Multisystem Inflammatory Syndrome in Children (MIS-C) Clinical Pathway

If highly suspicious for MIS-C or in shock, consult with tertiary pediatric center ASAP and consider initiating transfer process to tertiary pediatric center ASAP.

CLINICAL-HISTORICAL FEATURES
- GI Symptoms: Abdominal pain (mild/severe), vomiting, and/or diarrhea
- Rash: Polymorphic, maculopapular, petechial, NOT vesicular
- Extremity changes: Erythema and edema of the hands and feet
- Oral Mucosal changes: Erythema of oropharyngeal mucosa
- Conjunctivitis: Bilateral bulbar conjunctival injection without exudate
- Lymphadenopathy: Cervical > 1.5 cm
- Neurologic Symptoms: Headache, irritability, lethargy, altered mental status
- Epidemiologic Link to COVID: Patient with history of COVID disease or close contact with known Positive COVID case in past 4 weeks, or person placed in quarantine

CLINICAL/HISTORICAL FEATURES
- Fever/history of fever > 38.0°C for ≥ 3 days + ≥ 2 Clinical/Historical Features
- Follow ED/Hospital Sepsis Pathway and Order Sets
  - Additional diagnostic laboratory studies:
    - Add: COVID PCR, COVID Antibody, Troponin, BNP, D-dimer, Ferritin, ECG
    - Fluid resuscitation, vasopressors
    - Antibiotics: COVID PCR, COVID Antibody testing and consider
    - Laboratory studies/imaging for PICU patients with MIS-C
    - PICU Sepsis Pathway
    - Consider inotropes, vasopressors, milrinone
    - Consider bedside echocardiogram
    - Consults – Infectious Disease, Rheumatology, Cardiology, Hematology as indicated
    - Obtain COVID Antibody testing and consider repeating COVID PCR if initially negative at 48 hours
    - Consider differential diagnosis for MIS-C

Consider treatment AFTER multidisciplinary evaluation:
- Antibiotics
- Steroids, IVIG
- Aspirin, Anticoagulation
- Anticytokine therapy
- Monitoring Clinical, Lab, Imaging Response
- Discharge and Follow-Up Plan

Developed by the Wisconsin Emergency Medical Services for Children Program
Adapted from the Emergency Department, ICU and Inpatient Clinical Pathway for Evaluation of Possible Multisystem Inflammatory Syndrome (MIS-C), Children’s Hospital of Philadelphia, July 2020.

**Figure: Multisystem Inflammatory Syndrome in Children (MIS-C) Clinical Pathway**

- **ED Evaluation for Possible MIS-C**
  - ED Team Assessment
    - History & Physical Exam (PE)
    - COVID Eval re: exposure, diagnosis
  - Assess for Evidence of Inflammation
    - Consider Differential Diagnosis for MIS-C
  - Assess for Evidence of Shock
    - ED Sepsis Triage
    - Sepsis Huddle as clinically indicated
  - ED Sepsis Triage
  - History & Physical
- **Evaluation for Possible MIS-C Without Shock**
  - Fever/history of fever > 38.0°C for ≥ 3 days + ≥ 2 Clinical/Historical Features
  - Lab/clinical status
  - Labs or exam concerning but inconsistent with MIS-C
  - Labs or exam concerning but inconsistent with MIS-C
- **Suspected MIS-C with Shock**
  - Fever/history of fever > 38.0°C for ≥ 1 day + Evidence of myocardial dysfunction or Hypotension/vasopressor requirement
  - ≥ 2 Clinical/Historical Features
- **Initial Laboratory Testing**
  - CBC, CMP, CRP, ESR
  - Other testing as clinically indicated to identify cause of fever, based on clinical features
- **Discharge with PCP follow-up within 24-48 hours**
  - If progression or worsening of lab/clinical status
  - Transfer to Tertiary Care Center w/PICU

**Appendices (see page 2)**
- A. Common Features of Shock in Children
- B. Principal Clinical Features of Classic Kawasaki Disease
- C. Differential Diagnosis of MIS-C
If considering Kawasaki Disease, see Appendix B Clinical Features of Classic Kawasaki Disease and consult with a Kawasaki expert.

### Appendix A

**Common Features of Shock in Children**

*Hypotensive (decompensated) shock* is characterized by poor perfusion and an abnormally low blood pressure. It can be difficult to recognize children with *compensated shock*, as these children will have normal blood pressures. Other important clinical findings that may suggest either decompensated or compensated shock are:

- Tachycardia out of proportion to fever, or present despite resolution of fever
- Tachypnea
- Altered mental status
- Diminished urine output
- Cool extremities with weak pulses and prolonged capillary refill (> 3 seconds) OR warm extremities with bounding pulses and flash capillary refill (< 1 second)
- Children with cardiogenic shock and/or myocardial dysfunction may have hepatomegaly or crackles; it is important to assess for these signs initially and monitor for them as patients receive fluid resuscitation
- Acidosis (including low serum bicarbonate, base deficit on blood gas testing)
- Elevated lactate

### Appendix B

**Principal Clinical Features of Classic Kawasaki Disease**

May not all be present at the same time

**Fever**  
Presence of fever for ≥ 5 days as well as four of the five following additional features:

- **Oral changes** - Erythema and cracking of lips, strawberry tongue, and/or erythema of oral and pharyngeal mucosa
- **Conjunctivitis** - Bilateral bulbar conjunctival injection without exudate
- **Rash** - Maculopapular, diffuse erythroderma, or erythema multiforme-like
- **Extremity changes** - Erythema and edema of the hands and feet in acute phase and/or periungual desquamation in subacute phase
- **Lymphadenopathy** - Cervical lymphadenopathy (≥ 1.5 cm diameter), usually unilateral

**NOTE:** Kawasaki Disease (KD) can occur in the absence of full diagnostic criteria (incomplete KD), particularly in infants. Therefore consultation with an expert in KD is recommended if incomplete KD is being considered.

### Appendix C

**Differential Diagnosis of MIS-C**

- Acute COVID-19
- Kawasaki Disease
- Non-SARS-CoV-2 Viral Sepsis
- Toxic Shock Syndrome
- Bacterial Sepsis
- Systemic Onset Juvenile Idiopathic Arthritis
- Macrophage Activation Syndrome (MAS)
- Hemophagocytic Lymphohistiocytosis (HLH)

**REMINDER:** Wisconsin providers should report suspected cases of MIS-C to Wisconsin Department of Health Services through the Wisconsin Electronic Disease Surveillance System (WEDSS), or by calling the Communicable Diseases Epidemiology Section at (608) 267-9003.

**NOTE:** This clinical pathway is current at the time of publication and may need to be adapted for each patient based on practitioner judgement and evolving information on Multisystem Inflammatory Syndrome in Children (MIS-C).