome was onset of SARS-CoV-2 infection defined as either a SARS-CoV-2 PCR positive test OR the presence of any of the symptoms compatible with COVID-19. Additional secondary outcomes were development of serological positivity at Day 14 and safety up to 28 days from treatment initiation.

The baseline characteristics of the participants were similar between the two study arms, including coexisting disease, number of days of exposure before enrollment and randomization, and type of contact. A total of 138 (6%) study participants developed PCR-confirmed, symptomatic SARS-CoV-2 infection, with no statistical difference for this outcome between the control and intervention arms (6.2% vs. 5.7%, respectively; risk ratio 0.89; 95% CI, 0.54–1.46). There was also no statistical difference between the study arms in the incidence of either PCR-confirmed or symptomatically compatible COVID-19, which occurred in 18.2% of participants, 17.8% in the control arm and 18.7% in the intervention arm (risk ratio 1.04; 95% CI, 0.77–1.41). Similarly, there was no statistical difference between the arms in the rate of positivity for SARS-CoV-2 immunoglobulin (Ig) A and/or IgG (8.7% in the control arm and 14.3% in the intervention arm; risk ratio 1.6; 95% CI, 0.96–2.69). There were more adverse events among the hydroxychloroquine-treated participants (51.6%) than among the controls (5.9%), although most of the adverse events were mild, including gastrointestinal events, nervous system disorders, myalgia, fatigue, or malaise. No serious adverse events were attributed to the study drug.

This study had several limitations, including:

- It lacked a placebo comparator, which could have had an impact on safety reporting.
- Data regarding the extent of the exposure to the index cases was limited.
- For >50% of the study participants, the time from exposure to the index case to randomization was ≥4 days.

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Clinical Presentation of People with SARS-CoV-2 Infection

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Patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can experience a range of clinical manifestations, from no symptoms to critical illness. This section of the Guidelines discusses the clinical presentations of patients according to illness severity.

In general, adults with SARS-CoV-2 infection can be grouped into the following severity of illness categories. However, the criteria for each category may overlap or vary across clinical guidelines and clinical trials, and a patient's clinical status may change over time.

- *Asymptomatic or Presymptomatic Infection:* Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test or an antigen test), but who have no symptoms that are consistent with COVID-19.
- *Mild Illness:* Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
- *Moderate Illness:* Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have saturation of oxygen (SpO_2) ≥94% on room air at sea level.
- *Severe Illness:* Individuals who have SpO_2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mmHg, respiratory frequency >30 breaths per minute, or lung infiltrates >50%.
- *Critical Illness:* Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Patients with certain underlying comorbidities are at a higher risk of progression to severe COVID-19. Some of these comorbidities include being 65 years or older; having cardiovascular disease, chronic lung disease, diabetes, cancer, obesity, or chronic kidney disease; and being a recipient of immunosuppressive therapy.[1] Health care providers should monitor such patients closely until clinical recovery is achieved.

The optimal pulmonary imaging technique has not yet been defined for people with symptomatic SARS-CoV-2 infection who present to care. Initial evaluation for these patients may include chest X-ray, ultrasound, or, if indicated, computerized tomography. An electrocardiogram should be performed if indicated. Laboratory testing includes a complete blood count with differential and a metabolic profile, including liver and renal function tests. While not part of standard care, measuring the levels of inflammatory markers such as C-reactive protein (CRP), D-dimer, and ferritin may have prognostic value.[2-4]

The definitions for the severity of illness categories listed above also apply to pregnant patients. However, the threshold for certain interventions may be different for pregnant patients and nonpregnant patients. For example, oxygen supplementation is recommended for pregnant patients when SpO_2 falls below 95% on room air at sea level, to accommodate physiologic changes in oxygen demand during pregnancy and to assure adequate oxygen delivery to the fetus.[5] If laboratory parameters are used for monitoring and interventions, clinicians should be aware that normal physiologic changes during pregnancy can alter several laboratory values. In general, leukocyte cell count increases throughout gestation and delivery and peaks during the immediate postpartum period. This is mainly due to neutrophilia.[6] D-dimer and CRP levels also increase during pregnancy and are often higher in pregnant patients than in nonpregnant patients.[7] Detailed information on treating COVID-19 in pregnant

patients can be found in Special Considerations in Pregnancy, as well as in the pregnancy considerations subsection of each individual section of the Guidelines.

In pediatric patients, radiographic abnormalities are common and, for the most part, should not be used as the sole criteria to define the COVID-19 illness category. Normal values for respiratory rate also vary with age in children; thus, hypoxia should be the primary criteria used to define severe illness, especially in younger children. In a small number of children and in some young adults, SARS-CoV-2 infection may be followed by a severe inflammatory condition called multisystem inflammatory syndrome in children (MIS-C).[8,9] This syndrome is discussed in detail in Special Considerations in Children.

Asymptomatic or Presymptomatic Infection

Asymptomatic SARS-CoV-2 infection can occur, although the percentage of patients who remain truly asymptomatic throughout the course of infection is variable and incompletely defined. It is unclear at present what percentage of individuals who present with asymptomatic infection may progress to clinical disease. Some asymptomatic individuals have been reported to have objective radiographic findings that are consistent with COVID-19 pneumonia.[10,11] The availability of widespread virologic testing for SARS-CoV-2 and the development of reliable serologic assays for antibodies to the virus will help to determine the true prevalence of asymptomatic and presymptomatic infection. See Therapeutic Management of COVID-19 for recommendations regarding SARS-CoV-2-specific therapy.

Mild Illness

Patients with mild illness may exhibit a variety of signs and symptoms (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell). They do not have shortness of breath, dyspnea on exertion, or abnormal imaging. Most mildly ill patients can be managed in an ambulatory setting or at home through telemedicine or telephone visits. No imaging or specific laboratory evaluations are routinely indicated in otherwise healthy patients with mild COVID-19 disease. Older patients and those with underlying comorbidities are at higher risk of disease progression; therefore, health care providers should monitor these patients closely until clinical recovery is achieved. See Therapeutic Management of COVID-19 for recommendations regarding SARS-CoV-2-specific therapy.

Moderate Illness

Moderate COVID-19 illness is defined as evidence of lower respiratory disease during clinical assessment or imaging, with SpO_2 ≥94% on room air at sea level. Given that pulmonary disease can progress rapidly in patients with COVID-19, close monitoring of patients with moderate disease is recommended. If bacterial pneumonia or sepsis is strongly suspected, administer empiric antibiotic treatment, re-evaluate the patient daily, and de-escalate or stop antibiotics if there is no evidence of bacterial infection. See Therapeutic Management of COVID-19 for recommendations regarding SARS-CoV-2-specific therapy.

Severe Illness

Patients with COVID-19 are considered to have severe illness if they have SpO_2 <94% on room air at sea level, a respiratory rate of >30 breaths/min, PaO_2/FiO_2 <300 mmHg, or lung infiltrates >50%. These patients may experience rapid clinical deterioration. Oxygen therapy should be administered immediately using a nasal cannula or a high-flow oxygen device. See Therapeutic Management of COVID-19 for recommendations regarding SARS-CoV-2-specific therapy. If secondary bacterial pneumonia or sepsis is suspected, administer empiric antibiotics, re-evaluate the patient daily, and de-escalate or stop antibiotics if there is no evidence of bacterial infection.

Critical Illness

Severe cases of COVID-19 may be associated with acute respiratory distress syndrome, septic shock that may represent virus-induced distributive shock, cardiac dysfunction, elevations in levels of multiple inflammatory cytokines that provoke a cytokine storm, and/or exacerbation of underlying comorbidities. In addition to pulmonary disease, patients with COVID-19 may also experience cardiac, hepatic, renal, central nervous system, or thrombotic disease.

As with any patient in the intensive care unit (ICU), successful clinical management of a patient with COVID-19 includes treating both the medical condition that initially resulted in ICU admission and other comorbidities and nosocomial complications.

For more information, see Care of Critically Ill Patients with COVID-19.

Persistent Symptoms or Illnesses After Recovery from Acute COVID-19

There have been an increasing number of reports of patients who experience persistent symptoms after recovering from acute COVID-19. At this time, there is limited information on the prevalence, duration, underlying causes, and effective management strategies for these lingering signs and symptoms.[12] Some of the symptoms overlap with the post-intensive care syndrome that has been described in patients without COVID-19, but prolonged symptoms and disabilities after COVID-19 have also been reported in patients with milder illness, including outpatients.[13,14]

Some of the persistent symptoms that have been reported include fatigue, joint pain, chest pain, palpitations, shortness of breath, and worsened quality of life.[15,16] One study from China found that pulmonary function was still impaired 1 month after hospital discharge.[17] A study from the United Kingdom reported that among 100 hospitalized patients (32 received care in the ICU and 68 received care in hospital wards only), 72% of the ICU patients and 60% of the ward patients experienced fatigue and breathlessness at 4 to 8 weeks after hospital discharge. The authors of the study suggest that post-hospital rehabilitation may be necessary for some of these patients.[15]

Neurologic and psychiatric symptoms have also been reported among patients who have recovered from acute COVID-19. High rates of anxiety and depression have been reported in some patients using self-report scales for psychiatric distress.[16,18] Younger patients have been reported to experience more psychiatric symptoms than patients aged >60 years.[15,16]

Patients may continue to experience headaches, vision changes, hearing loss, loss of taste or smell, impaired mobility, numbness in extremities, tremors, myalgia, memory loss, cognitive impairment, and mood changes for up to 3 months after diagnosis of COVID-19.[19,20] More research is needed to better understand the pathophysiology and clinical course of these post-infection sequelae and to identify management strategies for patients.

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