defined by Centers for Disease Control (CDC)

MIS-C

(multisystem inflammatory syndrome in children)

when to consider evaluation for inpatient management

An individual aged <21 years +

fever* +

lab evidence of inflammation** +

clinically severe illness requiring hospitalization with involvement of 2 or more organ systems***

AND

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.

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

- * 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, lactic acid 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, arrythmia
- 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



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

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.

Laboratory and diagnostic tests for diagnosis of suspected MIS-C

Labs

Blood culture D-dimer, Fibrinogen

BNP Ferritin
CBC PT/INR/PTT
CRP Troponin I

CMP UA

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

clinical

change,

increased

suspicion

of MIS-C

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

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

Results of labs in combination with clinical presentation

with

Alternative diagnosis made

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



No alternative diagnosis found

Patient meets CDC criteria for MIS-C

If patient meets

CDC MIS-C definition, contact infection

control for reporting

to state.

 Continue current MIS-C therapies and escalate/wean based on response and clinical assessment

medication management of MIS-C

Mild MIS-C:

admitted to 3W.

No vasoactive requirement,
minimal/no respiratory
support, minimal organ injury

Moderate MIS-C:

ICU level care required
0-1 vasopressors,
significant supplemental oxygen
support, mild or isolated
organ injury

Severe MIS-C:

ICU level care required. More than 1 vasopressors, non-invasive or invasive ventilator support, moderate or severe organ injury including moderate to severe ventricular dysfunction

coronavirus MIS-C severity	medication	dose
all patients	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.)	
mild MIS-C	N/A. Consider IVIG on case per case basis. Consider IV methylprednisolone 2mg/kg/day IV divided q6-12 hours.	N/A.
moderate MIS-C	IVIG	2 g/kg (max 100g) IV over 12-16 hours
	Consider methylprednisolone	2mg/kg/day IV divided q 6-12 hours or 10-15mg/kg IV q 24 hours.
	Anakinra* (If refractory to IVIG)	2-10 mg/kg/day (max 100mg per dose) IV/SC
severe MIS-C	IVIG	2 g/kg (max 100g) IV over 12-16 hours
	Anakinra*	Dosing determined by rheumatology
	Consider methylprednisolone	20-30 mg/kg/day (max 1000 mg) for 1-3 days
complete or atypical Kawasaki disease	IVIG 2 g/kg (max 100g) IV over 12-16 hours	
	Aspirin (per cardiology and Kawasaki protocol: high dose/low dose)	
	Additional immunomodulators as needed in conjunction with appropriate consultants	
evidence of cardiac involvement (regardless of severity) • Abnormal ECG, ECHO • Elevated BNP/Troponin	IVIG 2 g/kg (max 100g) IV over 12-16 hours	

^{*}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		
	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	
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	

inpatient discharge of confirmed MIS-C or strong suspicion of MIS-C

Discharge medications for MIS-C	Very dependent on hospital course	
Rheumatology Follow up (required)	1-2 weeks after discharge (Rheumatology office: 937-641-3805	
Cardiology Follow up (required)	Timing dependent on patients' clinical presentation	
Other Follow-up	Schedule follow up with other subspecialties as deemed necessary.	

Inpatient at Dayton Children's Hospital with:

- 1. Diagnosis of COVID-MIS-C
 - or
- High suspicion of COVID-MIS-C and treatment using COVID-MIS-C pathway

Prior to Discharge:

Ensure follow-up with cardiology, timing dependent on patient's clinical condition.

Ensure follow up appointment in 1-2 weeks with pediatric rheumatology 937-641-3805

Ensure appropriate follow-up with all other applicable subspecialists

bibliography

- 1. Cavalli G, De Luca G, Campochiaro C, Della-Torte E, Ripa M, et al. Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study. Lancet Rheumatol. May 7, 2020. https://doi.org/10.1016/S2665-9913(20)30127-2
- 2. Capone CA, Subramony A, Sweberg T, Schneider J, Shah S, Rubin L, et al. Characteristics, Cardiac involvement, and Outcomes of Multisystem Inflammatory Disease of Childhood (MIS-C) Associated with SARS-CoV-2 Infection. 2020.
- 3. Clinical Guidance for Pediatric Patients with Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2 and Hyperinflammation in COVID-19. American College of Rheumatology. June 17, 2020.
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- 6. https://www.cdc.gov/mis-c/hcp/

