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

Clinical suspicion for Multi-System Inflammatory Syndrome in Children (MIS-C): Fever ≥100.4 °F (≥38 °C) for ≥3 days (OR fever ≥100.4 °F/≥38 °C for ≥24 hours with signs of shock/critical illness).	MIS-C CDC case definition
/ID-19 test ing or exposure to probable/confirmed COVID-19 case in the prior 60 days (or detection of antibody during current illness), no al ternative plausible diagnosis, <u>AND</u> any two of the following systems: signs of shock 31: abdominal pain, diarrhea, or vomiting 2V: chest pain, arrhythmia, or hypotension Mucocutaneous: rash, oral mucosal inflammation, conjunctivitis/conjunctival injection, or extremity swelling Initial Work Up and Management :	(updated Jan 2023); Fever ≥100.4 *F (≥38 °C) (subjective or documenter Requiring hospitalization Positive SARS-CoV-2 nucl acid/antigen up to 60 day prior, OR detection of antibody associated with current illness, OR close contact with confirmed/ prohable (OVUP.10 is co
sis/septic shock: follow the Septic Shock Pathway with the following caveats: t recognition of shock is crucial. Rapid push/pull administration of 10 ml/kg aliquots of fluid as tolerated with frequent reassessment for signs of sing heart failure, such as hepatomegaly, crackles, gallop, and other signs of fluid overload. Strong consideration should be given for early initiation of pic support. Studies (all potients): (see Appendix A for blood volumes and required tubes)	 probable COVID-19 in 60 days prior to hospitalizati CRP ≥3 mg/dL New onset manifestation 2 categories: Cardiac: coronary actery dilatation/
ad top and blue top tubes to hold for further studies; consider drawing and holding blood culture <u>Studies</u> (<i>abnormal</i> 1 st <i>tier labs¹</i> , <i>strong possibility of MIS-C based upon clinical presentation</i>): (see Appendix A for blood volumes and required <i>ppearing</i> : "coagulation panel" including D-dimer, troponin, NT-proBNP <i>earing</i> : add blood gas with lactate, ferritin, cortisol, blood culture, UA (volded specimen or bag; if abnormal, obtain mid-stream or cath for urine cx)	aneurysm, left ventricular ejection fraction <55%, or troponin elevation above normal o Shock
COVID-19 PCR (Appendix B: Instructions for Collection and Sending of COVID-19 Specimen), respiratory BIOFIRE er EKG, CXR 'ID-19 Special Precautions PPE until COVID-19 PCR results return	oral mucosal inflammation, conjunctivitis/ conjunctivitis/ conjunctival injecti or extremity findin
Disposition Considerations: er discharge from ED if: well appearing, no or mild elevation in labs, concrete plan in place for lab trending/follow up (may return to ED for lab follow mild symptoms of MIS-C (per ED and ID/Rheum), consider steroids – must have close follow up with ID and/or Rheumatology in place prior discharge. i:ents with normal labs and no clinical suspicion for MIS-C, f/u not necessarily required. er admission if: ill-appearing; clinical or laboratory picture strongly suggestive of MIS-C; markedly elevated inflammatory markers and/or lab or	 GI: abdom inal pain GI: abdom inal pain vom iting, diarrhea Hem at ol ogic: plate count <150 k/uL, A <1,000/uL No alternative plausible
evidence of end organ dy sfunction; tachy cardia out of proportion to clinical picture; abnormal ECG; altered mental status; meets criteria for ate or Incomplete Kawasaki Disease; clinical need to closely monitor disease progression; if unable to arrange outpatient follow up are admission to PICU if: strongly suggestive of moderate-severe MIS-C, signs of shock and/or multisystem organ involvement	diagnosis
	Absolute Lymphocyte Cor < 1000 Platelets 100 or >450k CRP ≥ 3 ESR >40 Na < 135
	Cardiology)
Treatment and Management	
I reatment may be started prior to CUVID-19 PCR and servingy tests result. Mild MIS-C (e.g., no hemodynamic instability, no cardiac dysfunction, mild abnormality in labs) ral prednisone/prednisolone taper per Rheumatology recommendations ication for methylprednisolone IV and/or IVIG therapy	DISCHARGE INSTRUCTIONS Call Rheumatology (or on-call) to schedule f/u in 2 weeks from discharge (5-9390)
ti void ASA if platelet count ≤80,000/uL) .ow dose 3-5 mg/kg/day (max 81 mg/day) if diagnosed MIS-C and KD-like features and/or thrombocytosis (platelet ≥450,000/uL) Continue ASA until normalization of platelet count and confirmed normal coronary arteries ≥6 weeks after diagnosis f coronary arteriopathy: follow Kawasaki Clinical Pathway in discussion with cardiologist if other cardiac abnormalities present, or doesn't meet above criteria: cardiology to direct antiplatelet/anticoagulation management	steroid taper per Rheumatology • For mod-severe MIS- C: Rx prednisolone/ prednisone taper:
	Initial Work Up and Management : is stapped is a back is crucial. Rapid push/pull administration of 10 m/l (Rapid push) (Rapid ministration of 10 m/l (Rapid push) (Rapid ministration of 10 m/l (Rapid push) (Rapid ministration of 10 m/l (Rapid push)) (Rapid Ministration and 10 m/l (Rapid Push)) (Rapid Ministration and 10 m/l (Rapid Push)) (Rapid Ministration and Rapid Push)) (Rapid Push)) (Rapid Push) (Rapid Push)) (Rapid Push) (Rapid Push)) (Rapid P

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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:
 - \circ $\;$ 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





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
 - o 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





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

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; **<u>DO NOT</u>** use the tube system
- When walking samples to Hartford Hospital, the staff member will <u>only</u> 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.





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).









Diagnosis or reason for testing: _

DIAGNOSTIC IMMUNOLOGY LABORATORY

Phone: 513-636-4685 • Fax: 513-636-3861 Lab Hours: Monday–Friday 8:00 AM – 5:00 PM EST www.cincinnatichildrens.org/DIL • CBDILabs@cchmc.org Ship First Overnight to: CCHMC - Julie Beach DIL - Rm R2328 3333 Burnet Avenue Cincinnati, OH 45229-3039

DIL — TEST REQUISITION FORM

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

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:

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

Alemtuzumab Plasma Level 2-3mL Southername	dium Heparin See #5 on page 2	Mitogen Stimulation	See #1 on page 2
ALPS Panel by Flow Need CBC/Diff result	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 Mrkrs: CD18/11b	1-3ml EDTA
□ Apoptosis (Fas, mediated)	10-20ml ACD-A	Neutrophil Oxidative Burst (DHR)	1-3ml EDTA
Note: Only draw Apoptosis on Wednesday for Thursday delivery		NK Function (STRICT 28 HOUR CUT-OFF)	See #1 on page 2
□ B Cell Panel Need CBC/Diff result	1-3ml EDTA – See #2 on page 2	Perforin/Granzyme B	1-3ml EDTA
BAFF	1-3ml EDTA – See #4 on page 2	D pSTAT5	1-3ml EDTA
CD40L / CD40FP / ICOS	3-5ml Sodium Heparin	S100A8/A9 Heterodimer 2 (0.3mL) Gold serum	aliquots, frozen w/in 4 hours of collection
CD45RA/RO	1-3ml EDTA	□ \$100A12 2 (0.3mL) Gold serum aliqu	ots, frozen w/in 4 hours of collection
CD52 Expression	1-3ml EDTA	□ SAP (XLP1)	1-3ml Sodium Heparin
CD107a Mobilization (NK Cell Degran)	See #1 on page 2	Soluble CD163	1-2ml EDTA - See #4 on page 2
Note: Only draw CD107a Mon	day – Wednesday	□ Soluble Fas-Ligand (sFasL) 1-3ml	EDTA/Red/Gold - See #4 on page 2
CTL Function	See #1 on page 2	Soluble IL-2R (Soluble CD25)	1-3ml EDTA - See #4 on page 2
CXCL9 2 (0.5ml) EDTA plasma aliquots, frozen w/in 8 hours of collection			
Cytokines, Intracellular	2-3ml Sodium Heparin	ΓΙ ΓΕΚ α/β ΓΕΚ Υ/δ 1-3ml EDIA	I-SIII EDTA
□ Cytokines (Circle One): Plasma or CSF Includes: IL-1b, 2, 4, 5, 6, 8, 10, IFN-g, TNF-a, and GM-CSF	3-5ml EDTA or 0.5-1ml CSF See #3 or #4 on page 2	T Cell Degranulation Assay Note: Only draw T Cell Degran I	See #1 on page 2 Nonday – Wednesday
If sending frozen, 2 (0.5mL) EDTA plasm	a aliquots frozen, preferred		
□ Foxp3 Need CBC/Diff result	1-3ml EDTA – See #2 on page 2	TCR V Beta Repertoire	2-3ml EDTA
GM-CSF Autoantibody (GMAb)	1-3ml Red/Gold - See #4 on page 2	Th-17 Enumeration	2-3ml Sodium Heparin
GM-CSF Receptor Stimulation	1-3ml Sodium Heparin	□ WASP	1-3ml Sodium Heparin
□ iNKT	1-3ml EDTA	WASP Transplant Monitor	1-3ml Sodium Heparin
□ Interleukin–18 (IL-18)	3ml Red/Gold - See #4 on page 2		1.2ml EDTA
If sending frozen, 2(0.3mL) red/gold serum aliquots frozen, preferred			
Lymphocyte Activation Markers	2-3ml Sodium Heparin	□ ZAP-70 (only for SCID)	1-3ml EDTA
Lymphocyte Subsets	1-3ml EDTA	C Other	
MHC Class I & II	1-3ml EDTA		

REFERRING PHYSICIAN	BILLING & REPORTING INFORMATION
Physician Name (print):	We do not bill patients or their insurance. Provide billing information here or on page 2.
Phone: () Fax: ()	Institution:
Email:	Address:
Date: / /	City/State/ZIP:
Referring Physician Signature	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: CBDILabs@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**