MULTI-SYSTEM INFLAMMATORY SYNDROME IN CHILDREN TEMPORALLY ASSOCIATED WITH COVID-19: INPATIENT WORKFLOW

DOCUMENT TYPE: GUIDELINE

Site Applicability

BC Children's Hospital – Inpatient Units

Guideline Statements

This document provides guidance for the identification of and investigations for MIS-C only.
It does not include the work-up and management of other entities on the differential diagnosis, including sepsis, which still need to be considered and managed according to clinical judgment.

Patients admitted to Pediatric Intensive Care Unit (PICU)

Isolation

Based on particular clinical features of the patient, please isolate as per routine PHSA IPAC guidelines which can be found at http://policyandorders.cw.bc.ca/ipac.

Resuscitation

Resuscitation with fluids should be provided rapidly if there is hemodynamic instability as most instability is likely to be fluid responsive and vasodilatory in nature, however because of the possibility of systolic cardiac compromise, monitor for signs and symptoms of fluid overload closely (new crackles, hepatomegaly, dilated cardiac silhouette). If shock is fluid-refractory, obtain echocardiogram early with early institution of inotropes as indicated.

Sepsis

Given the differential diagnosis of MIS-C patients includes sepsis, refer to the PICU Severe Sepsis or Septic Shock Order Set

Empiric antibiotic coverage: refer to BCCH Empiric Antibiotic Guide –
< 4 weeks old: Ampicillin + (Gentamicin or Cefotaxime) + Acyclovir*
> 4 weeks old: Cefotaxime +/- Vancomycin +/- Acyclovir (if neurologic abnormalities present)*

*If features of Toxic Shock syndrome present, add Clindamycin

Neurologic assessment

The following neurologic findings have been reported in children with MIS-C:

- Altered mental status (irritability, lethargy)
- Nuchal rigidity
- Aseptic meningitis
- Cerebral edema
- Cranial nerve palsies

Assessment of patient should include:

- History (if possible) of headache, neck stiffness, altered mental status, vision impairment, smell and/or taste impairment, balance/coordination problems, syncope
- Physical exam including mental status including GCS, cranial nerve exam (pupils, extraocular movements, cough/gag, bulbar function), strength in all 4 extremities, nuchal rigidity, finger-nose finger, gait (if possible)

If abnormal findings on neurologic exam, consider neurology consult, CSF sampling, EEG and brain imaging.

Consults

Consult Rheumatology, Cardiology and Infectious Diseases
Consider other services depending on patient's clinical features

Investigations

The differential diagnosis of these patients includes infection, Kawasaki Disease, myocarditis and other inflammatory conditions, etc. Obtain relevant investigations based on clinical judgement of the patient's features (including cultures, imaging, etc.).

In addition to full work up for possible infection and alternative diagnoses, ensure Full MIS-C Evaluation complete:

- CBC with differential
- ESR, CRP
- Electrolytes, BUN, creatinine
- LFTs (AST, ALT, GGT, bilirubin), LDH, Albumin, lactate
- Ferritin, d-dimer, PT/PTT
- Troponin, BNP
- SARS-CoV2 testing:
  - SARS CoV2 PCR: both respiratory (nasopharyngeal swab/sputum/BAL) AND stool specimens (sample type not yet validated but will be tested for this group)
  - SARS CoV2 serology: obtain pre-IVIG whenever possible; contact medical microbiology on call for approval: if serology approved complete a SARS-CoV2 serology request form (available on ePOPs) and send by secure email to misc@cw.bc.ca. Serology not available publicly in BC (as of May 26, 2020) but will be performed for this indication.
- Type and screen (for those receiving IVIG)
- EKG
- CXR
- Echocardiogram

Additional biobanking of patient samples

This process will involve obtaining verbal or written consent from family prior to collection of extra tubes of blood for BioBanking/research, and if feasible, should occur prior to IVIG or other immunomodulatory therapies. Discuss with rheumatology team for most up-to-date recommendations on process for consenting and collection of extra samples for research/BioBanking. If Rheumatology has not been consulted on a case and there is still interest in obtaining an extra blood sample to be stored at BCCH BioBank, contact the BioBank team to coordinate:

- If Monday to Friday 9-5 call local 7497 and if no one answers, leave a message and page (604-877-3796)
- If after hours email: biobank@cw.bc.ca

Medications

- Antibiotics (see Sepsis section above)
- Immune-modulating and anti-inflammatory therapies:

  These could include IVIG, Steroids, Aspirin, biologic agents such as Anakinra or Tociluzumab. Early initiation of IVIG +/- steroids in severely ill patients with suspected MIS-C has been recommended. **Decisions regarding the use of any of these agents should be made in consultation with Rheumatology.**
- Anticoagulation

  Currently there is no role for prophylactic or treatment anticoagulation in children with MIS-C. If there is a child who is already on therapeutic or prophylactic anticoagulation for prior indication and high-dose aspirin is being considered for management, consult hematology.
- Antiviral medications

  Not routinely recommended in patients with suspected MIS-C.

Ongoing monitoring

Clinical response

- Resolution of shock, neurologic impairment, any other clinical features; AND improving markers of inflammation including fever.
- Lack of clinical response within the first 36-48 hours: Consider further immunomodulator as per Rheumatology recommendation

Laboratory testing

The following are recommended daily for the monitoring of hyperinflammation while patients have evidence of shock and/or fever and /or persistence of symptoms:

- CBC and diff
- CRP
- PT/PTT/INR
- D-dimer
- Troponin
- Ferritin
- LDH
- BNP
- Lactate

Follow-up Echocardiogram

Frequency of follow-up echocardiograms will depend on patient's particular clinical features and should be guided by Cardiology.

**IMPORTANT: MIS-C is a reportable condition in BC. Suspected cases seen at BCCH must have a serology case requisition form emailed to misc@cw.bc.ca, after receiving approval for serology from the medical microbiologist on call. If this form is not completed, then it will be the responsibility of the MRP to ensure the case gets reported to the medical health officer.

If patient being discharged home from PICU, please refer to "Discharge criteria instructions and Follow-up Plan" section at the end of this document.

Patients admitted to ward

Isolation

Based on particular clinical features of the patient, please isolate as per routine PHSA IPAC guidelines which can be found at http://policyandorders.cw.bc.ca/ipac.

Close monitoring of clinical stability

Patients with MIS-C have been found to deteriorate rapidly from a hemodynamic standpoint. Monitor vital signs frequently to assess stability, need for fluid resuscitation and need for elevation of care.

Consults

Consult Rheumatology and Cardiology

Consider ID and other services based on clinical features.

Investigations

It is imperative that clinicians give due consideration to sepsis and other life-threatening infections whose clinical presentations overlap MIS-C. Having MIS-C on the differential diagnosis **should not delay** empiric antibiotic coverage in patients whose clinical picture may be in keeping with a serious bacterial infection.

The differential diagnosis of these patients includes infection/sepsis, other inflammatory conditions, etc. Obtain relevant investigations based on clinical judgement of the patient's features (including blood culture for any patient with fever or concern of sepsis).

In addition to full work up for possible infection and alternative diagnoses, ensure Full MIS-C Evaluation complete:

- CBC with differential
- ESR, CRP
- Electrolytes, BUN, creatinine
- LFTs (AST, ALT, GGT, bilirubin), LDH, Albumin, lactate
- Ferritin, d-dimer, PT/PTT
- Troponin, BNP
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Medications

➢ Immune-modulating and anti-inflammatory therapies:

These may include IVIG, Steroids, Aspirin, Anakinra or Tocilizumab.

- Early initiation of IVIG +/- steroids in severely ill patients with suspected MIS-C has been recommended.
- **Decisions regarding the use of any of these agents should be made in consultation with Rheumatology.**
- For patients with typical Kawasaki Disease, the first dose of IVIG can be given by CTU. For doses and monitoring, refer to the BCCH KD Order Set. Consult rheumatology within 24 hours of admission, regardless of treatment effect.

- For incomplete KD or other cases of suspected MIS-C, consult rheumatology prior to initiation of any treatment.

➢ **Antibiotics**

Based on the patient's clinical presenting features, infection is likely to be on the differential diagnosis and empiric antibiotics should be considered. Prior to initiating antibiotic therapy, obtain appropriate cultures.

➢ **Anticoagulation**

Currently there is no role for prophylactic or treatment anticoagulation in children with MIS-C. If there is a child who is already on therapeutic or prophylactic anticoagulation for prior indication and high-dose aspirin is being considered for management, consult hematology.

➢ **Antiviral medications**

Not routinely recommended in patients with suspected MIS-C.

Ongoing monitoring

Clinical response

- Resolution of fever, other clinical features and improving markers of inflammation
- Lack of clinical response within the first 36-48 hours: Consider further immunomodulator as per Rheumatology recommendation

Laboratory testing

Daily lab monitoring should be guided by Rheumatology recommendations.
The following may be considered for the monitoring of hyperinflammation while patients have evidence of fever and /or persistence of symptoms:

- CBC and diff
- CRP
- PT/PTT/INR
- D-dimer
- Troponin
- Ferritin
- LDH
- BNP
- Lactate

Follow-up Echocardiogram

Frequency of follow-up echocardiograms will depend on patient's particular clinical features and should be guided by Cardiology.

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Discharge criteria

These will vary depending on the clinical scenario and severity of presenting illness but generally should include:

- Lack of fever for 48 hours without antipyretics (excluding steroids)
- Improvement in the presenting clinical symptoms (e.g. diarrhea, rash, etc.)
- Improvement in lab markers
- If during influenza season, patient should receive influenza vaccination prior to discharge if not already received

Particular considerations:

- Patients on Aspirin (ASA) – the continuation of this medication should be guided by Rheumatology and Cardiology. They should avoid NSAIDS while on ASA.
- Patients who received Steroids during admission – A tapering schedule should be established prior to discharge based on guidance from Rheumatology.
- Patients who received IVIG – should not receive live virus vaccines for 11 months

Outpatient Follow-up

- General Pediatrics – follow up with pediatrician or family physician within 1 week of discharge. The discharge summary should include a summary of investigations and reasons to return (see below). The follow up physician should be copied.
- Cardiology – follow-up with repeat echocardiogram should occur in approximately 2 weeks with further follow-up established at the appointment.
- Rheumatology – Follow-up to be arranged depending on severity of illness, discharge medications, and availability of other physicians to see the patient. Rheumatology will provide follow up visit for patient prior to discharge.
- Other services (ID, GI, Neuro, Surgery, etc.) – will depend on clinical features and course of the patient
- All appointments should be arranged prior to discharge where possible.

Reasons to return to Emergency Department

- Fever > 38 degrees Celsius
- Recurrence of presenting symptoms or child becomes unwell with other symptoms.
- New appearance of respiratory distress or shortness of breath.

Version History

DATE	DOCUMENT NUMBER and TITLE	ACTION TAKEN
09-Jun-2020	C-05-07-60677 Multi-System Inflammatory Syndrome In Children Temporally Associated With Covid-19: Inpatient Workflow	Developed by BCCH MIS-C Working Group; Approved by Professional Practice Director
17-Aug-2020	“	Updated; Approved by Professional Practice Director

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