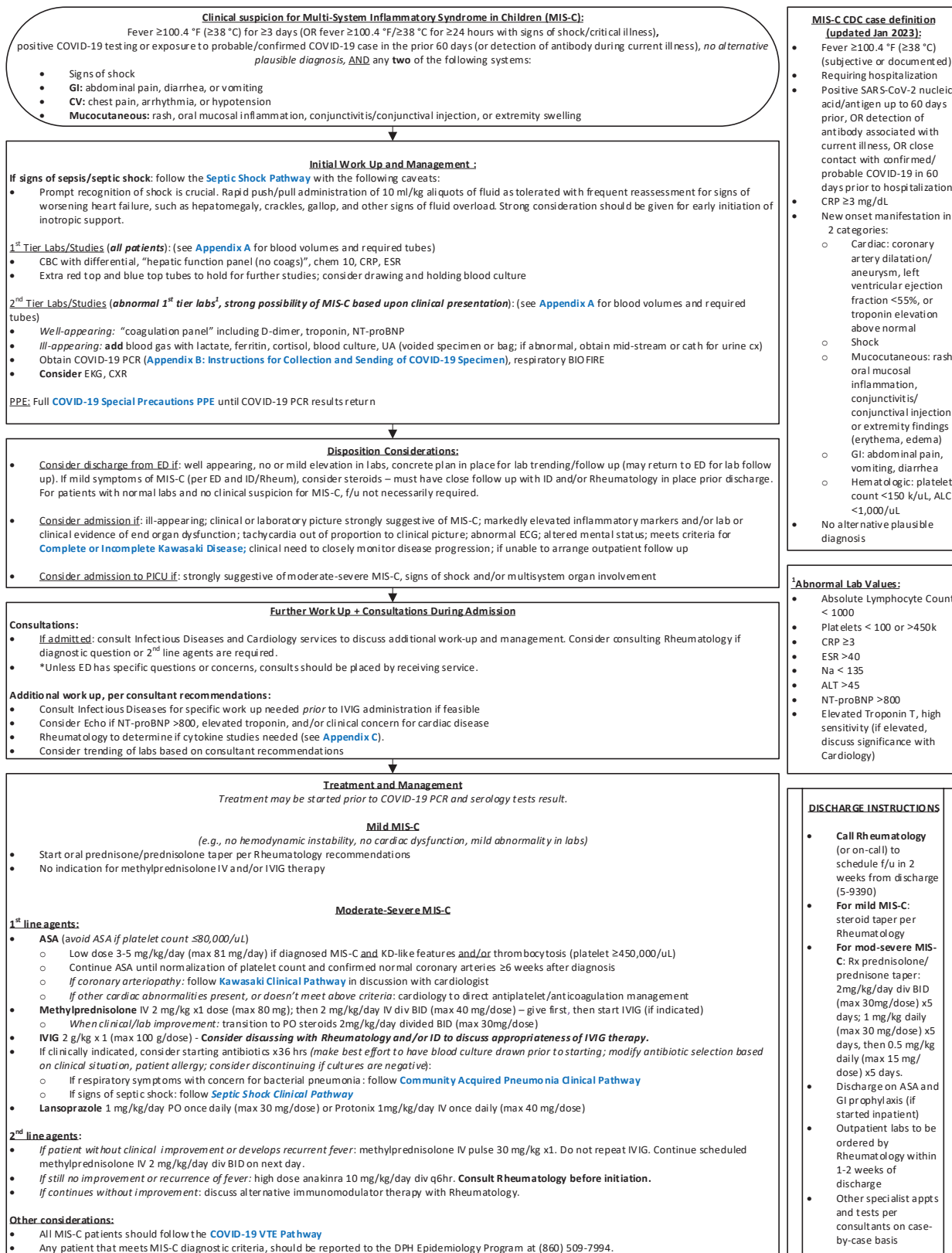


CLINICAL PATHWAY: Multi-System Inflammatory Syndrome in Children (MIS-C)

Clinical Pathway

THIS PATHWAY
SERVES AS A GUIDE
AND DOES NOT
REPLACE CLINICAL
JUDGMENT.



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This pathway is subject to change, based on evolving recommendations from the CDC and CT DPH.

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Appendix A: Blood Volumes and Required Tubes for Labs**Initial Work Up:**

- CBC with differential: Whole blood, Lavender EDTA, Minimum 1 mL, 4mL collection tube or microtainer
- “Liver function panel” (includes GGT and coags): Green top Lithium Heparin with gel-barrier, minimum 2mL whole blood, 1mL plasma (liver function) AND Full Blue top sodium citrate tube (coags)
- Chem 10: Green top Lithium Heparin with gel-barrier, minimum 2mL whole blood, 1 mL plasma.
- Blood gas with lactate: 1mL of whole blood into a heparin syringe on ice or full Green Lithium Heparin tube (blood gas); Grey top or Li Heparin on ice (lactate)
- Cortisol: Green top Lithium Heparin with gel-barrier, minimum 2mL whole blood, 1 mL plasma.
- Fibrinogen: Full Blue top sodium citrate tube
- D-dimer: Full Blue top sodium citrate tube
- CRP: Green top Lithium Heparin with gel-barrier, minimum 2mL whole blood, 1 mL plasma.
- ESR: Whole blood, Lavender EDTA, Minimum 1 mL, 4mL collection tube
- Procalcitonin: Green top Lithium Heparin with gel-barrier, minimum 2mL whole blood, 1 mL plasma.
- LDH: Green top Lithium Heparin with gel-barrier, minimum 2mL whole blood, 1 mL plasma.
- Ferritin: Green top Lithium Heparin with gel-barrier, minimum 2mL whole blood, 1 mL plasma.
- Troponin: Green top Lithium Heparin with gel-barrier, minimum 2mL whole blood, 1 mL plasma.
- NT-proBNP: Green top Lithium Heparin with gel-barrier, minimum 2mL whole blood, 1 mL plasma.
- CKMB: Green top Lithium Heparin with gel-barrier, minimum 2mL whole blood, 1 mL plasma.
- Blood culture: Bactec pedi bottle (no minimum amount needed)
- Hold extra red top tube for future studies, if able

****all tubes being sent need to be full if you wish the lab to run multiple tests off of the same tube – minimum volumes added together will not suffice****

- Lavender top EDTA tube (*not the bullet*):
 - Amount of blood: needs to be full
 - can run: CBC w diff, ESR
- Green top lithium heparin with gel barrier tube:
 - Amount of blood: needs to be full
 - Can run: liver function panel, chem 10, CRP, LDH, ferritin, triglyceride, troponin, NT-proBNP, CKMB, cortisol
- Blue top sodium citrate tube:
 - Amount of blood: needs to be full
 - Can run: coagulation tests, fibrinogen, D-dimer

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Additional Work Up:

- Type and Screen
- Triglycerides: Green top Lithium Heparin with gel-barrier, minimum 2 ml whole blood, 1 ml plasma
- Cytokine studies:
 - IL-6, Soluble IL-2, Soluble IL-2R, IL-1, IL-10 (sent as cytokine panel): Red top, preferred 1 ml serum
 - NK Function (not part of cytokine panel above): Green top, 10 ml whole blood
 - Soluble CD-163 (not part of cytokine panel above and is sent separately to Cincinnati): see [Appendix C Cytokine Studies Cincinnati Lab Requisition Form](#)
- CMV:
 - Serology:
 - Cytomegalovirus (CMV) Antibody, IgG: Red top serum, 1.0 mL (0.5 mL) min required
 - Cytomegalovirus (CMV) Antibody, IgM: Red top serum, 1.0 mL (0.5 mL) min required
 - PCR:
 - Cytomegalovirus DNA, QUANT, PCR: Send out to Quest, EDTA Lavender plasma, -1.0 mL
- EBV:
 - Serology:
 - All EBV serological testing: Red top serum, 1.0 mL (0.5 mL) min required
 - Molecular
 - EBV DNA, PCR, QUALITATIVE: Send out to Quest, 1 mL (0.3 mL minimum) serum from red gel barrier or red non-gel barrier tube or 1 mL Lavender EDTA plasma
 - EBV DNA, PCR, Quantitative: Send out to Quest, 1 mL (0.5 mL minimum) EDTA Lavender plasma or 1 mL (0.5 mL minimum) serum
- Parvovirus:
 - Antibodies: Send out to Quest, 2 mL (1 mL minimum) serum from a red top or SST tube
 - PCR: Send out to Quest, 1 mL (0.5 mL minimum) EDTA plasma

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Hartford Hospital Specimen

- Specimens must be collected in a viral transport tube
 - Both BIOFIRE and COVID-19 specimens may be sent with 1 single swab (reserve respiratory BIOFIRE for critically ill patients)
- Place COVID-19 sample in a green irreplaceable biohazard bag
- Patient's COVID-19 test requisition form (will have printed when COVID-19 test was ordered)
- Must hand carry sample to the HH Lab; **DO NOT** use the tube system
- When walking samples to Hartford Hospital, the staff member will only need to wear gloves for PPE. There is no need to don full PPE for sample transport.

LIAT Specimen

- Specimen must be collected in viral transport medium
- Label sample with barcoded patient demographic label that includes: the initials of the person collecting the sample, date and time of collection
- Patient sample should be placed in a green irreplaceable biohazard bag
- Must hand carry sample to COVID-19 specimen drop-off room (1C, room #1693) and fill out the log
- When walking samples to COVID-19 specimen drop-off room, the staff member will only need to wear gloves for PPE. There is no need to don full PPE for sample transport.



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CYTOKINE STUDIES

If Rheumatology determines that cytokine studies are needed, the following labs should be ordered:

- “Interleukin panel” and/or the below:
- IL-6
- Soluble IL-2
- IL-1
- IL-10
- NK Function
- Soluble CD-163
- Soluble IL-2R

Utilize [Cincinnati Children’s Test Requisition Form](#) (next page).



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DIL — TEST REQUISITION FORM

MUST BE RECEIVED MONDAY – FRIDAY WITHIN 1 DAY OF COLLECTION UNLESS OTHERWISE INDICATED

PATIENT INFORMATION (STICKER ALSO ACCEPTED)

Patient Name (Last, First, MI): _____, _____, _____ DOB (MM/DD/YYYY): ____/____/____

Medical Record #: _____ Collection Date (MM/DD/YYYY): ____/____/____ Time of Sample(HH:MM): _____

Legal Sex: ☐ Male ☐ Female BMT: ☐ Yes – Date: ____/____/____ ☐ No ☐ Unknown Relevant Medications: _____

Diagnosis or reason for testing: _____

TESTS OFFERED: THE MAX VOLUME LISTED IS THE PREFERRED WHOLE BLOOD VOLUME

☐ Alemtuzumab Plasma Level 2-3mL Sodium Heparin See #5 on page 2	☐ Mitogen Stimulation See #1 on page 2
☐ ALPS Panel by Flow <i>Need CBC/Diff result</i> 1-3ml EDTA – See #2 on page 2	☐ Neopterin (Circle One): Plasma or CSF 1-3ml EDTA or 0.5-1ml CSF See #3 or #4 on page 2
☐ Antigen Stimulation See #1 Below	☐ Neutrophil Adhesion Mrks: CD18/11b 1-3ml EDTA
☐ Apoptosis (Fas, mediated) 10-20ml ACD-A Note: Only draw Apoptosis on Wednesday for Thursday delivery	☐ Neutrophil Oxidative Burst (DHR) 1-3ml EDTA
☐ B Cell Panel <i>Need CBC/Diff result</i> 1-3ml EDTA – See #2 on page 2	☐ NK Function (STRICT 28 HOUR CUT-OFF) See #1 on page 2
☐ BAFF 1-3ml EDTA – See #4 on page 2	☐ Perforin/Granzyme B 1-3ml EDTA
☐ CD40L / CD40FP / ICOS 3-5ml Sodium Heparin	☐ pSTAT5 1-3ml EDTA
☐ CD45RA/RO 1-3ml EDTA	☐ S100A8/A9 Heterodimer 2 (0.3mL) Gold serum aliquots, frozen w/in 4 hours of collection
☐ CD52 Expression 1-3ml EDTA	☐ S100A12 2 (0.3mL) Gold serum aliquots, frozen w/in 4 hours of collection
☐ CD107a Mobilization (NK Cell Degran) See #1 on page 2 Note: Only draw CD107a Monday – Wednesday	☐ SAP (XLP1) 1-3ml Sodium Heparin
☐ CTL Function See #1 on page 2	☐ Soluble CD163 1-2ml EDTA - See #4 on page 2
☐ CXCL9 2 (0.5ml) EDTA plasma aliquots, frozen w/in 8 hours of collection	☐ Soluble Fas-Ligand (sFasL) 1-3ml EDTA/Red/Gold - See #4 on page 2
☐ Cytokines, Intracellular 2-3ml Sodium Heparin	☐ Soluble IL-2R (Soluble CD25) 1-3ml EDTA - See #4 on page 2
☐ Cytokines (Circle One): Plasma or CSF <i>Includes: IL-1b, 2, 4, 5, 6, 8, 10, IFN-g, TNF-a, and GM-CSF</i> If sending frozen, 2 (0.5mL) EDTA plasma aliquots frozen, preferred	☐ TCR α/β TCR γ/δ 1-3ml EDTA
☐ Foxp3 <i>Need CBC/Diff result</i> 1-3ml EDTA – See #2 on page 2	☐ T Cell Degranulation Assay See #1 on page 2 Note: Only draw T Cell Degran Monday – Wednesday
☐ GM-CSF Autoantibody (GMAb) 1-3ml Red/Gold - See #4 on page 2	☐ TCR V Beta Repertoire 2-3ml EDTA
☐ GM-CSF Receptor Stimulation 1-3ml Sodium Heparin	☐ Th-17 Enumeration 2-3ml Sodium Heparin
☐ iNKT 1-3ml EDTA	☐ WASP 1-3ml Sodium Heparin
☐ Interleukin-18 (IL-18) 3ml Red/Gold - See #4 on page 2 If sending frozen, 2(0.3mL) red/gold serum aliquots frozen, preferred	☐ WASP Transplant Monitor 1-3ml Sodium Heparin
☐ Lymphocyte Activation Markers 2-3ml Sodium Heparin	☐ XIAP (XLP2) 1-3ml EDTA
☐ Lymphocyte Subsets 1-3ml EDTA	☐ ZAP-70 (only for SCID) 1-3ml EDTA
☐ MHC Class I & II 1-3ml EDTA	☐ Other: _____

REFERRING PHYSICIAN

Physician Name (print): _____

Phone: (____) _____ Fax: (____) _____

Email: _____

Referring Physician Signature Date: ____/____/____

BILLING & REPORTING INFORMATION

We do not bill patients or their insurance. Provide billing information here or on page 2.

Institution: _____

Address: _____

City/State/ZIP: _____

Phone: (____) _____ Fax: (____) _____

ADDITIONAL BILLING INFORMATION – CONTINUED FROM PAGE 1

Institution: _____

Address: _____

City/State/ZIP: _____ Phone: (____) _____ Fax: (____) _____

Contact Name: _____

Phone: (____) _____ Fax: (____) _____ Email: _____

SEND ADDITIONAL REPORTS TO:

Name: _____ Name: _____

Fax Number: _____ Fax Number: _____

Laboratory Information

1. 5-10ml Sodium Heparin blood per test should be adequate for most patients unless they are lymphopenic. If you have volume constraints or an absolute lymphocyte count (ALC) of <1.0 K/uL, please see the Customized Volume Sheet on our website (www.cchmc.org/DIL) or call for adjusted volume requirements for the following tests: Antigen Stimulation, Mitogen Stimulation, CTL Function, NK Function, CD107a, or T Cell Degran.
2. Results of a concurrent CBC/Diff must accompany ALPS Panel, B Cell Panel, or Foxp3. Results will be used to calculate absolute cell counts.
3. CSF Samples: a) Fresh Specimens: Ship with frozen ice packs to keep at refrigeration temp (2-8°C/35-46°F) for receipt within 48 hours of collection.
b) Frozen Specimens: Freeze within 48 hours of collection. Ship samples frozen on dry ice.
4. Specimen Processing and Shipping Instructions **only** for tests marked with **"See #4"**.
a) Unspun whole blood: Ship as unspun whole blood at Room Temperature for receipt within 24 hours of collection.
b) Spun Specimens: See test line for acceptable specimen types. Spin and remove test-required serum or plasma from cells within 24 hours of collection. Freeze the separated plasma or serum immediately. Two aliquots per test are preferred. Ship frozen on dry ice. Once separated from cells, the serum or plasma must stay frozen until received by the DIL. Thawed samples will be rejected.
5. Specimen Processing and Shipping Instructions **only** for tests marked with **"See #5"**
a) Unspun whole blood: Ship as unspun whole blood at Room Temperature (20-25 °C) for receipt within 5 days of collection. Chilled specimens will be rejected.
b) Spun Specimens: Spin at 2000 g for 10 min and remove test-required plasma from cells in 500 µL aliquots within 5 days of collection. Freeze the separated plasma immediately. Two aliquots are preferred. Ship frozen on dry ice. Once separated from cells, the plasma must stay frozen until received by the DIL. Thawed samples will be rejected.

Visit our Clinical Lab Index at www.testmenu.com/cincinnatichildrens for detailed processing and testing information.

Additional Shipping & Handling Information

- **Testing is not performed and samples cannot be received on Saturdays/Sundays and certain holidays.**
- Samples should be sent as whole blood at room temperature and received in our laboratory within 1 day of collection, unless otherwise indicated. We recommend using a Diagnostic Specimen pack to ensure proper processing and timely delivery of samples to the lab.
- Call with any questions or help with minimizing collection requirements.
- Package securely to avoid breakage and extreme weather conditions.
- Include a completed copy of our test requisition form with each sample.
- First Overnight shipping is strongly recommended. Please call, email or fax the tracking number so that we may better track your specimen.

Billing Information

- The institution sending the sample is responsible for payment in full.
- We do not third-party bill patient insurance.

Laboratory Information

- Hours: Monday through Friday, 8:00 AM to 5:00 PM (Eastern Standard Time). Closed on Weekends and some major holidays.
- Phone: 513-636-4685
- Fax: 513-636-3861
- Email: CBDLabs@cchmc.org

Questions?

Please call 513-636-4685 with any questions regarding collection or billing.

****THE REQUISITION MUST BE FILLED OUT COMPLETELY. INCOMPLETE FORMS MAY RESULT IN THE COMPROMISE OF THE SPECIMEN INTEGRITY WHILE THE MISSING INFORMATION IS BEING OBTAINED****