UMMC GUIDANCE FOR MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) VERSION 3

Note: Guidance is based on expert consensus. Subspecialty consultation for individualized recommendations for suspected cases is strongly recommended. The Version 3 Guidelines also highlight that *at this time, given the high prevalence of COVID-19 in certain communities, seroreactivity to SARS-CoV-2 (nucleocapsid or spike protein) may no longer adequately distinguish between MIS-C and other overlapping syndromes, although a negative antibody test should prompt consideration of alternative diagnoses...*

* (https://emergency.cdc.gov/han/2020/han00432.asp)

### Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C)*

- A patient aged <21 years presenting with fever, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurologic); AND
- No alternative plausible diagnoses; AND
- Positive for recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within 4 weeks prior to the onset of symptoms

**COMMENTS:**

- Fever >38.0°C for >24 hours, or report of subjective fever lasting >24 hours
- Evidence of inflammation: an elevated CRP, ESR, fibrinogen, procalcitonin, d-dimer, ferritin, lactate dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin
- Reporting of these cases is completed via Infection Prevention (not necessary for providers to do this themselves)
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection

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**Figure 1 below used with Copyright License:** https://www.rheumatology.org/Portals/0/Files/ACR-COVID-19-Clinical-Guidance-Summary-MIS-C-Hyperinflammation.pdf

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### INITIAL LABS AND DIAGNOSTICS

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### INITIAL INPATIENT CONSULTS

- All children admitted with concern for MIS-C: Ped's ID, Ped's Cardiology, Ped's Rheumatology, Ped's Hematology
- If with concern for thrombosis/HU/MAS: Ped's Hem/Onc and Ped's Rheumatology
- If with severe abdominal pain: Ped's GI, Ped's Surgery
- If with neurologic findings: Ped's Neurology
- Additional consults based on presenting symptoms and clinical indications (Ped's Nephrology, Ped's Neurology, Dermatology)

*Please note Pediatric Cardiology UMMC Guidelines for MIS-C posted also at this website: https://intranet.unc.edu/Health%20Care/Coronavirus-Updates/files/Flowchart-Cardiac-Evaluation-Care-of-Children-MIS-C.pdf

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### PRELIMINARY MANAGEMENT PLANS FOR MIS-C

#### Therapeutic Categories:
- **Steroid Initial Dosing** – the use of steroid should be discussed with Ped's Rheumatology
- **Immuno modulators**– the use of anakinra or other biologics for refractory illness course should be discussed with Ped's Rheumatology and Ped's Hem/Onc
- **Anticoagulation** – the use of LMWH or other anticoagulation regimen should be discussed with Ped's Hem/Onc
- **GI prophylaxis with PPI** – while on steroid/corticosteroids primary team
- **Steroid taper** – with subspecialty consultation Ped's Rheumatology

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### IVIG

- All children meeting MIS-C criteria or with coronary ectasia should receive IVIG 2g/kg SLOW INFUSION and strongly considered dividing into two doses after subspecialty discussion (not to EXCEED 80 mg/kg/dose/infusion).
- If 2-19 years of age should dose per IBW if actual body weight is > IBW by 20%. (and adults with BMI >30kg/m2)
- Steroids should be considered also and discussed with PEDS Rheum and PEDS ID

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### OTHER MANAGEMENT CONSIDERATIONS

- **Antibiotics**: Ceftriaxone (alternative, ceftazidime) should be used as first-line empiric antibiotic coverage.
  - Add vancomycin if concerned for MRSA in infection, including skin or soft tissue source, pneumonia, Gram positive bacteremia
  - Add metronidazole if concerned for intra-abdominal infection.
  - Use cefepime (alternative, meropenem) for patients who are immunocompromised, have a history of multi drug resistant gram-negative bacterial infections, are critically ill, or if otherwise clinically indicated.
  - Consider further coverage for toxic shock syndrome or *Rickettsia* infection depending on patient presentation.
- **Anticoagulation**: Please consult Heme/Onc to discuss. Please consider contraindications to anticoagulation (i.e., platelet <50,000-80,000/uL, active bleeding, or significant bleeding risk). In general, low dose ASA 3-5 mg/kg/day should be given until normalization of platelet count and confirmed normal coronaries at >= 4 weeks after diagnosis. Enoxaparin should be considered also as prophylaxis (treatment dosing considered with coronary artery aneurysms with z score >=10 or patients with documented thrombosis or an ejection fraction <35%).
- Patients with GI symptoms: These patients have higher risk of bowel perforation with pulse steroids, consider...
risk/benefit of therapy in these patients. Please consult the hematologist for recommendations for steroids.

- Patients with Renal Injury: consult Peds Nephrology and pediatric pharmacy for assistance in dosing medications.

**ORGAN-SPECIFIC WORK-UP BASED ON PATIENT SYMPTOMS**

**Dermatologic:** Take photo of rash/upload to Epic. Consider the following tests (HSV, VZV, enterovirus PCR): Consider alternative rheumatologic diagnoses that present with fever and rash - Systemic JIA, Lupus, Kawasaki disease. GI: Consider GI pathogen PCR panel; C difficile toxin PCR; Stool culture. Neurologic: Head imaging - consider if with focal neurologic deficit, altered mental status, seizure, severe headache with meningeal signs. If no containments, perform lumbar puncture (cell count, protein, glucose, culture, meningoencephalitis panel) AND **CONSULT NEUROLOGY**

**FOLLOW-UP INPATIENT LAB & IMAGING**

<table>
<thead>
<tr>
<th>PICU</th>
<th>General Pediatric Floor</th>
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</thead>
<tbody>
<tr>
<td>- Cardiac enzymes &amp; BNP - every 48 hours (trend daily if abnormal)</td>
<td>- Cardiac enzymes &amp; BNP - weekly (trend daily if abnormal)</td>
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<tr>
<td>- 12L ECG every 1-2 days</td>
<td>- 12L ECG every 2 days</td>
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<tr>
<td>- ECHO - timing - discuss with Peds Cardiology</td>
<td>- ECHO - discuss with Peds Cardiology</td>
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<tr>
<td>Discuss with Peds Rheumatology regarding daily labs (CBC, diff, CMP, ferritin, fibrinogen, D-dimer, triglycerides) for patients concerning for cytokine storm</td>
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<tr>
<td>- Clinical change or abnormal trends/other labs warrant further evaluation to be determined by primary team</td>
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**DISCHARGE FOLLOW UP**

- Steroid taper plan should be determined and clarified with Pediatric Rheumatology. Please confirm that patient has prescription picked up and that patient is provided with prescription and medication dispense quantity prior to discharge. The prescription can be written as directions but please ensure steroids dispensed are sufficient for the wean period. Please call Rheum to clarify if there is any need.
- Ensure that plan for discharge ASA and enoxaparin are **clear** with Cardiology and Hematology **and the parent**, (e.g., if patient needs ASA if it is not given as an RX (tell the parents they have to get it separately). 
- Consider GI protective agent as many patients will be going home on ASA and steroid weans.
- All patients should have follow-up within 2 weeks post discharge with Pediatric Cardiology with repeat ECHO, ECG, and MIS-C clinic for Peds I, RHEUM, and HEME follow up. Prior to discharge, Pediatric Hematology should be contacted to discuss discharge plans for anticoagulation (email/contact Dr Cathy Gordon if there are needs for clarification).
- For appointments, prior to discharge, please email JEANIE CRAFT at jcraft@unc.edu. Make sure REF 300 is entered for Cardiology and CHAMBS MIS-C CLINIC (request 3 visits).
- **Exercise should be LIMITED** until outpatient Cardiology appointment clears the child for resumption of activity.
- Live vaccines are not to be administered within 11 months of IVIG due to decreased potential efficacy.
- Consider influenza shot (killed vaccine) if due, but ideally at least 1 month after cessation of steroids.
- CDC recommends deferring COVID-19 vaccination for eligible children to 3 months after MIS-C and clinical recovery has been achieved, including return to normal cardiac function; and onset of MIS-C occurred before any COVID-19 vaccination.

**LAST GUIDANCE UPDATE: JANUARY 2022**

Suggested readings and additional online resources for specialists caring for children with MIS-C:
