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

<table>
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<th>Consultations</th>
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<td>Blood gas with lactate</td>
<td>Echo (timing in conjunction with cardiology consultation, and with clinical consideration of phenotype)</td>
<td>Rheumatology</td>
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<td>Ferritin</td>
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<td>Hematology/Oncology</td>
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<td>Fibrinogen</td>
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<td>Surgery, if ECMO is being considered</td>
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<td>D-dimer</td>
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### 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

**Hasbro Children’s Hospital Contributors**

Brian Alverson, Pediatric Hospitalist Medicine
Sarah Welsh, Pediatric Critical Care Medicine
Ali Yalcindag, Pediatric Rheumatology
Lloyd Feit, Pediatric Cardiology
Michael Koster, Pediatric Infectious Disease/Pediatric Hospitalist Medicine
Frank Overly, Pediatric Emergency Medicine
Anthony Hayward, Immunology
Salley Pels, Pediatric Hematology/Oncology