



Date: November 8, 2021

BCD 2021-09

To: Wisconsin Clinicians, Hospitals, Clinics, Local and Tribal Health Departments

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## Increased Incidence of Multi-System Inflammatory Syndrome in Children

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#### Summary

- Since September 1, 2021, 25 children have been diagnosed with Multi-System Inflammatory Syndrome in Children (MIS-C).
- The Wisconsin Department of Health Services (DHS) expects the incidence of MIS-C diagnoses to increase over the next few months.
- The first COVID-19 vaccine for children 5-11 years old was approved in early November, so vaccination in this group is just beginning.
- DHS now prioritizes prompt reporting of suspected cases of MIS-C and Multi-system Inflammatory Syndrome in Adults (MIS-A).
- MIS-C is a rare but serious condition associated with COVID-19 in which different body parts become inflamed, including the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal organs. These patients may require intensive care unit admission for cardiac and/or respiratory support and testing for SARS-CoV-2 virus may be positive or negative.
- MIS-A is a rare but severe complication of COVID-19. Clinical manifestations include fever, cardiovascular, gastrointestinal, and mucocutaneous manifestations, and elevated markers of inflammation. Like MIS-C, it occurs after a delay of about two to six weeks from the initial SARS-CoV-2 infection. Recognizing the clinical manifestations of MIS-A can be more complicated than in MIS-C because of chronic comorbid conditions in adults and the potential phenotypic overlap with acute COVID-19. Cases of MIS-A appear to be much less common than MIS-C.
- Wisconsin clinicians and health departments are requested to report any cases of MIS-C or MIS-A that have occurred in their jurisdiction to DHS via the Wisconsin Electronic Disease Surveillance System (WEDSS) using the MIS-C or MIS-A disease incident. Case reports should be added to the notes section on the investigation tab or uploaded to the filing cabinet. Please include the clinical information listed in the body of this message. Refer to the case definitions for each syndrome below as there are differences in the presentations of MIS-C and MIS-A cases, and the case definitions have been updated by the Centers for Disease Control and Prevention (CDC) since originally presented.

## Background

### MIS-C

This inflammatory syndrome may occur days to weeks after acute COVID-19 illness and has features which overlap with Kawasaki Disease and Toxic Shock Syndrome. Inflammatory markers may be elevated, and fever and abdominal symptoms may be prominent. Rash may also be present. Myocarditis and other cardiovascular changes may be seen. Additionally, some patients have developed cardiogenic or vasogenic shock and required admission to an intensive care unit.

The syndrome may include:

- A child presenting with persistent fever, markers of inflammation (e.g., neutrophilia, elevated C-reactive protein, and lymphopenia), and evidence of multi-organ dysfunction (e.g., shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder). This may include children meeting full or partial criteria for Kawasaki disease.
- Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, and infections associated with myocarditis such as enterovirus. Clinicians should not delay seeking expert advice while waiting for results of these investigations.

Early recognition by pediatricians and prompt referral to an in-patient specialist, including to critical care, is essential. This syndrome should be considered by pediatricians and specialists, particularly when other microbial etiologies have not been identified.

Pediatricians and specialists should elicit any recent history of illness with COVID-19 or close contact with individuals who are known to have COVID-19 in children presenting with symptoms that are compatible with MIS-C.

Most patients who have presented with this syndrome have tested positive for the SARS-CoV-2 virus with a diagnostic molecular test, or were positive on a serologic test.

Testing and Treatment:

- Diagnostic testing to detect the presence of SARS-CoV-2, the virus that causes COVID-19, or corresponding antibody testing should be performed in patients who are under 21 years of age and present with symptoms compatible with MIS-C.
- Patients should receive supportive treatment. Health care providers should provide disease-specific treatments as appropriate.

Case Reporting:

- COVID-19-Associated MIS-C should be reported to DHS for any patient who meets the following CDC case definition:

#### CDC Case Definition for MIS-C

An individual aged <21 years presenting with fever<sup>i</sup>, laboratory evidence of inflammation<sup>i</sup>, and evidence of clinically severe illness requiring hospitalization, with multisystem ( $\geq 2$ ) 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 four weeks prior to the onset of symptoms

Fever  $>38.0^{\circ}\text{C}$  for  $\geq 24$  hours, or report of subjective fever lasting  $\geq 24$  hours

<sup>§</sup>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

## MIS-A

The CDC is collecting reported cases of MIS-A to learn more about this recently-described phenomenon.

Since June 2020, there have been several reports of MIS-A. CDC [recently published](#) a number of cases that fit the description of MIS-A. This report shows the way the syndrome appears in adults may be more complicated than in children. For example, a significant number of patients with MIS-A had no preceding respiratory symptoms and negative results on SARS-CoV-2 PCR testing, indicating that the syndrome may be a post-infectious process with variable timing of onset.

### CDC Case Definition for MIS-A

1. Age  $\geq 21$  years either with subjective fever or documented fever ( $\geq 38.0\text{ C}$ ) for  $\geq 24$  hours prior to or within three days of hospitalization\*; AND
2. A positive SARS-CoV-2 test during the current illness (by RT-PCR, serology, or antigen detection); AND
3. Laboratory evidence of severe inflammation\*\*; AND
4. Illness requiring hospitalization for  $\geq 24$  hours; AND
5. At least three of the following clinical criteria occurring within 3 days of hospitalization\*. At least one must be a primary clinical criterion.
  - Primary clinical criteria:
    - Severe cardiac illness†;
    - Rash AND non-purulent conjunctivitis
  - Secondary clinical criteria:
    - New-onset neurologic signs and symptoms‡
    - Shock or hypotension not attributable to medical therapy (e.g., sedation, renal replacement therapy);
    - Abdominal pain, vomiting, or diarrhea
    - Thrombocytopenia (platelets  $<150,000$  / microliter)

AND

6. No alternative plausible diagnosis for the above signs and symptoms (e.g., bacterial sepsis, exacerbation of a chronic medical condition)

\*This criterion must be met by the end of hospital day three, where the date of hospital admission is hospital day zero.

\*\*Elevated levels of at least two of the following: C-reactive protein, ferritin, IL-6, erythrocyte sedimentation rate, procalcitonin

†Includes myocarditis, pericarditis, coronary artery dilatation/aneurysm, or new onset:

- Right or left ventricular dysfunction (LVEF  $<50\%$ ), second/third degree A-V block, or ventricular tachycardia. Cardiac arrest alone does not meet this criterion.

‡Includes encephalopathy in a patient without prior cognitive impairment, seizures, meningeal signs, or peripheral neuropathy (including Guillain-Barré syndrome)

If any Wisconsin hospital providers or local health departments are aware of current or former patients meeting criteria for MIS-A, DHS requests that you please report clinical information about these cases using WEDSS. Cases of MIS-A should be reported in WEDSS using the MIS-A disease category.

All case reports of MIS-C and MIS-A should include the following information:

- History and Physical Examination
- Physician Consultations (Infectious Disease, Rheumatology, Cardiology Hematology, Dermatologic)
- Laboratory Results (Diagnostic and Chemistry)
- Radiology Results (if performed)
- Echocardiogram Results (if performed)
- Treatment Log
- Daily Vitals Log
- Discharge Summary

Wisconsin providers should report suspected cases of MIS-C and MIS-A to DHS via WEDSS, or by calling the Epidemiology Section at (608) 267-9003. The DHS epidemiology team will review any case reports and coordinate securing medical records and chart abstraction as necessary.

Questions about MIS-C or MIS-A reporting can be directed to the Communicable Disease Epidemiology Section at DHS by calling 608-267-9003 or via email to [DHSCDESOutbreaks@dhs.wisconsin.gov](mailto:DHSCDESOutbreaks@dhs.wisconsin.gov).