MIS-C
(multisystem inflammatory syndrome in children)

when to consider evaluation for inpatient management

**MIS-C** defined by Centers for Disease Control (CDC)

- Fever - 38.0°C or higher for 24 hours, or report of subjective fever for greater than 24 hours.
- One or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactate dehydrogenase (LDH), elevated neutrophils, reduced lymphocytes and low albumin.

Additional comment:
- Patients meeting criteria for Kawasaki disease should be reported if they also meet CDC definition for MIS-C.

*** Multisystem involvement examples:
- Cardiovascular: shock, increased troponin, elevated BNP, abnormal echocardiogram, arrhythmia
- Respiratory: pneumonia, pulmonary embolism, ARDS
- Renal: AKI, renal failure
- Neurologic: aseptic meningitis, stroke, seizure
- GI: increased LFTS, diarrhea, GI bleed, ileus, vomiting, abdominal pain
- Dermatologic: rash, mucositis, erythroderma

DISCLAIMER: This guide is to help aid and evaluate for potential MIS-C in outpatient guidelines. Providers are encouraged to use judgment beyond these guidelines and refer to the ED if they feel necessary.

An individual aged <21 years +
fever* +
lab evidence of inflammation** +
clinically severe illness requiring hospitalization with involvement of 2 or more organ systems***

AND

Positive for current or recent SARS-CoV-2 infection
- PCR NP swab
- Blood test SARS-CoV-2 IgG

OR
COVID-19 exposure within the 4 weeks prior to the onset of symptoms

AND

No alternative plausible diagnoses

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Concern for MIS-C: admit 3W or PICU (from ED or hospital transfer)

Providers are encouraged to consider and explore other etiologies (keep the differential broad). Many COVID-19 etiologies cause similar clinical presentations and laboratory changes. Premature diagnosis to MIS-C could result in a delayed diagnosis and ultimately harm to the patient. MIS-C and non MIS-C workup can occur simultaneously.

Algorithm for evaluation and management of inpatient admitted for ruling out MIS-C

Laboratory and diagnostic tests for diagnosis of suspected MIS-C

<table>
<thead>
<tr>
<th>Labs</th>
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</thead>
<tbody>
<tr>
<td>Blood culture</td>
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<tr>
<td>D-dimer, Fibrinogen</td>
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<tr>
<td>BNP</td>
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<tr>
<td>Ferritin</td>
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<tr>
<td>CBC</td>
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<tr>
<td>PT/INR/PTT</td>
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<tr>
<td>CRP</td>
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<tr>
<td>Troponin I</td>
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<tr>
<td>CMP</td>
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<tr>
<td>UA</td>
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</table>

Coronavirus labs

SARS-Cov-2 PCR NP swab, SARS-Cov-2 IgG

Diagnostics

CXR

ECG

Pediatric Echocardiogram Doppler 2D M-mode (Cardiology consult may be warranted at this time)

Other laboratory and diagnostic tests as indicated by clinical assessment

Urgency of additional testing is dependent on disease severity

Coronavirus available tests are still changing rapidly, listed tests current at time of publication. Use what is available in EPIC at time of patient evaluation

Results of labs in combination with clinical presentation

Unlikely to be MIS-C; other diagnosis more likely

- CR monitoring, pulse oximetry
- Consider repeat CRP, Ferritin, BNP and troponin based on clinical presentation
- Continue evaluation for alternative diagnosis
- Empiric antibiotic therapy if concern for acute bacterial infection.

Strong suspicion for MIS-C

- CR monitoring.
- Mild cases: supportive care/monitoring. Consider IVIG.
- IVIG indications:
  - Moderate or severe MIS-C
  - Patient meets criteria for Kawasaki’s disease (complete or atypical)
  - Evidence of cardiac involvement
    - Abnormal EKG or ECHO
    - Elevated troponin or BNP
- Aspirin: dosing per Kawasaki protocol if patient meets criteria, otherwise low dose (3-5mg/kg) for all cases of MIS-C
- Consults: to ID, rheumatology, and cardiology are usually indicated to help decide further use of biologic or other therapeutic interventions/monitoring

Refer to medication management appendix for further detail on interventions and classification of mild, moderate or severe MIS-C

If patient meets CDC MIS-C definition, contact infection control for reporting to state.

If no alternative diagnosis found

- Discontinue MIS-C therapies that are deemed no longer necessary
- Exit guideline

No alternative diagnosis found

- Patient meets CDC criteria for MIS-C
- Continue current CDC criteria for MIS-C therapies and escalate/wean based on response and clinical assessment
## Medication Management of MIS-C

<table>
<thead>
<tr>
<th>Coronavirus MIS-C Severity</th>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild MIS-C:</td>
<td>Consider broad spectrum antibiotics pending culture results: ceftriaxone +/- vancomycin. Consider additional anti-microbial dependent on patient presentation. Gastrointestinal prophylaxis with PPI. Continuous CR monitoring. Aspirin 3-5 mg/kg/day (81 – 325 mg per day. Subject to change based off cardiology recommendations/clinical presentation of patient.)</td>
<td>N/A. Consider IV on case per case basis. Consider IV methylprednisolone 2mg/kg/day IV divided q6-12 hours.</td>
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<tr>
<td>Moderate MIS-C:</td>
<td>IVIG</td>
<td>2 g/kg (max 100g) IV over 12-16 hours</td>
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<tr>
<td></td>
<td>Consider methylprednisolone</td>
<td>2mg/kg/day IV divided q 6-12 hours or 10-15mg/kg IV q 24 hours.</td>
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<tr>
<td></td>
<td>Anakinra* (if refractory to IVIG)</td>
<td>2-10 mg/kg/day (max 100mg per dose) IV/SC</td>
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<tr>
<td>Severe MIS-C:</td>
<td>IVIG</td>
<td>2 g/kg (max 100g) IV over 12-16 hours</td>
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<tr>
<td></td>
<td>Anakinra*</td>
<td>Dosing determined by rheumatology</td>
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<tr>
<td></td>
<td>Consider methylprednisolone</td>
<td>20-30 mg/kg/day (max 1000 mg) for 1-3 days</td>
</tr>
<tr>
<td>Complete or atypical Kawasaki disease</td>
<td>IVIG 2 g/kg (max 100g) IV over 12-16 hours</td>
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<td></td>
<td>Aspirin (per cardiology and Kawasaki protocol: high dose/low dose)</td>
<td>Additional immunomodulators as needed in conjunction with appropriate consultants</td>
</tr>
<tr>
<td>Evidence of cardiac involvement (regardless of severity)</td>
<td>IVIG 2 g/kg (max 100g) IV over 12-16 hours</td>
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<tr>
<td>• Abnormal ECG, ECHO</td>
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<tr>
<td>• Elevated BNP/Troponin</td>
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*Rheumatology approval prior to anakinra start to confirm dosing and indication

**DISCLAIMER:** Medication dosing is suggestive and based on current medical literature. The clinical presentation may warrant different therapies/doses that deviate from the above guidelines and should be evaluated on a case by case basis.

## General Inpatient Management of MIS-C

### Daily MIS-C Care

- **Monitoring:**
  - Continuous CR monitoring
  - Initial ECHO and EKG: then as recommended by cardiology or significant change in patient status
  - Repeat CXR as needed based on patient condition

- **Daily Labs:**
  - CBC, CRP, troponin I, CMP, Ferritin until patient status improved or plateaued; ESR, fibrinogen, coagulation studies, d-dimer as needed to monitor inflammation and patient specific indications
  - Other labs and frequency depending on organs involved and severity of illness
### bibliography


