Hackensack Meridian Children's Health

oneTEAM FOR SAFETY Hackensack Meridian Health

Multisystem Inflammatory Syndrome in Children (MIS-C)

Children generally have mild acute illness with COVID-19. However, a syndrome of multisystem inflammation has been recognized in some children and young adults. This potentially severe syndrome likely represents a post-infectious response to infection with SARS-CoV-2. There is much we do not know about this syndrome, including incidence, risks, disease spectrum, complications, optimal treatment, and potential sequelae. Although cardiogenic shock and death have been associated with this syndrome, most children have less severe illness and seem to respond readily to anti-inflammatory treatment. Early recognition and rapid initiation of anti-inflammatory seems to be key to preventing more severe complications.

This document serves as guidance to assist with early recognition, evaluation and treatment of children who may potentially have this syndrome and facilitate transfer to a children's hospital. Early recognition and treatment is vital to stop progressive inflammation and prevent progression to multi-organ system failure and shock.

The Center for Disease Control and Prevention (CDC) released a Health Advisory on May 14, 2020, which included a case definition for public health reporting. Although this definition provides a framework for identifying patients, it should not be used to diagnose or determine treatment for children with clinical suspicion of MIS-C.

CDC Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C)

- An individual aged <21 years presenting with fever[1], laboratory evidence of inflammation[2], 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

[1]Fever >38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours

[2]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

These recommendations are based on the best evidence at the time of publication. It is not meant to be a prescription for every patient. Clinical judgment based on each patient's unique situation remains vital.

Clinical Features

The clinical presentation of Pediatric Multisystem Inflammatory Syndrome Potentially Associated with COVID-19 include persistent fever and other signs of an inflammatory response. These features are not specific and overlap with Kawasaki disease—especially atypical or incomplete Kawasaki disease—toxic shock syndrome, and other infectious or inflammatory conditions. Early recognition and intervention can stop the progression of inflammation, decreasing the risk of multi-organ system failure and shock.

Presenting symptoms, listed by more frequently reported system to less

Persistent fever (> 101.3°F [38.5°C])

Gastrointestinal:
- Abdominal pain
- Diarrhea
- Vomiting

Dermatological
- Rash

Neurological:
- Headache
- Lethargy
- Confusion

Respiratory:
- Tachypnea
- Labored breathing

Head and Neck:
- Mucus membrane changes
- Sore throat

Musculoskeletal
- Swollen hands and feet

Other symptoms or exam findings (in no particular order):

Cardiovascular:
- Hypotension
- Chest pain
- Hepatosplenomegaly

Immunological:
- Lymphadenopathy

Ophthalmological:

- Red eye
- Non-exudative conjunctivitis/uveitis

Musculoskeletal

- Arthritis
- Myalgia/Myositis

Clinical findings:

Shock

Kawasaki disease (complete or incomplete)

Myocardial dysfunction (laboratory evidence and echocardiography)

Acute respiratory failure (usually secondary to cardiogenic shock)

Acute kidney injury

Serositis (pleural, pericardial, and/or ascitic effusions)

Abnormal results compatible with Pediatric Multisystem Inflammatory Syndrome Potentially Associated with COVID-19

Hematologic:

- Lymphopenia
- Neutrophilia
- Anemia
- Thrombocytopenia

Inflammatory Markers (Elevated)**:**

- C-reactive protein
- Erythrocyte sedimentation rate
- Ferritin
- D-dimer
- Fibrinogen
- Procalcitonin (if available)
- IL-6 (if available)

Cardiac Markers (Elevated)**:**

- Troponin
- BNP

Chemistry:

- Hypoalbuminemia
- Elevated BUN and/or creatinine
- Elevated LDH
- Transaminitis
- Hypertriglyceridemia

Coagulation:

- Coagulopathy

Urinalysis:

- Proteinuria

Echocardiography:

- Depressed left ventricular function
- Coronary artery dilatation or aneurysm
- Valvulitis (especially mitral valve regurgitation)
- Pericardial effusion

Chest Radiograph:

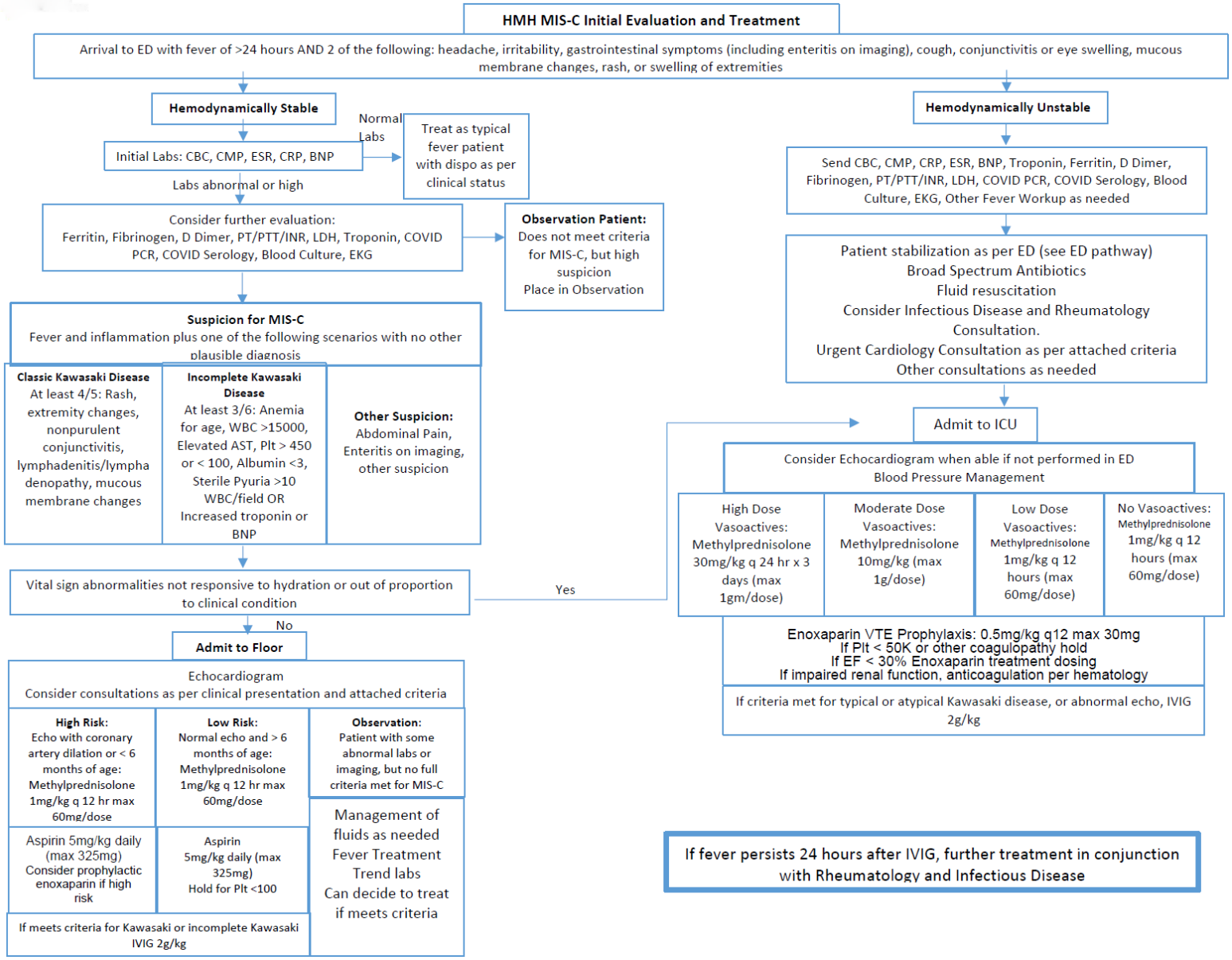
- Can be normal
- Patchy infiltrates
- Focal consolidation
- Pleural effusion
- Atelectasis

Chest CT:

- Similar to chest radiograph, although ground glass opacities have been seen
- Pulmonary embolus

Abdominal Ultrasound or CT of the abdomen with IV and oral contrast:

- Ascites
- Bowel and/or mesenteric inflammation
- Mesenteric lymphadenopathy
- Terminal ileitis
- Pericholecystic edema



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Lab Schedule

On Initial Presentation

- All patients with a diagnosis of MIS-C should have CBC, CMP, CRP, ESR, troponin, ferritin, D-Dimer, LDH, PT/PTT/INR, COVID PCR, COVID serology, blood culture
- Send blood gas with lactate if shock suspected at any point of admission
- If vomiting, amylase and lipase
- If diarrhea, consider GI Pathogen Panel (GiPP)

Consider daily labs as per patient status

- CBC, CMP, CRP
- Troponin and BNP if initially abnormal
- Ferritin, D-Dimer, PT/PTT/INR

Continued Care After Initial Treatment

Inpatient Treatment

- Continue methylprednisolone until afebrile for > 24 hours, then change to oral prednisone 1mg/kg BID
- Patient may be discharged once afebrile for 24-36 hours

Outpatient Follow Up

- Obtain CBC, CRP, ESR, and if elevated at discharge, ferritin, CBP, D-Dimer, PT/PTT/INR
- Steroid taper managed by rheumatology (for mild cases taper over 2-3 weeks, moderate to severe 6-8 weeks)

Cardiology Consult Indications

Urgent Echo:

- Hemodynamic compromise
- Significant dysrhythmia

Urgent Consultation

- BNP >400
- Troponin > 1

Non-Urgent Echo:

- KD Presentation without hemodynamic compromise
- Other dysrhythmia on ECG

Other Consult Indications

Hematology:

- Pancytopenia
- Hgb < 8.0
- DVT or other thrombus

Gastroenterology

- GI Bleeding
- Signs of pancreatitis
- Liver Failure

Neurology:

- Stroke
- Evidence of encephalitis
- Abnormal neurology examination

Consultations called overnight should be seen by 12pm to allow for timely team discussions

Care providers should wear personal protective equipment (PPE) as for patients with suspected or confirmed COVID-19

Patient must be on continuous cardiorespiratory monitor with blood pressure and pulse oximetry

For patients with respiratory failure, cardiac failure and/or shock, management and resuscitation follows PALS/ACLS guidelines.

> Fluid resuscitation must be adequate to maintain perfusion while monitoring for signs of worsening cardiac status

Testing and evaluation to be done as outlined above

Administer empiric antibiotics per local sepsis protocols after appropriate cultures have been obtained

If the syndrome is compatible with Kawasaki disease, treat with IVIG 2 gm/kg (maximum dose 100 gms) and aspirin per American Heart Association guidance, otherwise steroids are the preferred initial treatment

If aspirin is not being given, or if there is need to consider venous thromboembolism (VTE) prophylaxis, consultation with pediatric hematology is indicated (for anticoagulation guidance, refer to the pediatric guideline posted on the HMH Maestro COVID-19 site: https://HMHMaestro.org/covid-19-action-center/ → Protocols/Research → HMH Protocols and Policies → Pediatrics → Anticoagulation Guidelines for Patients with COVID-19)

Monitoring

Monitor closely for signs of respiratory or cardiovascular deterioration

Monitor for clinical signs of worsening inflammation:

- Worsening fever
- Cardiorespiratory deterioration
- Worsening gastrointestinal symptoms
- Increasing hepatosplenomegaly or lymphadenopathy
- Extending rash
- Worsening neurological symptoms
- Laboratory signs of increasing inflammation
- Falling blood cell counts
- Rising ferritin
- Unexpectedly low or falling ESR
- Rising fibrinogen or new onset low fibrinogen
- Rising ALT, AST or LDH
- Rising triglycerides
- Rising D-dimers
- Low serum sodium with worsening renal function

Contact Information for Consultations and Transport to a Children's Hospital:

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Consultation with **Pediatric Emergency Medicine**

K Hovnanian Children's Hospital (JSUMC): 732-776-4220
Joseph M Sanzari Children's Hospital (HUMC): 551-996-5430

Consultation with **Pediatric Intensivist** for continued management to PICU

K Hovnanian Children's Hospital (JSUMC): PICU: 732-776-4357
Joseph M Sanzari Children's Hospital (HUMC): PICU: 551-996-2403, Attending: 551-996-2000 x71816

Consultation with **Pediatric Cardiologist**

K Hovnanian Children's Hospital (JSUMC): Page Operator: 732-775-5500
Joseph M Sanzari Children's Hospital (HUMC): 201-441-9980, press 1

Consultation with **Pediatric Rheumatology**

K Hovnanian Children's Hospital (JSUMC): 551-996-5306
Joseph M Sanzari Children's Hospital (HUMC): 551-996-5306

Consultation with **Pediatric Neurology**

K Hovnanian Children's Hospital (JSUMC): Page Operator: 732-775-5500
Joseph M Sanzari Children's Hospital (HUMC): 551-996-3200

Consultation with **Pediatric Infectious Diseases**

K Hovnanian Children's Hospital (JSUMC): Page Operator: 732-775-5500
Joseph M Sanzari Children's Hospital (HUMC): 551-996-5308

Consultation with **Pediatric Hematology-Oncology**

K Hovnanian Children's Hospital (JSUMC): Page Operator: 732-775-5500
Joseph M Sanzari Children's Hospital (HUMC): 551-996-KIDS (551-996-5437)

To arrange **transport** to a Children's Hospital with multi-specialty consultants call the

K Hovnanian Children's Hospital (JSUMC): Transfer Center 732-776-3486
Joseph M Sanzari Children's Hospital (HUMC): Transfer Center 855-367-4862

Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19), CDC Health Advisory Issued May 14, 2020, (https://emergency.cdc.gov/han/2020/han00432.asp, accessed May 24, 2020)

Royal College of Paediatrics and Child Health, Guidance: Paediatric multisystem inflammatory syndrome temporally associated with COVID-19 (https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatric-multisystem-%20inflammatory%20syndrome-20200501.pdf, accessed May 7, 2020)

https://www1.nyc.gov/assets/doh/downloads/pdf/han/alert/2020/covid-19-pediatric-multi-system-inflammatory-syndrome.pdf (accessed May 7, 2020)

BW McCrindle, et al. Diagnosis, Treatment and Long-Term Management of Kawasaki Disease: A Scientific Statement for Health Professionals From the American Heart Association, *Circulation*, 2017;135:e927-e999 (https://www.ahajournals.org/doi/full/10.1161/cir.0000000000000484, accessed May 8, 2020)