Multisystem Inflammatory Syndrome in Children (MIS-C) Clinical Pathway
Emergency Department, Inpatient Unit, Pediatric Intensive Care Unit (PICU)

**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

**ED Evaluation for Possible MIS-C**

**ED Team Assessment**
- History & Physical Exam (PE)
- COVID Eval: 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
  - See Appendix A Common Features of Shock in Children

**Evaluation for Possible MIS-C Without Shock**

- Fever/history of fever ≥ 38.0°C for ≥ 3 days
- ≥ 2 Clinical/Historical Features
- * Review Appendix B Clinical Features of Classic Kawasaki Disease

**Evaluation for Possible MIS-C**

- Labs or exam concerning but inconsistent with MIS-C
- Consider differential diagnosis for MIS-C
- See Appendix C Differential Diagnosis of 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

**Labs and Physical Exam (PE) Reassuring**

- Labs or Physical Exam (PE)
- Reassuring
- Admit to Inpatient Pediatric Unit if available or consult with tertiary care center
- * Review Appendix B Clinical Features of Classic Kawasaki Disease

**Labs or exam concerning but inconsistent with MIS-C**

- Labs or exam concerning but inconsistent with MIS-C
- Consider differential diagnosis for MIS-C
- See Appendix C Differential Diagnosis of MIS-C

**Consult with Tertiary Care Center w/PICU regarding probable transfer, cardiac monitoring and patient status**

- Consider additional ancillary laboratory studies:
  - Troponin, BNP
  - ECG, COVID PCR, COVID Antibody testing

**Cardiology Consultation if**

- Abnormal ECG, BNP, Troponin
- Cardiac insufficiency on PE, e.g., delayed capillary refill, hepatomegaly, crackles
- Consider cultures (e.g., blood/urine), antibiotics

**Follow ED/Hospital Sepsis Pathway and Order Sets**

- Additional diagnostic laboratory studies
  - Add: COVID PCR, COVID Antibody, Troponin, BNP, D-dimer, Ferritin, ECG

**Admit to PICU at Pediatric Tertiary Care Center**

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

**Transfer to Tertiary Care Center w/PICU**

- Discharge with PCP follow-up within 24-48 hours
- If progression or worsening of lab/clinical status

*NOTE: If considering Kawasaki Disease, see Appendix B Clinical Features of Classic Kawasaki Disease and consult with a Kawasaki expert.*

- Developed by the Illinois MIS-C Workgroup
- 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.

**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

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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: In addition to reporting through I-NEDSS, hospitals should complete the MIS-C Case Report form when they suspect a case and submit to their local health department. The form can be accessed at https://www.cdc.gov/mis-c/pdfs/hcp/mis-c-form-printable.pdf

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).