### Multisystem Inflammatory Syndrome in Children (MIS-C)

**Clinical Presentation**

- Inflammatory illness associated with COVID-19 infection occurring up to 2-4 weeks post-infection in children and young adults
- Typically presents as refractory vasodilatory shock with fevers (for at least 4 days), GI complaints, and Kawasaki/toxic shock-like signs and symptoms; respiratory symptoms uncommon
- Progression of symptoms can be rapid
- Age <21 years
- Fever >38°C (100.4°F) or subjective fever for >24 hours
- Laboratory markers of inflammation
  - Elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes, and low albumin
- No alternative plausible diagnoses
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms
- Evidence of clinically severe illness requiring hospitalization with multisystem (>2) organ involvement, including:
  - Cardiac (eg, shock, elevated troponin, BNP, abnormal echocardiogram, arrhythmia)
  - Respiratory (eg, respiratory insufficiency, pneumonia, pulmonary infiltrates, pleural effusions)
  - Renal (eg, acute kidney injury or renal failure)
  - Hematologic (eg, disseminated intravascular coagulation, DVT)
  - Gastrointestinal (eg, elevated bilirubin or elevated liver enzymes)
  - Neurologic (eg, stroke, aseptic meningitis, encephalopathy)
  - Dermatologic (eg, rash, dry cracked lips/oral mucosa changes, conjunctivitis, strawberry tongue)

**Evaluation**

A tiered diagnostic approach is used in patients without life-threatening manifestations

- In those with shock, complete full diagnostic evaluation (Tier 1 and Tier 2)

**Tier 1 evaluation**

- CBC, complete metabolic panel, ESR, CRP, SARS-CoV-2 PCR, and/or serologies
- Proceed to Tier 2 if CRP ≥5 mg/dL or ESR >40 mm/h AND at least one suggestive laboratory feature (ALC <1000/µL, PLT <150,000/µL, Na <135 mmoles/L, neutrophilia, hypoalbuminemia)

**Tier 2 evaluation**

- BNP, troponin T, procalcitonin, ferritin, PT, PTT, D-dimer, fibrinogen, LDH, urinalysis, cytokine panel, triglycerides, SARS-CoV-2 serology, EKG, echocardiogram
- Consultations to Cardiology, Rheumatology, and Infectious Disease
- Consider referral to hospital with pediatric ICU support

### Diagnostic Criteria (Need All Six)

- Age <21 years
- Fever >38°C (100.4°F) or subjective fever for >24 hours
- Laboratory markers of inflammation
  - Including but not limited to one or more of the following:
    - Elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes, and low albumin
- No alternative plausible diagnoses
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### Commonly Used Treatments

- Inotropic support for shock (norepinephrine)
- Antibiotics often used for possible sepsis
- Use of anti-inflammatory medications and anticoagulation treatments have been variable

#### Anti-inflammatory medications

- Corticosteroids & IVIG are first line treatments, consider biologics if refractory
- Methylprednisolone 1 mg/kg q12h or high-dose methylprednisolone 30 mg/kg/day (if shock or life-threatening illness)
- IVIG 1-2 g/kg
- Biologics (eg, anakinra) as second line therapy if refractory to first line

#### Anticoagulation

- Aspirin
  - Commonly used due to concerns for coronary artery involvement
  - Low-dose at minimum (3-5 mg/kg/day; maximum 81 mg/day), high-dose also used
- Enoxaparin
  - Prophylactic doses often used due to hypercoagulable state associated with MIS-C (age 2 months - 18 yrs 40 kg; 0.5 mg/kg/dose SC q12h up to max of 40 mg SC qd)
  - If cardiomyopathy, often continued post-discharge for 2 weeks

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Centers for Disease Control and Prevention. [www.cdc.gov/mis-c/hcp](http://www.cdc.gov/mis-c/hcp)