New alert on COVID in Children:
In early May 2020, the UK first reported a cluster of pediatric patients who presented with a systemic inflammatory syndrome with common features with other pediatric inflammatory conditions, including Kawasaki disease, staphylococcal/streptococcal toxic shock syndromes, bacterial sepsis and macrophage activation syndrome. An alert was issued\(^1\) and a guidance document released by the Royal College of Paediatrics and Child Health\(^2\), and a case series was published from one centre in London\(^3\) describing 8 severe cases. Subsequently another case series was published from Italy\(^4\) describing an outbreak of severe Kawasaki-like disease during that country’s SARS-CoV-2 epidemic. In these two case series, not all children were confirmed to be SARS-CoV-2 positive by PCR, but most were positive for SARS-CoV-2 antibodies. Hence, contrary to described adult presentations with severe respiratory disease due to active infection, these cases are thought to represent a **post-infectious inflammatory** process.

In addition to the two initial published case series, large numbers of similar cases have been reported in North American cities with significant community transmission of SARS-CoV-2, including New York City and Montreal. On 14 May 2020, the CDC in the US released a similar alert\(^5\) about what they called the multisystem inflammatory syndrome in children (MIS-C), with similar clinical criteria for diagnosis as the UK; they mentioned that as of 12 May 2020, over 100 children had been diagnosed with this condition in New York State.

**Summary of common clinical presentations of PIMS (based on UK and Italian cohorts):**
- Presenting children were older than typical KD cases (UK median 8 years; Italy mean 7.5 vs 3.0 years)
- Fever, diarrhea, abdominal pain, conjunctivitis, and hypotension (warm shock) were common
- Patients often lacked prominent respiratory symptoms although CXR changes were common (e.g. pleural effusions, infiltrates)
- Other features were present in keeping with SARS-CoV-2 (lymphopenia)

**The above common symptoms seen in PIMS patients can be seen in the setting of the following clinical scenarios:**
1. "Classic Kawasaki Disease" meeting clinical/lab criteria - rash, conjunctivitis, dilated coronaries. Also with elevated BNP, elevated D-dimer, elevated platelets.
2. Atypical KD with some clinical manifestations, but normal coronaries, elevated BNP, elevated D-dimer, low platelets.
3. Shock/TSS presentation – appears less like KD, with abnormal cardiac function, GI symptoms.
4. Shock/TSS with more inflammatory presentation, elevated ferritin, elevated procalcitonin, elevated D-dimer, normal platelets.

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\(^5\) https://emergency.cdc.gov/han/2020/han00432.asp

**Version Date: 29 May 2020**
Pediatric care providers should be aware of this newly described syndrome. This document is meant to provide guidance on a case definition, initial investigations/management and the suggested multidisciplinary approach for suspected cases. This document will be updated as new information becomes available.

**PIMS Case Definition:**

A child presenting with persistent fever (>\(\geq\) 3 days*), laboratory evidence of inflammation and evidence of multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with additional features. This may include children fulfilling full or partial criteria for Kawasaki disease.

1. Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal toxic shock syndromes, and infections associated with myocarditis such as enterovirus (waiting for results of these investigations should not delay seeking expert advice).
2. SARS-CoV-2 PCR testing may be positive or negative
3. SARS-CoV-2 antibody testing positive (when available)

*Some patients may present with evidence of severe disease (e.g. hypotension, myocarditis, etc) at <3 days of symptoms; these patients should still be considered within the definition of PIMS.

**Reporting of Suspected PIMS Cases to Ottawa Public Health:**

Any patients meeting the above case definition or strongly suspected to be a PIMS case should be reported to Ottawa Public Health within 1-2 business days. The ID physician or MRP (Inpatient Pediatrics or PICU physician) should communicate with each other to decide who will report the case and ensure it is done. Cases may be reported by calling 613-580-6744 or by completing the Online COVID-19 Reporting Tool – [https://forms.ottawapublichealth.ca/physicians/Online-COVID-19-Reporting-Tool](https://forms.ottawapublichealth.ca/physicians/Online-COVID-19-Reporting-Tool)
Common Features

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent fever</td>
<td>High CRP</td>
</tr>
<tr>
<td>Hypotension</td>
<td>High D-dimer</td>
</tr>
<tr>
<td>Oxygen requirement</td>
<td>High ferritin</td>
</tr>
<tr>
<td>Evidence of cardiac dysfunction</td>
<td>Hypoalbuminemia</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>Lymphopenia</td>
</tr>
<tr>
<td>Abdominal pain/diarrhea</td>
<td>Neutrophilia</td>
</tr>
<tr>
<td></td>
<td>Abnormal fibrinogen</td>
</tr>
<tr>
<td></td>
<td>Absence of potential causative organisms</td>
</tr>
</tbody>
</table>

Possible Features

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>SARS-CoV-2 PCR testing may be positive or negative</td>
</tr>
<tr>
<td>Swollen hands and feet</td>
<td>SARS-CoV-2 antibody testing (IgG and/or IgM) positive</td>
</tr>
<tr>
<td>Meningeal signs, confusion, headache</td>
<td>Acute kidney injury, proteinuria</td>
</tr>
<tr>
<td>Lymphadenopathy, neck swelling</td>
<td>Coagulopathy</td>
</tr>
<tr>
<td>Mucous membrane changes</td>
<td>Raised CK</td>
</tr>
<tr>
<td>Odynophagia/sore throat</td>
<td>Raised LDH</td>
</tr>
<tr>
<td>Respiratory symptoms, cough</td>
<td>Raised triglycerides</td>
</tr>
<tr>
<td>Syncope</td>
<td>Raised troponin</td>
</tr>
<tr>
<td>History of exposure to COVID-19 infection</td>
<td>Thrombocytopenia, anemia</td>
</tr>
<tr>
<td></td>
<td>Transaminitis</td>
</tr>
</tbody>
</table>
Suspected PIMS case

**GUIDANCE DOCUMENT**

**Guidance Document for Pediatric Multisystem Inflammatory Syndrome (PIMS) potentially associated with COVID-19**

**Version Date:** 29 May 2020

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**Emergency Department Patients:**

For children assessed in ED and felt to show some features of PIMS, initiation of STANDARD INVESTIGATIONS above is recommended. If child is not deemed to require admission, a follow up plan (via ED follow up nurse call, and/or return to ED for reassessment and repeat of laboratory testing if abnormalities found on initial testing) should be decided prior to discharge. Discussion with subspecialists (Rheumatology, Cardiology, ID/Immunology as appropriate) may be helpful in deciding a management plan for these patients.

*This document was prepared by: Drs. Anne Pham-Huy (ID/Immunology), Lillian Lai (Cardiology), Johannes Roth (Rheumatology), Hilary Writer (PICU), Marc Zucker (Pediatric Medicine), Gina Neto (EM) and Jason Brophy (ID).*

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**SUGGESTED STANDARD INVESTIGATIONS:**

- CBC & diff, ESR, CRP, fibrinogen, D-dimer, PTT, INR, ferritin* (call lab to request ferritin STAT)
- Albumin, triglycerides, creatinine, urea, ALT, AST, bilirubin, CK, LDH, glucose, venous blood gas, lactate
- Urinalysis
- NP and throat swab for COVID-19 PCR
- Serum on hold (red top tube, if possible 5-10 cc) (for future SARS-CoV-2 antibody testing)
- Rule out infections:
  - NP swab for respiratory viruses (triplex)
  - Blood and urine cultures
  - Throat swab culture for Group A streptococcus
- CXR if respiratory symptoms or \( O_2 \) sats < 92%

**ADDITIONAL INVESTIGATIONS TO CONSIDER:**

- ECG
- Troponin for any admitted patient; echocardiogram and BNP as per Cardiology
- Rule out other infections:
  - NP swab for respiratory viruses (RV-16 PCR), stool for GI PCR panel EBV/CMV/HIV/Hepatitis A/B/C serologies
  - Wound bacterial culture of skin lesion (if applicable)
  - Vaginal swab for bacterial culture (if applicable)
- Early consultation to Rheumatology, Cardiology, Infectious Diseases/Immunology, +/- PICU (depending on presence of or signs of impending shock)

**ISOLATION:**

- Droplet-contact precautions (+ airborne precautions for AGMPs) pending COVID-19 PCR results.
- If PCR testing is negative, use of appropriate precautions according to clinical syndrome is recommended as per IPAC Manual.