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, LDH, ferritin, triglycerides
- *If suspected cardiac involvement*: add troponin, NT-proBNP, CKMB

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

Consults:
- Infectious Diseases for severe or progressive diseases (required), or at the discretion of primary team
- Rheumatology if suspected clinical (e.g., high fever, ARDS)/laboratory (e.g., ferritin >500 mcg/mL x2, coagulopathy, elevated triglycerides) evidence of cytokine storm syndrome (Appendix B) and need for escalation of treatment

General Treatment Considerations:
(See IDSA Guidelines on Treatment and Management of Patients with COVID-19 for more information)

- See Appendix A for High Risk and Increased Risk Factors for Severe COVID-19 in Children
- 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)[1], see MIS-C Clinical Pathway
- Consider other signs of systemic severe illness, in consultation with ID

Management options based on severity of illness and presence of high risk or increased risk factors (Appendix A)

Mild/Moderate Illness (>94% on RA and no supplemental O2 need):
- Any age + ≥1 High Risk Factor: remdesivir recommended
- Any age + ≥2 Increased Risk Factor **or** infant + 1 Increased Risk Factor: consider remdesivir
- Any age without any Increased or High Risk Factors: supportive management only

Severe Illness (≤94% on RA; needs supplemental O2 via low flow):
- Remdesivir x5 days
- **+/-** dexamethasone up to 10 days (or until discharge, whichever is shorter)

Critical Illness (high flow O2, CPAP, vent, ECMO, ARDS, end-organ dysfunction):
- Remdesivir 5-10 days
- **and** dexamethasone up to 10 days (or until discharge, whichever is shorter)

Medications:

Remdesivir:
- Obtain baseline CBC w diff, CMP if not already done
  - Additional labs at discretion of provider depending on severity of disease
- Weight-based dosing (once daily dosing):
  - 1.5 kg up to 3 kg: 2.5 mg/kg IV loading dose on day 1, followed by 1.25 mg/kg/dose from day 2 and on
  - 3 kg up to 40 kg: 5 mg/kg IV loading dose on day 1, followed by 2.5 mg/kg/dose from day 2 and on
  - ≥40 kg: 200 mg IV loading dose on day 1, followed by 100 mg from day 2 and on

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)

Laboratory Monitoring:
The labs obtained and frequency of labs will be dependent on the patient's clinical status and judgment of the healthcare team.

- Consider: CBC with differential, chem 10, PT/PTT, fibrinogen, D-dimer, CRP, ferritin
- Additional labs in consultation with Infectious Diseases and/or Rheumatology

Discharge Considerations:
- Follow up with ID as needed; follow up with Rheumatology if consulted
- 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]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, *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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Examples of Factors Associated with Progression to Severe COVID-19

High Risk Factors:

Example Health Condition	Example Therapeutics That Predispose to Substantial Immunosuppression
Fewer than 1% peripheral B-cells assessed in past 6 months	B-cell depleting agents in past 12 months (e.g., rituximab, ofatumumab, ocrelizumab, others)
Congenital agammaglobulinemia	CAR-T therapy in past 12 months
Graft versus host disease	Abatacept
Hematological malignancy on therapy	Tyrosine kinase inhibitor (e.g., ibrutinib, acalabrutinib, others)
HIV infection with CD4 <200 cells/mm^3	High-dose corticosteroids (≥20 mg prednisone or equivalent for ≥4 weeks)
Other severe primary immunodeficiency	Anthracycline derivatives
Solid organ transplant	
Solid tumor on immunosuppressive therapy	
Stem cell transplant <2 years	

Increased Risk Factors (not high risk)

These factors vary in the degree of risk they confer. For those that confer less risk, the benefit of antiviral therapy will likely be lower.

Example Health Condition	Example Therapeutics That Are Less Likely to Predispose to Substantial Immunosuppression but May Increase Risk of Severe COVID-19
Chronic heart disease, cyanotic or otherwise hemodynamically significant	Anti-IL-6
Chronic liver disease	Anti-IL-12 and 23
Chronic lung diseases other than asthma	Corticosteroids 10-20 mg (0.25-0.5 mg/kg) for ≥4 weeks
Conditions associated with moderate immunocompromise (e.g., acute lymphoblastic leukemia in maintenance; solid tumors receiving conventional chemotherapy; HSCT >6 months prior; immunomodulatory therapy; solid organ transplantation)	
Diabetes mellitus	
End-stage renal disease	
HIV with CD4 >200 cells/mm^3	
Neurodevelopmental conditions inclusive of Down syndrome	
Obesity	
Pregnancy (current or within 6 weeks of pregnancy)	
Prematurity with ongoing sequelae affecting at least 1 organ system (e.g., chronic lung disease, neurodevelopmental sequelae)	
Sickle cell disease	

Source: Infectious Disease Society of America. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. *Clin Infect Dis.* 2024. Pages e250-e349. DOI: 10.1093/cid.ciac724.

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Patients With Evidence of Cytokine Storm Syndrome

(e.g., high fever, worsening coagulopathy, ARDS, elevated ferritin >500 mcg/ml)

- Consult Rheumatology to discuss need for additional labs and escalation of treatment
- Additional laboratory studies may be suggested, including 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

- Treatment recommendations may include 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 (should not be given in cases of severe leukopenia or transaminitis)
  - **Anakinra**: 2 mg/kg/dose (max 100 mg/dose) IV q6 hrs
  - **Steroids:** should be added if not already receiving, as per pathway

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