# UNC Children’s COVID-19 Guidelines

## Page 1: Overall Management Algorithm

### Inclusions
- Children between 3 months and 22 years of age

Note: for children under 3 months of age with COVID-19, recommend management as per routine with a viral infection in this age group.

### Initial Diagnostic Tests

<table>
<thead>
<tr>
<th>Acute COVID-19</th>
<th>MIS-C</th>
<th>Asymptomatic Infection</th>
</tr>
</thead>
</table>
| - Prominent respiratory symptoms  
- PCR (+), IgG (+) or (-)  
- No features of MIS-C | - MIS-C findings below: often GI, derm, cardiac, may resemble Kawasaki  
- **Consider differential diagnosis**, including sepsis!  
- PCR (+) or (-); IgG usually (+)  
- MOST have known COVID-19 history | - Patient presented for another reason (e.g., trauma, planned procedure)  
- NO consistent symptoms at time of screening |

### Admission Criteria

| Oxygen requirement  
- Signs/symptoms of sepsis  
- Felt to be at high risk of decompensation and further monitoring needed  
- **Admit to PICU** if sepsis or requiring HFNC or greater support | Admit ALL patients with suspected MIS-C. Refer to Pediatric ED MIS-C pathway for more details.  
- **Admit to PICU** if shock, concern for heart failure, or requiring HFNC or greater support | As indicated based on presenting condition |

### Consults

| Required  
- Pulmonary (in-person)  
- Infectious Diseases (in-person)  
- Hematology (virtual OK) | Required  
- Rheumatology (in-person)  
- Infectious Diseases (in-person)  

**If cardiac involvement**  
- Cardiology (in-person)  
- Others as indicated | - Consults only as indicated for underlying condition  
- Consider discussing with or consulting ID, Rheum, Pulm, or others if diagnosis is in doubt |

### Supportive Care and Monitoring

| Monitors, cont pulse ox  
- Oxygen support as needed  
- NPO/IV fluids as indicated | Monitors, cont pulse ox  
- Telemetry if cardiac involvement  
- Echocardiogram | As appropriate for underlying condition |

### Labs (daily, space as appropriate)

| CBC/diff, CMP, LDH, CRP, ESR  
- DIC panel, troponin, pro-BNP  
- Consider CTA chest if PE suspected | CBC/diff, CMP, LDH, CRP, ESR, troponin, pro-BNP, blood culture, D-dimer (or DIC panel)  
- COVID-19 PCR AND IgG  
- CXR, EKG  
- Echocardiogram ASAP | - Consider CXR  
- Consider labs as for acute COVID-19 and MIS-C as indicated  
- Consider COVID-19 IgG  
- Evaluation of underlying condition as indicated |

### Treatment Considerations

| Anticoagulation (most, see page 5)  
No O2 requirement: **consider remdesivir** if considered high-risk.  
+ O2 requirement: remdesivir +/- dexamethasone. Page 2 for details.  
If high-risk, not on O2, and >=12 years old, may **consider** monoclonal antibody therapy (see page 2) | Commonly used  
- IVIG  
- Methylprednisolone  
- Aspirin  

Selection and dosing per Rheumatology | Treatment not indicated unless determined to be symptomatic.  
For **high-risk** patients age 12 and older, may consider monoclonal antibody therapy. See UNC Health definitions of "high-risk." |
<table>
<thead>
<tr>
<th>Agent</th>
<th>Dosing and Regimen</th>
<th>Considerations</th>
<th>Adverse Effects and Interactions</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remdesivir</td>
<td>&lt;40 kg: 5 mg/kg IV x1, followed by 2.5 mg/kg IV daily</td>
<td>Requires ASP or ID approval. May be ordered by primary team.</td>
<td>Nausea, vomiting, elevation of hepatic transaminases (monitor closely)</td>
<td>Recommended in patients admitted for COVID-19 and requiring supplemental oxygen or greater support.</td>
</tr>
<tr>
<td></td>
<td>≥40 kg: 200mg IV x1, followed by 100mg IV daily Course: 5 days</td>
<td>Criteria (abbreviated): SpO2 &lt;94% on RA, eGFR &gt; 30. ALT &lt; 5x ULN. Hospitalized &lt;10 days; intubated &lt;5 days. Not pregnant.</td>
<td>Under EUA: Daily LFTs required. ALT must be &lt;5x ULN to start therapy; therapy must be discontinued if ALT rises &gt;5x ULN.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>&lt;40 kg: 0.15 mg/kg PO/IV daily</td>
<td>Proven benefit for adults requiring oxygen or greater respiratory support. Other corticosteroids would likely have similar effect.</td>
<td>Hypertension +/- PRES, bradycardia, delirium</td>
<td>Consider if requiring low-flow oxygen, especially if consistent or escalating requirement.</td>
</tr>
<tr>
<td></td>
<td>&gt;40 kg: 6 mg PO/IV daily</td>
<td></td>
<td></td>
<td>Recommended if requiring HFNC or greater respiratory support.</td>
</tr>
<tr>
<td></td>
<td>Alternatives: prednisolone 1 mg/kg daily (40 mg max), methylpred 0.8 mg/kg daily (32 mg max)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin OR Low molecular-weight heparin</td>
<td>See Page 5 for anticoagulation recommendations.</td>
<td></td>
<td></td>
<td>Used in most cases of COVID-19. See page 5 for detailed recommendations.</td>
</tr>
<tr>
<td>Convalescent plasma</td>
<td>Single dose of 1 or 2 units of plasma (200-500 mL) from a single COVID-19 recovered</td>
<td>Experimental therapy only. Requires eIND from FDA for patients &lt;18 years. Requires informed consent.</td>
<td>Adverse effects appear comparable to standard FFP transfusions.</td>
<td>Not recommended. Recent data has not supported a therapeutic benefit.</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>8 mg/kg/dose x1, max 800 mg Monoclonal antibody against IL-6</td>
<td>In adult patients, recommended if receiving HFNC or greater support, or if worsening and high CRP (&gt;75).</td>
<td>Avoid if: already immune suppressed, neutropenic, platelets &lt;50K, ALT &gt;5x ULN, concern for pre-existing chronic infection such as TB or Strongyloides</td>
<td>Consider only in critical COVID-19. Not generally recommended. Used in addition to other therapies (steroids, remdesivir, etc.).</td>
</tr>
<tr>
<td>Baricitinib</td>
<td>≥9 years: 4 mg PO daily &lt;9 years: 2 mg PO daily</td>
<td>JAK inhibitor used as anti-inflammatory.</td>
<td>Thrombosis is more common; patients must be on thromboprophylaxis unless contraindicated.</td>
<td>Not generally recommended. May be considered as alternative to tocilizumab when tocilizumab unavailable or contraindicated.</td>
</tr>
<tr>
<td>Available under EUA for acute COVID-19 down to age 2</td>
<td>Can be dispersed in water and taken PO or via NG or GT</td>
<td></td>
<td></td>
<td>Do not co-administer with tocilizumab.</td>
</tr>
<tr>
<td>Casirivimab/Imdevimab Or Bamlanivimab/Etesivimab</td>
<td>As of this writing, Casirivimab/Imdevimab is the only preferred product due to efficacy against newer variants.</td>
<td>Monoclonal antibodies against the spike protein. 1-2 hour infusion with at least 1 hour observation. No benefit in patients hospitalized for COVID-19.</td>
<td>Infusion reactions (fever, chills, hypotension) may occur. Anaphylaxis may rarely occur.</td>
<td>Rarely recommended inpatient. Occasionally may be used in patients admitted for another reason and found to have COVID-19 and meeting criteria for treatment.</td>
</tr>
<tr>
<td>Agent</td>
<td>Dosing and Regimen</td>
<td>Considerations</td>
<td>Adverse Effects and Interactions</td>
<td>Recommendation</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------</td>
<td>----------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>Severe: 30 mg/kg daily x 3 days Moderate: 10 mg/kg daily x 3 days Mild: 1-2 mg/kg day Consider starting with IV MP then transition to oral and taper</td>
<td>Consider administering in the morning</td>
<td>Hypertension +/- PRES, bradycardia, delirium</td>
<td>Used very often in MIS-C. May be used alone without IVIG. Use in addition to IVIG with organ-threatening disease or shock and/or refractory to IVIG. Dose is based on severity of illness.</td>
</tr>
<tr>
<td>Prednisolone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVIG</td>
<td>1-2 gm/kg/dose x1 (maximum 70-100 gm/dose) May consider additional dose if no improvement or rebound after 1st dose</td>
<td>Pre-medication is not required prior to IVIG administration Can be divided over 2 days if needed</td>
<td>Increased risk for clot or thrombosis if other risk factors present; aseptic meningitis; hemolytic anemia</td>
<td>Used in most cases of MIS-C.</td>
</tr>
<tr>
<td>Aspirin</td>
<td>3-5 mg/kg/day, max dose 81 mg</td>
<td>Anti-platelet and anti-inflammatory</td>
<td>Slightly increased risk of bleeding.</td>
<td>Use in almost all MIS-C cases.</td>
</tr>
<tr>
<td>Anakinra</td>
<td>1-2 mg/kg/day SC; May consider increasing up to a maximum of 10 mg/kg/day</td>
<td>IL-1 receptor antagonist Use may be limited by pharmacy availability</td>
<td>Generally well-tolerated with favorable profile. Administered in sepsis trials without untoward effects. Short half-life. Use with caution in renal insufficiency</td>
<td>Considered in severe cases only.</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>8-12 mg/kg/dose IV x1; May consider additional dose if no improvement</td>
<td>IL-6 receptor monoclonal antibody Use may be limited by pharmacy availability</td>
<td>Elevated transaminases, thrombocytopenia, neutropenia, hypersensitivity reaction, GI perforation. Use with caution/avoid with cytopenia or transaminitis.</td>
<td>May consider for severe cases or treatment resistance to IVIG +/- steroids</td>
</tr>
<tr>
<td>Infliximab</td>
<td>5-10 mg/kg/dose IV x1</td>
<td>TNF inhibitor Use may be limited by pharmacy availability</td>
<td>TB reactivation, hypersensitivity reaction</td>
<td>Consider in patients with KD features or treatment resistance to IVIG +/- steroids</td>
</tr>
</tbody>
</table>
**UNC Children’s COVID-19 Guidelines**  
*Page 4: Evaluation of Suspected MIS-C*

### EVALUATION OF PEDIATRIC PATIENTS SUSPECTED TO HAVE MIS-C

1. Vital signs per unit routine  
2. CBC/D, CMP, LDH, CRP, ESR, DIC panel, troponin, pro-BNP  
3. COVID PCR and COVID IgG if not already done  
4. EKG and consider telemetry  
5. Baseline CXR if not already done  
6. Obtain echocardiogram as soon as possible  
7. If considering initiation of immunosuppressive therapy (see Page 3), consult pediatric rheumatology

### MIS-C CASE DEFINITION

1. Individual <21-years-old presenting with fever >24 hours, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurologic); **AND**  
   2. **No alternative plausible diagnosis; AND**  
   3. Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to onset of symptoms

### EXAMPLES OF ORGAN SYSTEM INVOLVEMENT
- Cardiac: shock, elevated troponin, elevated pro-BNP, coronary arteritis, abnormal echocardiogram, arrhythmia  
- Gastrointestinal: severe abdominal pain, vomiting, diarrhea, elevated transaminases  
- Hematologic: elevated d-dimers, coagulopathy, lymphopenia, thrombocytosis or thrombocytopenia  
- Mucocutaneous: petechia or purpura, polymorphous rash, mucositis, conjunctivitis  
- Neurologic: headache/irritability, altered mental status, seizures, focal neurologic deficits  
- Respiratory: ARDS, pulmonary embolism  
- Renal: acute kidney injury or failure

### LABORATORY EVIDENCE OF INFLAMMATION
- Elevated CRP and/or ESR  
- Elevated d-dimer  
- Elevated ferritin  
- Elevated IL-6  
- Elevated neutrophils and/or reduced lymphocytes
UNC Children's COVID-19 Guidelines
Page 5: Anticoagulation Management in Pediatric COVID-19

START
Patient admitted with acute COVID-19 OR MIS-C

Initial Labs
CBC/diff, retic, CMP, DIC panel, FVIII, AT3, ferritin, LDH

Determine Thrombosis Risk Group

Group A: Therapeutic Anticoagulation
Any of the following:
- Confirmed DVT/PE or other indication for therapeutic anticoagulation
- High suspicion of DVT/PE but not documented. Strongly consider if O2 requirement if >5L HFNC
- Hemodialysis with repetitive clotting of dialysis tubing
- MIS-C with coronary artery aneurysm and Z-score >=10
- MIS-C with documented VTE or ejection fraction (EF) < 35%

High-risk Acute COVID-19
Treat with
- Enoxaparin (target anti-Xa level 0.6-1; monitor renal function)
or
- UFH (Heparin Pediatric Nomogram: Thrombosis Panel, target hep correlation or anti-Xa: 0.3-0.7 U/ml). Consider heparin for first 48 hours if clinically unstable

UNC Medical Center: Heparin Guideline

High-risk MIS-C
Dual therapy with therapeutic enoxaparin + aspirin 3-5 mg/kg/day; max 81 mg/day for MIS-C with CAA with Z-score>10.0

Group B: Prophylactic Anticoagulation
- Hospitalized and D-dimer >5x ULN with or without non-COVID-19 VTE risk factors
- Hospitalized with D-dimer <5x ULN with >3 non-COVID-19 VTE risk factors (see Table 1 below)
- Consider Pediatric Hematology consult if initial D-dimer >10x ULN (>2,500 ng/mL) or rising

Prophylaxis with
- Enoxaparin (monitor renal function)
or
- UFH (Heparin Pediatric Nomogram: Sub-Therapeutic Panel)

*Order via Peds VTE PPX order set

UNC Health: VTE Prophylaxis Guideline

Group C: Antiplatelet Therapy
- MIS-C and KD-like features and/or thrombocytosis (PLT > 450K)
- Coronary artery aneurysms with z-score 2.5-10

Low-dose aspirin (3-5 mg/kg/day; max 81 mg/day). Avoid if platelet count < 80K.

Daily Labs
CBC/diff, DIC Panel (consider less frequent if stable)

Table 1. Risk Factors for Hospital-Associated VTE in Children
- Central venous catheter
- Mechanical ventilation
- Prolonged length of stay (eg, anticipated >3 days)
- Complete immobility (eg, Braden Q Mobility Score =1)
- Obesity (BMI > 95th percentile)
- Active malignancy, nephrotic syndrome, CF exacerbation, sickle cell disease vaso-occlusive crisis, or flare of underlying inflammatory disease (eg, lupus, JIA, IBD)
- Congenital or acquired heart disease with venous stasis or impaired venous return
- Previous history of VTE
- First-degree family history of VTE before age 40 or unprovoked VTE
- Known thrombophilia (eg Protein S, Protein C, or anti-thrombin deficiency; Factor V Leiden; factor II G0210A; persistent antiphospholipid antibodies
- Pubertal, post-pubertal, or age > 12 years
- Estrogen-containing oral contraceptive pill
- Status-post splenectomy for underlying hemoglobinopathy

Table 2. Management After Hospital Discharge
- Continued anticoagulant thromboprophylaxis post-discharge from hospital can be considered in patients with COVID-19 or MIS-C who have markedly elevated D-dimer levels at discharge and superimposed clinical risk factors for VTE with a planned duration of the sooner of clinical risk factor resolution or 30d post discharge
- Patients with MIS-C and documented thrombosis or an EF <35% should receive therapeutic anticoagulation with enoxaparin until at least two weeks after discharge from the hospital
  - Indications for longer outpatient therapeutic enoxaparin dosing include: CAA with z-score >10 (indefinite treatment), documented thrombosis (treatment 2 3mos pending thrombus resolution), or ongoing moderate to severe left ventricular dysfunction
- Any patient with COVID-19 discharged from the hospital should be educated about the 4 main symptoms of DVT (swelling, pain, redness, warmth), PE (SOB, SP, tachycardia, cough/gemoptysis), CTVL (worsening headache, nausea/vomiting, changes in vision, or focal neuro deficits). www.clotconnect.org
- Anticoagulation of choice: enoxaparin if <15 yo or apixaban if >15 yo AND weight of>50 kg.
- Patients on anticoagulation should have a pediatric hematology consultation AND follow up within 2 weeks of discharge.
- Patients on aspirin therapy for MIS-C or KD should have a pediatric cardiology consultation AND follow up within 2 weeks of discharge.
Special Precautions during follow-up:

<table>
<thead>
<tr>
<th>AS needed only</th>
<th>AS needed only</th>
<th>Infectious Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>In person, with echocardiogram.</td>
<td>In person, with echocardiogram.</td>
<td>Virtual OK</td>
</tr>
<tr>
<td>If cardiac involvement, at 2 weeks and 4 weeks, in-</td>
<td>If discharged on anticoagulation, virtual follow-up.</td>
<td>Virtual OK</td>
</tr>
<tr>
<td>person preferred</td>
<td>Within 2 weeks with labs, in-person preferred</td>
<td>Virtual OK</td>
</tr>
<tr>
<td>Within 2 weeks with labs, in-person preferred</td>
<td>Within 2 weeks</td>
<td>Virtual OK</td>
</tr>
<tr>
<td>If discharged on anticoagulation, virtual follow-up.</td>
<td>If discharged on anticoagulation, virtual follow-up.</td>
<td>Virtual OK</td>
</tr>
<tr>
<td>2 months after discharge with PFTs</td>
<td>2-month in-person: PFTs and 6-minute walk test</td>
<td>Pulmonology</td>
</tr>
<tr>
<td>Prior to subspecialist follow-up.</td>
<td>1-month symptom check (virtual OK)</td>
<td>Pulmonology</td>
</tr>
<tr>
<td>Revert: rash (in some cases, labs may be needed</td>
<td>or virtual generally OK.</td>
<td>Primary Care Physician</td>
</tr>
<tr>
<td>As needed, lab follow-up.</td>
<td>Consider check-in 3-5 days after discharge. Phone</td>
<td>Acute COVID-19 Service</td>
</tr>
</tbody>
</table>

When in doubt, use full precautions.

The child and their family members should be screened for symptoms and history of COVID-19 prior to the visit. However, family members are highly likely to have been infected, so they are not likely to be contagious at the time of discharge. Regardless of PCR status, especially if they are less than 3 years old, they may be contagious for up to 3 days after resolution of fever and respiratory symptoms. Family members are highly likely to have been infected.

Acute COVID-19 service:

Contact PCP at discharge

MIS-C

These are guidelines only. Follow-up plans must be individualized for each patient.
In many cases, data are limited. For all these patient groups, families should be advised to take particular care to avoid infection, and patients with these conditions who test positive require careful follow-up. Additional conditions of similar severity that are not listed here may also be considered risk factors.

### Putative Risk Factors

<table>
<thead>
<tr>
<th>Putative Risk Factors</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunocompromised Status</strong></td>
<td>Strikingly, immunocompromised status has not been a common risk factor for severe acute infection. Immunocompromised patients may be at greater risk of prolonged illness/shedding.</td>
</tr>
<tr>
<td>Hematopoietic stem cell transplant recipient</td>
<td></td>
</tr>
<tr>
<td>Solid organ transplant recipient</td>
<td></td>
</tr>
<tr>
<td>Receiving anticancer chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Primary immunodeficiency</td>
<td></td>
</tr>
<tr>
<td>HIV infection</td>
<td></td>
</tr>
<tr>
<td>Chronic steroid therapy</td>
<td></td>
</tr>
<tr>
<td>Other immunosuppressive medications (e.g., TNF blockade)</td>
<td></td>
</tr>
<tr>
<td><strong>Hematologic Disease</strong></td>
<td>Limited data, but patients likely at increased risk for severe pneumonia.</td>
</tr>
<tr>
<td>Sickle-cell disease</td>
<td></td>
</tr>
<tr>
<td><strong>Symptomatic cardiac disease</strong></td>
<td>Limited data. Caution and careful follow-up are advised</td>
</tr>
<tr>
<td>Major congenital heart defects</td>
<td></td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td><strong>Significant pulmonary disease</strong></td>
<td>Baseline compromised pulmonary function likely increases the risk of requiring hospitalization and risk of severe disease. Many hospitalized patients have had baseline OSA or poorly controlled asthma.</td>
</tr>
<tr>
<td>Severe chronic lung disease with lung function &lt;50% or ≥2 hospitalizations in the past year</td>
<td></td>
</tr>
<tr>
<td>Oxygen while awake and/or asleep</td>
<td></td>
</tr>
<tr>
<td>Tracheostomy</td>
<td></td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td></td>
</tr>
<tr>
<td>Asthma requiring daily controller</td>
<td></td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic or endocrine disease</strong></td>
<td>These are clear risk factors in adults. Most adolescents with severe COVID-19 in our hospital have been obese.</td>
</tr>
<tr>
<td>Diabetes mellitus requiring insulin</td>
<td></td>
</tr>
<tr>
<td>Obesity (BMI &gt;95th percentile or &gt;30)</td>
<td></td>
</tr>
<tr>
<td>Metabolic disorders significantly affecting multiple organ systems</td>
<td></td>
</tr>
<tr>
<td><strong>Medically complex</strong></td>
<td>These patients have diminished tolerance for an acute infection.</td>
</tr>
<tr>
<td>Technology dependence associated with developmental delay and/or genetic abnormalities</td>
<td></td>
</tr>
</tbody>
</table>