COVID-19 Associated Hyperinflammatory Response Syndrome

Emerging Phenotype Across Europe:
- Fever, diarrhea, abdominal pain
- Lymphopenic, elevated inflammatory markers
- Toxic shock syndrome/Kawasaki like illness with similar inflammatory patterns
- Some occurring at the time of COVID infection with some 2 weeks after the peak

Case Definition
1. A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP and lymphopenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with additional. This may include children fulfilling 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 chikungunya such as enterovirus (waiting for results of these investigations should not delay seeking expert advice).
3. SARS-CoV-2 PCR testing may be positive or negative.

Signs/Symptoms
- All:
  - Persistent fever >38.5°C
  - Oxygen requirement, Hypotension
- Some:
  - Abdominal pain, Confusion, Conjunctivitis, Cough, Diarrhea, Headache, Lymphadenopathy, Mucus membrane changes, Neck swelling, Rash, Respiratory symptoms, sore throat, Swollen hands and feet, Syncope, Vomiting

Lab:
- All:
  - Abnormal fibrinogen, Absence of potential causative organisms (other than SARS-CoV-2), High CRP, High D-Dimers, High ferritin, Hypoalbuminemia, Lymphopenia
- Most:
  - Neutrophilia in most—normal neutrophils in some
- Some:
  - Acute kidney injury, Anemia, Coagulopathy, High IL-10 (if available), High IL-6 (if available), Proteinuria, Raised CK, Raised LDH, Raised triglycerides, Raised troponin, Thrombocytopenia, Transaminist

Disease Course
- Systems:
  - Shock 88%, Depressed LV function 42%, Dilated coronaries 26%, Hypoxia 27%, Elevated BNP 100%, Elevated troponin 70%
  - Support
  - Vasopressors support 70-94%, Incubation 24-68%, ECMO 5-12%
  - Therapies
    - Fluid resuscitation 100%, Steroids 51-94%, IVIG 18-62%, Anakinra 8-24%, Tocilizumab 0-6%, Antivirals 6-5%, Anticoagulation 65%, Antiplatelet 6%

Lab testing:
- 23/37 positive for Sars-CoV-2 PCR or IgG

Approaches to Workup and Treatment
- Labs: earlier the better, try to trend
  - CBC/diff, ESR/CRP, LFT's w/ LDH, Ferritin, Coags, D-Dimer, Cytokine panel
- Imaging:
  - CXR, High Res CT, ECHO specifically for KD features
- Team Approach
  - PICU, ID, Rheum, Cards, Immun
- Treatment:
  - Consider immunomodulatory therapy (anti-IL1, anti IL6, IVIG, steroids)
  - Enroll trials as able

Imaging and ECG
- Echo and ECG—myocarditis, valvulitis, pericardial effusion, coronary artery dilatation
- CXR—patchy symmetrical infiltrates, pleural effusion
- Abdominal Ultrasound—calculus, ileus, lymphadenopathy, ascites, hepatosplenomegaly
- CT chest—as for CXR—may demonstrate coronary artery abnormalities if contrast