CLINICAL CARE OPTIONS®
INFECTIOUS DISEASE

Covid-19 diagnosis & treatment

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Screening and Diagnosis

Epidemiology

- The COVID-19 pandemic has exploded since cases were first reported in China in December 2019. As of April 15, 2022, more than 503 million cases of COVID-19—caused by SARS-CoV-2 infection—have been reported globally, including more than 6.2 million deaths

serious COVID-19 disease is higher in ;

people aged ≥60 years,

those living in a nursing home or long-term care facility,

those with chronic medical conditions.

In an analysis of more than 1.3 million laboratory-confirmed cases of COVID-19 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.[2]

- Data on comorbid health conditions among patients with COVID-19 indicate ;
- 32% had cardiovascular disease,
- 30% had diabetes,
- 18% had chronic lung disease.
- Other conditions include
- cancer, kidney disease, liver disease (especially in patients with cirrhosis), obesity, sickle cell disease, and other immunocompromising conditions. Transplant recipients and pregnant people are also at a higher risk of severe COVID-19

SARS-CoV-2 Variants

- The Omicron (B.1.1.529) variant was designated a VOC in November 2021 , the Omicron subvariants BA.1, BA.1.1, and BA.2
- Delta (B.1.617.2) was first identified in India and was the dominant variant in July 2021
- Alpha (B.1.1.7) variant, which was first seen in the United Kingdom
- the Beta (B.1.351) variant, which was originally identified in South Africa
- Gamma (P.1) variant, which was identified in Manaus, Brazil

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
- The spectrum of illness can range from asymptomatic infection to severe pneumonia with acute respiratory distress syndrome and death
- mild (defined in this study as no pneumonia or mild pneumonia), severe (defined as dyspnea, respiratory frequency ≥30 breaths/min, oxygen saturation ≤93%, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen [PaO_2/FiO_2] <300 mm Hg, and/or lung infiltrates >50% within 24 to 48 hours),
- critical (defined as respiratory failure, septic shock, and/or multiple organ dysfunction syndrome or failure)

- [30] 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.[2] Other reported symptoms have included, but are not limited to, diarrhea, dizziness, rhinorrhea, anosmia, dysgeusia, sore throat, abdominal pain, anorexia, and vomiting.

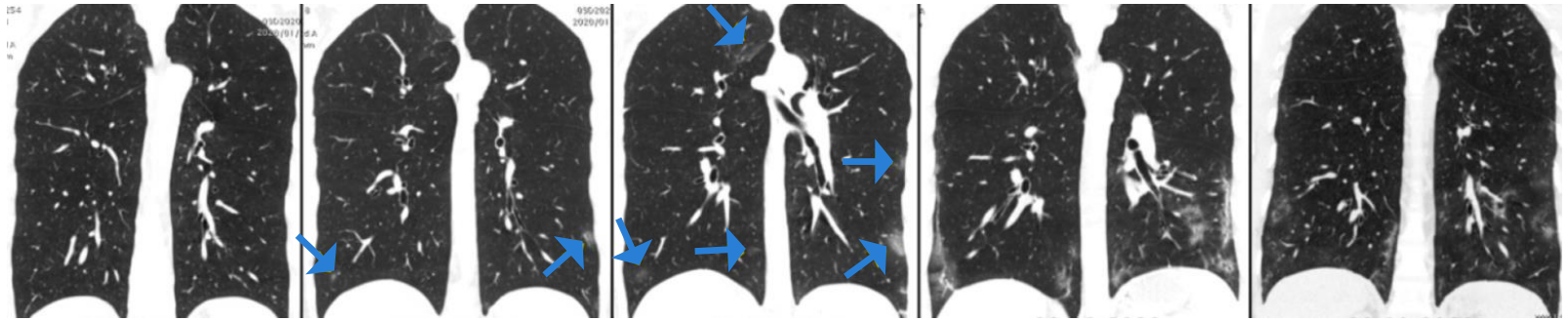
- The abnormalities seen in chest X-rays of patients with COVID-19 vary, but bilateral multifocal opacities are the most common.
- The abnormalities seen in computed tomography of the chest also vary, but the most common are bilateral peripheral ground-glass opacities, with areas of consolidation developing later in the clinical course of COVID-19.[31] Imaging may be normal early in infection and can be abnormal in the absence of symptoms

Chest CT Abnormalities

- Most common hallmark features on chest CT images include bilateral peripheral ground-glass opacities and consolidations of the lungs with peak lung involvement between 6 days and 11 days post-symptom onset[1-3]
- In a study in Wuhan, China, chest CT imaging demonstrated a sensitivity of 97% and specificity of 25% with RT-PCR as the reference (N = 1014)[4]
  - 60% to 93% of patients had initial positive lung CT consistent with COVID-19 *before* the initial positive RT-PCR result

29-Yr-Old Man Presenting With Fever for 6 Days[4]

→ Ground-glass opacities



Day 6 Day 9 Day 11 Day 17 Day 23

1. Bernheim. Radiology. 2020;295:685. 2. Pan. Radiology. 2020;295:715. 3. Wang. Radiology. 2020;296:E55. 4. Ai. Radiology. 2020;296:E32.

Slide credit: clinicaloptions.com

WHO: Suspect Case Definition

Acute onset of fever and cough OR ≥ 3 of the following: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status

And 1 of the following within 14 days of symptom onset:

- Residing or working in an area with high risk of transmission*
- Residing or travel to an area with community transmission
- Working in a healthcare setting

OR:

Patient with severe acute respiratory illness (acute respiratory infection with history of fever or measured fever ≥ 38°C and a cough; onset within last 20 days; requires hospitalization)

*Closed residential settings, humanitarian settings such as camp and camp-like settings for displaced persons.

WHO COVID-19 Case Definition. Updated August 7, 2020. https://www.who.int/publications/i/item/WHO-2019-nCoV-Surveillance_Case_Definition-2020.1

WHO: Probable Case Definition

Acute onset of fever and cough OR ≥ 3 of the following: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status

AND:

Contact of probable or confirmed case or epidemiologically linked to a cluster with at least 1 confirmed case

OR:

Suspect case with chest imaging showing findings suggestive of COVID-19 disease*

OR:

Recent onset of loss of smell or taste in the absence of any other identified cause

OR:

Unexplained death in an adult with respiratory distress who was a contact of a probable or confirmed case or epidemiologically linked to a cluster with at least 1 confirmed case

*Hazy opacities with peripheral and lower lung distribution on chest radiography; multiple bilateral ground glass opacities with peripheral and lower lung distribution on chest CT; or thickened pleural lines, B lines, or consolidative patterns on lung ultrasound.

WHO COVID-19 Case Definition. Updated August 7, 2020. https://www.who.int/publications/i/item/WHO-2019-nCoV-Surveillance_Case_Definition-2020.1

Common COVID-19 Diagnostic Methods: RNA

Viral Nucleic Acid Assays	
Typically indicate	▪ Current infection
Specimen sources	▪ Upper (eg, nasopharyngeal swabs or washes, oropharyngeal swabs, nasal aspirates) or lower (eg, sputum, bronchoalveolar lavage fluid, tracheal aspirates) respiratory tract
Considerations	▪ Primary method for COVID-19 diagnosis with multiple RT-PCR kits available ▪ False negatives may result from improper sampling or handling, low viral load, or viral mutations ▪ SARS-CoV-2 RNA undetectable by ~ Day 14 following onset of illness in some cases/samples

Udugama. ACS Nano. 2020;14:3822. Lee. Front Immunol. 2020;11:879.

Slide credit: clinicaloptions.com

WHO: Interim Guidance on Laboratory Testing for SARS-CoV-2 in Suspected Symptomatic Human Cases

- Routine confirmation of SARS-CoV-2 infection is based on the detection of unique sequences of RNA by nucleic acid amplification tests such as RT-PCR
- 1 or more negative results do not rule out the possibility of SARS-CoV-2 infection

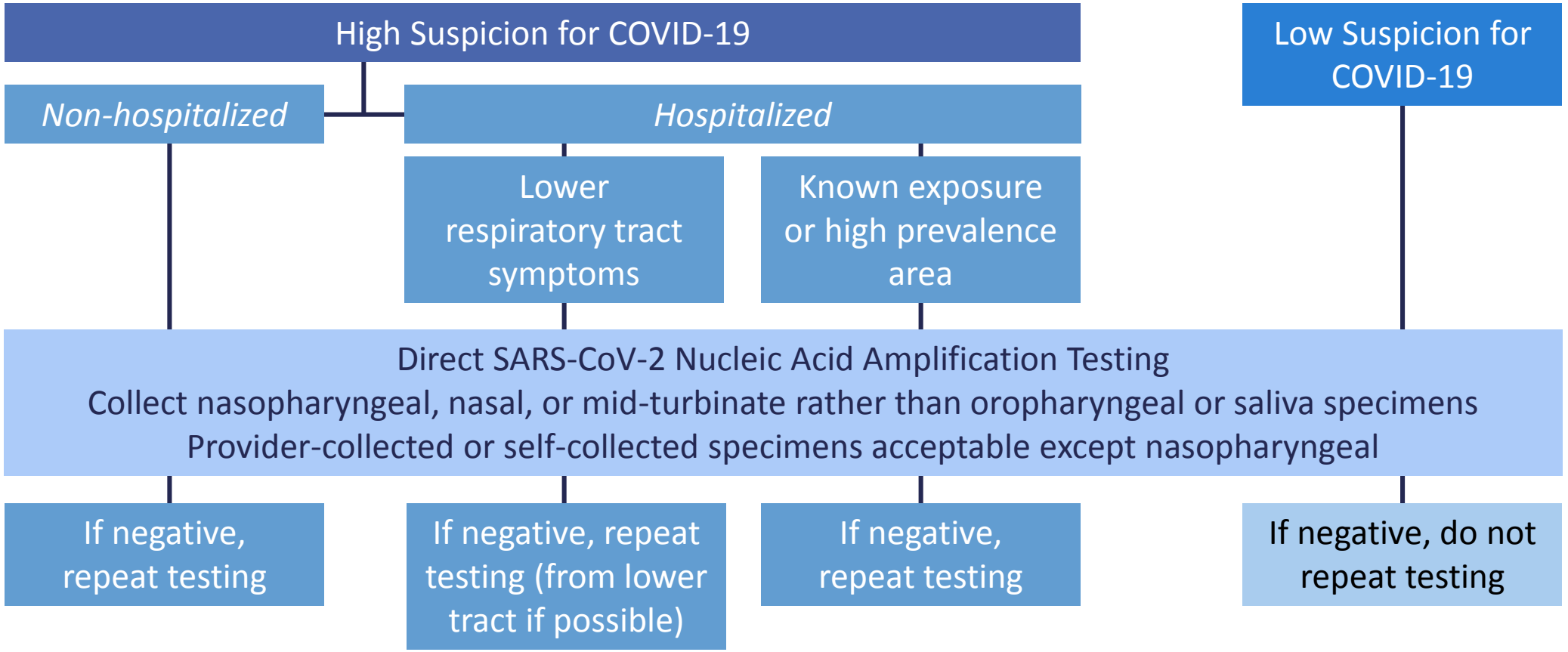
Factors Potentially Leading to Negative Result in an Infected Individual
Poor specimen quality
Timing of specimen collection (very early or late in infection)
Specimen was not handled appropriately
Technical reasons inherent in test (virus mutation or PCR inhibition)

"If a negative result is obtained from a patient with a high index of suspicion for COVID-19, particularly when only upper respiratory tract specimens were collected, additional specimens, including from the lower respiratory tract if possible, should be collected"

https://www.who.int/publications-detail/laboratory-testing-strategy-recommendations-for-covid-19-interim-guidance

Slide credit: clinicaloptions.com

IDSA: SARS-CoV-2 Nucleic Acid Testing of Symptomatic Individuals

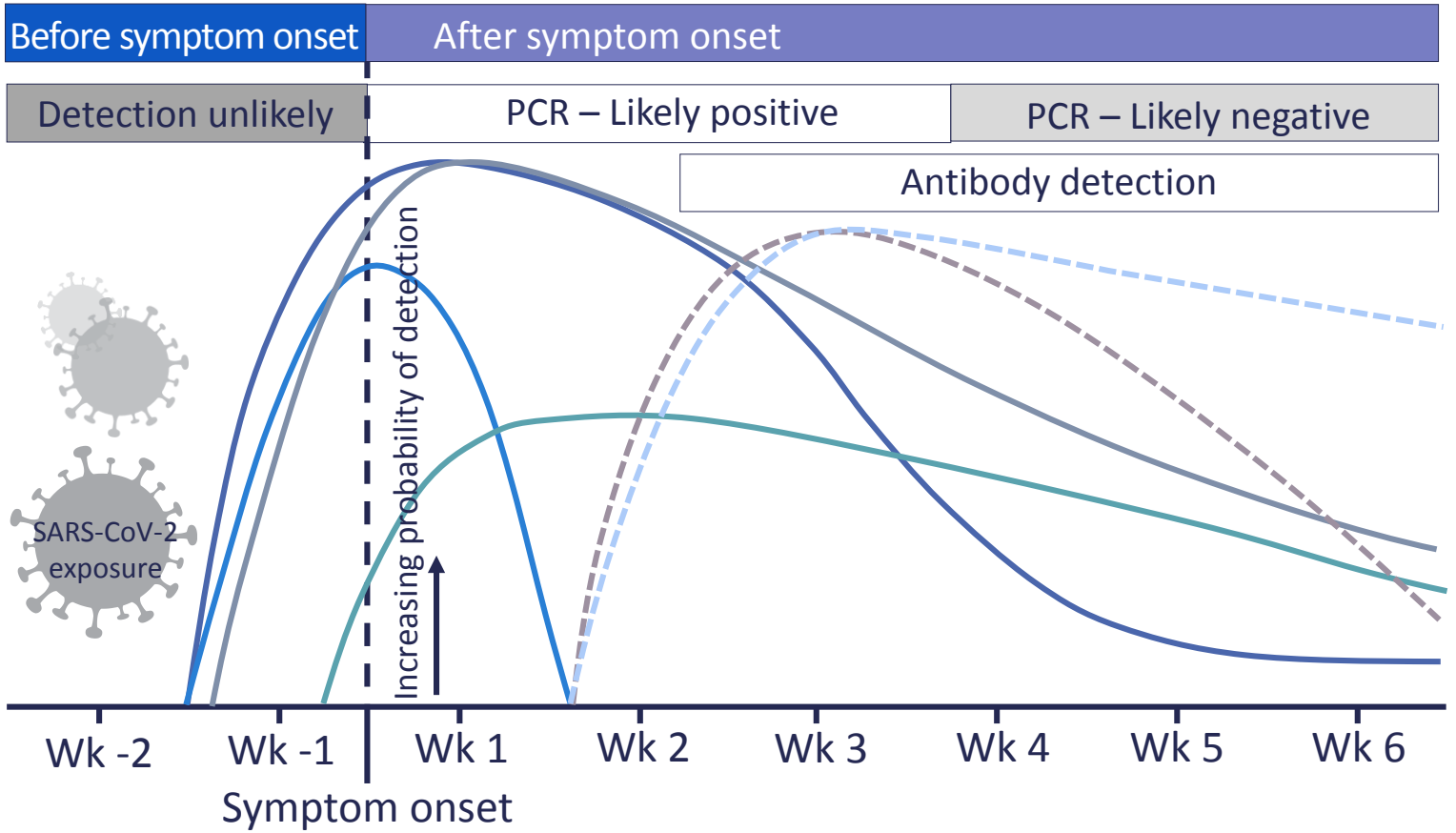


Prioritize testing for symptomatic patients. If resources adequate, consider testing select asymptomatic individuals (eg, exposed, immunosuppressive procedure, major time-sensitive surgery, aerosol-generating procedure with limited PPE).

IDSA. COVID-19 Guideline, Part 3: Diagnostics. Version 1.0.1.

Slide credit: clinicaloptions.com

Temporal Considerations for Diagnosis



- Nasopharyngeal swab PCR
- Virus isolation from respiratory tract
- Bronchoalveolar lavage/sputum PCR
- Stool PCR
- IgM antibody
- IgG antibody

Sethuraman. JAMA. 2020;323:2249. Reproduced with permission from JAMA. 2020. doi:10.1001/jama.2020.8259.

Slide credit: clinicaloptions.com

Testing for SARS-CoV-2 Infection

- (the Panel) recommends using either a nucleic acid amplification test (NAAT) or an antigen test with a sample collected from the upper respiratory tract (e.g., nasopharyngeal, nasal midturbinate, anterior nasal) to diagnose acute SARS-CoV-2 infection **(AIII)**.
- A NAAT should not be repeated in an asymptomatic person (with the exception of health care workers) within 90 days of a previous SARS-CoV-2 infection, even if the person has had a significant exposure to SARS-CoV-2 **(AIII)**.

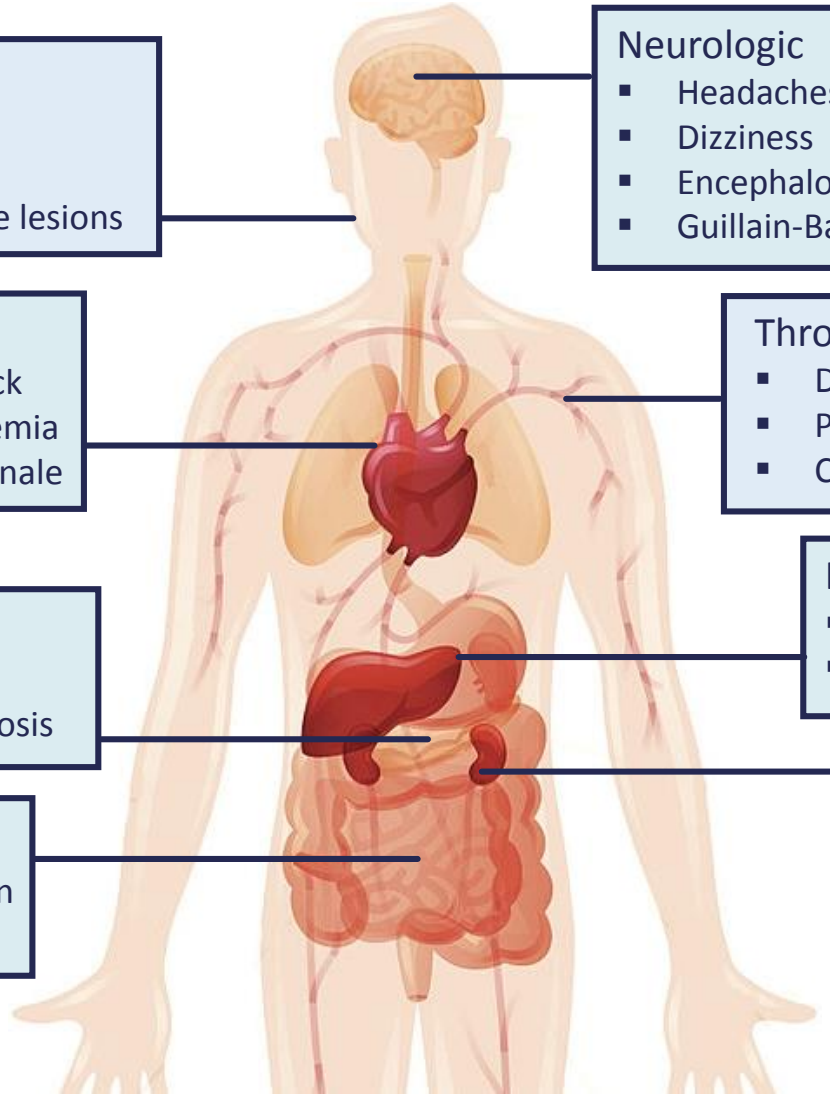
- SARS-CoV-2 reinfection has been reported in people after an initial diagnosis of the infection; therefore, clinicians should consider using a NAAT for those who have recovered from a previous infection and who present with symptoms that are compatible with SARS-CoV-2 infection if there is no alternative diagnosis **(BIII)**.
- The Panel **recommends against** diagnosing acute SARS-CoV-2 infection solely on the basis of serologic (i.e., antibody) test results **(AIII)**.
- There is insufficient evidence for the Panel to recommend either for or against the use of SARS-CoV-2 serologic testing to assess for immunity or to guide clinical decisions about using COVID-19 vaccines or anti-SARS-CoV-2 monoclonal antibodies

Clinical Management Summary

- Two main processes are thought to drive the pathogenesis of COVID-19. **Early in the clinical course, the disease is primarily driven by the replication of SARS-CoV-2**. Later in the clinical course, the disease appears to be driven by a dysregulated immune/inflammatory response to SARS-CoV-2 that leads to tissue damage. Based on this understanding, it is anticipated that therapies that directly target SARS-CoV-2 would have the greatest effect early in the course of the disease, while immunosuppressive/anti-inflammatory therapies are likely to be more beneficial in the later stages of COVID-19. The clinical spectrum of SARS-CoV-2 infection includes asymptomatic or presymptomatic infection and mild, moderate, severe, and critical illness.

- Common laboratory findings in patients with COVID-19 include;
- leukopenia and lymphopenia,elevated levels of aminotransferase, C-reactive protein, D-dimer, ferritin, and lactate dehydrogenase
- Although COVID-19 is primarily a pulmonary disease, emerging data suggest that it also leads to cardiac,[32,33] dermatologic,[34] hematologic,[35] hepatic,[36] neurologic,[37,38] renal,[39,40] and other complications. Thromboembolic events also occur in patients with COVID-19, with the highest risk occurring in critically ill patients

Extrapulmonary Manifestations



Dermatologic
- Petechaie
- Livedo reticularis
- Erythematous rash
- Urticaria
- Vesicles
- Pernio-like lesions

Neurologic
- Headaches
- Dizziness
- Encephalopathy
- Guillain-Barré
- Ageusia
- Myalgia
- Anosmia
- Stroke

Cardiac
- Takotsubo cardiomyopathy
- Myocardial injury/myocarditis
- Cardiac arrhythmias
- Cardiogenic shock
- Myocardial ischemia
- Acute cor pulmonale

Thromboembolism
- Deep vein thrombosis
- Pulmonary embolism
- Catheter-related thrombosis

Hepatic
- Elevated ALT/AST
- Elevated bilirubin

Endocrine
- Hyperglycemia
- Diabetic ketoacidosis

Renal
- Acute kidney injury
- Proteinuria
- Hematuria

Gastrointestinal
- Diarrhea
- Nausea/vomiting
- Abdominal pain
- Anorexia

Gupta. Nat Med. 2020;26:1017.

Slide credit: clinicaloptions.com

NIH Guidelines: Defining a COVID-19 Severity Spectrum

Stage	Characteristics
Asymptomatic or presymptomatic infection	▪ Positive test for SARS-CoV-2 but no symptoms
Mild illness	▪ Varied symptoms (eg, fever, cough, sore throat, malaise, headache, muscle pain) but no shortness of breath, dyspnea, abnormal imaging
Moderate illness	▪ $SpO_2 \geq 94\%$ and lower respiratory disease evidenced by clinical assessment or imaging
Severe illness	▪ $SpO_2 < 94\%$, $PaO_2/FiO_2 < 300$, respiratory rate > 30 breaths/min, or lung infiltrates > 50%
Critical illness	▪ Respiratory failure, septic shock, and/or multiorgan dysfunction

NIH COVID-19 Treatment Guidelines. Management of persons with COVID-19. Last updated June 11, 2020.

Slide credit: clinicaloptions.com

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 what percentage of individuals who present with asymptomatic infection progress to clinical disease. Some asymptomatic individuals have been reported to have objective radiographic findings consistent with COVID-19 pneumonia

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. 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

These comorbidities include;

being aged ≥65 years; having cancer, cardiovascular disease, chronic kidney disease, chronic liver disease, chronic lung disease, diabetes, advanced or untreated HIV infection, or obesity; being pregnant; being a cigarette smoker; being a transplant recipient; and receiving immunosuppressive therapy.[1] Health care providers should monitor such patients closely until clinical recovery is achieved

Medical Management of Mild COVID-19

WHO[1]
▪ Isolate suspected/confirmed cases to contain SARS-CoV-2 transmission; isolation can occur at home, in a designated COVID-19 health or community facility
▪ Treat symptoms (eg, antipyretics for fever, adequate nutrition, appropriate rehydration)
▪ Educate patients on signs/symptoms of complications that, if developed, should prompt pursuit of urgent care

NIH[2,3]
▪ Majority of cases managed in ambulatory setting or at home (eg, by telemedicine)
▪ Close monitoring advised for symptomatic patients with risk factors for severe disease; rapid progression possible
▪ No specific lab tests indicated if otherwise healthy
▪ In non-hospitalized patients, do not initiate anticoagulants or antiplatelet therapy to prevent VTE or arterial thrombosis unless other indications exist

1. WHO Interim Guidance. Clinical management of COVID-19. May 27, 2020.
2. NIH COVID-19 Treatment Guidelines. Management of persons with COVID-19. Last updated June 11, 2020.
3. NIH COVID-19 Treatment Guidelines. Antithrombotic therapy in patients with COVID-19. Last updated May 12, 2020.

Moderate Illness

- Moderate illness is defined as evidence of lower respiratory disease during clinical assessment or imaging, with SpO2 ≥94% on room air at sea level. Given that pulmonary disease can progress rapidly in patients with COVID-19, patients with moderate disease should be closely monitored. If bacterial pneumonia or sepsis is suspected, administer empiric antibiotic treatment, re-evaluate the patient daily, and de-escalate or stop antibiotics if there is no evidence of bacterial infection.

Medical Management of Moderate COVID-19

Management[1]

- Monitor closely, as pulmonary disease can rapidly progress
- Administer empiric antibiotics if bacterial pneumonia/sepsis strongly suspected; re-evaluate daily and de-escalate/stop treatment if no evidence of infection
- Use hospital infection prevention and control measures; limit number of individuals/providers entering patient room
- Use AIIRs for aerosol-generating procedures; staff should wear N95 respirators or PAPRs vs surgical masks

Isolation (Home vs Healthcare Facility)[2]

- Dependent on clinical presentation, requirement for supportive care, presence of vulnerable household contacts; if high risk of deterioration, hospitalization preferred

Initial Evaluation[1]

- May include chest x-ray, ultrasound, or CT
- Perform ECG if indicated
- Obtain CBC with differential and metabolic profile including liver/renal function
- Inflammatory markers (eg, CRP, D-dimer, ferritin) may be prognostically valuable

1. NIH COVID-19 Treatment Guidelines. Management of persons with COVID-19. Last updated June 11, 2020.
2. WHO Interim Guidance. Clinical management of COVID-19. May 27, 2020.

Severe Illness

- Patients with COVID-19 are considered to have severe illness if they have SpO2 <94% on room air at sea level, a respiratory rate >30 breaths/min, PaO2/FiO2 <300 mm Hg, 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

Medical Management of Severe COVID-19

Severe Pneumonia Treatment[1]

- Equip patient care areas with pulse oximeters, functioning oxygen systems, and disposable, single-use, oxygen-delivering interfaces
- Provide immediate supplemental oxygen to patients with emergency signs (eg, obstructed/absent breathing, severe respiratory distress, central cyanosis, shock, coma, or convulsions) and anyone with $SpO_2 < 90\%$
- Monitor for clinical deterioration (eg, rapidly progressive respiratory failure, shock); provide immediate supportive care
- Practice cautious fluid management in patients without tissue hypoperfusion and fluid responsiveness

Acute Coinfection Treatment[1]

- Administer empiric antimicrobials within 1 hr of initial assessment based on clinical judgment, patient host factors, and local epidemiology; knowledge of blood cultures before antimicrobial administration ideal
- Assess daily for antimicrobial de-escalation

Evaluation[2]

- Perform evaluations outlined for **moderate** disease

1. WHO Interim Guidance. Clinical management of COVID-19. May 27, 2020.
2. NIH COVID-19 Treatment Guidelines. Management of persons with COVID-19. Last updated June 11, 2020.

Critical Illness

- SARS-CoV-2 infection can cause acute respiratory distress syndrome, virus-induced distributive (septic) shock, cardiac shock, an exaggerated inflammatory response, thrombotic disease, and exacerbation of underlying comorbidities.
- Successful clinical management of a patient with COVID-19, as with any patient in the intensive care unit (ICU), includes treating both the medical condition that initially resulted in ICU admission as well as other comorbidities and nosocomial complications

Infectious Complications in Patients With COVID-19

- ***Coinfections at presentation:***

influenza and other respiratory viruses, Community-acquired bacterial pneumonia

- ***Reactivation of latent infections:***

chronic hepatitis B virus ,

latent tuberculosis infections reactivating in patients with COVID-19 who receive immunomodulators as treatment,

Reactivation of herpes simplex virus and varicella zoster virus infections have also been reported.

severe and disseminated strongyloidiasis have been reported in patients with COVID-19 during treatment with tocilizumab and corticosteroids

- ***Nosocomial infections****:*

hospital-acquired pneumonia (including ventilator-associated pneumonia), line-related bacteremia or fungemia, catheter-associated urinary tract infection, and *Clostridioides difficile*–associated diarrhea.

- ***Opportunistic fungal infections****:*

Invasive fungal infections, including aspergillosis and mucormycosis,

SARS-CoV-2 Reinfection and Breakthrough Infection

- Furthermore, an investigation of Omicron infection after Delta infection in 4 U.S. states identified 10 cases of reinfection occurring <90 days after a symptomatic infection (1 reinfection required hospitalization).[29] The majority of reinfection cases (70%) occurred in people who were unvaccinated. Fewer patients were symptomatic during reinfection than during initial infection. Among patients who were symptomatic, the median duration of symptoms was shorter with reinfection than with the initial infection

- Breakthrough SARS-CoV-2 infection appears to be less likely to lead to severe illness than infection in people who are unvaccinated. An analysis of electronic health record data from a large U.S. sample of 664,722 patients seen from December 2020 to September 2021 found that full vaccination was associated with a 28% reduced risk for a breakthrough infection.[31] That study also found that the time to breakthrough infection was shorter for patients with immunocompromising conditions (i.e., people with HIV or solid organ or bone marrow transplant recipients) than for those with no immunocompromising conditions

Persistent Symptoms and Other Conditions After Acute COVID-19

- Some patients may experience persistent symptoms or other conditions after acute COVID-19.
- It has been referred to as post-COVID-19 condition, post-COVID syndrome, post-acute sequelae of SARS-CoV-2, or, colloquially, “long COVID,” and affected patients have been referred to as “long haulers.” MIS-C and multisystem inflammatory syndrome in adults (MIS-A) are serious, postinfectious complications of acute COVID-19
- The CDC has defined post-COVID-19 conditions as new, returning, or ongoing symptoms that people experience ≥4 weeks after being infected with SARS-CoV-2

nonneurologic, persistent symptoms included fatigue or muscle weakness, joint pain, chest pain, palpitations, shortness of breath, and cough.

cerebrovascular disorder, dysrhythmia, inflammatory heart disease, ischemic heart disease, heart failure, thromboembolic disease) at 12 months

headaches, vision changes, hearing loss, impaired mobility, numbness in extremities, restless legs syndrome, tremors, memory loss, cognitive impairment, sleep difficulties, concentration problems, mood changes, and loss of sense of smell or taste.

of new-onset diabetes after COVID-19

General Management of Nonhospitalized Patients With Acute COVID-19

- Management of nonhospitalized patients with acute COVID-19 should include providing supportive care, considering the use of COVID-19-specific therapy for patients who have a high risk for disease progression, taking steps to reduce the risk of SARS-CoV-2 transmission (including isolating the patient), and advising patients on when to contact a health care provider and seek an in-person evaluation **(AIII)**.
- When possible, patients with symptoms of COVID-19 should be triaged via telehealth visits to determine whether they require COVID-19-specific therapy and in-person care **(AIII)**.
- Patients with dyspnea should be referred for an in-person evaluation by a health care provider and should be followed closely during the initial days after the onset of dyspnea to assess for worsening respiratory status **(AIII)**.
- Management plans should be based on a patient's vital signs, physical exam findings, risk factors for progression to severe illness, and the availability of health care resources **(AIII)**.

Tier	Risk Group
1	• Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status (see Immunocompromising Conditions below); or • Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors).
2	• Unvaccinated individuals not included in Tier 1 who are at risk of severe disease (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors)
3	• Vaccinated individuals at high risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with clinical risk factors) Note: Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients within this tier in this situation should be prioritized for treatment.
4	• Vaccinated individuals at risk of severe disease (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors) Note: Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients within this tier in this situation should be prioritized for treatment.

Immunocompromising Conditions

- Patients who are within 1 year of receiving B cell-depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab)
- Patients receiving Bruton's tyrosine kinase inhibitors
- Chimeric antigen receptor T cell recipients
- Post-hematopoietic cell transplant recipients who have chronic graft-versus-host disease or who are taking immunosuppressive medications for another indication
- Patients with hematologic malignancies who are on active therapy
- Lung transplant recipients

- Patients who are within 1 year of receiving a solid organ transplant (other than lung transplant)
- Solid organ transplant recipients who had recent treatment with T cell- or B cell-depleting agents for acute rejection
- Patients with severe combined immunodeficiencies
- Patients with advanced or untreated HIV

Clinical Risk Factors

- [2] cancer, cardiovascular disease, chronic kidney disease, chronic lung disease, diabetes, immunocompromising conditions or receipt of immunosuppressive medications, obesity (i.e., body mass index ≥30), and pregnancy

Clinical Management of Adults Summary

Patient Disposition	Panel's Recommendations
Does Not Require Hospitalization or Supplemental Oxygen	For All Patients: • All patients should be offered symptomatic management (AIII). • The Panel recommends against the use of dexamethasone[a] or other systemic corticosteroids in the absence of another indication (AIIb). For Patients Who Are at High Risk of Progressing to Severe COVID-19[b] Preferred Therapies. Listed in order of preference: • Ritonavir-boosted nirmatrelvir (Paxlovid)[c,d] (AIIa) • Remdesivir[d,e] (BIIa) Alternative Therapies. For use ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate. Listed in alphabetical order • Bebtelovimab[f] (CIII) • Molnupiravir[d,g] (CIIa)

Discharged from Hospital Inpatient Setting in Stable Condition and Does Not Require Supplemental Oxygen	**The Panel recommends against continuing the use of remdesivir (AIIa), dexamethasone[a] (AIIa), or baricitinib (AIIa) after hospital discharge.**
Discharged from Hospital Inpatient Setting and Requires Supplemental Oxygen For those who are stable enough for discharge but still require oxygen[h]	There is insufficient evidence to recommend either for or against the continued use of remdesivir or dexamethasone.
Discharged from ED Despite New or Increasing Need for Supplemental Oxygen When hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured [i]	The Panel recommends using dexamethasone 6 mg PO once daily for the duration of supplemental oxygen (dexamethasone use should not exceed 10 days) with careful monitoring for AEs (BIII). Because remdesivir is recommended for patients with similar oxygen needs who are hospitalized,[j] clinicians may consider using it in this setting. As remdesivir requires IV infusions for up to 5 consecutive days, there may be logistical constraints to administering remdesivir in the outpatient setting.

Disease Severity	Recommendations for Antiviral or Immunomodulator Therapy		Recommendations for Anticoagulant Therapy
	Clinical Scenario	Recommendation	
Hospitalized for Reasons Other Than COVID-19	Patients with mild to moderate COVID-19 who are at high risk of progressing to severe COVID-19[a]	See Therapeutic Management of Nonhospitalized Adults With COVID-19.	For patients without an indication for therapeutic anticoagulation: • Prophylactic dose of heparin, unless contraindicated (AI); (BIII) for pregnant patients
Hospitalized but Does Not Require Oxygen Supplementation	All patients	The Panel recommends against the use of dexamethasone (AIIa) or other systemic corticosteroids (AIII) for the treatment of COVID-19.[b]	
	Patients who are at high risk of progressing to severe COVID-19[a]	Remdesivir[c] (BIII)	

Hospitalized and Requires Conventional Oxygen[d]	**Patients who require minimal conventional oxygen**	**Remdesivir[e] (BIIa)**	**For nonpregnant patients with D-dimer levels above the ULN who do not have an increased bleeding risk:** • **Therapeutic dose of heparin[g] (CIIa) For other patients:** • **Prophylactic dose of heparin, unless contraindicated (AI); (BIII) for pregnant patients**
	Most patients	Use dexamethasone plus remdesivir[e] (BIIa). If remdesivir cannot be obtained, use dexamethasone (BI).	
	Patients who are receiving dexamethasone and who have rapidly increasing oxygen needs and systemic inflammation	Add PO baricitinib[f] or IV tocilizumab[f] to 1 of the options above (BIIa).	

Hospitalized and Requires HFNC Oxygen or NIV	**Most patients**	**Promptly start 1 of the following, if not already initiated:** • **Dexamethasone plus PO baricitinib[f] (AI)** • **Dexamethasone plus IV tocilizumab[f] (BIIa)** **If baricitinib, tofacitinib, tocilizumab, or sarilumab cannot be obtained:** • **Dexamethasone[h] (AI)** **Add remdesivir to 1 of the options above in certain patients (CIIa).[i]**	**For patients without an indication for therapeutic anticoagulation:** • **Prophylactic dose of heparin, unless contraindicated (AI); (BIII) for pregnant patients** **For patients who are started on a therapeutic dose of heparin in a nonICU setting and then transferred to the ICU, the Panel recommends switching to a prophylactic dose of heparin, unless there is another indication for therapeutic anticoagulation (BIII).**
Hospitalized and Requires MV or ECMO	Most patients	Promptly start 1 of the following, if not already initiated: • Dexamethasone plus PO baricitinib[f] (BIIa) • Dexamethasone plus IV tocilizumab[f] (BIIa) If baricitinib, tofacitinib, tocilizumab, or sarilumab cannot be obtained: • Dexamethasone[h] (AI)	

Oxygenation and Ventilation

- ***Goal of Oxygenation*** The optimal oxygen saturation (SpO2) in adults with COVID-19 is uncertain. However, a target SpO2 of 92% to 96% seems logical considering that indirect evidence from experience in patients without COVID-19 suggests that an SpO2 <92% or >96% may be harmful. Regarding the potential harm of maintaining an SpO2 <92%, a trial randomly assigned ARDS patients without COVID-19 to either a conservative oxygen strategy (target SpO2 of 88% to 92%) or a liberal oxygen strategy (target SpO2 ≥96%). The trial was stopped early due to futility after enrolling 205 patients, but in the conservative oxygen group there was increased mortality at 90 days (between-group risk difference of 14%; 95% CI, 0.7% to 27%) and a trend toward increased mortality at 28-days (between-group risk difference of 8%; 95% CI, -5% to 21%).1 Regarding the potential harm of maintaining an SpO2 >96%, a meta-analysis of 25 randomized trials involving patients without COVID-19 found that a liberal oxygen strategy (median SpO2 of 96%) was associated with an increased risk of in-hospital mortality compared to a lower SpO2 comparator

Supplements

- **Vitamin C** • There is insufficient evidence for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of vitamin C for the treatment of COVID-19.
- **Vitamin D** • There is insufficient evidence for the Panel to recommend either for or against the use of vitamin D for the treatment of COVID-19.
- **Zinc** • There is insufficient evidence for the Panel to recommend either for or against the use of zinc for the treatment of COVID-19. • The Panel **recommends against** using zinc supplementation above the recommended dietary allowance for the prevention of COVID-19, except in a clinical trial **(BIII)**.

Prevention of SARS-CoV-2 Infection

- The COVID-19 Treatment Guidelines Panel (the Panel) recommends COVID-19 vaccination as soon as possible for everyone who is eligible according to the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices **(AI)**.
- The Panel recommends using **tixagevimab 300 mg plus cilgavimab 300 mg (Evusheld)** administered as 2 consecutive 3-mL intramuscular (IM) injections **(BIIb)** as SARS-CoV-2 pre-exposure prophylaxis (PrEP) for adults and adolescents (aged ≥12 years and weighing ≥40 kg) who do not have SARS-CoV-2 infection, who have not been recently exposed to an individual with SARS-CoV-2 infection, **AND** who:

- Are moderately to severely immunocompromised and may have an inadequate immune response to COVID-19 vaccination; *or*
- Are not able to be fully vaccinated with any available COVID-19 vaccines due to a history of severe adverse reactions to a COVID-19 vaccine or any of its components.
- The Panel recommends repeat dosing of **tixagevimab 300 mg plus cilgavimab 300 mg** administered as IM injections every 6 months **(BIIb)**.

- **Tixagevimab plus cilgavimab is not a substitute for COVID-19 vaccination and should not be used in unvaccinated individuals for whom COVID-19 vaccination is recommended.**
- The Panel recommends against the use of **bamlanivimab plus etesevimab** and **casirivimab plus imdevimab** for post-exposure prophylaxis (PEP), as the Omicron variant and its subvariants, which are not susceptible to these agents, are currently the dominant SARS-CoV-2 variants circulating in the United States **(AIII)**.

General Prevention Measures

- Transmission of SARS-CoV-2 is thought to occur primarily through exposure to respiratory droplets. Exposure can occur when someone inhales droplets or particles that contain the virus (with the greatest risk of transmission occurring within 6 feet of an infectious source) or touches their mucous membranes with hands that have been contaminated with the virus. Exhaled droplets or particles can also deposit the virus onto exposed mucous membranes

- Less commonly, airborne transmission of small droplets and particles of SARS-CoV-2 to people farther than 6 feet away can occur; in rare cases, people passing through a room that was previously occupied by an infectious person may become infected. SARS-CoV-2 infection via airborne transmission of small particles tends to occur after prolonged exposure (i.e., >15 minutes) to an infectious person who is in an enclosed space with poor ventilation

- The risk of SARS-CoV-2 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 reduce the spread of infectious droplets from individuals with SARS-CoV-2 infection to others. Frequent handwashing also effectively reduces the risk of infection

Recommendation for Ending Isolation

- **For people who are mildly ill with SARS-COV-2 infection and not moderately or severely immunocompromised;**
- Isolation can be discontinued at least 5 days after symptom onset (day 0 is the day symptoms appeared, and day 1 is the next full day thereafter) if fever has resolved for at least 24 hours (without taking fever-reducing medications) **and** other symptoms are improving
- Loss of taste and smell may persist for weeks or months after recovery and need not delay the end of isolation.

- A high-quality mask should be worn around others at home and in public through day 10. A test-based strategy may be used to remove a mask sooner.
- If symptoms recur or worsen, the isolation period should restart at day 0.
- People who cannot wear a mask, including children < 2 years of age and people of any age with certain disabilities, should isolate for 10 days
- In certain high-risk congregate settings that have high risk of secondary transmission, CDC recommends a 10-day isolation period for residents.

For people who test positive, are asymptomatic (never develop symptoms) and not moderately or severel immunocompromised

- Isolation can be discontinued at least 5 days **after the first positive viral test** (day 0 is the date the specimen was collected for the positive test, and day 1 is the next full day thereafter)
- A high-quality mask should be worn around others at home and in public through day 10. A test-based strategy may be used to remove a mask sooner.
- If a person develops symptoms within 10 days of testing positive, their 5-day isolation period should start over (day 0 changes to the first day of symptoms).

- People who cannot wear a mask, including children < 2 years of age and people of any age with certain disabilities, should isolate for 10 days
- In certain high-risk congregate settings that have high risk of secondary transmission, CDC recommends a 10-day isolation period for residents.

For people who are moderately ill and not moderately or severely immunocompromised:

- Isolation and precautions can be discontinued 10 days after symptom onset (day 0 is the day symptoms appeared, and day 1 is the next full day thereafter)

For people who are severely ill and not moderately or severely immunocompromised

- Isolation should continue for at least 10 days after symptom onset (day 0 is the day symptoms appeared, and day 1 is the next full day thereafter)
- Some people with severe illness (e.g., requiring hospitalization, intensive care, or ventilation support) may remain infectious beyond 10 days. This may warrant extending the duration of isolation and precautions for up to 20 days after symptom onset (with day 0 being the day symptoms appeared) **and** after resolution of fever for at least 24 hours (without the taking fever-reducing medications) **and** improvement of other symptoms.

- Serial testing prior to ending isolation can be considered in consultation with infectious disease experts

For people who are moderately or severely immunocompromised (regardless of COVID-19 symptoms or severity)

- Moderately or severely immunocompromised patients may remain infectious beyond 20 days. For these people, CDC recommends an isolation period of at least 20 days, and ending isolation in conjunction with serial testing and consultation with an infectious disease specialist to determine the appropriate duration of isolation and precautions.

The criteria for serial testing to end isolation are:

- Results are negative from at least two consecutive respiratory specimens collected ≥ 24 hours apart (total of two negative specimens) tested using an antigen test or nucleic acid amplification test
- Also, if a moderately or severely immunocompromised patient with COVID-19 was symptomatic, there should be resolution of fever for at least 24 hours (without the taking fever-reducing medication) and improvement of other symptoms. Loss of taste and smell may persist for weeks or months after recovery and need not delay the end of isolation
- Re-testing for SARS-CoV-2 infection is suggested if symptoms worsen or return after ending isolation and precautions

thanks your Attention