



From the Editor

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Severe Inflammatory Syndrome in Children Testing Positive for Current or Recent COVID-19 Infection

COVID 19 has resulted in a global and economic catastrophe unlike anything seen in 100 years. Until recently, we thought children were mostly spared from the disease, or if they did acquire it, cases would be mild and short-lived. Reports from the Centers for Disease Control and Prevention (CDC) (2020) confirmed that only 2% of COVID-19 cases in the United States were children.

Reports over the past few weeks tell us this is no longer the case. In a cross-sectional study of 46 North American pediatric intensive care units (PICUs) between March 14 and April 3, 2020, 48 children were admitted to 14 PICUs in the United State and none in Canada. Of this number, a total of 40 children (83%) had preexisting underlying medical conditions, 35 (73%) presented with respiratory symptoms, and 18 (38%) required invasive ventilation, and the hospital mortality rate was 4.2% (Shekerdemian et al., 2020). Although it is true at this point in time that severe illness is less frequent and early hospital outcomes in children are better than in adults, COVID-19 can result in a significant disease burden in children.

Of particular concern is a new condition first observed in the United Kingdom that has been named “pediatric inflammatory multisystem syndrome” (PIMS). The condition is seen in children who have been infected with COVID-19, recovered from it, and later have an immune response that results in significant levels of inflammation in organ systems and symptoms. Children who have PIMS typically did not have obvious symptoms when they were infected with COVID-19, like cough, and generally, were healthy prior to developing PIMS. The syndrome is not contagious. As mentioned, to have it, a child must have had COVID-19 previously, and it is believed that for the child to have the antibodies, he or she must be past the contagious stage of the disease (Children’s Hospital of Los Angeles [CHLA], 2020).

PIMS is so new that there remain many unanswered questions about how and why it affects children. What we do know about the syndrome’s symptoms include the following (Belluck, 2020):

1. Symptoms can include fever, rash, reddish eyes, swollen lymph nodes, and sharp abdominal pain.
2. Symptoms do not usually include two common features of COVID-19: cough and shortness of breath.
3. The syndrome can resemble Kawasaki disease, but physicians emphasize the two conditions are not the same.
 - Kawasaki disease can produce coronary aneurysms when left untreated; the new syn-

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drome seems to mostly involve inflammation of coronary arteries and other blood vessels.

- Shock is rare with Kawasaki disease; the new syndrome has sent children into a type of toxic shock.
4. The syndrome seems to be less lung-specific, but most children need some additional oxygen, and a few have required ventilators.
 5. The inflammatory response can affect many parts of the body.

Cases have been seen in children of all ages, from infants to teenagers. Although some children with the syndrome have preexisting conditions, many of these children have been previously healthy. It is unclear how many children have developed the syndrome, but the numbers appear small so far (Belluck, 2020). As of May 12, 2020, New York state has reported 73 cases (CDC, 2020), and a handful of cases have been reported in other states (e.g., Louisiana, Mississippi, California). At least 50 cases have been reported in Europe. At the time of this writing, three children in New York and one in England have died (Riphagen et al., 2020).

The International PICU-COVID-19 Collaboration, coordinated by Jeffrey Burns, MD, MPH, chief of Critical Care Medicine at Boston Children’s Hospital, convened a Zoom conference on May 2, 2020, to compare notes about PIMS (Fliesler, 2020). Pediatric experts in intensive care, cardiology, rheumatology, infectious disease, and Kawasaki disease reviewed data from several dozen cases in Europe and the United States, offered guidance for clinicians, and presented an agenda for research. Attendees made two conclusions: 1) thus far, PIMS is rare; and 2) clinicians who suspect a case should consult promptly with pediatric infectious disease, rheumatology, or critical care specialists. Some children’s medical status declines rapidly; thus, they should be cared for in hospitals with tertiary pediatric/cardiac intensive care units.

Figure 1.
Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C)

- An individual aged younger than 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 COVID-19 exposure within the 4 weeks prior to the onset of symptoms.

*Fever greater than 38.0°C (100.4° F) for 24 hours or more, or report of subjective fever lasting 24 hours or longer.

**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.

Source: CDC, 2020.

Early symptoms mimic many common childhood illnesses. The panel suggested that all clinicians adopt the following case definition for PIMS, put forth by the Royal College of Paediatrics and Child Health (2020, p. 1):

1. A child presenting with persistent fever, inflammation (defined as neutrophilia, elevated c-reactive protein [CRP], and lymphopaenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal, or neurological disorder), with additional features. The child may fulfill full or partial criteria for Kawasaki disease.
2. Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis, such as enterovirus. However, waiting for results of these investigations should not delay seeking expert advice.
3. SARS-CV-2 polymerase chain reaction (PCR) testing may be positive or negative.

On May 14, 2020, the CDC issued an official health advisory on the syndrome, calling it multisystem inflammatory syndrome in children (MIS-C). The case definition is nearly identical to that put forth above by the Royal College of Paediatrics and Child Health for PIMS. See Figure 1 for the CDC's case definition.

According to CHLA (2020), the current treatment for MIS-C is a similar protocol to what is used to treat Kawasaki disease. The goal is to reduce the inflammation to avoid long-term damage to arteries in the child's body and heart. This is accomplished through transfusions of plasma, which reduces the body's own immune response that is causing the inflammation. More serious cases have required a ventilator for a few days. It is unclear at this time if there will be any long-term effects (Belluck, 2020).

Things are moving very quickly as COVID-19 reveals more of itself and related issues. There is much more to learn about this mysterious syndrome. To support this effort, the CDC is funding a \$2.1 million study of 800 children who have been hospitalized after testing positive for the coronavirus through Boston Children's Hospital. The study aims to understand why some children are more vulnerable to the disease than others.

This is what we know today. The CDC tells us it is currently unknown if multisystem inflammatory syndrome is specific to children or if it also occurs in adults. We also know little about risk factors, pathogenesis, clinical course, or treatment. The CDC is requesting health care providers to report suspected cases to public health authorities to better characterize this newly recognized condition in the pediatric population.

Take a deep breath and hang on tight. This could be a long ride. ■■■

References

- Belluck, P. (2020, May 11). A new coronavirus threat to children. *The New York Times*. <https://www.nytimes.com/article/kawasaki-disease-coronavirus-children.html>
- Centers for Disease Control and Prevention (CDC). (2020). *Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). Emergency preparedness and response*. <https://emergency.cdc.gov/han/2020/han00432.asp>
- Children's Hospital of Los Angeles (CHLA). (2020). *Multisystem inflammatory syndrome in children (MIS-C): What parents should know*. <https://www.chla.org/blog/health-and-safety-tips/pediatric-inflammatory-multisystem-syndrome-pims-what-parents-should-know>
- Fliesler, N. (2020). COVID-19 and serious inflammatory syndrome in children: Unpacking recent warnings. *Discoveries*. <https://discoveries.childrenshospital.org/covid-19-inflammatory-syndrome-children/>
- Riphagen, S., Gomez, Z., Gonzalez-Martinez, C., Wilkinson, N., & Theocharis, P. (2020). Hyperinflammatory shock in children during COVID-19 pandemic. *The Lancet*. [https://doi.org/10.1016/S0140-6736\(20\)31094-1](https://doi.org/10.1016/S0140-6736(20)31094-1)
- Royal College of Paediatrics and Child Health. (2020). *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>
- Shekerdemian, L.S., Mahmood, N.R., Wolfe, K.K., Riggs, B.J., Ross, C.E., McKiernan, C.A., Heidemann, S.M., Kleinman, L.C., Sen, A.I., Hall, M.W., Priestley, M.A., McGuire, J.K., Boukas, K., Sharron, M.P., & Burns, J.P. (2020). Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units [Epub ahead of print]. *JAMA Pediatrics*. <https://doi.org/10.1001/jamapediatrics.2020.1948>

Additional Reading

- CDC COVID-19 Response Team. (2020). Coronavirus Disease 2019 in Children – United States, February 12-April 2, 2020. *MMWR Morbidity and Mortality Weekly Report*. <https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm>