CLINICAL PATHWAY:
Inpatient Therapies for COVID-19

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Inclusion Criteria:
Positive for COVID-19 infection **AND** requiring hospitalization **due to COVID-19 infection**

Initial Management:

Labs:
- CBC with differential, CMP
- Additional labs at the discretion of the provider depending on severity of illness: PT/PTT, fibrinogen, D-dimer, CRP, ESR, procalcitonin, LDH, ferritin, triglycerides
- *If suspected cardiac involvement*: add troponin, NT-proBNP, CKMB
- *If ferritin >500 mcg/ml*: obtain cytokine panel[1] (IL-6, IL-1, NK cell activity)

Studies:
- EKG (if clinically indicated)
- Chest X-ray (if clinically indicated)

Consults:
- Infectious Diseases (required)
- Rheumatology if suspected clinical/laboratory evidence of cytokine storm syndrome[2] and need for escalation of treatment

General Treatment Considerations:
(See NIH Guideline for Treatment of COVID-19 in Hospitalized Children for more information)
- See Appendix A for Comorbidities Associated with Severe COVID-19 in Children
- Consider placing patient in prone position
- Management is primarily supportive in nature with a focus on treatment of pneumonia, respiratory failure, ARDS, sepsis and septic shock (see Septic Shock Pathway).
- Please utilize VTE Prophylaxis Clinical Pathway to determine interventions to prevent or treat for thrombosis
- If concern for Multi-system Inflammatory Syndrome in Children (MIS-C)[3], see MIS-C Clinical Pathway
- Consider other signs of systemic severe illness, in consultation with ID

Medication Options:

Remdesivir:
- FDA approved for patients ≥28 days old and weighing ≥3 kg who are:
  - hospitalized **due to** COVID-19, **or**
  - hospitalized due to other reasons but have mild-moderate COVID-19 and are at high risk for progression to severe COVID-19 (see Appendix A)
- Obtain baseline CBC w diff, CMP if not already done
  - Additional labs at discretion of provider depending on severity of disease
- Dosing:
  - ≥28 days old **and** weighing 3 kg to <40 kg:
    - 5 mg/kg IV load on day 1, followed by maintenance 2.5 mg/kg from day 2 and on
  - ≥40 kg:
    - 200 mg IV load on day 1, followed by maintenance 100 mg daily from day 2 and on
- Duration:
  - Hospitalized **due to COVID-19**: 5 days (extend up to 10 days if on mechanical ventilation/ECMO or there is no clinical improvement after 5 days of therapy)
  - Hospitalized **due to other reasons** with mild-moderate COVID-19: 3 days total
- Considerations:
  - If patient is on chloroquine phosphate or hydroxychloroquine sulfate at baseline (i.e., lupus), co-administration with remdesivir is not recommended

Dexamethasone:
- Consider using in combination with remdesivir for patients with increasing oxygen needs
- Dosing:
  - 0.15 mg/kg IV or PO once daily (max 6 mg/dose)
- Duration:
  - Up to 10 days (or until discharge, whichever is shorter)

Baricitinib:
- Consider for patients requiring HFNC, BIPAP, mechanical ventilation or ECMO **and** do not have rapid (e.g., within 24 hours) improvement in oxygenation after initiation of dexamethasone; to be used in consultation with ID
- Dosing:
  - 2 yrs old – <9 yrs of age: 2 mg once daily
  - ≥9 yrs old: 4 mg once daily
  - Dosing adjustments are recommended for laboratory abnormalities, including renal impairment
- Duration:
  - For 14 days (or until discharge, whichever is shorter)

Laboratory Monitoring:
The lab schedule is recommended based on algorithms used at other medical centers. The labs obtained and frequency of labs will be dependent on the patient's clinical status and judgment of the healthcare team.

- CBC with differential, chem 10, PT/PTT, fibrinogen, D-dimer, CRP, procalcitonin, ferritin
- *For patients who are on remdesivir:* LFTs, if baseline LFTs are abnormal
- *In patients with suspected clinical or lab evidence of cytokine storm syndrome[2]:* add LFTs, LDH, triglycerides

Discharge Considerations:
- Follow up with ID (and Rheumatology, if involved)
- Refer to COVID-19 Cardiology Return to Play Algorithm

Important References:
Refer to CT Children's COVID-19 Intranet site, under "Care for COVID-19 Patient" for more resources.

[1]**Cytokine studies**
- IL-1 and IL-6: 1 ml in red top
  - IL-1 levels are done at Quest labs on Wed with ~7 day turnaround time
  - IL-6 levels are done at Quest labs on Tues with ~5-12 day turnaround time
- NK cell killer activity is done at Quest Labs from Tues-Fri with a 4-8 day turnaround time. A 5 ml (preferred 10 ml) sample in a green sodium heparin tube must be sent to the lab between 2-3 PM Mon-Thurs for direct shipping to Quest

[2]**For patients with evidence of CYTOKINE STORM SYNDROME**
(*e.g., high fever, worsening coagulopathy, ARDS, elevated ferritin*):
- Consult Rheumatology for escalation of treatment
- Begin treatment with one of the following:
  - **Tocilizumab:** <30kg: 12mg/kg IV x 1 dose; ≥30 kg: 8mg/kg (max 800mg/dose) IV x 1 dose; A 2nd dose can be given separated by at least 12 hours based on clinical response (caution should be used in cases of leukopenia or transaminitis) **or**
  - **Anakinra**: 2 mg/kg/dose (max 100 mg/dose) IV q6hr
  - If these treatments are unavailable, may consider emapalumab
  - Steroids should be added if not already receiving, following consultation with the ID and Rheumatology services

[3]If there is a clinical suspicion for **Multi-System Inflammatory Syndrome in Children (MIS-C),** please follow the MIS-C Clinical Pathway.

Clinical *suspicion* would include:
Fever ≥100.4°F/≥38°C for ≥3 days (or fever ≥100.4°F/≥38°C for ≥24 hours with signs of shock/critical illness), positive COVID-19 testing or exposure in the prior 60 days (or detection of antibody during current illness), *no alternative plausible diagnosis*, AND any **two** of the following systems:
- Signs of shock
- GI: abdominal pain, diarrhea, or vomiting
- CV: chest pain, arrhythmia, or hypotension
- Mucocutaneous: rash, oral mucosal inflammation, conjunctivitis/ conjunctival injection, or extremity swelling

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This pathway is subject to change, based on evolving recommendations from the CDC and CT DPH.

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Definite Risk Factors

- Cardiovascular disease
- Neurologic disease
- Seizure disorders
- Prematurity
- Diabetes (type 1 and 2)
- Obesity
- Chronic lung disease
- Immunocompromise

Probable Risk Factors

- Neurodisability*
- Trisomy 21*
- Chronic GI and liver disease*
- Chronic kidney disease *
- Moderate immunosuppression
- Sickle cell disease

Unlikely Risk Factors

- Asthma
- Sex (male)

*Downgraded because of small sample sizes or non-significant effects after adjusting for comorbidities.

Reference: Willis AI, Oliveira CR, Abzug MJ, et al. Guidance for prevention and management of COVID-19 in children and adolescents: A consensus statement from the Pediatric Infectious Diseases Society Pediatric COVID-19 Therapies Taskforce. *Journal of the Pediatric Infectious Diseases Society*. 2024 Feb 10:piad116. DOI: 10.1093/jpids/piad116.

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