Cincinnati Children's Hospital Medical Center
COVID-19 MIS-C Algorithm
Version 1.13
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COVID-19 ASSOCIATED MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C)
GUIDANCE FOR EVALUATION AND MANAGEMENT

Background:
The purpose of this document is to provide guidance regarding which patients should be evaluated for MIS-C, the initial evaluation of suspected MIS-C, and the management of patients who meet the MIS-C case definition.

Case definition (note: this is a purposely broad definition for reporting purposes and NOT designed as a clinical pathway)[1]

2023 MIS-C Surveillance case definition	
Age	Age <21 years
Fever	Subjective or documented fever 38C or higher
Illness Severity	Illness with clinical severity requiring hospitalization or resulting in death
Alternative Diagnosis	A more likely alternative diagnosis is not present
Laboratory markers of inflammation	C-reactive protein 3.0 mg/dL or more
Organ involvement	New onset of manifestations in 2 or more of the following categories:
Cardiac	• I-left ventricular ejection fraction <55% • Coronary artery dilatation, aneurysm, or ectasia • Troponin elevated above laboratory normal range or indicated as elevated in a clinical note
Shock	Clinician diagnosis as documented in clinical note
Hematologic	• Thrombocytopenia (platelet count, <150,000 cells/µL) • Lymphopenia (absolute lymphocyte count <1,000 cells/ µL)
Gastrointestinal	• Abdominal pain • Vomiting • Diarrhea
Dermatologic/Mucocutaneous	• Rash • Inflammation of the oral mucosa • Conjunctivitis or conjunctival injection • Extremity findings
COVID-19 Exposure or Testing	• Positive viral test within the last 60 days prior to illness onset • Currently positive COVID PCR test • Known exposure to COVID-19 infection in the last 4-6 weeks

Patients to be evaluated for *suspected* MIS-C:

- Patients with unexplained fever for ≥3 days AND diarrhea, vomiting, abdominal pain, conjunctivitis, non-vesicular rash, swelling of hands/feet or altered mental status
- Patients with any unexplained fever and shock
    - Note: even if there is an apparent explanation for fever, persistent fever should prompt further evaluation particularly if there is a suspected COVID exposure

Tiered approach for initial evaluation for *suspected* MIS-C: See Appendix I

- Note: COVID-19 serology should be interpreted in the context of clinical history including prior known or suspected prior infection, vaccination status, and possible maternal transfer for infants

Patients with suspected Kawasaki disease (complete or incomplete) but negative SARS-CoV-2 testing and no documented COVID exposure should be evaluated and managed per AHA guidelines (7)

Evaluation and Management principles for patients who *meet the MIS-C Case Definition*

- **Consider and potentially treat other diagnostic possibilities in patients meeting the MIS-C case definition.**
- **Evaluate all patients with signs of shock for sepsis; perform a sepsis huddle, send cultures, and start antibiotics.**
- Patients with MIS-C may be placed in standard precautions unless SARS-CoV-2 PCR+
- Consult Cardiology and order echocardiogram to assess myocardial function. Timing of echo to be determined by the patients' clinical status and cardiology, ideally prior to the initiation of IVIG whenever possible, including in patients without signs of shock. Repeat echocardiogram with any clinical worsening or per cardiology recommendations. Consult heart failure for any patient with significant myocardial dysfunction (EF<40%)
- If case definition is met, and Tier 1 and 2 labs are resulted and concerning for MIS-C, consult rheumatology if not already involved. Overnight rheumatology consults should be reserved for patients in critical care or who are at risk for rapid decompensation. Consider ID consultation if there are specific questions regarding evaluation.
- Management decisions including IVIG treatment should be made by primary team (hospital medicine or critical care) in consultation with rheumatology and cardiology. It is acceptable to delay IVIG treatment in clinically stable patients to ensure adequate monitoring for vital sign changes during infusion. Patients in need of urgent treatment should be assessed for PICU/CVICU care
- Inpatient unit assignment should be discussed between primary team (hospital medicine or critical care) and cardiology:
    - Patients not needing ICU care should have frequent monitoring until stable >24h (watcher status w/ frequent PEWS, MRT for any concerns)
    - Patients who develop shock, coronary artery dilation, or myocardial dysfunction should be transferred to PICU or CVICU via MRT
- Trend above labs q24-48 h until clinically improving
- Infection Prevention & Control will report patients to the CDC

TREATMENT

MILD DISEASE (no signs of shock, no myocardial dysfunction)

- Admit to Hospital Medicine
- Low dose aspirin
- IVIG
- Methylprednisolone/Prednisone 1mg/kg BID for 2 weeks followed by taper over 2-3 weeks; consider adding PPI

Patients with MILD DISEASE who worsen or are REFRACTORY TO TREATMENT (continued fever >36h after IVIG, worsening clinical condition, new cardiac dysfunction or shock):

- Transfer to ICU for shock and/or new cardiac dysfunction
- Continue low dose aspirin and methylprednisolone/prednisone
- Consider pulse dose methylprednisolone and/or biologics in consultation with rheumatology

MODERATE/SEVERE disease (shock, cardiac dysfunction, or significant coronary artery dilation)

- Admit or Transfer to ICU
- Perform sepsis huddle, send cultures and initiate antibiotics if not initiated
- Inotropic support as needed; ECMO should be considered early in patients with refractory shock
- Low dose aspirin; discuss high-dose aspirin with cardiology for any coronary changes
- Anticoagulation as needed per cardiology and ICU team
    - Central venous catheterization, age >12 years, malignancy, ICU admission, and D-dimer level elevated to greater than 5 times the upper limit of normal are independent risk factors for thrombosis in MIS-C. Higher intensity anticoagulation should be considered in children with MIS-C on an individual basis, taking into consideration the presence of these risk factors balanced with the patient's risk of bleeding
- IVIG
- Methylprednisolone/Prednisone for 2 weeks followed by taper over 2-3 weeks. Consider pulse methylprednisolone for 1-3 days in severely ill patients after discussions between primary and consulting teams. Consider adding PPI
- Consider biologics (anakinra, tocilizumab, infliximab) in consultation with rheumatology

Medication	Dosing	Notes
Aspirin	**Low dose (antiplatelet):** 3-5 mg/kg/dose once daily **High dose (anti-inflammatory):** 20-25 mg/kg/dose every 6 hours	Round aspirin dose to nearest ½ 81 mg tablet size
IVIG	2 gm/kg/dose IV (max 100 gm) for 1 dose	Retreatment not recommended
Methylprednisolone	2mg/kg/day until clinically improved followed by taper over 2-3 weeks **Pulse dose:** 30mg/kg/day (max 1000mg/day) for 1-3 days followed by 2mg/kg/day divided q8-q12. Continue high dose until clinically improved (can consolidate to daily) then taper over 2-3 weeks	Add a proton pump inhibitor for patients receiving steroids + aspirin to decrease risk for GI bleed
Biologic dosing recommendations:		
Medication	Dosing	Notes
Anakinra	2-4 mg/kg/dose (max 100mg/dose) SQ twice daily (may increase to 3 times daily) for 3 days	
Infliximab	10mg/kg/dose IV once	

References:

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Appendix I: Tiered approach for initial evaluation of suspected MIS-C