Beaumont
CHILDREN'S

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 ≥ 38ºC 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)

AND

No alternative diagnosis

AND

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 (>38ºC) + 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

FURTHER LABORATORY TESTING IF HIGH SUSPICION FOR MIS-C

Discuss further laboratory workup with Pediatric ID, Pediatric Cardiology, and Pediatric ICU prior to ordering

- **Hematologic**: PT/PTT (if not already done), Fibrinogen; Ferritin; D-Dimer
- **Inflammatory Markers**: Procalcitonin; Lactic Acid Dehydrogenase (LDH); Interleukin 6 (IL-6); Cytokine panel; Creatine Kinase
- **Cardiac Evaluation**: Troponin 1; BNP; Triglycerides ; EKG; ECHO
- **Respiratory Evaluation**: Chest X-Ray
- **Infectious Evaluation**:SARS-CoV-2 serology (if not already done)

HEMODYNAMIC INSTABILITY OR SEPTIC SHOCK

Emergency Department
Pediatric ICU

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

IMMUNOMODULATORY TREATMENT

Pediatric ID

- **Immune Globulin (10%)** 2 grams/kg/dose IV x 1 dose (*max*: 120 grams) infused over 10-12 hours

AND

- **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)

Clinically worsening or minimal improvement after 24-48 hours

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:

- Abdel-Haq, N., Asmar, B.I., Deza Leon, M.P. *et al.* SARS-CoV-2-associated multisystem inflammatory syndrome in children: clinical manifestations and the role of infliximab treatment. *Eur J Pediatr* (2021).
- American Academy of Pediatrics (AAP). Multisystem Inflammatory Syndrome in Children (MIS-C) Interim Guidance. Last updated 2/2/2021. Available at: http://services.aap.org
- Centers for Disease Control and Prevention (CDC). Information for Healthcare Providers about Multisystem Inflammatory Syndrome in Children (MIS-C). Last updated: 2/17/2021. Available at: www.cdc.gov/mis-c.
- Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. American College of Rheumatology Clinical Guidance for Pediatric Patients with Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2 and Hyperinflammation in COVID-19. Version 1. *Arthritis Rheumatol* 2020; 72; 1791-1805. doi: https://onlinelibrary.wiley.com/doi/10.1002/art.41454.

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