UNC CHILDREN'S PATHWAY FOR EVALUATION AND TREATMENT OF PATIENTS WITH CONCERN FOR MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C)

EMERGENCY DEPARTMENT MANAGEMENT (INPATIENT MANAGEMENT ON PAGE 3)

Patient presents with **fever AND TWO** or more of the following:
GI sx, Rash, Conjunctivitis, Oral changes, Cough, Headache/Irritability, Extremity swelling, Lymphadenopathy
OR
Fever > 4 days and no obvious source

*Please consider alternate diagnoses such as Kawasaki Disease, Incomplete Kawasaki, and Toxic Shock Syndrome. **See page 2 for MIS-C Context & Definitions***

*See Kawasaki criteria and lab testing in **Appendix A***

Does the patient have unstable vitals?

YES → Initiate early goal directed therapy for sepsis (Sepsis Bundle)

NO → Common causes of fever evident on initial eval?

YES → Evaluate and manage as appropriate

NO

Lab evaluation to include:

CBC w/ diff	Troponin	COVID-19 PCR and nucleopcapsid IgG
CMP	BNP	CXR
LDH	DIC Panel	EKG
CRP and ESR	Blood Culture	Echocardiogram ASAP
Ferritin	*Other testing as clinically indicated*	

Critically ill?

YES → At UNC Medical Center?

NO → Transfer Patient to UNC Children's Hospital Patient Logistics Center 984-974-5000

YES → Admit to PICU* Inpatient management on Page 3

NO → Labs abnormal?

YES → Admit to hospitalist service and consult Peds ID and Rheum. Cardiology if cardiac involvement**. Inpatient management on Page 3

NO → Admit to hospitalist service. Inpatient management on Page 3

***PICU admission crtieria for MIS-C patient: shock, concern for heart failure, requiring HFNC or greater support**

**** Cardiac involvement= EF < 55%, elevated troponin, hemodynamic compromise**

CONTEXT

On May 14, 2020 the CDC defined a pediatric multi-system inflammatory syndrome temporally associated with COVID-19 as Multisystem Inflammatory Syndrome in Children (MIS-C). Clinical features of this syndrome are similar to those seen in other diseases including Kawasaki Disease (KD), Toxic Shock Syndrome (TSS), and Macrophage Activation Syndrome (MAS)/Hemophage Lymphohistiocytosis Syndrome (HLH). This pathway was adapted from existing clinical guidance from the Children's Hospital at NYU Langone to maximize diagnostic opportunity and to provide a streamlined approach to initial management.

Management of your patient may require a more individualized approach.

MIS-C CASE DEFINITION

1. Individual <21 years old presenting with fever >24 hours, 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**
2. No alternative plausible diagnosis; **AND**
3. 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 onset of symptoms**

EXAMPLES OF ORGAN SYSTEM INVOLVEMENT

Cardiac: shock, elevated troponin, elevated pro-BNP, coronary arteritis, abnormal echocardiogram, arrhythmia

Gastrointestinal: severe abdominal pain, vomiting, diarrhea, elevated transaminases

Hematologic: elevated d-dimers, coagulopathy, lymphopenia, thrombocytosis or thrombocytopenia

Mucocutaneous: petechia or purpura, polymorphous rash, mucositis, conjunctivitis

Neurologic: headache/irritability, altered mental status, seizures, focal neurologic deficits

Respiratory: ARDS, pulmonary embolism

Renal: acute kidney injury or failure

LABORATORY EVIDENCE OF INFLAMMATION

Elevated CRP and/or ESR, D-dimer, Ferritin, IL-6, Neutrophils and/or Reduced lymphocytes

INPATIENT MANAGEMENT FOR MIS-C

CONSULTS	**Required** • Pediatric Rheumatology (in-person) • Pediatric Infectious Diseases (in-person) **If cardiac involvement (depressed EF (<55%), elevated troponin, hemodynamic compromise)** • Pediatric Cardiology
SUPPORTIVE CARE & MONITORING	• Monitors, continuous pulse ox • Telemetry if cardiac involvement • Echocardiogram • Assess patient hypercoagulability risk (see page 4) **Labs (daily, space as appropriate)** • CBC/diff, CMP, CRP • BNP, troponin (if initially abnormal) • F/u EKG and echo as indicated

TREATMENT CONSIDERATIONS FOR MIS-C

Agent	Dosing and Regimen	Considerations	Adverse Effects and Interactions	Recommendation
Methylprednisolone **Prednisolone** **Prednisone**	**Mild:** 2 mg/kg day Start with IV methylprednisolone then transition to oral **Moderate**: 5-10 mg/kg daily x 3 days **Severe**: 30 mg/kg daily (MAX 1 Gram) x 3 days	Consider administering in the morning	Hypertension +/- PRES, bradycardia, delirium	**Used in almost all MIS-C cases**. May be used alone without IVIG. Use in addition to IVIG with organ-threatening disease or shock and/or refractory to IVIG. Dose is based on severity of illness.
IVIG	1-2 gm/kg/dose x1 (MAX 70-100 gm/dose)	Pre-medication is not required prior to IVIG administration Can be divided over 2 days if needed	Increased risk for clot or thrombosis if other risk factors present; aseptic meningitis; hemolytic anemia	**Used in almost all MIS-C cases**.
Aspirin (Full anticoagulation management recs on page 4)	3-5 mg/kg/day, **MAX DAILY DOSE 81 mg**	Anti-platelet and anti-inflammatory	Avoid if baseline PLT< 100K; slightly increased risk of bleeding.	**Used in almost all MIS-C cases.** Almost all patients should be discharged on aspirin UNLESS being sent home on lovenox. No dual therapy.

ANTICOAGULATION MANAGEMENT IN MIS-C

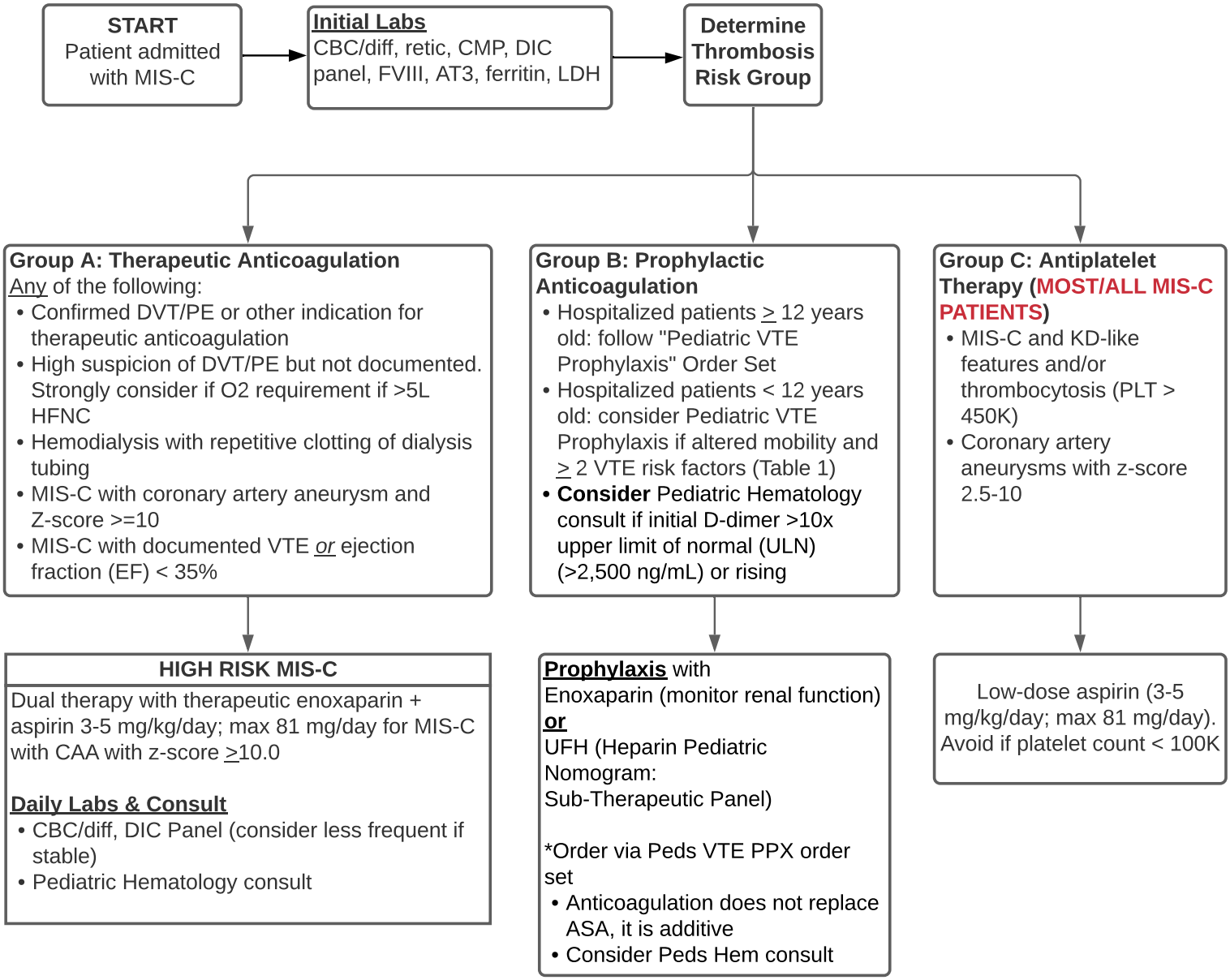

Table 1. Risk Factors for Hospital-Associated VTE in Children

• Central venous catheter • Mechanical ventilation • Prolonged length of stay (eg, anticipated >3 days) • Complete immobility (eg, Braden Q Mobility Score = 1) • Obesity (BMI > 95th percentile) • Active malignancy, nephrotic syndrome, Cystic fibrosis exacerbation, sickle cell disease vaso-occlusive crisis, or flare of underlying inflammatory disease (eg, lupus, JIA, IBD) • Congenital or acquired heart disease with venous stasis or impaired venous return • ICU admission • D-dimer level elevated to > 5 times ULN	• Previous history of VTE • First-degree family history of VTE before age 40 or unprovoked VTE • Known thrombophilia (eg Protein S, Protein C, or anti-thrombin deficiency; Factor V Leiden; factor II G0210A; persistent antiphospholipid antibodies • Pubertal, post-pubertal, or age > 12 years • Estrogen-containing oral contraceptive pill • Status-post splenectomy for underlying hemoglobinopathy

POST-DISCHARGE FOLLOW-UP RECOMMENDATIONS

MIS-C Service	Contact PCP at discharge
Primary care physician	Consider check-in 3-5 days after discharge. Ensure adequate follow-ups. Monitor for recrudescence (e.g., fever, rash). Labs may be needed prior to subspecialist follow-up.
Pulmonology	As-needed if significant respiratory compromise during hospitalization
Hematology	If discharged on anticoagulation, virtual follow-up within 2 weeks
Rheumatology	Within 2 weeks with labs, in-person preferred
Cardiology	If cardiac involvement, at 2 weeks and 4 weeks, in-person, with echocardiogram.
Infectious Diseases	As needed only

Updated 2/1/22

Contact Dr. Aliese Sarkissian (aliese@email.unc.edu) or Dr. Daniel Park (daniel.park@unc.edu) for clarifications or edits

APPENDIX A

Evaluation of Suspected Kawasaki Disease

Adapted from McCrindle BW, Rowley AH, Newburger JW et al. Diagnosis, treatment, and long-term management of Kawasaki disease: A scientific statement for health professionals from the American Heart Association. Circulation 2017; 135:e927