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*
  - PaO_2 < 65 mm Hg or O_2Sat < 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:

- Imunocompromised 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)

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PHARMACOLOGIC MANAGEMENT

No criteria for admission

- **Instructions for self-quarantine** (as per Public Health guidelines)
- **Acetaminophen** 650 mg po q4-6h PRN, *avoid if severe hepatic impairment*

Offer enrolment in outpatient clinical trial and contribution to COVID biobank (patient to contact ext.32033 or COVID.Research@muhc.mcgill.ca)

At least one admission criterion

Follow Admission guide for COVID-19 (and IPC guidelines for isolation)

Call coordinator for COVID-19 treatment trials at ext.32033

MILD disease
(O_2 Sat > 92%, no supplemental O_2)

- **Acetaminophen** 650 mg po q4-6h PRN (*avoid if severe hepatic impairment*) AND
- **Dalteparin**[1] 200 U/kg S/C die if expected hospitalization > 3 days (until clinical improvement, *or* x 14 days whichever comes first) (*avoid* if eGFR < 30 mL/min or if contra-indications*) AND
- Offer enrolment in clinical trial
- **NO empiric antibiotics**[3]

MODERATE disease
(Need supplemental O_2 to maintain O_2 Sat > 92%)

- **Acetaminophen** 650 mg po q4-6h PRN (*avoid if severe hepatic impairment*) AND
- **Dalteparin**[1] 200 U/kg S/C die until clinical improvement, *or* x 14 days (whichever comes first) (*avoid* if eGFR < 30 mL/min or if contra-indications*) AND
- **Dexamethasone**[2] 6 mg po daily x 10 days (IV only if cannot tolerate po) AND
- Offer enrolment in clinical trial
- **NO empiric antibiotics**[3]

Consider **Remdesivir**[4] ONLY if **early** stage 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.**

SEVERE disease
(High-flow nasal cannula, invasive or non-invasive mechanical ventilation to maintain O_2 Sat > 92%)

****CONSULT ID****

- **Acetaminophen** 650 mg po q4-6h PRN (*avoid if severe hepatic impairment*) AND
- **Dalteparin**[1] 5000 units S/C daily
- **Dexamethasone**[2] 6 mg po/IV daily x 10 days AND
- Offer enrolment in clinical trial AND
- **Empiric antibiotics**[3] **(reassess after 48 hours, maximum duration 7 days)**
  - **Ceftriaxone**[5] 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
- **Tocilizumab**[7] 8mg/kg (max 800mg) **IF patient < 24h** since meeting severity criteria ***OR*** criteria for **COVID-19 cytokine storm**[8] [may be repeated after 12-24h; max 2 doses]

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. O_2) 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 adjustement

*** 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 bleeing; 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 sensitifvity 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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