Multisystem Inflammatory Syndrome in Children (MIS-C): Guidance for Ambulatory Care Providers

Multisystem inflammatory syndrome in children (MIS-C) appears to be an inflammatory response to a prior SARS-CoV-2 infection. Patients with MIS-C reported to the New York City (NYC) Department of Health and Mental Hygiene have ranged in age from infancy to young adulthood. Most MIS-C patients present with fever, laboratory evidence of inflammation, and multisystem abnormalities which are usually not respiratory in nature. Rash, abdominal pain, vomiting, and/or diarrhea have been present in at least half of the MIS-C cases in NYC. Clinical features of MIS-C could resemble those seen in other diseases, including Kawasaki disease and/or toxic shock syndrome.

Signs and Symptoms

Signs and symptoms related to MIS-C can be transient. If a caregiver or another clinician has noted a sign or symptom consistent with MIS-C during a patient’s febrile illness that is not observed during your own evaluation, consider the previous report to be accurate and representative of an evolving illness. Children and adolescents diagnosed with MIS-C could also have bacterial (e.g., cervical lymphadenitis, urinary tract infection) or viral co-infections (e.g., Epstein-Barr virus, parvovirus).

Illness Assessment

Children may have a history of a COVID-like illness, or of being exposed to a person with COVID-like illness, in the preceding one to two months. While there continues to be community transmission of SARS-CoV-2 in NYC, providers should consider MIS-C even if there is no known history of COVID-19 illness or exposure.

Refer ill-appearing children with a possible MIS-C case to the emergency department (ED) of the children’s hospital where they typically obtain care, or to the closest ED where care by pediatric subspecialists is available, when possible. For MIS-C, a multidisciplinary approach to evaluation and treatment that involves pediatric subspecialists is critical, as is access to clinical and diagnostic laboratory testing with rapid turnaround time for results. Cases can progress rapidly to shock.

For well-appearing children with an illness potentially compatible with MIS-C who do not meet criteria for ED referral initially, close follow-up is recommended. Laboratory testing may be considered, but is not essential for the evaluation of MIS-C in the ambulatory care setting for an otherwise well-appearing child. If laboratory testing is conducted, increasing inflammatory markers (e.g., C-reactive protein) can be indicative of disease progression.
Laboratory Testing

More than 75% of NYC children meeting criteria for MIS-C have had laboratory evidence of SARS-CoV-2 infection (i.e., positive by viral RNA-based test and/or serology). However, detection of antibody to SARS-CoV-2 should not be considered solely diagnostic of MIS-C, and documenting current or past infection by viral RNA and/or serology does not change management of patients with MIS-C. Still, conducting this testing for children with possible MIS-C may help to more fully characterize patients with MIS-C and enable a better understanding of this emerging syndrome.
Evaluation of Multisystem Inflammatory Syndrome in Children (MIS-C) in the Ambulatory Setting

**STEP 1 - Assess for severe symptoms**
(e.g., concern for shock or sepsis [hypotension, tachycardia, and/or hypoperfusion], altered mental status, lethargy, seizures, severe abdominal pain, or otherwise ill- appearance)

- Ill-appearing child
  - REFER IMMEDIATELY TO NEAREST ED*

- Well-appearing child

**STEP 2 - Consider the diagnosis of Multisystem Inflammatory Syndrome in Children (MIS-C) if FEVER lasting at least 48-72 hours AND signs/symptoms from 2 or more of the following symptom categories:**

- **GI Symptoms** (e.g., nausea, abdominal pain, vomiting, diarrhea)
- **Rash** (variable in appearance, including but not limited to maculopapular, scarlatiniform)
- **Conjunctivitis** (e.g., bilateral bulbar conjunctival injection without exudate)
- **Oral mucosal changes** (e.g., erythema and cracking of lips, strawberry tongue, and/or erythema of oropharyngeal mucosa)
- **Extremity changes** (e.g., erythema and/or edema of the hands and feet)
- **Neurologic or Psychiatric Symptoms** (e.g., headache, irritability, cranial nerve palsy)
- **Lymphadenitis** (neck swelling causing significant pain and/or sore throat)

**Fever PLUS signs/symptoms from 2 or more symptom categories?**

- **YES**
  - Consider MIS-C and alternative diagnoses

- **NO**
  - Consider MIS-C and alternative diagnoses, provide anticipatory guidance, and **re-evaluate** the next day and repeat **Steps 1, 2**

**STEP 3 – Additional evaluation**
If laboratory testing is performed, consider CBC with differential, Comprehensive Metabolic Panel (e.g. “Chem-20”), C-reactive protein (CRP), SARS-CoV-2 serology

- **Abnormal results on lab testing**
  - Consider ED referral for more extensive evaluation, including additional laboratory testing and subspecialty consultation.

- **Normal results on lab testing**
  - Re-evaluate the next day, **repeat Steps 1, 2**, and consider repeat laboratory testing as indicated by clinical course.

- **Lab testing not performed**
  - Re-evaluate the next day, **repeat Steps 1, 2**

* When possible, the patient should be referred to an ED where consultation by pediatric subspecialists is available.

The NYC Health Department may change recommendations as the situation evolves. 6.24.20