Multi-system Inflammatory Syndrome in Children (MIS-C) Temporally Associated with COVID-19
Hasbro Children's Hospital Clinical Guideline
Last updated July 2021

This clinical guideline is a working, iterative document given the nature of this emerging clinical syndrome, with growing evidence and experience. The guideline will be updated as recommendations evolve.

MIS-C Case Definition (WHO/CDC)

CDC Case Definition for MIS-C: Reporting Purposes Only	• Fever (≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours) • Lab evidence of inflammation: ≥1: elevated CRP, ESR, fibrinogen, procalcitonin, d-dimer, ferritin, LDH, IL-6, neutrophils, reduced lymphocytes or albumin • Clinically severe illness requiring hospitalization • Multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological) • No alternative plausible diagnoses • Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms	
Key Findings with MIS-C	• High fevers (universal) • Severe abdominal pain/diarrhea in most • +/- rash, oral mucosal changes, conjunctivitis • Respiratory failure uncommon	• Key lab findings: ○ ↑ CRP, D-dimer, ferritin, markedly elevated BNP ○ ↓ lymphocytes, sodium, platelets
Kawasaki Disease AHA Criteria	*Typical Kawasaki:* Fever ≥ 5 days PLUS 4 of 5 of: • Changes in lips/oral cavities • Conjunctivitis • Rash • Erythema/edema of hands/feet • Lymphadenopathy > 1.5cm	*Incomplete/Atypical Kawasaki:* Fever ≥ 5 days PLUS 2-3 criteria OR infants with fever ≥ 7 days without explanation • CRP < 3 and ESR < 40: Serial clinical and lab evaluation if fevers persist. ECHO if peeling develops. • CRP ≥ 3 and/or ESR ≥ 40: Treat if positive ECHO OR ≥ 3 lab findings: (↓ **Hgb** for age, **platelet** ≥ 450,000 after 7th day of fever, **albumin** ≤ 3 g/dL, ↑ **ALT**, **WBC** ≥ 15,000/mm^3, **urine** ≥ 10 WBC)

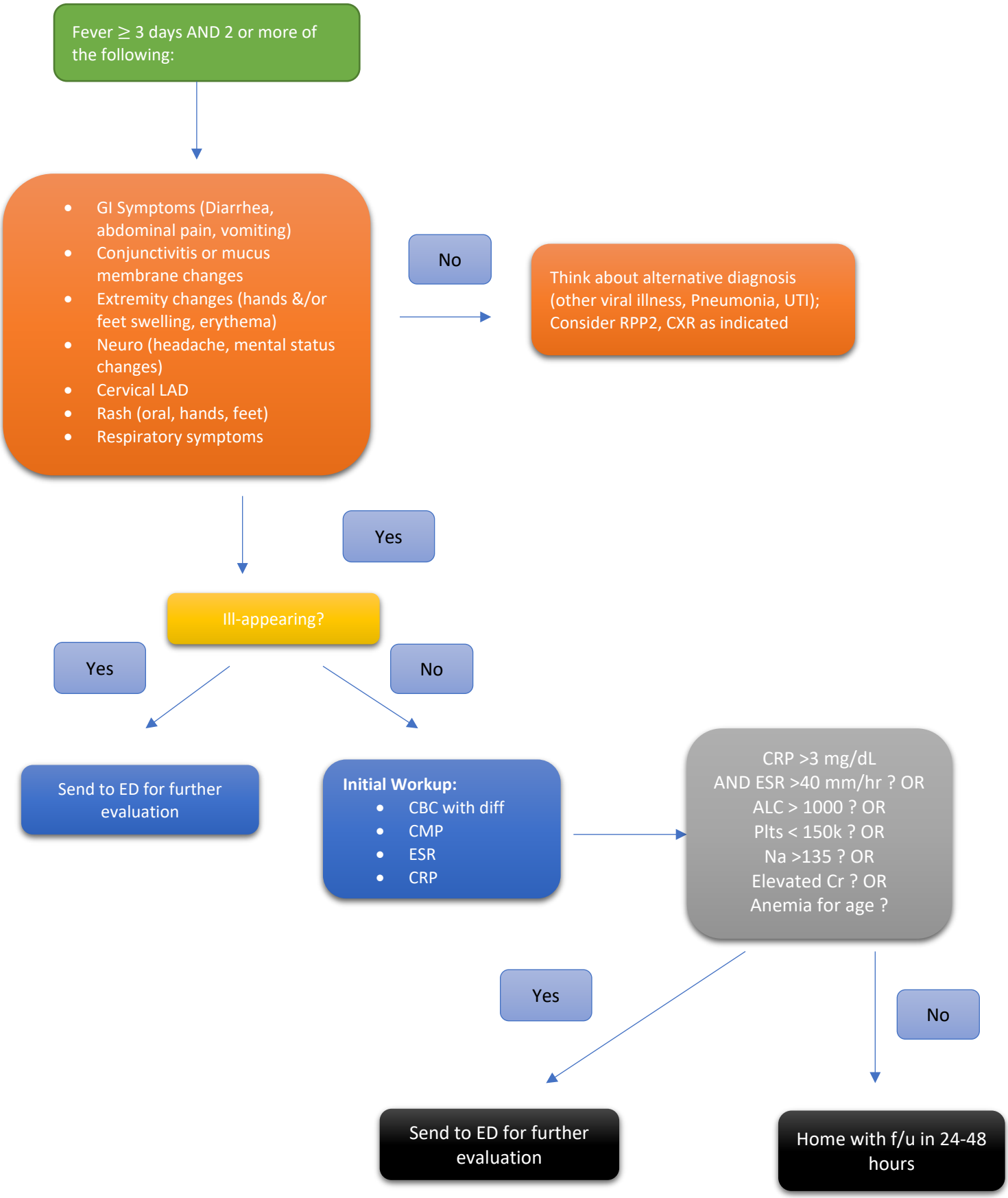
RI DOH/CDC Reporting

1. Report MIS-C case to CDC and RIDOH
    a. Responsibility of primary team at discharge
    b. Place a Significant Event note in the EMR noting that RiDOH/CDC reporting has been completed
2. Complete CDC form (https://www.cdc.gov/mis-c/pdfs/hcp/mis-c-form-fillable.pdf)
    a. Email completed form and patient facesheet to Karen Luther (Karen.Luther@health.ri.gov via lifespan email (using PHI in subject line) OR
    b. Send fax patient facesheet and completed form to: Karen Luther RN, MPH fax: 401-222-2488

AAP Interim Guidance: https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/multisystem-inflammatory-syndrome-in-children-mis-c-interim-guidance/

Additional resources:
https://www.rheumatology.org/Portals/0/Files/ACR-COVID-19-Clinical-Guidance-Summary-MIS-C-Hyperinflammation.pdf
https://www.chop.edu/clinical-pathway/multisystem-inflammatory-syndrome-mis-c-clinical-pathway

Outpatient MIS-C Algorithm



Multisystem Inflammatory Syndrome in Children(MIS-C) Pathway

Fever (>100.4F) ≥24 hours
*Typically high grade

No → Seek alternative diagnosis (viral illness, UTI, appendicitis)

Further workup at the discretion of provider

-consider RP2, UA, CXR, abd US as indicated.

Yes

≥ 2 Clinical features

Gastrointestinal (more common)
- Diarrhea, abdominal pain, vomiting

Dermatologic (more common)
- Rash, desquamation, non-vesicular

Conjunctivitis
- Non exudative conjunctivitis

Oral Mucosal change
- Erythema and cracked lips, erythema of oropharynx, strawberry tongue

Extremity changes
- Erythema and edema of hands and feet

Lymphadenopathy
- Cervical, unilateral, >1.5cm

Neurologic
- Headache, irritability, altered mental status

Respiratory, Renal

***Epidemiologic Link to COVID**
- **Positive test/ exposure in the past >4 weeks**

No → Seek alternative diagnosis (viral illness, UTI, appendicitis)

Yes

Initial lab workup:
CBC w/diff, CMP, ESR, CRP, UA
↑CRP >3 mg/dL or ESR >40 mm/hr
AND at least 1:
↓Lymphopenia (<1000)
↓Thrombocytopenia (<150K)
↓Hyponatremia (<135)

Consultations as indicated:

Rheumatology
- Unsure of MIS-C diagnosis
- Refractory disease

Infectious Disease
- Unsure of MIS-C diagnosis
- fever workup

Cardiology
- Evaluate cardiac dysfunction
- KD features

Hematology/Oncology
- Thromboprophylaxis

Normal → **Reassuring exam & labs** → **Close follow up with PCP**

Abnormal → **Extended workup:**

↑ D-dimer	-EKG
↑ ferritin	-Covid Ab
↑ fibrinogen	-PT/INR
↑ BNP	-Blood
↑ Troponin	

Abnormal D-dimer
-Consult Hematology/Oncology
-Thromboprophylaxis per per Pediatric COVID-19/MIS-C Thromboprophylaxis guideline

Abnormal BNP, Troponin, EKG
-Consult Cardiology
-Consider echo

Abnormal → **Treat if symptoms and lab concerning for MIS-C [Multidisciplinary approach]**

Mild MIS-C
- Normal echo and no KD features
- Febrile but clinically well

Admit to hospitalist team
- **PO Prednisolone/Prednisone** 1mg/kg/dose 2XDay
OR **IV Methylprednisolone** 1mg/kg/dose 2XD (max 30mg/dose)
- **Duration:** 5 days plus 10 days of Prednisolone
Day 1-5: 1mg/kg/dose 2XD
Day 6-10: 0.5mg/kg/dose 2XD
Day 11-15: 0.5mg/kg/dose 1XD

Moderate MIS-C
- Cardiac dysfunction
- KD/incomplete KD features
Hemodynamically stable.

Admit to hospitalist team/PICU
- **IV Methylprednisolone**
1mg/kg/dose 2XD (max 30mg/dose)
- **IVIG 2g/kg, ASA**

Severe MIS-C
- Shock/end organ dysfunction
- KD features/cardiac dysfunction

Admit to PICU
- **IV Methylprednisolone**
1mg/kg/dose 2XD (max 30mg/dose)
- **IVIG 2g/kg, ASA**