HDVCH Guidelines for Management of Pediatric Patient with MIS-C – June 16, 1505

An emerging condition associated with current or recent SARS-CoV-2 infection
Spectrum Health Contact: Andrea Hadley

Multisystem Inflammatory Syndrome in Children (MIS-C) is a clinical entity believed to follow a SARS-CoV-2 infection or exposure. The clinical presentation is accompanied by significant hyper-inflammation similar to that of Kawasaki Disease or Toxic Shock Syndrome and can lead to organ dysfunction and shock. The pathogenesis is unclear however it is thought to develop 4-6 weeks after an infection when macrophage activation and acquired immunity is occurring.

The CDC has since released a health advisory statement to alert health care providers and organize a case reporting system. Both the Centers for Disease Control and the World Health Organization have developed case definitions to guide the clinical diagnosis. See the links below and the full case definitions are copied on page 4 of this document for your reference as well.
CDC MIS-C definition
WHO MIS-C definition

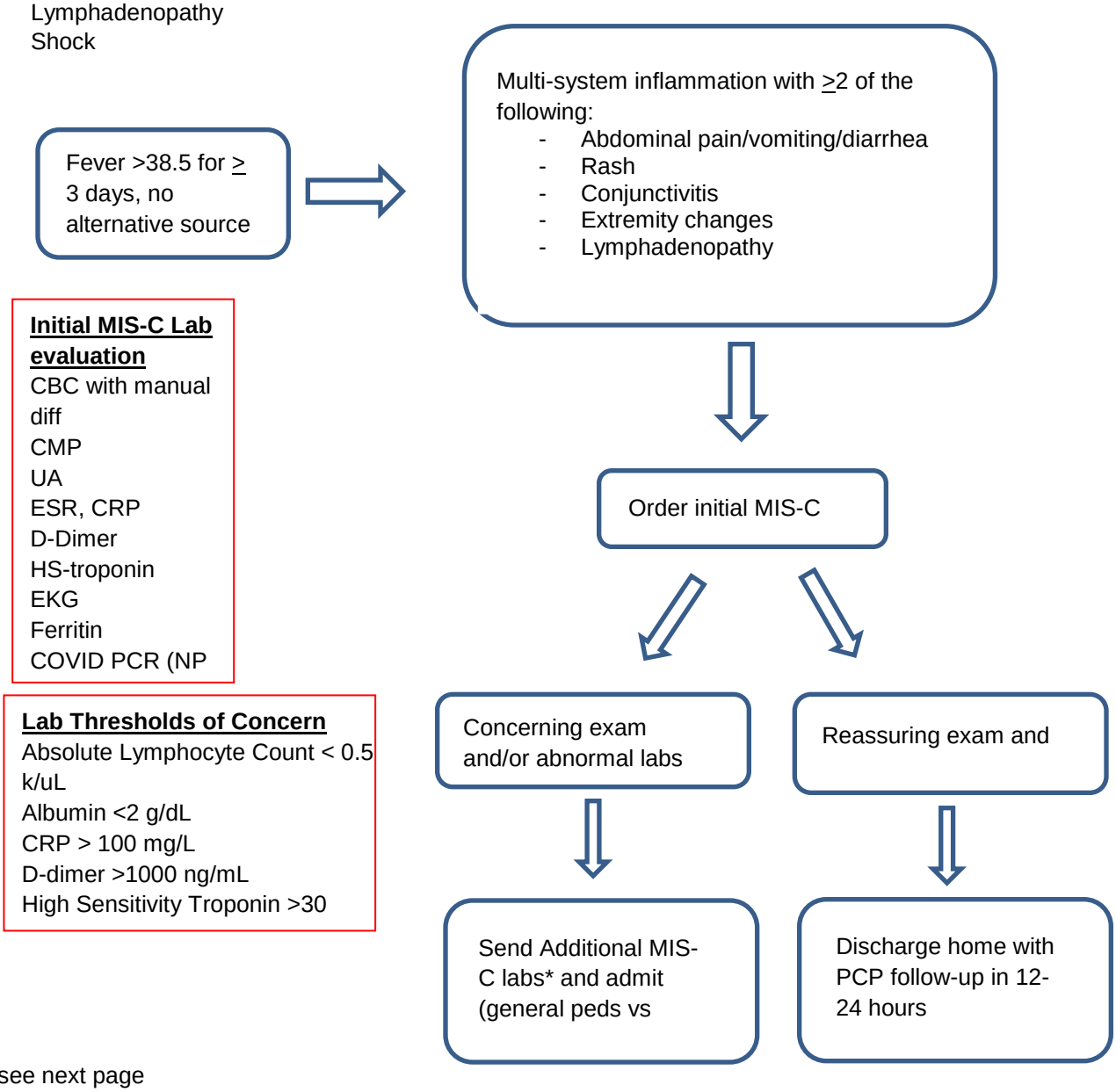
Children with MIS-C will most consistently present with prolonged fever and GI complaints (abdominal pain, vomiting, and diarrhea). Additional features include rash, extremity swelling, conjunctivitis, lymphadenopathy and appear very similar to Kawasaki Disease. The most concerning feature of MIS-C is progression to cardiovascular abnormalities (myocarditis, coronary aneurysms, ventricular dysfunction), and potentially shock. Children with MIS-C rarely exhibit respiratory complaints and death is rare.

Initial Workup/ED Evaluation

As MIS-C is an inflammatory syndrome, the initial laboratory workup is focused on uncovering signs of inflammation. Moreover, as the disease progresses, patients often develop end-organ dysfunction, in particular cardiac involvement and coagulopathies, and the recommended testing seeks to screen for those concerns as well.

Concerning presenting signs and symptoms:

- Persistent fever, not fully responsive to antipyretics
- GI complaints such as abdominal pain (may mimic appendicitis) and/or diarrhea
- Rash
- Conjunctivitis
- Headache
- Respiratory symptoms
- Sore throat
- Lymphadenopathy
- Shock



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Inpatient Evaluation

Additional MIS-C Labs to be collected for admitted patients

COVID PCR (NP swab x 2 total, 24 hrs apart)	PT/INR, PTT
COVID serologies if not sent	Fibrinogen
Film Array if COVID PCR negative	LDH
Blood Cx	Triglycerides
UA/UCx	BNP
VBG	Cytokine Panel
Procalcitonin	Echo
Peripheral Smear	CK

Daily lab monitoring

CBC with manual diff	CMP
ESR, CRP	Ferritin
PT, PTT	Fibrinogen
D-dimer	BNP, troponin if original values were elevated

Vital Sign Monitoring

Continuous cardiorespiratory monitoring and continuous pulse oximetry

Isolation

Place patient in severe respiratory isolation until COVID PCR is negative x 2 (24 hours apart)
Negative pressure not needed unless pt likely to undergo aerosolizing procedures

VTE prophylaxis

Complete VTE assessment within epic on admission and reassess daily. Chemical prophylaxis with lovenox is recommended for COVID patients >12 years of age who are hospitalized and who do not have a contra-indication. For patients <12 years of age, VTE prophylaxis is recommended for moderate or severe COVID 19 infection or if otherwise indicated per VTE assessment. However, for MIS-C, evidence based guidelines have not been developed at this time. VTE prophylaxis should be strongly considered for any patient with suspected MIS-C, especially if D-dimer is elevated, and this should be discussed with hematology team on a case by case basis. Risks and benefits should be discussed with the patient/family.

Subspecialty consultations

ID consult if MIS-C is being considered. ID team will be responsible for reporting the disease and for outpatient follow-up (labs, echo). ID will recommend additional consultations as indicated to rheumatology, cardiology, heme/onc, immunology. Cardiology will need to be consulted if EKG, BNP/troponin or Echo are abnormal, or there are other concerns.

Disease Reporting

ID team will be responsible for reporting if there is sufficient evidence to make the diagnosis

Treatment considerations

Treatment approach will be individualized and may include supportive care, IVIG, steroids, immunomodulators as further evidence develops.

CDC case definition:

A. Age < 21 years
B. Clinical presentation including **all** of the following:
   1. Fever >38.0C (100.4F) for >/= 24 hours or subjective fever lasting >/= 24 hours
   2. Laboratory evidence of inflammation, including but not limited to:
      - Elevated CRP
      - Elevated ESR
      - Elevated fibrinogen
      - Elevated procalcitonin
      - Elevated D-dimer
      - Elevated ferritin
      - Elevated LDH
      - Elevated IL-6 level
      - Neutrophilia
      - Lymphcytopenia
      - Hypoalbuminemia
   3. Severe illness requiring hospitalization
   4. Multisystem (2 or more) involvement
      - Cardiovascular
      - Renal
      - Respiratory
      - Hematologic
      - Gastrointestinal
      - Dermatologic
      - Neurologic
C. No alternative plausible diagnosis
D. Recent or current SARS-CoV-2 infection or exposure, with **any** of the following:
   - Positive SARS-CoV-2 RT-PCR
   - Positive serology
   - Positive antigen test
   - COVID-19 exposure within the 4 weeks prior to the onset of symptoms

   <u>Additional comments</u>
   - 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

WHO case definition:

A. Age 0-19 years
B. Fever for >/= 3 days
C. **At least 2** of the following clinical signs:
   - Rash, bilateral nonpurulent conjunctivitis, or mucocutaneous inflammation signs (oral, hands, feet)

- Hypotension or shock
- Cardiac dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiographic findings or elevated troponin/BNP
- Evidence of coagulopathy (prolonged PT or PTT; elevated D-dimer)
- Acute gastrointestinal symptoms (diarrhea, vomiting, or abdominal pain)

D. Elevated markers of inflammation, such as ESR, CRP, procalcitonin
E. No other obvious microbial cause of inflammation, including bacterial sepsis and staphylococcal or streptococcal toxic shock syndromes
F. Evidence of COVID-19, with any of the following:
   - Positive SARS-CoV-2 RT-PCR
   - Positive serology
   - Positive antigen test
   - Likely contact with an individual with COVID-19