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## Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019

### Summary

On May 14, 2020, the U.S. Centers for Disease Control and Prevention issued a health alert regarding children with signs and symptoms of a severe multisystem inflammatory syndrome (MIS-C) potentially associated with SARS-CoV-2 infection.<sup>1</sup> Patients have presented with persistent fever and a constellation of symptoms including hypotension, multiorgan involvement and elevated inflammatory markers. As this is an unusual illness and is associated with a reportable condition, hospitals and health care providers should immediately report cases meeting the MIS-C case definition to their respective local health departments. Local health departments should report cases to CDPH.

### Background

Compared with adults, cases of COVID-19 in children have been reported less often and have been less severe. In contrast, children with MIS-C have presented with persistent fever and a constellation of symptoms shared by Kawasaki disease (KD) or Toxic Shock Syndrome (TSS) including hypotension, multiorgan (e.g., cardiac, gastrointestinal, renal, hematologic, dermatologic or neurologic) involvement and elevated inflammatory markers.<sup>2</sup> Respiratory symptoms were not present in all cases. Some patients have needed respiratory or blood pressure support in a pediatric intensive care unit. Fatalities have been reported. These children tested positive for current or recent infection with SARS-CoV-2 based on reverse-transcriptase polymerase chain reaction (RT-PCR) or serologic assay or had an epidemiologic link to a COVID-19 case.

MIS-C has been reported in the United Kingdom, Europe<sup>3</sup> and New York State<sup>4</sup>. At least one child with KD and COVID-19 but not MIS-C has been described in California<sup>5</sup>. In a case series from the United Kingdom that included eight children including one fatality<sup>6</sup>, 75% of patients

<sup>1</sup> <https://emergency.cdc.gov/han/2020/han00432.asp>

<sup>2</sup> 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>.

<sup>3</sup> Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, Bonanomi E, D'Anitga L. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet*. 2020. Advance online publication, doi: 10.1016/S0140-

6736(20)31129-6 [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31103-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31103-X/fulltext)

<sup>4</sup> [http://dmna.ny.gov/covid19/docs/all/DOH\\_COVID19\\_PediatricInflammatorySyndrome\\_050620.pdf](http://dmna.ny.gov/covid19/docs/all/DOH_COVID19_PediatricInflammatorySyndrome_050620.pdf)

<sup>5</sup> <https://hosppeds.aappublications.org/content/hosppeds/early/2020/04/06/hped.2020-0123.full.pdf>

<sup>6</sup> Riphagen S, Gomez X, Gonzales-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet*. 2020. Advance online publication, doi: 10.1016/S0140-6736(20)31094

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31094-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31094-1/fulltext)



were of Afro-Caribbean descent and 62.5% were male. All eight patients tested positive for SARS-CoV-2 through antibody testing.

The New York City Health Department<sup>7</sup> released a health alert on May 4, 2020 describing 15 patients aged 2-15 years of age hospitalized with a syndrome compatible with MIS-C between April 17 and May 1. All patients had subjective or measured fever and more than half reported rash, abdominal pain, vomiting, or diarrhea. Respiratory symptoms were reported in less than half of these patients. While only 4 of the 15 patients were PCR positive for SARS-CoV-2, 6 patients with negative PCR results were positive by serology. More than half of the patients required blood pressure support and five required mechanical ventilation. As of May 12, 2020, the New York State Department of Health identified 102 patients with similar presentations, many of whom tested positive for SARS-CoV-2 infection by RT-PCR or serologic assay.

There is limited information currently available about risk factors, pathogenesis, clinical course, and treatment for MIS-C.

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

- An individual aged <21 years presenting with fever<sup>8</sup>, laboratory evidence of inflammation<sup>9</sup>, 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

Individuals who fulfill full or partial criteria for Kawasaki disease 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.

### **Actions for Health Care Providers and Local Health Departments**

- Hospitals and health care providers should immediately report cases meeting the MIS-C case definition to their local health departments using a Confidential Morbidity Report (CMR).
- Local Health Departments should report cases to the California Department of Public Health via CalREDIE, using the condition “Multisystem Inflammatory Syndrome in Children (MIS-C) associated with Novel Coronavirus 2019”. If the electronic form is not

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<sup>7</sup> <https://www1.nyc.gov/assets/doh/downloads/pdf/han/alert/2020/covid-19-pediatric-multi-system-inflammatory-syndrome.pdf>

<sup>8</sup> Fever >38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours

<sup>9</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

yet available in CalREDIE, please complete a paper form of the CDC MIS-C Reporting form and upload with the initial CalREDIE report.

- Because MIS-C is separate from COVID-19 reporting in CalREDIE, cases which also meet criteria for SARS-CoV-2 should also be reported using the novel coronavirus condition (“Novel Coronavirus 2019”).

### **Actions for Health Care Providers**

Health care providers should:

- Monitor children with confirmed COVID-19 for potentially serious complications.
- Test children with potential MIS-C, including with symptoms and signs of KD or TSS, by both a RT-PCR test (detects current infection) and by a serologic assay (detects past infection) approved or given Emergency Use Authorization by the U.S. Food and Drug Administration.
- Immediately refer patients with MIS-C or features of TSS or KD to a specialist in pediatric infectious disease, rheumatology, and/or critical care, as indicated. Early diagnosis and treatment of patients is critical to preventing long-term complications.