# Multisystem Inflammatory Syndrome (MIS-C) Inpatient

## Evidence-Based Outcomes Center

Patient with Clinical Features suspicious for MIS-C w/out an alternative explanation

- Fever/history of fever ≥3d + evidence of ≥2 system involvement, consider COVID-19 exposure

Consider Differential Diagnosis

Multisystem Inflammatory Syndrome in Children (MIS-C) Inpatient

**Lab results consistent with MIS-C**

Elevated:
1. CRP: ≥ 3 mg/dL (median 20 mg/dL)
2. ESR: > 40
3. Ferritin: > 500 mg/L
4. BNP: > 400 pg/ml
5. D-dimer: > 3000ng/ml

Decreased:
Hgb: < 9
Platelets < 150
Albumin < 2.5

**History/symptoms/ labs c/w MIS-C**

Assess disease severity

Severe illness or moderate illness with worsening labs or limited response to fluid resuscitation. Consider evaluation for PICU placement.

Moderate/Severe → Admit to PICU

Mild/Moderate → Admit PCRS/PUI

**Initial Care:**
**Monitoring:**
- vitals per unit protocol
- Isolation guidelines

**Testing:**
- Confirm completion of initial labs (see ED pathway)
- Repeat SARs-CoV2 test, 12 hours from initial test
- Daily CBC, CMP, CRP and trend other abnormal labs
- Daily EKG, if initial abnormal

**Consults:**
- ID: treatment recommendations
- Cards: discuss timing of initial ECHO
- Heme: VTE prophylaxis, hematologic abnormalities
- Rheum: for severe disease, early use of Anikinra therapy

**Initial Care**
**Monitoring:**
- vitals q4 with BPs (arm only)
- admit to Telemetry
- Isolation guidelines

**Testing:**
- Confirm completion of initial labs (see ED pathway)
- Repeat SARs-CoV2 test, 12 hours from initial test
- Daily CBC, CMP, CRP and trend other abnormal labs
- Repeat daily EKG, if initial abnormal or vital sign changes

**Consults:**
- ID: treatment recommendations
- Cards: will consult and review timing/need for ECHO
- Heme: if VTE prophylaxis needed or hematologic abnormalities

**Treatment**
1. IVIG (2g/kg) via infusion protocol x1 dose
2. Steroids
3. VTE Prophylaxis
4. Consider early use of Anakinra
5. Vasopressor support and/or ECMO per PICU management
6. Pepcid prophylaxis

*Daily multidisciplinary team assessment/huddle*

**Treatment**
1. IVIG (2g/kg) via infusion protocol x1 dose
2. Steroids
3. ASA: Low dose 3-5mg/k/dose q day
4. VTE Prophylaxis
5. Pepcid prophylaxis

*If presentation consistent with KD, follow KD Pathway

*Daily multidisciplinary team assessment/huddle*

Clinical Improvement?

Yes → **Discharge Criteria:**
1. CRP < by 50%
2. Afebrile 24 hrs.
3. Stable EKG, BNP improving (if abnormal)
4. No $0_2$ requirement
5. Follow up arranged

No →
- Revisit treatment strategy
- Consider Anakinra if refractory or worsening illness

Discharge Orders:
Appointments Scheduled
1. Follow up with PCP:
   48 hrs.
2. Follow up with Cardiology:
   2 wks. after discharge
   4-6 wks. for Echo/eval
3. Follow up with ID in 2 weeks
4. Follow up with Heme in 2 weeks if dc on Lovenox

Discharge Medications:
1. Steroid taper
2. Gastritis prophylaxis while on steroids
3. Low dose ASA

dell children's Ascension

PEDIATRIC EBOC

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# MIS-C Clinical Features:

- **Fever** > 38.0 ** **AND**
- **No other plausible explanation for presentation AND**
- **Evidence of > 2 systems of involvement**:
  - **GI:** abdominal pain, nausea/vomiting, diarrhea
  - **Neuro:** headache, vision changes, altered mental status
  - **Cardiac:** unexplained tachycardia, signs of acute heart failure, cardiogenic shock
  - **Renal:** Oliguria
  - **Mucocutaneous:** mimic typical or atypical KD
  - Skin: polymorphic, petechial, maculopapular exanthem, eythroderma
  - Mucosa: red/cracked lips, strawberry tongue
  - Eye: bulbar, non-purulent conjunctivitis
  - Extremity: palmar/plantar erythema, edema
  - Lymph: Cervical adenopathy > 1.5cm
  - Other: severe sore throat, arthralgias

* Respiratory complaints less common, should prompt investigation of other causes or cardiac/pulmonary embolism as a source

* Consider more detailed evaluation if prior history of COVID or close contact with known positive COVID case in past 4 weeks

** CDC Criteria is > 38.0 for > 24 hours, but fevers typically persist > 3 days

# Differential Diagnosis for patient with possible MIS-C:

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| Differential Diagnosis | Clinical Features |
|---|---|
| **Toxic Shock Syndrome (STSS)** | Severe, abrupt onset illness due to toxin-producing GAS or *staphylococcus aureus*<br>Signs/Symptoms: fever, diffuse erythematous exanthem/erythroderma (desquamates in 1-2 weeks), hypotension, & multi-system organ involvement |
| **Endemic (Murine) Typhus** | *Rickettsia typhi*, transmitted by infected rat flea; ask exposure history<br>Triad of fever, headache, rash (macular to petechial - spreads trunk to extremities)<br>Lab abnormalities: thrombocytopenia, anemia, hyponatremia, & elevated LFTs<br>Diagnosis: *Rickettsia typhi titers*<br>Treatment: Doxycycline |
| **Hemophagocytic Lymphohistiocytosis (HLH)** | Hyperinflammatory syndrome related to immune dysregulation of cytotoxic T lymphocytes & natural killer cells<br>Fever, splenomegaly, cytopenias, hypertriglyceridemia, elevated ferritin, elevated CD25, decreased/absent NK function |
| **Kawasaki Disease** | See Kawasaki Disease Pathway |
| **EVALI** | E-cigarette/Vaping Associated Lung Injury<br>Recognized by CDC, 8/2019 - possible link to vaping THC, vitamin E acetate<br>Definition: e-cigarette/vaping in previous 90 days AND infiltrate on chest XR/ ground glass appearance on CT AND no plausible infectious source (neg RRP, neg flu) AND no evidence of other cause<br>Symptoms: fever, cough/respiratory distress/shortness of breath, GI symptoms (N/V/abdominal pain), weight loss, fatigue |

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## Disease Severity:

| Disease Severity | Criteria |
|---|---|
| **Mild** | Normal blood pressure<br>No oxygen requirement<br>Normal ECHO (if completed) |
| **Moderate** | Hypotension with limited response to fluids OR<br>Supplemental O2 required OR<br>Mild ventricular dysfunction on ECHO |
| **Severe** | Requiring vasoactive support OR<br>O2 requirement necessitating HFNC (above floor max) or ventilatory support OR<br>Mod to severe ventricular dysfunction on ECHO |

## Steroid Therapy:

| Disease Severity | Initial Steroid Therapy |
|---|---|
| **Mild** | Prednisolone 2 mg/kg/day divided bid x 5 days (max 60 mg) followed by the steroid taper<br>* May consider NO steroid therapy if mild disease similar to classic KD (discuss with multidisciplinary team) |
| **Moderate or Severe** | Methylprednisolone (high dose, IV) 30 mg/kg/day (max 1 gram) for 3 days. Transition to oral therapy of prednisolone 2 mg/kg/day divided bid x 5 days (max 60 mg) followed by the steroid taper |

## Steroid Taper:

- Prednisolone: 1 mg/kg/day divided BID x 5 days (max 30 mg/day), and then 0.5 mg/kg/day DAILY x 5 days (max 15 mg/day).
- All children should receive gastritis prophylaxis while completing steroid treatment.

# VTE Prophylaxis

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**Venothromboemobolism (VTE) Prophylaxis:**

Consider prophylactic anticoagulation with Enoxaparin if:

1. Personal for first degree relative with history of VTE OR
2. An indwelling central venous catheter and ≥ 2 risk factors OR
3. 4 risk factors

**Risk Factors**

Post pubertal age
Decreased mobility from baseline
Burns
Active malignancy
Indications of venous stasis or cardiac low flow state
Estrogen therapy
Active systemic inflammation
Flare of inflammatory disease
Obesity
Severe Dehydration
Recent surgery or trauma

*Reference: Pediatric Blood Cancer. 2020;67:e28485. © 2020 https://doi.org/10.1002/pbc.28485*

**Enoxaparin Dosing / Monitoring:** Refer to Enoxaparin (Lovenox) Pedi/NEO Order Set. Use prophylaxis dosing in the order set.

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Approved by the Multisystem Inflammatory Syndrome (MIS-C) Workgroup Team

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