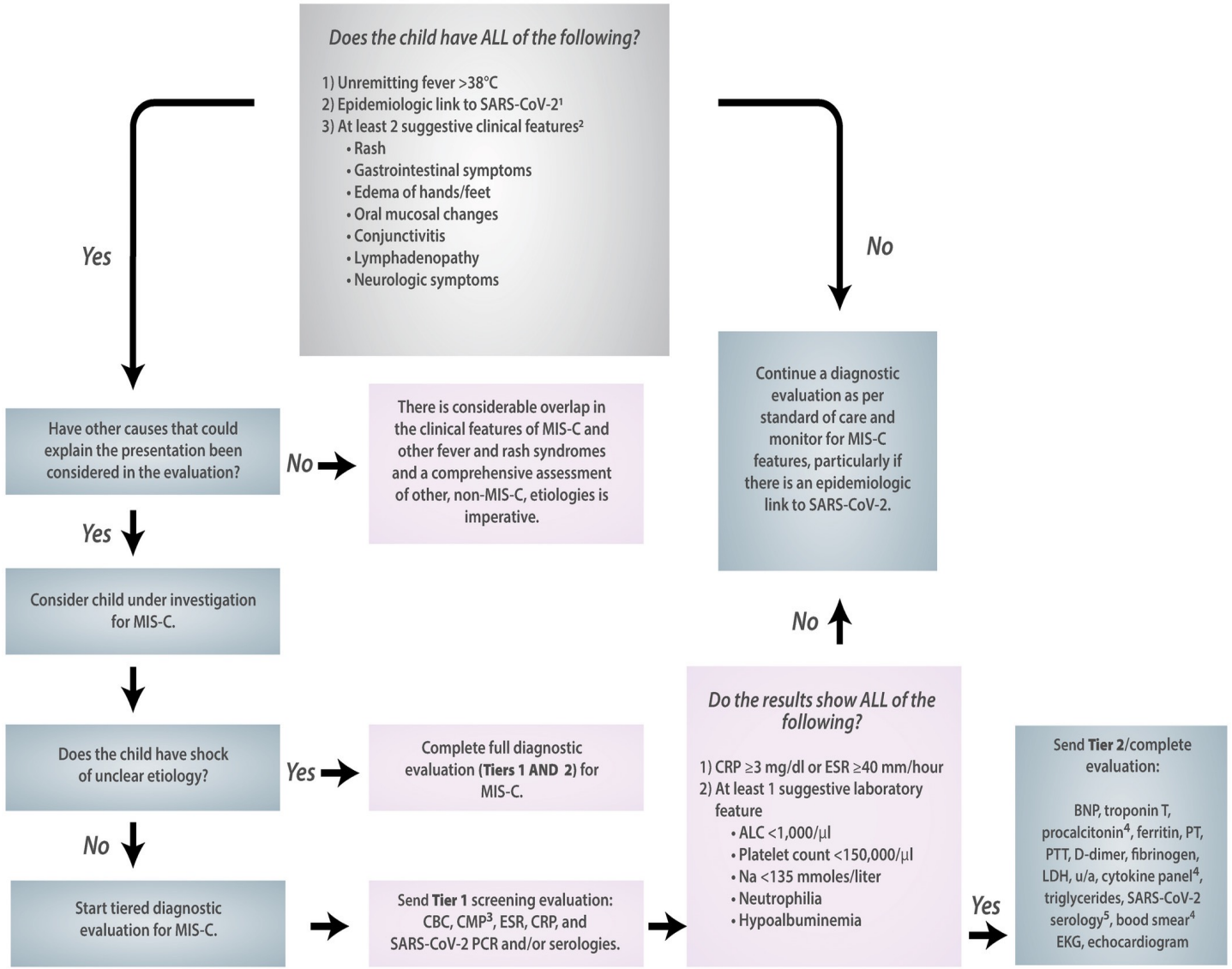
American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With SARS–CoV-2 and Hyperinflammation in Pediatric COVID-19: Version 3



Arthritis & Rheumatology, First published: 03 February 2022, DOI: (10.1002/art.42062)

Table 1. Case definitions of MIS-C*

Criteria	RCPCH†	CDC	WHO‡
Age	All children (age not defined)	<21 years	0–19 years
Fever	Persistent fever (≥38.5°C)	Temperature ≥38.0°C for ≥24 hours *or* subjective fever for ≥24 hours	Fever for ≥3 days
Clinical symptoms	Both of the following: 1. single or multiorgan dysfunction; *and* 2. additional features	Both of the following: 1. severe illness (hospitalized); *and* 2. ≥2 organ systems involved	At least 2 of the following: 1. rash, conjunctivitis, and mucocutaneous inflammation; 2. hypotension or shock; 3. cardiac involvement; 4. coagulopathy; 5. acute GI symptoms
Inflammation	All 3 of the following: 1. neutrophilia; *and* 2. increased CRP; *and* 3. lymphopenia	Laboratory evidence of inflammation including, but not limited to, 1 or more of the following: 1. ↑CRP; 2. ↑ESR; 3. ↑fibrinogen; 4. ↑procalcitonin; 5. ↑D-dimer; 6. ↑ferritin; 7. ↑LDH; 8. ↑IL-6; 9. neutrophilia; 10. lymphopenia; 11. hypoalbuminemia	Elevated inflammation markers, including any of the following: 1. ↑ESR; 2. ↑CRP; 3. ↑procalcitonin
Link to SARS–CoV-2	Positive or negative by PCR	Current or recent findings of the following: 1. positive by PCR; 2. positive by serology; 3. positive by antigen test; *or* 4. COVID-19 exposure within prior 4 weeks	Evidence of COVID-19 by the following: 1. positive by PCR; 2. positive by antigen test; 3. positive by serology; *or* 4. likely COVID-19 contact
Exclusion	Other infections	No alternative diagnosis	No obvious microbial cause

* Case definitions of multisystem inflammatory syndrome in children (MIS-C) are adapted from recommendations from the World Health Organization (WHO) (8) and Centers for Disease Control and Prevention (CDC) (10) for MIS-C, as well as the Royal College of Paediatrics and Child Health (RCPCH) for pediatric inflammatory multisystem syndrome temporally associated with SARS–Cov-2 (9). For laboratory parameters, ↑ indicates elevated levels. GI = gastrointestinal; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; LDH = lactate dehydrogenase; IL-6 = interleukin-6; PCR = polymerase chain reaction.

† In the RCPCH case definition, additional features include abdominal pain, confusion, conjunctivitis, cough, diarrhea, headache, lymphadenopathy, mucous membrane changes, neck swelling, rash, respiratory symptoms, sore throat, swollen hands and feet, syncope, and vomiting.

‡ In the WHO case definition, cardiac involvement is defined as the presence of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including findings on echocardiogram or elevated levels of troponin/N-terminal pro–B-type natriuretic peptide).

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Usual onset is 2-6 wks after acute COVID

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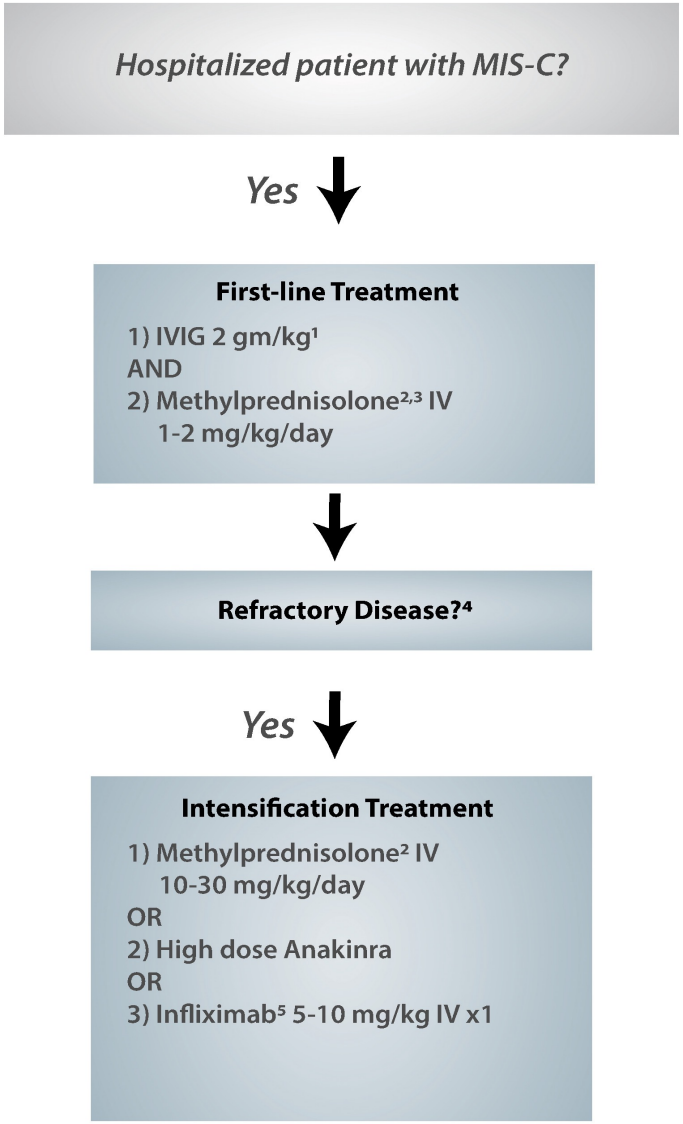

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MIS-C vs Kawasaki's

Guidance statement	Level of consensus
MIS-C and KD may share overlapping clinical features, including conjunctival infection, oropharyngeal findings (red and/or cracked lips, strawberry tongue), rash, swollen and/or erythematous hands and feet, and cervical lymphadenopathy.	High
Several epidemiologic, clinical, and laboratory features of MIS-C may differ from KD in the following ways: 1. There is an increased incidence of MIS-C in patients of African, Afro-Caribbean, and Hispanic descent, but a lower incidence in those of East Asian descent. 2. Patients with MIS-C encompass a broader age range, have more prominent GI and neurologic symptoms, present more frequently in a state of shock, and are more likely to display cardiac dysfunction (ventricular dysfunction and arrhythmias) than children with KD. 3. At presentation, patients with MIS-C tend to have lower platelet counts, lower absolute lymphocyte counts, and higher CRP levels than patients with KD. 4. Ventricular dysfunction is more frequently associated with MIS-C whereas KD more frequently manifests with coronary artery aneurysms; however, MIS-C patients without KD features can develop CAA.	Moderate to high
Epidemiologic studies of MIS-C suggest that younger children are more likely to present with KD-like features, while older children are more likely to develop myocarditis and shock.	Moderate

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