



Clinical Guidance: Evaluating Febrile Children for Multisystem Inflammatory Syndrome in Children (MIS-C)

June 25, 2020

The following is guidance based on expert opinion derived from the small number of the MIS-C cases reported and extrapolated from related syndromes, including Kawasaki disease and Kawasaki shock syndrome. It is meant to help IHS providers recognize and treat MIS-C as early as possible. These recommendations will likely change as more data become available and are not intended to replace clinical judgment.

Background: Although very rare, the emergence of Multisystem Inflammatory Syndrome in Children (MIS-C) has changed the way medical providers should evaluate fever in pediatric patients. MIS-C is a serious inflammatory disorder that appears to arise days to weeks after SARS-CoV-2 infection (the causative agent for COVID-19) and can present with a wide range of findings, including features of Kawasaki's Disease as well as cardiogenic shock.

Current CDC Case Definition:

- An individual aged <21 years presenting with fever*, laboratory evidence of inflammation**, 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 exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms.

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

***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*

Purpose: This guideline is intended to provide interim guidance which will assist IHS medical providers in the early recognition and management of MIS-C.

Recommendation: Carefully consider the diagnosis of MIS-C in pediatric patients presenting with any of the following:

- Fever for ≥ 4 days
- Fever for ≥ 3 days PLUS any of the following clinical/historical features:
 - Abdominal pain or diarrhea without a clear source
 - Conjunctivitis
 - Diffuse rash

- Mucositis (red or cracked lips, strawberry tongue)
- Hand or foot swelling
- Epidemiological link to COVID-19 (personal history of COVID-19 or close contact in past six weeks)
- Fever of any duration with shock and two of the above clinical/historical features

History and physical should be obtained with the following differential diagnosis in mind:

- Bacterial Infection/ Sepsis
- Kawasaki Disease
- Viral Infection (e.g., Adenovirus, Enteroviruses, EBV)
- Toxic Shock Syndrome
- Staph Scalded Skin Syndrome
- Rocky Mountain Spotted Fever
- Myocarditis
- Hypersensitivity Drug Reaction (e.g., DRESS, SJS, or Serum Sickness-like Reaction)

Laboratory Tests should initially include CBC with differential, Chem 7, CRP, ESR. Additional lab tests may be indicated as part of an evaluation for alternate causes (e.g., UA, blood cultures, LFTs) or to further evaluate a likely case of MIS-C (e.g., anti SARS-CoV-2 antibodies, COVID-19 antigen PCR, troponin, d-Dimer).

Initial Management: ***Patients presenting in shock should be immediately resuscitated per ED sepsis protocols, admitted/transferred to a Pediatric ICU, and evaluated for MIS-C.***

For stable patients, either of the following should prompt appropriate consultation and hospital admission for possible MIS-C:

- CRP ≥ 3 mg/dl OR
- ESR > 40 mm/hr

Patients with reassuring history, physical, and labs can be discharged home with follow-up in ≤ 48 hours and instructions to return if fever does not resolve in 72 hours or if other symptoms consistent with MIS-C develop.

Reporting: Healthcare providers should report any patient who meets the case definition to local, state, and territorial health departments. After hour phone numbers for health departments are available at the [Council of State and Territorial Epidemiologists website](#). For additional reporting questions, please contact CDC's 24-hour Emergency Operations Center at 770-488-7100.

References:

Centers for Disease Control and Prevention (CDC). <https://www.cdc.gov/mis-c/hcp/>

Children's Hospital of Philadelphia. <https://www.chop.edu/clinical-pathway/multisystem-inflammatory-syndrome-mis-c-clinical-pathway>

Seattle Children's Hospital. <https://seattlechildrens.sharefile.com/share/view/s4cc2c13eb974ed48>