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Surveillance, research needed to identify optimal treatments for MIS-C

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Godfred-Cato S, et al. "COVID-19-Associated Multisystem Inflammatory Syndrome in Children - United States, March-July 2020." *MMWRMorb Mortal Wkly Rep.* 2020;69:1074-1080.

A cluster of eight previously healthy children with hyperinflammatory shock and clinical features similar to atypical Kawasaki disease or toxic shock syndrome was first reported from the United Kingdom in April. The cases occurred in children who were positive for SARS-CoV-2 on polymerase chain reaction (PCR) test, had a positive SARS-CoV-2 serology test or had an epidemiologic link to a COVID-19 case.

Following case reports in Europe, the New York State Department of Health identified 102 patients with a similar clinical presentation. On May 14, the Centers for Disease Control and Prevention (CDC) issued a Health Alert Network advisory notice to providers formally naming this condition multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19, which included a case definition with the intention of being more inclusive.

Characteristics of MIS-C

As of July 29, a total of 570 MIS-C patients who met the case definition had been reported to CDC (see figure). The median patient age was 8 years (range: 2 weeks-20 years), and 55.4% were male, 40.5% were Hispanic or Latino, 33.1% were non-Hispanic Black and 13.2% non-Hispanic White. Whereas 66% of MIS-C patients did not have underlying medical conditions, obesity was the most common underlying medical condition (25.6%) followed by chronic lung disease (8.4%).

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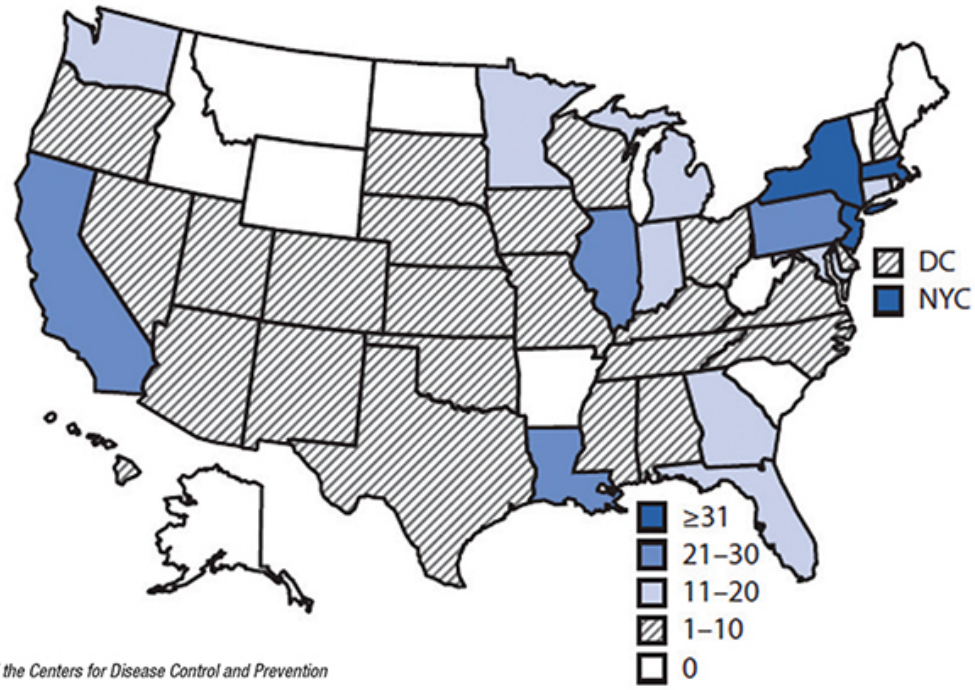
Geographic distribution of 570 reported cases of multisystem inflammatory syndrome in children — United States, March–July 2020



Courtesy of the Centers for Disease Control and Prevention

Abbreviations: DC = District of Columbia; NYC = New York City.

Four or more organ systems were involved in 490 (86%) patients. Most patients had gastrointestinal (90.9%), cardiovascular (86.5%) or dermatologic or mucocutaneous (70.9%) involvement. Severe complications were common, including cardiac dysfunction (40.6%), shock (35.4%), myocarditis (22.8%), coronary artery dilatation or aneurysm (18.6%) and acute kidney injury (18.4%). Overall, 364 patients (63.9%) were treated in an intensive care unit, and 10 patients (1.8%) died.

This study divided the MIS-C cases into three groups by underlying similarities using latent class analysis with specific indicator variables, a statistical modeling technique that is well-suited to describe different manifestations of a novel clinical syndrome. A total of 203 (35.6%) patients (Class 1) had a clinical course consistent with previously published MIS-C reports characterized predominantly by shock, cardiac dysfunction, gastrointestinal symptoms and markedly elevated inflammatory markers. Almost all Class 1 patients (98%) had positive SARS-CoV-2 serology test results with or without positive PCR test results.

Respiratory manifestations, including pneumonia or acute respiratory distress syndrome, that appeared to overlap with acute COVID-19 were more common in 169 (29.6%) patients (Class 2). This group had the highest rates of PCR positivity: 84%.

The remaining 198 (34.7%) patients (Class 3) were younger than other groups (the median age was 6 years) and more commonly met the criteria for complete Kawasaki disease (6.6%).

Importantly, Class 1 patients had the highest prevalence (21.1%) of coronary artery abnormalities compared with Class 2 (15.8%) and Class 3 (18.2%).

One of the study's limitations is that the CDC's broad case definition might have led to the unintentional inclusion of children whose illnesses overlapped with acute COVID-19 and Kawasaki disease.

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Among all 570 patients, 527 (92.5%) were treated. The treatments included intravenous immunoglobulin (80.5%), steroids (62.8%), antiplatelet agents (58.6%), anticoagulation agents (44.2%) and vasoactive agents (41.9%). To date, there are no established guidelines on the management of MIS-C, and randomized controlled trials are urgently needed. AAP interim guidance on the treatment approach for MIS-C is available at https://bit.ly/3lveqY2.

Pathogenesis of MIS-C and vaccine safety concern

Although the pathogenesis of MIS-C remains unknown, it is hypothesized that MIS-C results from immune-mediated injury triggered by SARS-CoV-2 infection based on evidence of hyperinflammation and the delayed onset in relation to SARS-CoV-2 infection coincident with antibodies development. While elucidating the exact mechanism of this new syndrome is critical, the hypothesis of immune-mediated pathogenesis of MIS-C associated with natural SARS-CoV-2 infection, potentially involving a delayed aberrant cellular or humoral adaptive immune response, raises concern for MIS-C as a possible serious adverse event in children who receive COVID-19 vaccines. Therefore, once COVID-19 vaccines become available for children, it is crucial to evaluate MIS-C as a possible COVID-19 vaccine safety outcome through the U.S. vaccine safety monitoring systems.

Further surveillance and research are critical

Suspected MIS-C cases should be reported to local or state health departments. While a specific ICD-10-CM code for MIS-C has not yet been developed, the AAP has released coding guidance on MIS-C based on COVID-19 status at https://downloads.aap.org/AAP/PDF/COVID 2020.pdf. Appropriate coding for MIS-C is crucial to identify cases of MIS-C through electronic medical record systems for future studies and surveillance.

Since Dr. Tomisaku Kawasaki first described Kawasaki disease in the 1960s, we now encounter a novel mysterious syndrome in the era of the COVID-19 pandemic. Continued surveillance and research are needed to understand this syndrome further and provide insights into optimal treatments for MIS-C.

Question

What percentage of MIS-C patients reported to the CDC from March to July 2020 developed coronary artery abnormalities?

A. 1%

B. 6%

C. 12%

D. 18%

E. 24%

Answer: *D*

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