Multisystem Inflammatory Disease in Children (MIS-C) Quicksheet

October 2024

Multisystem Inflammatory Syndrome in Children (MIS-C)

In spring 2020, doctors recognized a new pattern of severe illness affecting children who had recently experienced otherwise unremarkable COVID-19 infections. The illness was named Multisystem Inflammatory Syndrome in Children (MIS-C) in the US and was characterized by fever, body-wide inflammation, and disease in several body systems severe enough to result in hospitalization. Disease incidence peaked in 2020 and declined substantially over the following 3 years. By 2024, MIS-C incidence had decreased to fewer than 10 cases per year in California.

MIS-C patients are, by definition, under 21 years of age and most cases occur in school age children. It remains unknown why only certain children develop MIS-C after COVID-19 infections and why disease incidence has declined so dramatically. COVID-19 is not unique in causing inflammatory disease after recovery from infection; the pattern has been seen with both viruses and bacteria. To better understand the potential causes, optimal treatment, and outcomes of MIS-C, CDPH conducts surveillance for MIS-C cases in conjunction with the CDC.

Reporting MIS-C cases

Clinicians should:

- Report **any hospitalized person under 21 years of age with a recent COVID-19 infection and new onset of fever and systemic inflammation affecting more than 1 organ system** to patient's local health department (LHD). Provide or assist LHD in obtaining hospital records sufficient to complete the MIS-C Case Report Form. At a minimum this will include the discharge summary and all labs/studies.
- Also report any person whose death certificate lists MIS-C as a cause of death or a condition contributing to death.

Contact CDPH at covmis-c@cdph.ca.gov for assistance with reporting or request for clinical consultation.

Case Definition

To meet the case definition a patient must satisfy all clinical criteria AND satisfy linkage to a recent COVID-19 infection in one of three ways (see below). A patient may also meet the case definition based on vital records criteria alone (see below).

Clinical Criteria

- <21 years of age
- Subjective or documented fever (temperature ≥38.0° C, 100.4°F)
- Clinical severity requiring hospitalization or resulting in death.
- Evidence of systemic inflammation indicated by C-reactive protein ≥3.0 mg/dL
- Absence of a more likely alternative diagnosis*
- New onset manifestations in at least two of the following categories:
    1. Cardiac involvement indicated by:
        - Left ventricular ejection fraction <55%, **OR**
        - Coronary artery dilatation, aneurysm, or ectasia, **OR**
        - Troponin elevated above laboratory normal range,

or indicated as elevated in a clinical note.

2. Mucocutaneous involvement indicated by:
   - Rash, **OR**
   - Inflammation of the oral mucosa (e.g., mucosal erythema or swelling, drying or fissuring of the lips, strawberry tongue), **OR**
   - Conjunctivitis or conjunctival injection (redness of the eyes), **OR**
   - Extremity findings (e.g., erythema [redness] or edema [swelling] of the hands or feet)
3. Shock**
4. Gastrointestinal involvement indicated by:
   - Abdominal pain, **OR**
   - Vomiting, **OR**
   - Diarrhea
5. Hematologic involvement indicated by:
   - Platelet count <150,000 cells/μL **OR**
   - Absolute lymphocyte count (ALC) <1,000 cells/μL

** If documented by the clinical treatment team, a final diagnosis of Kawasaki Disease should be considered an alternative diagnosis and these cases should not be reported.*

*** Clinician documentation of shock meets this criterion.*

Linkage to recent COVID-19 infection

- Confirmatory laboratory evidence:
  - Detection of SARS-CoV-2 ribonucleic acid (RNA) in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen using a diagnostic molecular amplification test (e.g., polymerase chain reaction [PCR]), **OR**
  - Detection of SARS-CoV-2 specific antigen in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen, **OR**
  - Detection of SARS-CoV-2 specific antibodies^ in serum, plasma, or whole blood associated with current illness resulting in or during hospitalization.

****Positive molecular or antigen results from self-administered testing using over-the-counter test kits meet laboratory criteria.*

^Includes a positive serology test regardless of COVID-19 vaccination status. Detection of anti-nucleocapsid antibody is indicative of SARS-CoV-2 infection, while anti-spike protein antibody may be induced either by COVID-19 vaccination or by SARS-CoV-2 infection.

- Epidemiology Linkage
  - Close contact‡ with a confirmed or probable case of COVID-19 disease in the 60 days prior to hospitalization.

‡Close contact is generally defined as being within 6 feet for at least 15 minutes (cumulative over a 24-hour period). However, it depends on the exposure level and setting; for example, in the setting of an aerosol-generating procedure in healthcare settings without proper personal protective equipment (PPE), this may be defined as any duration.

Vital Records Criteria

- A person aged <21 years of age whose death certificate lists MIS-C or multisystem inflammatory syndrome as an underlying cause of death or a significant condition contributing to death.

Case Classification

Confirmed:

- Meets clinical criteria AND confirmatory laboratory evidence linkage criteria

Probable:

- Meets clinical criteria AND epidemiologic linkage criteria

Suspect:

- Meets the vital records criteria

Infection control precautions for possible MIS-C cases

MIS-C is not infectious, however, the patient may still be infectious with the initial COVID-19 infection.

If patient may be infectious and is in a healthcare setting, please follow CDC infection control guidance for SARS-CoV-2. If patient is not in a healthcare setting, please follow CDC guidance for Preventing Spread of Respiratory Viruses When You're Sick

Additional Resources

- CDPH MIS-C web page
- CDC MIS web page
- CDC Clinical Treatment
- MIS-C Case Reporting Form