SSM Health Cardinal Glennon Children's Hospital

Evaluation and Management of Multi-System Inflammatory Syndrome in Children (MIS-C)

Clinical Practice Guideline

Approved by SSM Health Cardinal Glennon Clinical Practice Guidelines Committee May 23, 2024

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SSMHealth Cardinal Glennon Access Center Transfer Line
888-229-2424

1. SSMHealth Cardinal Glennon CPG Home

2. Resources

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Approved by SSM Cardinal Glennon Clinical Practice Guidelines Committee May 23, 2024
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MIS-C DEFINITION:
Any illness in a person aged < 21 years that meets:

- Clinical criteria AND Lab criteria (Confirmed) - *See Box 1*
- Clinical criteria AND Epidemiologic Criteria (Probable) - *See Box 1*
- Vital Records Criteria (Suspected) - *See Box 1*

EVALUATE ANY PATIENT < 21 YEARS BASED ON CLINICAL JUDGEMENT
The above case definition does not define who should have a diagnostic evaluation

STANDARD INITIAL ASSESSMENT IN A PATIENT WITH SUSPECTED MIS-C

- Vital signs, including Temperature, Heart Rate, Blood Pressure, SpO2, Respiratory Rate
- History and Physical Exam
  - Evaluate for evidence of inflammation
  - Utilize Epic Haiku to photograph any dermatologic or mucosal findings, if available
- COVID-19 exposure and diagnosis history
- Consider Differential Diagnosis, including, but not limited to:
  - Bacterial sepsis
  - Kawasaki Disease
  - Staph Scalded Skin Syndrome (SSSS)
  - Toxic Shock Syndrome
  - Myocarditis
  - Serum sickness
  - Tick-borne Illness
  - Viral Infections

POSSIBLE MIS-C

PRESENCE OF SHOCK?
Clinical evidence of decreased cardiac output or hypotension/vasopressor requirement

NO

OBTAIN
- CBC with differential
- CMP
- ESR and CRP
- Troponin
- COVID-19 PCR
- Consider:
  - COVID-19 serology
  - Blood culture
  - Other testing as clinically indicated

CRP ≥ 3mg/dL (30mg/L) PLUS at least two of the following:
- Elevated troponin
- Mucocutaneous symptoms (*see Box 1*)
- Gastrointestinal involvement (*see Box 1*)
- Hematologic Involvement (*see Box 1*)

NO

ALL OF THE FOLLOWING ARE PRESENT:
- Vitals, exam, and remainder of labs are reassuring
- Patient is able to tolerate oral intake
- Ability to follow up with PCP in 24-48 hours
- Reliable transportation and means of communicating with health care professionals

YES

Discharge Home
- Follow up with PCP in 24-48 hours

NO

Admit to General Pediatrics
- Consult Infectious Disease at attending discretion
- Consider initiating treatment (see Page 2)
- Consider alternative diagnoses and additional workup to evaluate for alternative diagnoses
- Consider further evaluation as noted above, if not previously obtained

YES

- Obtain Labs
  - BNP
  - Ferritin
  - D-dimer
  - PT/PTT
- Obtain procedures/imaging
  - Echocardiogram (urgent vs emergent)
  - Chest x-ray
  - EKG
- Consider
  - Blood cultures
  - Antibiotics

YES

- Evaluate and treat for sepsis
  - Stabilize circulation, airway, breathing as clinically indicated
  - Blood cultures, Fluids, pressors, antibiotics as clinically indicated
- Obtain Labs
  - CBC with differential
  - CMP
  - ESR and CRP
  - COVID-19 PCR +/- serologies
  - Respiratory PCR panel
  - BNP
  - Troponin
  - Ferritin
  - Fibrinogen
  - D-dimer
  - PT/PTT
- Obtain Imaging/Procedures
  - EKG
  - Chest X-ray
  - Echocardiogram
- Consult, as indicated:
  - Pediatric Infectious Disease
  - Pediatric Cardiology
  - Pediatric Rheumatology
- Obtain any additional labs, imaging, and provide treatments as indicated

Admit to PICU
- Consider initiating treatment (see Page 2)

Box 1: Clinical Definition Criteria

- Clinical Criteria
  - An illness characterized by all of the following in the absence of a more likely alternative diagnosis

Subjective OR documented fever ≥ 38°C	Clinical severity requiring hospitalization or resulting in death	Evidence of systemic inflammation indicated by C-reactive protein (CRP) ≥ 3.0mg/dL (30mg/L)	New-onset inflammation in at least two of the following categories: 1) Cardiac a. Left ventricular ejection fraction < 55% b. Coronary artery dilation, aneurysm, or ectasia c. Troponin elevated above laboratory normal range or indicated as elevated in a clinical note 2) Mucocutaneous a. Rash b. Oral mucosal inflammation (erythema or swelling, drying/fissuring of the lips, strawberry tongue) c. Conjunctivitis or conjunctival injection d. Extremity findings (erythema or edema of the hands or feet) 3) Shock 4) Gastrointestinal a. Abdominal pain b. Vomiting c. Diarrhea 5) Hematologic a. Platelet count < 150,000 cells/μL b. Absolute lymphocyte count (ALC) < 1,000 cells/μL

- Laboratory Criteria - One of the following

Detection of SARS-CoV-2 RNA in a clinical specimen** up to 60 days prior to or during hospitalization	Detection of SARS-CoV-2 specific antigen in a clinical specimen** up to 60 days prior to or during hospitalization	Detection of SARS-CoV-2 specific antibodies^ in serum, plasma, or whole blood associated with current illness resulting in or during hospitalization
** = Includes self-administered testing using over-the-counter test kits ^ = Includes a positive serology test regardless of COVID-19 vaccination status		

- Epidemiologic Linkage Criteria
  - Close contact with a confirmed or probable case of COVID-19 disease in the 60 days prior to hospitalization
    - Close contact defined as being within 6 feet for at least 15 minutes over a 24 hour period
- Vital Records Criteria
  - A person who's death certificate lists MIS-C or multisystem inflammatory syndrome as an underlying cause of death or a significant condition contributing to death

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DECISION TO TREAT HOSPITALIZED PATIENT WITH MIS-C
- Multi-disciplinary decision to proceed with treatment

FIRST LINE THERAPY
- IVIG 2 gram/kg (max 100 grams)

AND
- Methylprednisolone IV 1-2mg/kg/day (max 60mg daily)

AND
- Aspirin by mouth, 3-5mg/kg/day (max 81mg daily)

CONSIDERATIONS
- IVIG
  - Consider split dosing (1gm/kg daily for 2 days) or concomitant diuretic use if depressed cardiac function
  - Give over 12 hours
- Methylprednisolone
  - May use alternative steroid at equivalent dosing
  - May omit if mild disease or a contraindication to glucocorticoids
- Aspirin
  - Contraindicated if active bleeding, significant bleeding risk, or platelets < 80,000/uL
  - Consider additional anti-coagulation therapy in select cases
    - Presence of central venous catheterization, age > 12 years, malignancy, ICU admission
    - D-dimer elevated to > 5 times upper limit of normal
    - Expanding coronary artery aneurysms or coronary artery Z-score > 10.0
    - Documented thrombosis
    - Left ventricular ejection fraction < 35%

Resolution of fevers, improvement in clinical and lab evidence of inflammation and/or end-organ involvement?

NO

INTENSIFICATION TREATMENT
- Consult Pediatric Rheumatology
- Continue aspirin
- Methylprednisolone IV 10-30mg/kg/day

OR
- High-dose Anakinra

OR
- Infliximab 5-10mg/kg IV for 1 dose

CONSIDERATIONS
- Methylprednisolone
  - May use alternative steroid at equivalent dosing
- Infliximab
  - Do not use if concern or features of Macrophage Activation Syndrome (MAS)
- Aspirin
  - Contraindicated if active bleeding, significant bleeding risk, or platelets < 80,000/uL
  - Consider additional anti-coagulation therapy in select cases
    - Presence of central venous catheterization, age > 12 years, malignancy, ICU admission
    - D-dimer elevated to > 5 times upper limit of normal
    - Expanding coronary artery aneurysms or coronary artery Z-score > 10.0
    - Documented thrombosis
    - Left ventricular ejection fraction < 35%

Resolution of fevers, improvement in clinical and lab evidence of inflammation and/or end-organ involvement?

NO

OFF PATHWAY
- Sub-specialty consultation (Infectious disease, rheumatology, cardiology) and further treatment recommendations
- Consider alternative diagnosis
- Continue aspirin
- Continue steroids

YES

YES

DISCHARGE HOME

Additional Discharge Requirements
- If no other reason for ongoing hospitalization
- Reliable transportation for return appointments
- Reliable ability to communicate with health care professionals

Follow-up appointments
- PCP within 1 week of discharge
- If rheumatology involved, rheumatology in 2-3 weeks
- If rheumatology not involved, infectious disease in 2-3 weeks
- If cardiology involved, follow up at 14 days and 4-6 weeks

Follow-up testing
- Echocardiogram at 14 days
- Echocardiogram at 4-6 weeks

Medications
- Low-dose aspirin (3-5mg/kg/day, max 81mg) for a minimum of 4 weeks, until cleared by cardiology
- Anti-coagulation
  - If initiated, evaluate for the need to continue, as well as appropriate duration and follow-up
- Steroids
  - Stop at discharge for mild cases that respond to therapy
  - Taper over 2-3 weeks for patients with moderate to severe disease or prolonged high-dose steroid use