Multisystem Inflammatory Syndrome in Children (MIS-C) Temporally Associated with COVID-19: Guidance for Clinicians in B.C.

September 4, 2020

The Canadian Pediatric Society issued a Public Health Alert on May 12, 2020 to notify health practitioners of an acute inflammatory syndrome temporally linked to COVID-19 that has been reported in children and teenagers.

Children with this condition present with symptoms of systemic inflammation, and can have clinical similarities to Kawasaki Disease, toxic shock syndrome and macrophage activation syndrome. Prominent features include fever, abdominal pain, cardiac involvement and rash, among others. There may be a spectrum of disease severity and phenotypes in children affected by COVID-19-associated inflammation. A preliminary case definition has been developed by the World Health Organization and amended for use in B.C. (see Appendix A).

If you see a child with features that could be in keeping with MIS-C obtain a comprehensive history of exposure to a person with COVID-19. Children with unexplained fever and inflammation (elevated WBC, CRP), and those in early phases of an acute illness should be followed closely for progression of their illness. Care may involve serial monitoring of clinical and laboratory parameters, cardiac imaging, therapies targeting inflammation, and close follow up post-discharge (see Appendix B). Children admitted to a general pediatrics ward for MIS-C warrant close monitoring for clinical deterioration. Affected patients can become critically ill quickly and there have been deaths reported.

When evaluating patients for MIS-C, it is imperative that clinicians give due consideration to sepsis and other life-threatening infections whose clinical presentations overlap with MIS-C. Evaluation for MIS-C should not delay empiric antibiotic coverage in patients whose clinical picture may be in keeping with a serious bacterial infection.

Children with possible MIS-C require evaluation by a pediatric specialty team experienced in the diagnosis of Kawasaki Disease and other inflammatory conditions of childhood. Consultation with pediatric rheumatology cardiology, infectious disease, and critical care is recommended, ideally at a tertiary pediatric centre. If you have a possible case of MIS-C, page the infectious diseases physician on call at BC Children’s Hospital for further discussion and
triaging. If cardiac imaging is needed, please liaise with the pediatric cardiologist BC Children’s Hospital. Both specialists can be reached through central paging at 1-604-875-2000.

**Cases of MIS-C are reportable under the Reporting Information Affecting Public Health Regulation and Public Health Act.** Please contact your local Medical Health Officer to report cases of MIS-C. They can provide guidance regarding further testing required to confirm COVID-19 and liaise with the consultant pediatric specialists. They can be reached through your local public health department or hospital switchboard.
Appendix A: BC Case Definition for MIS-C

Person under investigation
Children 0-19 years of age requiring hospitalization with fever ≥ 3 days

AND two of the following:

a) Acute gastrointestinal symptoms (abdominal pain, vomiting, diarrhoea)
b) Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet)
c) Hypotension or shock
d) Features of myocardial dysfunction, or pericarditis, or valvulitis, or coronary abnormalities (ECHO findings or elevated Troponin/BNP/NT-proBNP)
e) Evidence of coagulopathy (abnormal PT, PTT, elevated d-dimer)

AND
Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin

AND
No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes and no alternative plausible obvious diagnosis

Confirmed case
Meets criteria for a MIS-C person under investigation

AND
Evidence of SARS-CoV-2 infection (positive PCR test or serology), or close contact with a confirmed or probable (lab-probable or epi-link probable) COVID-19 case

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2 Confirmed and lab-probable cases have positive or indeterminate NAAT results, respectively. COVID-19 cases are further defined here: [http://www.bccdc.ca/health-professionals/clinical-resources/case-definitions/covid-19-novel-coronavirus](http://www.bccdc.ca/health-professionals/clinical-resources/case-definitions/covid-19-novel-coronavirus)
Appendix B: Laboratory tests and investigations to consider for MIS-C

<table>
<thead>
<tr>
<th><strong>Lab tests</strong></th>
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<tbody>
<tr>
<td>CBC and differential</td>
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<tr>
<td>CRP</td>
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<tr>
<td>Liver function tests (Alb, AST, ALT, GGT, Alk Phos, Bilirubin)</td>
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<tr>
<td>Electrolytes, BUN, creatinine</td>
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<tr>
<td>LDH</td>
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<td>Ferritin</td>
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<td>d-dimer</td>
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<tr>
<td>PT, PTT</td>
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<td>Troponin</td>
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<td>BNP</td>
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<td>Nasopharyngeal swab or other suitable respiratory and gastrointestinal specimen in consultation with the local medical microbiologist for SARS-CoV-2 PCR</td>
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<td>Serology for SARS-CoV-2: Serology will be made available for this indication at BCCH; page medical microbiologist on call at BCCH (via 604-875-2161) to coordinate appropriate collection and shipment for testing</td>
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<td>Additional studies to rule out an alternative microbiologic etiology</td>
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<tr>
<td>EKG</td>
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<td>Chest X-ray</td>
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For further clinical guidance see [Clinical Reference Group Recommendation: Pediatric Clinical Guidance for COVID-19](#).
Resources:

BCCDC Pediatric Clinical Guidance for COVID-19:
http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-19_Pediatric_clinical_guidance.pdf (hopefully can replace link soon with updated version)

Canadian Pediatric Society Public Health Alert:

World health organization scientific brief on multisystem inflammatory syndrome in children and adolescents with COVID-19:

Royal College of Paediatrics and Child Health UK Guidance on pediatric multisystem inflammatory syndrome temporally associated with COVID-19:

Boston Children’s Hospital news release on pediatric multisystem inflammatory syndrome temporally associated with COVID-19:

CDC guidance on MIS-C with alternative case definition:
https://emergency.cdc.gov/han/2020/han00432.asp

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Preliminary guidance for clinicians in British Columbia about:
Multisystem inflammatory syndrome in children (MIS-C) temporally associated with COVID-19