

**CONSIDERATION OF MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN
(MIS-C) ASSOCIATED WITH COVID-19**

<i>Clinical features</i>	<p>Fever >38.5 °Celsius of any duration</p> <p align="center">AND</p> <p>Tachycardia, hypotension and/or oxygen requirement</p> <p align="center">AND</p> <p>Evidence of multi-organ dysfunction</p>	<p>Persistent fever >38.5 °Celsius for 5 days *</p> <p align="center">plus/minus</p> <p>Additional Clinical Features of MIS-C (See Boxes A and B)</p>	
<i>Initial Action Steps</i>	<p>Consider early PICU consult</p> <p>Order MIS-C Full Panel (See Box C)</p>	<p>Order MIS-C Screening Blood Work (See Box D)</p>	
<i>Assessment of MIS-C Screen</i>		<p><i>Are at least 2 of the following present?</i></p> <ol style="list-style-type: none"> 1. CBC abnormalities consistent with MIS-C (e.g. neutrophilia, lymphopenia, anemia or thrombocytopenia) 2. CRP > 100 3. Ferritin > 500 4. Albumin < 30 	
		YES	NO
<i>Next Action Steps</i>		<p>Contact General Pediatrics and Rheumatology to discuss potential admission and/or further work-up</p>	<p>Manage as per usual care by the ED team</p>

* Physicians should use their clinical judgement:

- Patients with an obvious cause for their fever (e.g. Streptococcal pharyngitis or pneumonia) may not require MIS-C screening blood work
- Patients with less than 5 days of fever and 2 or more concerning symptoms for MIS-C (see Box A) may require screening blood work

Box A. Additional clinical features of Multisystem Inflammatory Syndrome in Children (MIS-C)

- Abdominal pain, diarrhea and/or vomiting
- Non-exudative conjunctivitis
- Oral mucosal changes
- Hand and foot erythema or edema
- Diffuse erythematous rash
- Headache or neck stiffness

Box B. Features that help distinguish patients with MIS-C from those with Kawasaki disease (KD)

	KD	MIS-C
Age	<ul style="list-style-type: none"> • Typically 1 to 5 years of age 	<ul style="list-style-type: none"> • Often older than typical KD patients
Clinical features	<ul style="list-style-type: none"> • Classic KD features present <ul style="list-style-type: none"> ○ Nonpurulent conjunctivitis ○ Oral mucosal changes ○ Cervical lymphadenopathy ○ Rash ○ Peripheral edema 	<ul style="list-style-type: none"> • Classic KD features present, but more likely to be incomplete • More respiratory and gastrointestinal symptoms • Meningeal signs may be present • More likely to have signs of cardiovascular involvement
Laboratory features	<ul style="list-style-type: none"> • Leukophilia • Normal/increased lymphocytes • Increased platelet counts • Mild to moderately high ferritin • Normal CK 	<ul style="list-style-type: none"> • May have leukopenia • Lymphopenia • Thrombocytopenia • Higher ferritin levels • Elevated CK
Clinical course		<ul style="list-style-type: none"> • More severe disease course • More likely to have myocarditis and shock • More IVIG resistance • Increased rates of cytokine storm (e.g. secondary HLH)

Box C. MIS-C Full Panel

- CBC including differential, blood film
- CRP
- Ferritin
- Albumin
- ALT, AST, GGT, LDH, bilirubin
- Electrolytes, urea, creatinine
- Glucose
- Blood gas
- INR, PTT, fibrinogen, D-Dimer
- Triglycerides
- CK, troponin
- Save full red top tube for COVID-19 serological testing prior to IVIG
- Blood culture
- NPS for respiratory viruses plus SARS-CoV-2
- Urinalysis

Box D. MIS-C Screening Blood Work

- CBC including differential
- CRP
- Ferritin
- Albumin
- ALT
- Creatinine

APPENDIX A

Centers for Disease Control and Prevention Case Definition of Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19)

- An individual aged <21 years presenting with feverⁱ, laboratory evidence of inflammationⁱⁱ, and evidence of clinically severe illness requiring hospitalization, with multisystem (≥ 2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **AND**
- No alternative plausible diagnoses; **AND**
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms

ⁱ Fever $\geq 38.0^{\circ}\text{C}$ for ≥ 24 hours, or report of subjective fever lasting ≥ 24 hours

ⁱⁱ Including, but not limited to, 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), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin

Additional comments

- *Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C*
- *Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection*

Source: <https://emergency.cdc.gov/han/2020/han00432.asp>

APPENDIX B

World Health Organization Preliminary Case Definition of Multisystem Inflammatory Syndrome in Children and Adolescents Temporally Associated with COVID-19

Children and adolescents 0–19 years of age with fever \geq 3 days

AND 2 of the following:

1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
2. Hypotension or shock.
3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

AND

Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.

AND

No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

AND

Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

Source: <https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>