

See and Not Miss The MIS-C:

What Pediatricians & Parents Need to Know About

Multisystem Inflammatory Syndrome in Children Related to COVID-19

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As of May 21st, there were 54,031 confirmed cases of COVID-19 in children in the United States. Children represent only 4.2% of all the confirmed cases nationally. It appears that children escaped the burden of severe lung disease associated with COVID-19. However SARS-CoV-2, posed a new challenge for the pediatricians in the form of a novel inflammatory syndrome.

On April 26th, pediatricians in the United Kingdom reported a severe inflammatory syndrome with Kawasaki like features in otherwise healthy children.¹ These children tested positive for SARS-CoV-2 based on either reverse transcriptase polymerase chain reaction assay or /and serology. The initial UK case series described eight children presenting with persistent fevers, hypotension, and multi-organ involvement with evidence of inflammation. None of these children had respiratory symptoms.

Similarly, characterization on 35 children with cardiac failure in midst of COVID-19 was published from France and Switzerland.² In Bergamo Province, a 30-fold increase in Kawasaki-like disease was observed in children. This followed a rapid recognition of analogous cases in New York. As of June 1st, there were over 200 cases with three pediatric deaths. New York State continues to collect data on children presenting with signs and symptoms suggestive of this inflammatory condition.

New York State has been on the forefront of developing guidelines on management. Our pediatric emergency departments quickly adapted screening procedures for children presenting with prolonged fevers (≥ 3 days). Instantaneously fever work ups for children included inflammatory and multi-organ system labs. Treatment regimens were promptly tried drawing an analogy to some components of Kawasaki disease. Most Centers are using intravenous immunoglobulins (IVIG) as the first-line agent, along with other immunosuppressive such as steroids and/or IL-1 blockers (Anakinra).

On May 14th, the Centers for Disease Control and Prevention (CDC) defined this new inflammatory syndrome temporally related to recent exposure of SARS-CoV-2 as the “Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19.

Centers for Disease Control has the following case definition:

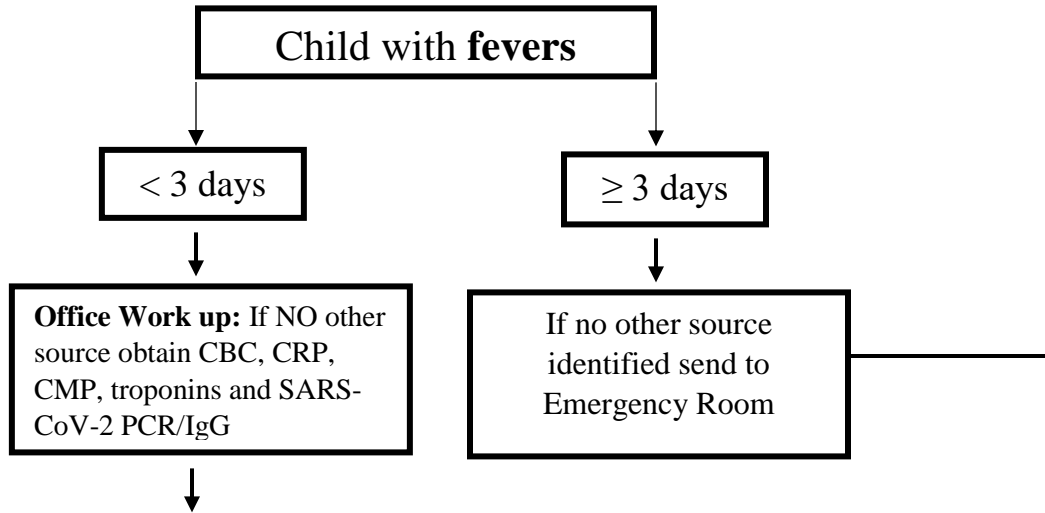
Any child or young adult less than 21 years of age presented with:
Fevers Laboratory evidence of inflammation Severe illness requiring hospitalization Multisystem organ involvement (≥ 2) such as cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurologic
AND No alternate plausible diagnosis
AND Evidence of recent or current SARS-CoV-2 by PCR, serology or antigen, or COVID-19 exposure 4 weeks prior to the onset of symptoms

This led to increased awareness by pediatricians as well as parents of MIS-C primarily from the news media. Despite development of plans for expeditious management strategies in the pediatric emergency room, there exists little guidance for pediatric offices in this regard. As the number of cases surge, a wide spectrum of MIS-C is acknowledged. In this blog, we provide a clinical pathway to triage children with fevers and concern of MIS-C presenting to the pediatrician's office.

What is MIS-C? It is likely a post inflammatory response to recent infection by SARS-CoV-2. The clinical spectrum ranges from severe presentations such as shock-like presentation, macrophage activation syndrome (MAS) or hemophagocytic lymphohistiocytosis (HLH) syndrome to Kawasaki-like disease and milder variants manifesting as fevers and lab evidence of inflammation only. Abdominal pain is often a significant part of the presentation as well.

This is a general guidance and should be interpreted and applied with caution. It is expected to evolve as more information becomes available. Clinical judgment should supersede this clinical pathway.

Clinical decision-making pathway for MIS-C in a child presenting to Pediatric office with fevers



Inflammation	*Mild	Severe	Severe
Organ Involvement	No liver, kidney, heart involvement	No liver, kidney, heart involvement	Involvement of heart, liver or kidney
Next step			
Follow up	Follow-up outpatient in 24 hours with repeat labs and refer to cardiology for Echo if still elevated	Send to emergency room for admission and follow-up labs and Echo	Sent to emergency room for further workup, admission and treatment consideration
*Mild CRP 10-40, Severe > 40 mg / L			

ED Work up			
Clinical	Laboratory		SARS-CoV-2
	Inflammatory	Organ involvement	
<input type="checkbox"/> Shock-like presentation <input type="checkbox"/> Kawasaki-like presentation <input type="checkbox"/> Fever only	<input type="checkbox"/> ↑ WBC <input type="checkbox"/> ↑ CRP <input type="checkbox"/> ↑ Procalcitonin <input type="checkbox"/> ↑ Ferritin <input type="checkbox"/> ↑ ESR <input type="checkbox"/> ↑ D-dimer	<input type="checkbox"/> ↑ Troponins <input type="checkbox"/> ↑ Transaminases <input type="checkbox"/> ↑ Creatinine	<input type="checkbox"/> PCR <input type="checkbox"/> Serology <input type="checkbox"/> Exposure
Obtain baseline echocardiogram, consider treatment with intravenous immunoglobulins +/- steroids +/- IL-1 blockers +/- IL-6 monoclonal			

How to educate parents on MIS-C:

Parents should be encouraged to contact pediatrician if there is any concern about child's health. While this inflammatory condition sounds frightening, the American Academy of Pediatrics reassures that this condition is rare. A blast email, phone texts, or phone calls to patient's families in this regard will help with increased awareness as well as accessibility.

A script from American Academy of Pediatrics can be used, "MIS-C has been compared to another rare childhood condition, known as Kawasaki disease. Although it is different, if you notice any of the following symptoms please call your pediatrician:

- Fevers lasting for more than 24 hours
- Red eyes and/or a skin rash
- Abdominal pain, diarrhea or vomiting
- Child seems confused or overly sleepy
- Trouble breathing

In addition, please let your pediatrician know if the child was tested positive for COVID-19 or exposed to this virus. Based on this information, the pediatrician will determine whether the child can be seen in the office, via telemedicine or you would need to go to the emergency department."

As a pediatrician, please remember to report any such cases to the New York State Department of Health at (866) 692-3641.

References:

- 1- 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>pdf iconexternal icon.
- 2- Zahra Belhadjer, MD, et al. Acute heart failure in multisystem inflammatory syndrome in children (MIS-C) in the context of global SARS-CoV-2 pandemic.
10.1161/CIRCULATIONAHA.120.0483601
- 3- <https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/children/mis-c.html>