Centers for Disease Control and Prevention

Coronavirus Disease 2019 (COVID-19)

Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)

Updated May 15, 2020

Summary of Recent Changes

Revisions were made on May 15, 2020, to reflect the following:

- Updated information for pediatric management

Revisions were made on May 12, 2020, to reflect the following:

- New information about COVID-19-Associated Hypercoagulability
- Updated content and resources to include new NIH Treatment Guidelines
- Minor revisions for clarity

This interim guidance is for clinicians caring for patients with confirmed infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19). CDC will update this interim guidance as more information becomes available.

Clinical Presentation

Incubation period

The incubation period for COVID-19 is thought to extend to 14 days, with a median time of 4-5 days from exposure to symptoms onset.[1-3] One study reported that 97.5% of persons with COVID-19 who develop symptoms will do so within 11.5 days of SARS-CoV-2 infection.[3]

Presentation

The signs and symptoms of COVID-19 present at illness onset vary, but over the course of the disease, most persons with COVID-19 will experience the following[1,4-9]:

- Fever (83–99%)
- Cough (59–82%)
- Fatigue (44–70%)
- Anorexia (40–84%)
- Shortness of breath (31–40%)
- Sputum production (28–33%)
- Myalgia (11–35%)

Atypical presentations have been described, and older adults and persons with medical comorbidities may have delayed presentation of fever and respiratory symptoms.[10,11] In one study of 1,099 hospitalized patients, fever was present in only 44% at hospital admission but later developed in 89% during hospitalization.[1] Headache, confusion, rhinorrhea, sore throat, hemoptysis, vomiting, and diarrhea have been reported but are less common (<10%).[1,4-6] Some persons with COVID-19 have experienced gastrointestinal symptoms such as diarrhea and nausea prior to developing fever and lower respiratory tract signs and symptoms.[9] Anosmia or ageusia preceding the onset of respiratory symptoms has been anecdotally reported[12], but more information is needed to understand its role in identifying COVID-19.

Several studies have reported that the signs and symptoms of COVID-19 in children are similar to adults and are usually milder compared to adults.[13-17] For more information on the clinical presentation and course among children, see Information for Pediatric Healthcare Providers.

Asymptomatic and Pre-Symptomatic Infection

Several studies have documented SARS-CoV-2 infection in patients who never develop symptoms (asymptomatic) and in patients not yet symptomatic (pre-symptomatic).[14,16,18-28] Since asymptomatic persons are not routinely tested, the prevalence of asymptomatic infection and detection of pre-symptomatic infection is not well understood. One study found that as many as 13% of RT-PCR-confirmed cases of SARS-CoV-2 infection in children were asymptomatic.[14] Another study of skilled nursing facility residents infected with SARS-CoV-2 from a healthcare worker demonstrated that half were asymptomatic or pre-symptomatic at the time of contact tracing evaluation and testing.[25] Patients may have abnormalities on chest imaging before the onset of symptoms.[19,20] Some data suggest that pre-symptomatic infection tended to be detected in younger individuals and was less likely to be associated with viral pneumonia.[19,20]

Asymptomatic and Pre-Symptomatic Transmission

Epidemiologic studies have documented SARS-CoV-2 transmission during the pre-symptomatic incubation period[19,29-31], and asymptomatic transmission has been suggested in other reports.[21,22,32] Virologic studies have also detected SARS-CoV-2 with RT-PCR low cycle thresholds, indicating larger quantities of viral RNA, and cultured viable virus among persons with asymptomatic and pre-symptomatic SARS-CoV-2 infection.[23,25,28,33] The exact degree of SARS-CoV-2 viral RNA shedding that confers risk of transmission is not yet clear. Risk of transmission is thought to be greatest when patients are symptomatic since viral shedding is greatest at the time of symptom onset and declines over the course of several days to weeks.[33-36] However, the proportion of SARS-CoV-2 transmission in the population due to asymptomatic or pre-symptomatic infection compared to symptomatic infection is unclear.[37]

Clinical Course

Illness Severity

The largest cohort of >44,000 persons with COVID-19 from China showed that illness severity can range from mild to critical:[38]

- Mild to moderate (mild symptoms up to mild pneumonia): 81%
- Severe (dyspnea, hypoxia, or >50% lung involvement on imaging): 14%
- Critical (respiratory failure, shock, or multiorgan system dysfunction): 5%

In this study, all deaths occurred among patients with critical illness and the overall case fatality rate was 2.3%.[38] The case fatality rate among patients with critical disease was 49%.[38] Among children in China, illness severity was lower with 94% having asymptomatic, mild or moderate disease, 5% having severe disease, and <1% having critical disease.[14] Among U.S. COVID-19 cases with known disposition, the proportion of persons who were hospitalized was 19%.[39] The proportion of persons with COVID-19 admitted to the intensive care unit (ICU) was 6%.[39]

Clinical Progression

Among patients who developed severe disease, the medium time to dyspnea ranged from 5 to 8 days, the median time to acute respiratory distress syndrome (ARDS) ranged from 8 to 12 days, and the median time to ICU admission ranged from 10 to 12 days.[5,6,10,11] Clinicians should be aware of the potential for some patients to rapidly deteriorate one week after illness onset. Among all hospitalized patients, a range of 26% to 32% of patients were admitted to the ICU.[6,8,11] Among all patients, a range of 3% to 17% developed ARDS compared to a range of 20% to 42% for hospitalized patients and 67% to 85% for patients admitted to the ICU.[1,4-6,8,11] Mortality among patients admitted to the ICU ranges from 39% to 72% depending on the study.[5,8,10,11] The median length of hospitalization among survivors was 10 to 13 days.[1,6,8]

Risk Factors for Severe Illness

Age is a strong risk factor for severe illness, complications, and death.[1,6,8,10,11,38-41] Among more than 44,000 confirmed cases of COVID-19 in China, the case fatality rate was highest among older persons: ≥80 years: 14.8%, 70–79 years: 8.0%, 60–69 years: 3.6%, 50–59 years: 1.3%, 40–49 years: 0.4%, <40 years: 0.2%.[38,42] Early U.S. epidemiologic data suggests that

the case fatality was highest in persons aged ≥85 years (range 10%–27%), followed by 3%–11% for ages 65–84 years, 1%–3% for ages 55–64 years, and <1% for ages 0–54 years.[39]

Patients in China with no reported underlying medical conditions had an overall case fatality of 0.9%, but case fatality was higher for patients with comorbidities: 10.5% for those with cardiovascular disease, 7.3% for diabetes, and approximately 6% each for chronic respiratory disease, hypertension, and cancer.[42] Heart disease, hypertension, prior stroke, diabetes, chronic lung disease, and chronic kidney disease have all been associated with increased illness severity and adverse outcomes.[1,6,10,11,38,42,43] Accounting for differences in age and prevalence of underlying condition, mortality associated with COVID-19 in the United States was similar to China.[24,39,40]

Reinfection

There are no data concerning the possibility of re-infection with SARS-CoV-2 after recovery from COVID-19. Viral RNA shedding declines with resolution of symptoms, and may continue for days to weeks.[10,33,34] However, the detection of RNA during convalescence does not necessarily indicate the presence of viable infectious virus. Clinical recovery has been correlated with the detection of IgM and IgG antibodies which signal the development of immunity.[36,44-46]

Viral Testing

Diagnosis of COVID-19 requires detection of SARS-CoV-2 RNA by reverse transcription polymerase chain reaction (RT-PCR). Detection of SARS-CoV-2 viral RNA is better in nasopharynx samples compared to throat samples.[33,47] Lower respiratory samples may have better yield than upper respiratory samples.[33,47]. SARS-CoV-2 RNA has also been detected in stool and blood.[13,34,44,48] Detection of SARS-CoV-2 RNA in blood may be a marker of severe illness.[52] Viral RNA shedding may persist over longer periods among older persons and those who had severe illness requiring hospitalization. (median range of viral shedding among hospitalized patients 12–20 days).[10,33-36]

Infection with both SARS-CoV-2 and with other respiratory viruses has been reported, and detection of another respiratory pathogen does not rule out COVID-19.[50]

For more information about testing and specimen collection, handling and storage, visit Evaluating and Testing Persons for Coronavirus Disease 2019 (COVID-19) and Frequently Asked Questions on COVID-19 Testing at Laboratories.

Laboratory and Radiographic Findings

Laboratory Findings

Lymphopenia is the most common lab finding in COVID-19 and is found in as many as 83% of hospitalized patients.[1,5] Lymphopenia, neutrophilia, elevated serum alanine aminotransferase and aspartate aminotransferase levels, elevated lactate dehydrogenase, high CRP, and high ferritin levels may be associated with greater illness severity.[1,5,6,8,10,51] Elevated D-dimer and lymphopenia have been associated with mortality.[8,10] Procalcitonin is typically normal on admission, but may increase among those admitted to the ICU.[4-6] Patients with critical illness had high plasma levels of inflammatory makers, suggesting potential immune dysregulation.[5,52]

Radiographic Findings

Chest radiographs of patients with COVID-19 typically demonstrate bilateral air-space consolidation, though patients may have unremarkable chest radiographs early in the disease.[1,5,53] Chest CT images from patients with COVID-19 typically demonstrate bilateral, peripheral ground glass opacities.[4,8,38,54-63] Because this chest CT imaging pattern is non-specific and overlaps with other infections, the diagnostic value of chest CT imaging for COVID-19 may be low and dependent upon radiographic interpretation.[55,64] One study found that 56% of patients who presented within 2 days of diagnosis had a normal CT[56]. Conversely, other studies have also identified chest CT abnormalities in patients prior to the detection of SARS-CoV-2 RNA.[54,65] Given the variability in chest imaging findings, chest radiograph or CT alone is not recommended for the diagnosis of COVID-19. The American College of Radiology also does not recommend CT for screening or as a first-line test for diagnosis of COVID-19. (See American College of Radiology Recommendations).

Clinical Management and Treatment

The National Institutes of Health published guidelines on prophylaxis use, testing, and management of patients with COVID-19. For more information, please visit: National Institutes of Health: Coronavirus Disease 2019 (COVID-19) Treatment Guidelines . The recommendations were based on scientific evidence and expert opinion and will be updated as more data become available.

Mild to Moderate Disease

Patients with a mild clinical presentation (absence of viral pneumonia and hypoxia) may not initially require hospitalization, and many patients will be able to manage their illness at home. The decision to monitor a patient in the inpatient or outpatient setting should be made on a case-by-case basis. This decision will depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and the ability of the patient to self-isolate at home. Patients with risk factors for severe illness (see People Who Are at Higher Risk for Severe Illness) should be monitored closely given the possible risk of progression to severe illness in the second week after symptom onset.[5,6,10,11]

For information regarding infection prevention and control recommendations, please see Interim Infection Prevention and Control Recommendations for Patients with Confirmed Coronavirus Disease 2019 (COVID-19) or Persons Under Investigation for COVID-19 in Healthcare Settings.

Severe Disease

Some patients with COVID-19 will have severe disease requiring hospitalization for management. Inpatient management revolves around the supportive management of the most common complications of severe COVID-19: pneumonia, hypoxemic respiratory failure/ARDS, sepsis and septic shock, cardiomyopathy and arrhythmia, acute kidney injury, and complications from prolonged hospitalization, including secondary bacterial infections, thromboembolism, gastrointestinal bleeding, and critical illness polyneuropathy/myopathy.[1,4-6,10,11,38,66-69]

More information can be found at National Institutes of Health: Coronavirus Disease 2019 (COVID-19) Treatment Guidelines and Healthcare Professionals: Frequently Asked Questions and Answers. Additional resources and guidance documents on the treatment and management of COVID-19, including inpatient management of critically ill patients, are provided below.

Hypercoagulability and COVID-19

Some patients with COVID-19 may develop signs of a hypercoagulable state and be at increased risk for venous and arterial thrombosis of large and small vessels.[70,71] **Laboratory abnormalities** commonly observed among hospitalized patients with COVID-19-associated coagulopathy include:

- Mild thrombocytopenia
- Increased D-dimer levels
- Increased fibrin degradation products
- Prolonged prothrombin time

Elevated D-dimer levels have been strongly associated with greater risk of death.[70,72-75]

There are several reports of hospitalized patients with **thrombotic complications**, most frequently deep venous thrombosis and pulmonary embolism.[76-78] Other reported manifestations include:

- Microvascular thrombosis of the toes
- Clotting of catheters
- Myocardial injury with ST-segment elevation
- Large vessel strokes[79-82]

The pathogenesis for COVID-19-associated hypercoagulability remains unknown. However, hypoxia and systemic inflammation secondary to COVID-19 may lead to high levels of inflammatory cytokines[83] and activation of the coagulation pathway.

There are limited data available to inform clinical management around prophylaxis or treatment of venous thromboembolism in COVID-19 patients.

Several national professional associations provide resources for up-to-date information concerning COVID-19-associated hypercoagulability, including management of anticoagulation. This is a rapidly evolving topic, with new information released often.

More information on hypercoagulability and COVID-19 is available from the American Society of Hematology and National Institutes of Health: Coronavirus Disease 2019 (COVID-19) Treatment Guidelines – Antithrombotic Therapy in Patients with COVID-19.

Pediatric Management

Illness among pediatric patients with COVID-19 is typically milder than among adults, with most children presenting with symptoms of upper respiratory infection. However, severe outcomes have been reported in children including SARS-CoV-2 associated deaths. CDC and partners are investigating reports of multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19 and have released a related health advisory through its Health Alert Network (HAN).

For expanded guidance on the management of children with COVID-19 and associated complications, see Information for Pediatric Healthcare Providers and the Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children.

Investigational Therapeutics

The National Institutes of Health have published interim guidelines for the medical management of COVID-19 which include information on therapeutic options for COVID-19 currently under investigation. No U.S. Food and Drug Administration (FDA)-approved drugs have demonstrated safety and efficacy in randomized controlled trials when used to treat patients with COVID-19, although FDA has granted an Emergency Use Authorization for the use of remdesivir to treat severe cases. Use of investigational therapies for treatment of COVID-19 should ideally be done in the context of enrollment in randomized controlled trials, so that beneficial drugs can be identified. For the latest information, see Information for Clinicians on Therapeutic Options for COVID-19 Patients. For information on registered trials in the United States, see ClinicalTrials.gov.

Discontinuation of Transmission-Based Precautions or Home Isolation

Patients who have clinically recovered and are able to discharge from the hospital but who have not been cleared from their Transmission-Based Precautions may continue isolation at their place of residence until cleared. For recommendations on discontinuation of Transmission-Based Precautions or home isolation for patients who have recovered from COVID-19 illness, please see:

- Interim Guidance for Discontinuation of Transmission-Based Precautions and Disposition of Hospitalized Patients with COVID-19
- Interim Guidance for Discontinuation of In-Home Isolation for Patients with COVID-19
- Discontinuation of In-Home Isolation for Immunocompromised Persons with COVID-19.

CDC Resources

- Healthcare Professionals: Frequently Asked Questions and Answers
- Information for Pediatric Healthcare Providers
- Evaluating and Testing Persons for Coronavirus Disease 2019 (COVID-19)
- Frequently Asked Questions on COVID-19 Testing at Laboratories
- Infection Control Guidance for Healthcare Professionals about COVID-19
- Interim Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed Coronavirus Disease 2019 (COVID-19) or in Healthcare Settings
- COVIDView: A Weekly Surveillance Summary of U.S. COVID-19 Activity

Additional resources

- World Health Organization. Interim Guidance on Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected
- Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)
- Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016
- Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children
- Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America
- ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19 Infection
- National Institutes of Health: Coronavirus Disease 2019 (COVID-19) Treatment Guidelines
- Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19 Infection

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