

Managing outpatients with COVID-19

- All symptomatic patients should be tested for COVID-19 by SARS-CoV-2 RT-PCR or antigen assay and isolated until test results are available.
 - Patients with symptoms highly suspicious for COVID-19, no alternative explanation for symptoms and a negative antigen assay, should have a PCR assay.
- All patients who are SARS-CoV-2 (+) should be isolated following testing:
 - **Asymptomatic (+):** 10 days following their (+) result
 - **Symptomatic, not immunocompromised* (+):** 10 days following the onset of symptoms and ≥ 24 hours without fever (≥ 100.4 F), without antipyretics
 - **Symptomatic, immunocompromised* (+):** 20 days following the onset of symptoms, improving symptoms, and ≥ 24 hours without fever (≥ 100.4 F) without antipyretics
 - **Symptomatic, following critical care hospitalization (+):** 20 days following the onset of symptoms, improving symptoms, and ≥ 24 hours without fever (≥ 100.4 F) without antipyretics

Evaluating symptomatic patients with COVID-19

- The **incubation period** of COVID-19 following exposure to SARS-CoV-2 is 2-14 days.
- **Onset of symptoms:** 99% of symptomatic patients become ill by day 10.
- **Infectious period:** 2 days before symptom onset until 10 days after; viral load in the nasopharynx peaks about day 5.
- **Viral shedding:** 95% of infected people stop shedding virus by day 10 and are no longer infectious, but shedding may be prolonged in patients who are critically ill or severely immunocompromised*.
- **Virus transmission:** most efficient within households; $\geq 20\%$ of infections are spread by asymptomatic people.
- **Severity of illness:** $\sim 85\%$ of patients have mild-moderate symptoms; $\sim 10\%$ have severe symptoms; $\sim 5\%$ require critical care.
 - **Mild-moderate infection** lasts about 14 days, but symptoms may linger for months, even in young healthy patients.
 - **Severe infection** usually becomes apparent by 7-13 days after onset of symptoms and is associated with “cytokine storm”. Median time from onset to admission to a critical care unit is 12 days.
- **Presentation** is variable, most common is a flu-like illness and patients usually have multiple symptoms (Table 1). Common laboratory abnormalities are listed in Table 2.
- Secondary bacterial infections in outpatients are extremely unusual; $< 3\%$ of patients have secondary bacterial pneumonia at hospital admission.

*Immunocompromised: primary immunodeficiency (i.e., common variable immune deficiency [CVID], HIV with CD4 < 200 , solid organ or hematopoietic cell transplant, recent chemotherapy, current immunosuppressant therapy (> 20 mg prednisone for > 14 days), treatment for autoimmune disease, etc.

Table 1. Symptoms reported by patients with COVID-19

<i>Symptoms</i>	<i>Percent reporting</i>
Fever	44-94%
Cough	68-83%
Taste/smell alterations	70%
Upper respiratory symptoms	5-61%
Dyspnea	11-40%
Myalgias	11-15%
Headache	8-14%
“Brain fog”	9%
GI symptoms	3-17%
Asymptomatic	≥20%

Table 2. Common laboratory abnormalities in COVID-19

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- Lymphopenia
 - Anemia
 - Elevated ALT/AST/GGT/LDH
 - Elevated D-dimer
 - Elevated CK
 - Elevated CRP, ESR, ferritin
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Initial evaluation of symptomatic patients with COVID-19

COVID-19 can rapidly progress to severe illness, especially among patients at high risk for complications; respiratory complications are most likely to occur from day 7-13.

When first evaluating patients, it is important to determine where they are in the course of their COVID-19 infection:

- Acute COVID-19: (days 1-7) symptoms are due to high viral load
- Post-acute COVID-19: (>8 days) is predominated by inflammatory response

Initial evaluation of symptomatic patients with COVID-19 (continued)

Appropriate management of patients includes the assessment of the following:

1. Patient’s age and presence of any conditions or co-morbidities that are high-risk (Table 3) for complicated COVID-19
2. Date of symptom onset
3. Date and place of SARs-CoV2 test, if available
4. Workplace or household to determine if contacts should be quarantined (this is especially important for health care providers or residents of congregate living facilities)
5. Home and social factors: is there anyone available to care for the patient?
6. Level of dyspnea (any patient with dyspnea should be advised to obtain a pulse oximeter)
 - a. **Mild:** does not interfere with activities of daily living (ADLs)
 - b. **Moderate:** shortness of breath when climbing a single flight of stairs, performing light housekeeping, etc.
 - c. **Severe:** can’t speak in complete sentences or perform any ADLs
7. Change in mental status: is the patient confused, somnolent, falling?
8. Signs of dehydration: dizziness, inability to maintain hydration, concentrated urine
9. Is the patient febrile? Does the patient have a thermometer?
10. If a telemedicine visit is possible:
 - a. If they are capable, ask the patient to march in place for one minute, then check pulse oximeter, and/or assess for tachypnea, cyanosis, use of accessory muscles for breathing
11. Schedule a telemedicine visit follow-up as indicated at the following intervals (see Table 4):
 - a. **Asymptomatic – advise to call if symptoms develop**
 - b. **Low severity – day 5 of symptoms**
 - c. **Moderate severity – days 4, 7 and 10 of symptoms**
 - d. **Post hospital discharge – day 2, then as needed**

Table 3. Conditions that increase risk for complications in COVID-19

High risk conditions/co-morbidities	Possible high-risk conditions/co-morbidities
Age ≥65 years	Moderate-severe asthma
Type II diabetes mellitus	Cystic fibrosis
Obesity (BMI ≥30 kg/m ²)	Pulmonary fibrosis
Chronic lung/renal disease	Chronic liver disease
Coronary artery disease, heart failure	Thalassemia
Malignancy	Hypertension
Pregnancy	Dementia, cerebrovascular disease
Sickle cell disease	Immunosuppression dues to hematopoietic cell transplant, chronic steroids or other immunosuppressants
Tobacco use	
Down Syndrome	

Table 4. Severity level for symptomatic outpatients with COVID-19

<i>Symptoms</i>	<i>Action</i>
<p>Low</p> <ul style="list-style-type: none"> Resting SpO₂ >94%, no tachypnea (RR <22 BPM) and mild symptoms in a low-risk* patient 	<ul style="list-style-type: none"> Order COVID-19 testing Phone or telemedicine visit for evaluation
<p>Moderate</p> <ul style="list-style-type: none"> Resting SpO₂ 90-94%, tachypnea or dyspnea limiting ADLs High-risk* patient with SpO₂ 90-97% or any dyspnea, tachypnea, chest pain 	<ul style="list-style-type: none"> Order COVID-19 testing Telemedicine visit for evaluation Consider in-person evaluation @ UAB COVID-19 Respiratory Clinic if symptomatic patient’s onset was within previous 21 days Consider referral to UAB Post-COVID clinic if symptomatic patient’s onset was ≥22 days ago
<p>Severe</p> <ul style="list-style-type: none"> Resting SpO₂ <90%, or severe dyspnea, chest pain High-risk patient* with SpO₂ <95%, severe dyspnea, tachypnea, chest pain, orthostasis or altered mental status 	<ul style="list-style-type: none"> Direct admit to UAB or send for evaluation to UAB Emergency Dept., local ED or urgent care center

General recommendations for treatment of symptomatic outpatients

- Current treatment of most outpatients with acute COVID-19 is supportive and can be managed by a primary care provider via phone or telemedicine visit.
- Most patients who are low severity (Table 4) do not require chest X-rays or laboratory testing.
- Patients ≥65 years of age or those with certain high-risk co-morbidities may be eligible to receive monoclonal antibody therapy within the first 10 days of illness.
- See section below on ***Monoclonal Antibody infusion therapy*** for eligibility and details.

There are currently no data from randomized, controlled clinical trials to support the use of the following agents for COVID-19:

- ***Corticosteroids - oral, intramuscular or IV corticosteroids given within the first 7 days of COVID-19 to patients not requiring supplemental oxygen may increase viral load and disease severity***
- Azithromycin or other antibacterial agents
 - Side effects include nausea, diarrhea, increased drug resistance
- Ivermectin or other antiparasitic agents
- Hydroxychloroquine, chloroquine, colchicine
- Zinc
- Famotidine
- Ritonavir/lopinavir
- Fluvoxamine

General recommendations for treatment of symptomatic outpatients (continued)

- Encourage hydration, especially in patients with insensible fluid loss (fever, diarrhea)
- Cough suppression when cough interferes with ADLs or sleep
- Fever suppression
- Pain management
- Treatment of gastrointestinal symptoms
- Treatment of dyspnea
- Advise rest as needed with frequent re-positioning and ambulation
- Advise patients about the warning signs that indicate clinical deterioration and should prompt emergency care (Table 5.)
- Set reasonable expectations about recovery time and advise patients about the variable and sometimes prolonged course of COVID-19; in general:
 - Low severity – recovery in 10-14 days
 - Moderate severity – recovery in 3-6 weeks
 - Critical illness or with co-morbidities – recovery may be prolonged

1. Hydration

- a. Water
- b. Gatorade, Gatorade Zero, Propel, etc.
- c. More expensive: over-the-counter formulations or oral packets: (*Ceralyte, Cerasport, Emergen-C Electro Mix, Naturalyte, Normalyte, Pedialyte*, etc.)
- d. Avoid caffeine-containing beverages

2. Cough Suppression

- a. Cough drops, over-the-counter cough suppressant formulations
 - i. Productive cough use formulations with expectorants, i.e., guaifenesin
 - ii. Dry cough: use formulations with suppressants, i.e., dextromethorphan
- b. Cough not responsive to above, consider:
 - i. Benzonatate, formulations with dextromethorphan + codeine or promethazine + dextromethorphan.

3. Fever suppression and pain management

- a. Acetaminophen – avoid in patients with liver disease or otherwise contraindicated
 - i. 325 mg tablets/capsules: 2 tabs/caps every 4-6 hours, not to exceed 10 tabs/caps per day
 - ii. 500 mg tablets: 2 tabs every 6 hours, not to exceed 6 tabs/day
 - iii. 650 mg tablets: 2 tabs every 8 hours, not to exceed 6 tabs/day
- b. Non-steroidal anti-inflammatory drugs (NSAIDs) – avoid when contraindicated
 - i. Ibuprofen 200 mg tablets/capsules: 2-3 tabs/caps every 6-8 hours, not to exceed 12 tabs/day
- c. Fever unresponsive to a single agent
 - i. Acetaminophen alternating with NSAIDs, for example:
 1. Acetaminophen – 325-650 mg, 2 tabs/caps at 8:00 AM, 4:00 PM, 12:00 AM
 2. Ibuprofen 200 mg tablets/capsules – 2-3 tabs at 12:00 PM, 8:00 PM

General recommendations for treatment of symptomatic outpatients (continued)

4. Treatment of gastrointestinal symptoms

- a. Nausea
 - i. Ondansetron
 - ii. Promethazine
 - iii. Meclizine
- b. Diarrhea
 - i. Over-the-counter
 - 1. bismuth formulations (e.g., *Pepto-Bismol*)
 - 2. loperamide (*Imodium*)

5. Treatment of dyspnea

- a. All patients with dyspnea should be encouraged to get a pulse oximeter and instructed how to use it.
- b. Dyspnea, chest tightness:
 - i. Consider inhalational albuterol, ipratropium, corticosteroids; avoid nebulizers if possible due to risk of aerosolization
- c. Patients can try sleeping while laying on their stomach or side

6. Warning signs (Table 5)

- a. A small proportion (15%) of patients will have severe or critical illness
- b. Progression to severe disease usually occurs 7-13 days following onset of illness.

Table 5. Warning signs that should prompt patients to seek emergency care

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- Severe or increasing shortness of breath
 - Gasping for air
 - Coughing up blood
 - Pain/pressure in chest that is severe or could be cardiac in nature
 - Confusion, severe drowsiness or repeated falls
 - Inability to eat, drink or walk
 - Sustained (>1 hour) resting pulse oximeter reading of <90%
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COVID-19 vaccine

- Eligible patients who have had COVID-19 should receive a COVID-19 vaccine 90 days following onset of their illness.
- Patients who develop COVID-19 following their first dose of vaccine should receive the second dose 90 days following the onset of COVID-19.

Monoclonal antibody infusion therapy

- Intravenous monoclonal antibody infusion therapies have been authorized for use in high-risk outpatients with low-moderate severity COVID-19 in the first 10 days of illness.
- **Monoclonal antibody infusion must be given within the first 10 days of illness, prior to hospitalization.**
- There are currently 2 drugs available at UAB under an Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration (FDA) for patients ≥ 12 years of age:
 - **Bamlanivimab** (Lilly Pharmaceuticals)
 - **Casirivimab plus Imdevimab** (Regeneron Pharmaceuticals)
- These treatments have been shown to:
 - Decrease the presence of circulating SARS-CoV-2 virus
 - Decrease symptoms of COVID-19
 - Reduce the risk of hospitalization by $>70\%$ for high-risk patients
- Pregnancy is not an absolute contraindication for monoclonal antibody therapy
- Co-morbidities or conditions that increase the risk for severe COVID-19 and are required for eligibility:
 - Morbid obesity (Body Mass Index [BMI] > 35 kg/m²)
 - Type II diabetes mellitus
 - Chronic renal disease
 - Immunosuppression (from a condition or medication)
 - Age ≥ 65 years
 - Age ≥ 55 years with any of the following co-morbidities:
 - Significant cardiovascular disease or heart failure
 - Hypertension
 - Chronic lung disease
- Treatment is given at the UAB West Pavilion Infusion Center and takes between 2½ - 3 hours to complete.
 - Treatment protocols are overseen by Edgar Turner Overton, MD and Sonya Heath, MD, UAB Division of Infectious Diseases.
 - A one hour intravenous infusion is followed by a one hour observation period.
 - As part of the evaluation, the following laboratory work is usually performed:
 - Complete blood count with differential,
 - Complete metabolic panel (CMP),
 - C-reactive protein (CRP),
 - D-dimer
 - Additional laboratory work can be requested for the visit.
 - The patient's UAB provider may order additional lab work in IMPACT and message Drs. Heath and Overton in IMPACT regarding the request for additional testing.
 - Post-infusion follow-up phone call is provided by members of the Infusion Team, but primary care providers are expected to follow-up with their patients after therapy as well.

How to refer a patient for monoclonal antibody infusion therapy

- Eligible patients must have:
 - Proof of a positive COVID-19 antigen or PCR assay test
 - Onset of symptoms within the previous 10 days
 - If you are a UAB provider and have an eligible patient, or would like to have a patient evaluated for eligibility:
 - Send an IMPACT message in the patient's electronic medical record to:
 - Edgar Turner Overton, MD and Sonya Heath, MD, Division of Infectious Diseases
 - Include the following information:
 - Best phone number to reach the patient
 - Date of onset of COVID-19 symptoms
 - Date of positive test confirming COVID-19
 - Eligible conditions or co-morbidities
 - **Non UAB patient or provider:**
 - Please submit the patient's name and contact information as a referral to the UAB COVID-19 Respiratory Clinic through the following website:
<https://www.uabmedicine.org/web/medicalprofessionals/covid-respiratory-referral-form>

Useful Websites

Brigham and Women's Hospital COVID-19 Guidelines <https://bwh.covidprotocols.org>

National Institutes of Health COVID Treatment Guidelines

<https://www.covid19treatmentguidelines.nih.gov>

Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19

<https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>

Clinical Care Guidance for Healthcare Professionals about Patients with Coronavirus (COVID-19)

<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care.html>