
September 22, 2021

KEY MESSAGES AND ACTION ITEMS:

- Given the recent surge in COVID-19 infections across Chicago and Illinois, clinicians should familiarize themselves with the clinical presentation, evaluation, management, and reporting requirements for Multisystem Inflammatory Syndrome in Children (MIS-C).
- MIS-C is a rare but severe post-infectious sequela of COVID-19 in children marked by fever, elevated inflammatory markers, and severe illness involving two or more organ systems.
- In Chicago and nationally, increases in MIS-C cases are seen 3 to 4 weeks following surges in COVID-19 cases in the community, reflecting the delay between initial SARS-CoV-2 infection and subsequent inflammatory response. It often occurs after asymptomatic or mild infections, so a lack of known exposure or infection following periods of high local transmission should not rule out the diagnosis.
- Follow the MIS-C Clinical Pathway for cases of suspected MIS-C, including timely transfer to intensive care.
- Report MIS-C in Chicago residents to CDPH by following instructions on the HAN page: https://www.chicagohan.org/covid-19/mis-c OR follow the two steps below:
  1) Fill out the MIS-C case report form link available at https://redcap.link/misc_afm and upload it confidentially through the same portal (here).
  2) Enter suspect MIS-C cases into the COVID-19 I-NEDSS module – subsection “Multisystem Inflammatory Syndrome”.

Background: In the spring of 2020, clinicians in the United Kingdom reported observation of a severe inflammatory syndrome in children with recent proven, or highly suspected history of, COVID-19. Since the first recognition of this syndrome, increased cases of MIS-C have been reported on local and national levels following peaks in acute COVID infection. On May 21, 2020 (updated March 1, 2021) the Illinois Department of Public Health issued a Health Advisory with interim guidance, a MIS-C clinical pathway developed by the Illinois MIS-C Workgroup, and public health reporting requirements. Given the recent surge in Delta variant COVID-19 infections across Chicago and Illinois, clinicians should familiarize themselves with the clinical presentation, evaluation, management and reporting requirements for MIS-C.

In order to prepare for identification of additional MIS-C cases, CDPH prepared an annual report (attached) of cases reported in Chicago residents under 21 years-old, during April 2020 to June 2021. Chicago observed 60 MIS-C cases in this time period with no reported deaths. Important findings include:

- The median age was 10 years (IQR=7.2); 62% of reported cases were among males; 50% Black, non-Latinx, 37% Latinx, and 7% White, non-Latinx.
- 77% of the MIS-C cases had no reported significant comorbidity. The most commonly identified comorbidity among cases was obesity; 15% of all cases had a BMI greater than 30.
- 31 of 59 (52%) cases did NOT report having a preceding COVID-like illness but 53 of 60 (88%) had a positive SARS-CoV-2 serology test.
The median number of days between MIS-C illness onset and hospital admission was 3 days.

Higher rates of MIS-C were reported in the Southwest and West sides of Chicago, similar to the overall rates of COVID-19 disease in these regions.

Frequencies of involved organ system and associated laboratory abnormalities are detailed with similarities to other recent publications.5,6,7

**Clinical Presentation:** Patients with MIS-C usually present with persistent fever, abdominal pain, vomiting, diarrhea, skin rash, mucocutaneous lesions and, in severe cases, with hypotension and shock. They have elevated laboratory markers of inflammation (e.g., CRP, ferritin), and in a majority of patients laboratory markers of damage to the heart (e.g., troponin; B-type natriuretic peptide (BNP) or proBNP). The child may have been infected from an asymptomatic contact and, in some cases, the child and their caregivers may not even know they had been infected. See CDC resources8,9 for healthcare providers: “How to Recognize MIS-C”.

**MIS-C 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°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

Notes:
- 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 and report to CDPH by the process below.
- ICD-10-CM Diagnosis Code for MIS-C and MIS-A: M35.81

**Clinician Recommendations:**

- Clinicians should maintain awareness for signs and symptoms of MIS-C for at least 4-6 weeks after periods of local high COVID transmission.
- Refer to the MIS-C Clinical Pathway developed by the Illinois MIS-C Workgroup for children with suspected MIS-C to ensure timely triage, treatment and multidisciplinary consultation.
- Children with MIS-C may require ICU-level care and early transfer should be considered if severe features are present in accordance with MIS-C Clinical Pathway.
- AAP Interim Management Guidance and a CDC COCA call are also available for review.10,11

**MIS-C Reporting:**

1. **Case Report Form:** Complete the case report form (CRF) linked online at https://redcap.link/misc_afm, then scan and upload it through the same portal (preferred).
   - Alternatively, you could send the CRF by encrypted email to maria.joseph@cityofchicago.org.
   - Ideally, the case report form includes information on patient discharge but notification of the suspect case should occur right away. We may need to follow-up to obtain this information later.
   - If you need support filling out the form, please email maria.joseph@cityofchicago.org and indicate a point of contact and direct phone number for our investigators to reach you to obtain appropriate medical records to submit the form to CDC.
2. **I-NEDSS entry**: Enter suspect MIS-C cases into the COVID-19 I-NEDSS module – subsection “Multisystem Inflammatory Syndrome”. At this time, there does not have to be a positive COVID test in order to enter into the module. It can be an epi link, COVID-like illness, or a positive molecular, antigen, or antibody test. If your lab or a commercial send out lab does not have the ability to run serologic testing, consider drawing serum and saving it prior to any treatments.

**Additional information and References:**

2. CDC Health Alert: [https://emergency.cdc.gov/han/2020/han00432.asp](https://emergency.cdc.gov/han/2020/han00432.asp)
5. MMWR on MIS-C: [COVID-19–Associated Multisystem Inflammatory Syndrome in Children — United States, March–July 2020 | MMWR (cdc.gov)](https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6921a2.htm)
8. CDC MIS-C page: [Information for Healthcare Providers about Multisystem Inflammatory Syndrome in Children (MIS-C) | CDC](https://www.cdc.gov/mis/mis-c/hcp/provider-resources/index.html)
12. CDPH MIS-C HAN page: [https://www.chicagohan.org/covid-19/mis-c](https://www.chicagohan.org/covid-19/mis-c)