



## **Clinical Guideline: Pediatric Multi-System Inflammatory Syndrome (PMIS) Temporally Associated with COVID-19**

*Developed by, and used with permission of, Hasbro Children's Hospital*

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This clinical guideline is a working, iterative document given the nature of this new clinical syndrome, with growing evidence and experience. The guideline will be updated as recommendations evolve. **Any suspected cases (see [CDC HAN 432](#) for case definition) should be reported to RIDOH immediately at 401-654-6990 during business hours or 401-276-8046 after hours.**

### **Description of Patients**

- Likely pediatric/young adult patients (wide age range, with average age of 8-11 years)
- Signs and symptoms are consistent with post-infectious immune response/cytokine storm syndromes
- Often exposure to COVID-19 (family member positive or with fever/respiratory symptoms, mild or no symptoms for the patient) but not always known
- Often two to three weeks (or more) post exposure or mild symptoms
- As above, similarities with many immune response syndromes such as Kawasaki Disease with shock, cytokine release syndrome after CAR-T therapy, HLH, MAS
- Presenting with, or can rapidly progress to, shock, often cardiogenic
- Some male predominance
- Some degree of obesity prevalence
- Excludes patients with typical Kawasaki disease, other etiologies of shock such as TSSS, gram negative bacteremia, and others

### **Presenting Signs and Symptoms**

- Fever refractory to anti-pyretics
- GI symptoms/diarrhea
- Rash (can be desquamating)
- Neurologic symptoms/altered mental status
- Tachycardia
- Hypotension
- Poor perfusion
- Hypoxia

### **Common Laboratory Findings**

- Elevated D-dimer
- Elevated ferritin
- Elevated CRP/ESR
- Elevated troponin
- Elevated BNP
- Lymphopenia, sometimes with neutrophilia
- Hyponatremia
- Almost always COVID-19 PCR negative, often COVID-19 IgG/IgM antibody positive

### **Signs and Symptoms to Consider Referral/Transfer to Emergency Department**

Clinical suspicion and history consistent with syndrome, with special attention to:

- Tachycardia (with or without fever)
- Refractory fever
- Altered mental status
- Hypotension
- Decreased urine output
- Hypoxia

## Suggested Initial Hospital Workup/Evaluation

Laboratory tests	Imaging/Other diagnostics	Consultations
CBC with differential Blood culture Blood gas with lactate Ferritin Fibrinogen D-dimer PT/INR PTT TEG (thromboelastography) Triglycerides CRP Troponin BNP CK-MB CMP/M/P LDH COVID-19 PCR COVID-19 IgM/IgG RPP Urinalysis Type and screen  If possible: <ul style="list-style-type: none"> <li>• IL-6</li> <li>• Soluble IL-2 receptor</li> <li>• IL-1</li> </ul>	CXR 12-lead EKG Echo (timing in conjunction with cardiology consultation, and with clinical consideration of phenotype)	Cardiology Infectious Disease Rheumatology Hematology/Oncology Surgery, if ECMO is being considered

### **Clinical Decision-Making Regarding Admission Status**

- Patients with suspicion for PMIS should be admitted given the small amount of clinical experience with this new presentation as well as reports of rapid decline.
- Patients who are hemodynamically stable may be admitted to wards with cardiorespiratory monitoring and frequent clinical re-assessment.
- Patients with persistent tachycardia, any worsening perfusion, or other metrics of declining cardiac output should be evaluated by the FAST Team with low threshold for immediate transfer to PICU.

### **Therapies and Interventions**

- If hypotensive, consider appropriate early inotropic support (often vasoplegia/warm shock with benefit from norepinephrine) prior to third fluid bolus, or earlier in patients who appear adequately hydrated.
- Echocardiogram can guide fluid resuscitation management by identifying possible myocardial dysfunction and assessing preload.
- Consider fluid management carefully as respiratory failure in patients has tended to occur after significant fluid resuscitation.
- Give early consideration of the need for central access.
- Give empiric antibiotics for sepsis
- Initiate thromboprophylaxis as per Pediatric COVID-19 Thromboprophylaxis guideline and in consultation with Pediatric Hematology/Oncology.
- Kawasaki-predominant phenotype: initiate IVIG (may require up to 2 doses; 2 g/kg/dose) and then consider anakinra
- Cytokine release syndrome predominant phenotype: initiate anakinra, and then consider IVIG. May also consider tocilizumab with elevated IL-6 with consideration of drug availability.
- Consider initiating steroids in conversation with consultants (steroids may be a component of ARDS management or refractory shock management as well)
- Standing anti-pyretics
- Discuss ECMO early for refractory cardiogenic shock

### **Diagnostic Monitoring**

- Serial echocardiograms as clinically indicated
- Trend CBC, troponin, BNP, ferritin, fibrinogen, PT/INR, PTT, d-dimer as clinically indicated and in conjunction with consultant guidance

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