

Management of suspected/confirmed COVID-19 (adults)



SARS-CoV-2 causes a self-limited influenza-like illness in the majority of cases, but can progress to severe illness with ARDS and multiorgan failure in 2-3% of infected patients. Severe illness usually begins about 1 week after onset of illness and may be characterized by a severe hyperimmune response or cytokine storm (COVID-CS). Older age and certain underlying comorbidities are risk factors for severe disease.

Excellent supportive care remains the cornerstone of management. Eligible patients will be offered enrollment in **clinical treatment trials** (standard of care + trial medications) to ensure access to best treatment options. Prescription of investigational or off-label products (antivirals, convalescent plasma, host-directed immunotherapy) *outside* of clinical trials is **discouraged** but may be considered on a case-by-case basis, with ID approval. Since the vast majority of patients with COVID-19 do not have bacterial superinfection at presentation, empiric therapy with antibiotics is **discouraged**. This document will be regularly updated based on new knowledge and information.

DEFINITIONS:

Suspected COVID-19 case: fever and/or new onset/exacerbation of respiratory symptoms and/or new onset diarrhea

Confirmed COVID-19 case: as above + lab detection of SARS-CoV-2 in respiratory sample

Recommended Admission Criteria (use clinical judgment)

- Respiratory criteria:
 - Dyspnea at rest or during minimal activity (sitting, talking, coughing, swallowing), *OR*
 - Respiratory rate > 22/min, *OR*
 - PaO₂ < 65 mm Hg or O₂Sat < 90%, *OR*
 - Infiltrate on CXR (worsening CXR if baseline abnormal)
- Non-respiratory criteria:
 - Systolic BP < 100 or signs of sepsis/septic shock, *OR*
 - Altered mental status *OR*
 - Concern for high risk of complications/severe disease if managed as outpatient - based on comorbidities* and living situation

*Conditions associated with increased risk of severe COVID-19:

- Immunocompromised state (solid or hematopoietic transplant recipient with engraftment < 30 days; HIV with CD4 < 200; recipient of immunosuppressive therapy including high dose steroids)
- Active malignancy (undergoing chemo/radio/immunotherapy)
- Serious cardiovascular disease
- Severe lung disease (severe asthma, COPD, CF, pulmonary fibrosis)
- Chronic kidney disease
- Sickle cell disease
- Diabetes
- Pregnancy
- Obesity (BMI > 30)

PHARMACOLOGIC MANAGEMENT

<p>No criteria for admission</p>	<ul style="list-style-type: none"> • Instructions for self-quarantine (as per Public Health guidelines) • Acetaminophen 650 mg po q4-6h PRN, <i>avoid if <u>severe</u> hepatic impairment</i> <p><i>Offer enrolment in outpatient clinical trial and contribution to COVID biobank (patient to contact ext.32033 or COVID.Research@muhc.mcgill.ca)</i></p>
<p>At least one admission criterion</p>	<p style="text-align: center;"><i>Follow Admission guide for COVID-19 (and IPC guidelines for isolation)</i> <i>Call coordinator for COVID-19 treatment trials at ext.32033</i></p> <p>MILD disease (O₂ Sat > 92%, no supplemental O₂)</p> <ul style="list-style-type: none"> • Acetaminophen 650 mg po q4-6h PRN (<i>avoid if <u>severe</u> hepatic impairment</i>) AND • Dalteparin¹ 200 U/kg S/C die if expected hospitalization > 3 days (until clinical improvement, or x 14 days whichever comes first) (<i>avoid</i> if eGFR < 30 mL/min or if contra-indications*) AND • Offer enrolment in clinical trial • <u>NO empiric antibiotics³</u>
<p>MODERATE disease (Need supplemental O₂ to maintain O₂ Sat > 92%)</p>	<ul style="list-style-type: none"> • Acetaminophen 650 mg po q4-6h PRN (<i>avoid if <u>severe</u> hepatic impairment</i>) AND • Dalteparin¹ 200 U/kg S/C die until clinical improvement, or x 14 days (whichever comes first) (<i>avoid</i> if eGFR < 30 mL/min or if contra-indications*) AND • Dexamethasone² 6 mg po daily x 10 days (IV only if cannot tolerate po) AND • Offer enrolment in clinical trial • <u>NO empiric antibiotics³</u> <p><i>Consider Remdesivir⁴ ONLY if <u>early stage</u> of disease (< 10 days from onset of symptoms): 200 mg IV x 1 then 100 mg IV (infuse over 30-120 min) q24h x 4 d. Need ID approval.</i></p>
<p>SEVERE disease (High-flow nasal cannula, invasive or non-invasive mechanical ventilation to maintain O₂ Sat > 92%)</p>	<p style="text-align: center;">**CONSULT ID**</p> <ul style="list-style-type: none"> • Acetaminophen 650 mg po q4-6h PRN (<i>avoid if <u>severe</u> hepatic impairment</i>) AND • Dalteparin¹ 5000 units S/C daily • Dexamethasone² 6 mg po/IV daily x 10 days AND • Offer enrolment in clinical trial AND • Empiric antibiotics³ (reassess after 48 hours, maximum duration 7 days) <ul style="list-style-type: none"> - Ceftriaxone⁵ 2 g IV q24h If < 5 days since admission - Piperacillin-tazobactam^{5,6} 4.5 g IV q6h if > 5 days since admission or severe immunocompromise • Tocilizumab⁷ 8mg/kg (max 800mg) IF patient < 24h since meeting severity criteria OR criteria for COVID-19 cytokine storm⁸ [may be repeated after 12-24h; <u>max 2 doses</u>]

ADDITIONAL CONSIDERATIONS

¹ Dalteparin:

- **For Mild and Moderate disease: Therapeutic anticoagulation (TAC) superior to prophylactic anticoagulation** (net benefit in terms of organ-support free days, irrespective of D-dimer levels) in patients admitted for > 3 days. **If disease is mild, we recommend to start TAC only if predicted to remain in hospital for > 3 days.** TAC is to be continued **until significant clinical improvement (e.g. no need for supp. O₂) or x 14 days** (whichever comes first).

- **Severe disease: TAC potentially more harmful than prophylactic anticoagulation.** If patient was on TAC when became critically ill, consider continuing same dosage.
- **If eGFR < 30 mL/min, replace LMWH with unfractionated heparin (UFH):** bolus 80 U/kg then 18 U/kg/h - follow MUHC PPO for monitoring and dose adjustment

*** Contra-indications to TAC:**

- GI bleed in last 3 months; recent major surgery (< 14 days); bleeding disorder (e.g. hemophilia)
- Thrombolysis within previous 7 days
- Brain tumor, brain metastases (unless recent imaging shows no bleed); cerebral aneurysm or intracerebral arteriovenous malformation; history of intracranial bleeding; presence of an epidural or spinal catheter
- Other physician-perceived contra-indication to anticoagulation

² Dexamethasone:

- **Monitor glycemia (CBGM) and adjust glycemic control.** If non-diabetic, CBGM for 48-72 hours; consider initiating insulin sliding scale if glucose > 10-12
- **For patients with severe immunocompromise:** use of dexamethasone on a case-by-case basis
- **For patients on steroids for another indication:** if high dose, continue same steroid formulation; if low dose, switch to dexamethasone 6 mg po/IV die; can replace with Hydrocortisone 50 mg IV q8h

³ Empiric antibiotics:

- **Mild-moderate disease: vast majority of patients do not have and do not develop bacterial co-infection** - empiric antibiotics are not recommended.
- **Severe disease: secondary bacterial infections occur in about 15%.** Collect blood and sputum samples before starting antibiotics and reassess choice of antibiotics within 48 h.

⁴ Remdesivir:

- Only **modest benefit** with reduction in time to recovery; no effect on mortality; **benefits expected only in early stages when virus actively replicating** (low likelihood of significant viral replication after 10d of symptoms). **Potential adverse events: liver and renal** (monitor LFTs and creat daily)

⁵ Hypersensitivity reactions:

- If type I hypersensitivity to penicillin, replace piperacillin-tazobactam with meropenem 1 g IV q8h;

⁶ Renal dose adjustment for piperacillin-tazobactam:

- CrCl 20-40 mL/min: 4.5 g IV q8h; CrCl <20 mL/min: 2.25 g IV q6 h; HD: 2.25 g IV q8h

⁷ Tocilizumab (anti-IL6 receptor antibody):

- **Risk of serious bacterial infection – avoid if known bacterial superinfection/sepsis**
- Risk of allergic reaction, liver failure - monitor creat and LFTs; caution if LFTs > 1.5x ULN at baseline

⁸ Proposed criteria to identify COVID-19 cytokine storm (COVID-CS):

SARS-CoV2+ AND ground glass opacities on CXR/CT + Ferritin > 250 ng/mL + CRP > 46 mg/L + at least one from each cluster	
Cluster 1	
Albumin	< 28 g/L
% lymphocytes	< 10.2% of total WBC
Absolute neutrophils	> 11.4/mm ³
Cluster 2	
ALT	> 60 IU/L
AST	> 87 IU/L
D-dimers	> 4,930 ng/mL
LDH	> 416 IU/L
Troponin I high sensitivity	> 1090 ng/L
Cluster 3	
Anion gap	< 6.8 mmol/L
Chloride	> 106 mmol/L
Potassium	> 4.9 mmol/L
Ratio Urea:Creatinine (urea in mmol/L x 1000 divided by creatinine in umol/L)	> 100:1 (pre-renal AKI)

These criteria have a sensitivity of 0.85 and specificity of 0.80 in identifying COVID-CS compared with clinical consensus; correlate with > risk of mortality and longer length of stay if criteria met in 1st week of hospitalization (ref: <https://ard.bmj.com/content/80/1/88>)

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