### Guidelines for the Treatment of Multisystem Inflammatory Syndrome in Children (MIS-C)

*This is a living document that will be updated as more data emerge.*

#### MIS-C CASE DEFINITION (CDC)
- Age younger than < 21 years old
- Fever ≥ 38°C for ≥ 24 hours
- Laboratory evidence of inflammation including but not limited to increased C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes, low albumin
- Clinically severe illness requiring hospitalization
- Involvement of ≥ 2 organs (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurologic)
- No alternative diagnosis
- Positive for current/recent SARS-CoV-2 or exposure to a suspected/confirmed COVID-19 case within the 4 weeks prior to onset of symptoms

### INITIAL PRESENTATION & SYMPTOMS OF ORGAN DYSFUNCTION

**For all patients with High Suspicion for MIS-C:**

**Immediately discuss management with Pediatric Infectious Disease (ID) & Pediatric Cardiology**

**AND**

Admit to the Pediatric ICU or Pediatric Progressive Care Unit for blood pressure & continuous cardiopulmonary monitoring.

**High Suspicion for MIS-C (if other causes are ruled out):**

Persistent fever (>38°C) + Link to SARS-CoV-2 + At least TWO suggestive clinical features (marked as * below)

- **Cardiac**: Tachycardia; myocarditis
- **Dermatologic***: Skin rash (polymorphic, maculopapular, or petechial); oral mucocutaneous lesions (red or cracked lips; strawberry tongue, or erythema)
- **Gastrointestinal***: Abdominal pain, diarrhea, nausea/vomiting
- **Hematologic**: Thrombosis
- **Immunologic**: Lymphadenopathy*
- **Kawasaki-like disease**: Conjunctivitis (bilateral without exudate)*, edema of hands & feet*, rash, coronary artery enlargement/aneurysm
- **Neurologic***: Altered mental status; encephalopathy; focal neurologic deficits; papilledema
- **Renal**: Acute kidney injury
- **Respiratory**: Respiratory distress (any severity); tachypnea
- **Systemic**: Hemodynamic instability; hyper inflammatory features; hypotension; shock

### INITIAL LABORATORY TESTING (ON PRESENTATION)

**High Suspicion for MIS-C (further workup is required):**

CRP ≥ 50 mg/L OR ESR ≥ 40 mm/hr

AND

At least ONE of the following laboratory features: Lymphocytes < 1 bil/L; Platelets < 150 bil/L; Na < 135 mmol/L; Elevated Neutrophils; Hypoalbuminemia

- **General**: Comprehensive Metabolic Panel
- **Hematologic**: CBC with Differential
- **Inflammatory Markers**: Erythrocyte Sedimentation Rate (ESR); C-reactive protein (CRP)
- **Microbiology**: SARS-CoV-2 PCR and/or SARS-CoV-2 serology
HEMODYNAMIC INSTABILITY OR SEPTIC SHOCK

Emergency Department
- Fluid resuscitation
- Vasoactive medications (e.g., Epinephrine or Norepinephrine) if necessary

Pediatric ICU

IMMUNOMODULATORY TREATMENT

Pediatric ID
- **Immune Globulin (10%)** 2 grams/kg/dose IV x 1 dose (max: 120 grams) infused over 10-12 hours
- **Methyprednisolone** 0.5 mg/kg/dose IV every 6 hours x 5 days (max: 40 mg/dose)

ANTIPLATELET THERAPY

Pediatric ID
- **Aspirin (low dose)** 3-5 mg/kg/dose PO every 24 hours (max: 81 mg/dose)
  - Avoid use in patients with active bleeding (or at bleeding risk) or with thrombocytopenia (platelets < 50 bil/L)

IMMUNOMODULATORY TREATMENT (REFRACTORY DISEASE)

Pediatric ID
- **Infliximab-dyyb** 5 mg/kg/dose IV (max: 500 mg/dose) every 24 hours x 2 doses.
  - Pharmacy manager approval: Required prior to initiation of therapy.
  - **Premedication:** Not required (patients will remain on methylprednisolone)
  - **Administration:** Infuse each dose over 2 hours.
  - **Monitoring:** refer to the guideline for Management of Infusion-Related Reactions to Infliximab, Infliximab-dyyb, and Vedolizumab in Pediatric Patients

References:


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