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CDC HEALTH ADVISORY

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Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19)

Summary
The Centers for Disease Control and Prevention (CDC) is providing 1) background information on several cases of a recently reported multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19); and 2) a case definition for this syndrome. CDC recommends healthcare providers report any patient who meets the case definition to local, state, and territorial health departments to enhance knowledge of risk factors, pathogenesis, clinical course, and treatment of this syndrome.

Background
On April 26, 2020, clinicians in the United Kingdom (UK) recognized increased reports of previously healthy children presenting with a severe inflammatory syndrome with Kawasaki disease-like features.[1] The cases occurred in children testing positive for current or recent infection by SARS-CoV-2, the novel coronavirus that causes COVID-19, based on reverse-transcriptase polymerase chain reaction (RT-PCR) or serologic assay, or who had an epidemiologic link to a COVID-19 case. Patients presented with a persistent fever and a constellation of symptoms including hypotension, multiorgan (e.g., cardiac, gastrointestinal, renal, hematologic, dermatologic and neurologic) involvement, and elevated inflammatory markers.[2] Respiratory symptoms were not present in all cases.

Eight cases, including one death, from the UK were described in a recent publication.[3] In the limited sample of 8 children, it was reported that 75% of the patients were of Afro-Caribbean descent and 62.5% were male. The report also indicated that all 8 patients tested positive for SARS-CoV-2 through antibody testing, including the patient that died.[3]

During March and April, cases of COVID-19 rapidly increased in New York City and New York State. In early May 2020, the New York City Department of Health and Mental Hygiene received reports of children with multisystem inflammatory syndrome. From April 16 through May 4, 2020, 15 patients aged 2-15 years were hospitalized, many requiring admission to the intensive care unit. As of May 12, 2020, the New York State Department of Health identified 102 patients (including patients from New York City) with similar presentations, many of whom tested positive for SARS-CoV-2 infection by RT-PCR or serologic assay. New York State and New York City continue to receive additional reports of suspected cases.

Additional reports of children presenting with severe inflammatory syndrome with a laboratory-confirmed case of COVID-19 or an epidemiological link to a COVID-19 case have been reported by authorities in other countries.[4]

It is currently unknown if multisystem inflammatory syndrome is specific to children or if it also occurs in adults.

There is limited information currently available about risk factors, pathogenesis, clinical course, and treatment for MIS-C. CDC is requesting healthcare providers report suspected cases to public health authorities to better characterize this newly recognized condition in the pediatric population.

Recommendations
Healthcare providers who have cared or are caring for patients younger than 21 years of age meeting MIS-C criteria should report suspected cases to their local, state, or territorial health department.

For additional information, please contact CDC's 24-hour Emergency Operations Center at 770-488-7100. After hour phone numbers for health departments are available at the Council of State and Territorial Epidemiologist website (https://resources.cste.org/epiafterhours).

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

- An individual aged <21 years presenting with fever[i], laboratory evidence of inflammation[ii], 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

[i]Fever ≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours
[ii]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

Additional comments
- 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

References
[1] https://www.cdc.gov/kawasaki/index.html
[2]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.
[3]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
[4]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

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