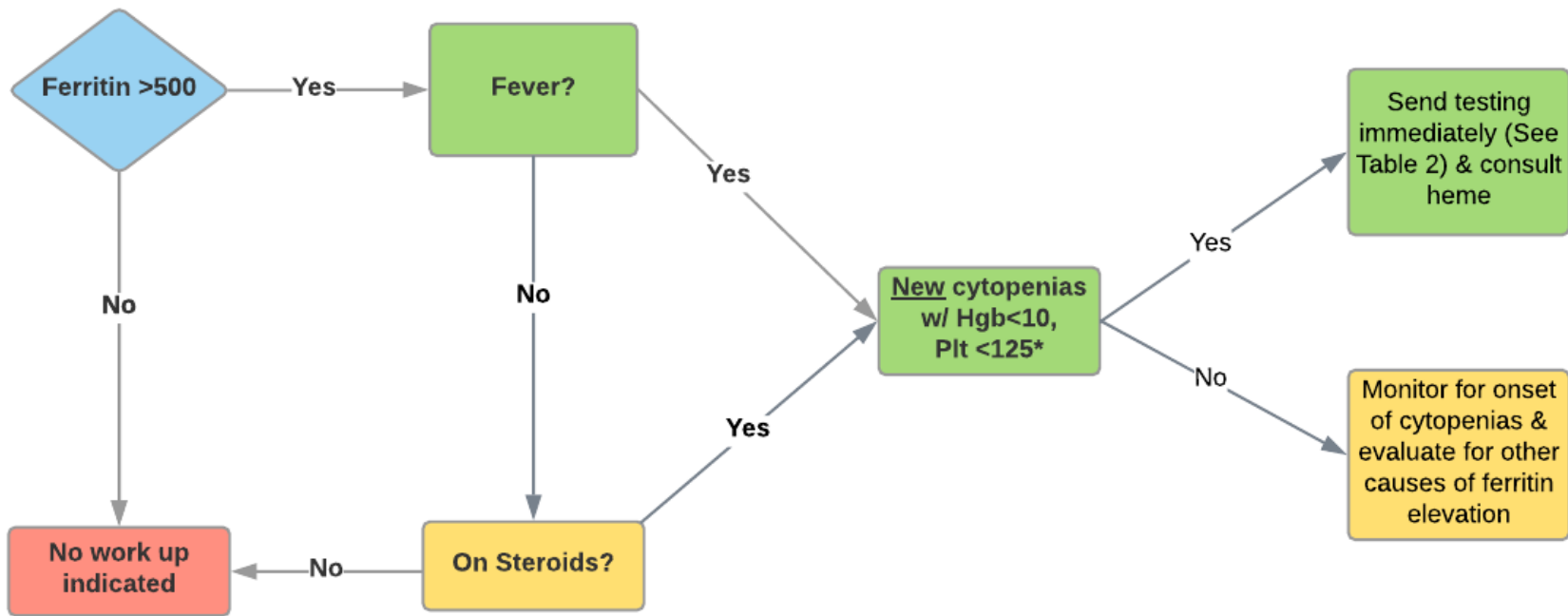


# Does My Patient Warrant an Expedited HLH Evaluation?



## General Considerations

- Hemophagocytosis sensitivity 83%, specificity 60%<sup>4</sup>
  - Simply a marker of macrophage activity
    - Can be physiologic or pathologic
- Significantly elevated ferritin (even >50,000) is NOT specific for HLH in the adult population<sup>5</sup>
- Benign hematology consult team should be involved early if high suspicion
- Consider timely in-person multi-disciplinary meeting in cases that are not clear cut
- Diagnostic Immunology Laboratory Form for sIL2R & NK activity: <https://www.cincinnatichildrens.org/service/c/cancer-blood/hcp/clinical-laboratories/test-requisition-forms>
- Number to obtain results (available prior to appearing in Epic): 513-636-4685

\*Selected for screening to be more sensitive than official diagnostic criteria

Table 1. Diagnostic Criteria <sup>1</sup>	Institutional Guidelines for Meeting the Criteria
Fever	T > 38.3°C
Splenomegaly	By physical exam (unless imaging otherwise indicated)
Cytopenias affecting ≥2 lineages	Hgb <9 g/dL Platelets <100 x 10 <sup>9</sup> /L Neutrophils < 1.0 x 10 <sup>9</sup> /L
Hypertriglyceridemia and/or hypofibrinogenemia	Triglycerides ≥ 265 mg/dL and/or Fibrinogen ≤ 150 mg/dL
Hemophagocytosis in bone marrow, spleen or lymph nodes	Need for and type of biopsy to be determined by hematology consultant.
Low or absent NK cell activity	Only send if requested by hematology consultant. Green top tube by paper form. WBC >1K: 1 tube 1>WBC>0.2: call for # tubes required WBC<0.2: do NOT send Must be drawn after 11am on weekday & received by lab before 1pm on M-Th. Results available by phone in 4-5 business days.
Ferritin ≥ 500	Trend daily
Soluble IL-2 Receptor (sIL2R) ≥ 2400	1 lavender top tube by paper form. Must be drawn same day & received by lab before 1pm on M-Th. Results available by phone in 1-2 business days.

<sup>1</sup>Henter JI et al. HLH-2004:diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer*. 2007;48(2):124-131.

<sup>2</sup>Rouphael NG et al. Infections associated with haemophagocytic syndrome. *Lancet Infect Dis*. 2007 Dec;7(12):814-22.

<sup>3</sup>Fukaya S et al. Clinical features of haemophagocytic syndrome in patients with systemic autoimmune diseases: analysis of 30 cases. *Rheumatology (Oxford)*. 2008 Nov;47(11):1686-91.

<sup>4</sup>Goel S et al. Sensitivity and specificity of bone marrow hemophagocytosis in hemophagocytic lymphohistiocytosis. *Ann Clin Lab Sci*. 2012 Winter; 42(1):21-5.

<sup>5</sup>Schram AM et al. Marked hyperferritinemia does not predict for HLH in the adult population. *Blood*. 2015 Mar 5; 125(10):1548-52.

Table 2. Work Up and Evaluating for the Trigger	
Immediate testing (for all suspected case)	BMP, LFTs, CBC, PT/PTT, LDH, ferritin, triglycerides, sIL2R, HIV 1/2 routine test, hepatitis B surface ag/ab and core ab, hepatitis C ab, blood cultures, CXR, EBV PCR
Additional testing if trigger unknown	Infectious work up: <ol style="list-style-type: none"> <li>HLH has been associated with viral, bacterial, fungal, parasitic and mycobacterial infections in the literature with EBV being the most common infectious trigger.<sup>2</sup> Additional testing should be done in the appropriate clinical context based on symptoms, exposures and host risk factors.</li> <li>Recommend ID consult to guide appropriate work up.</li> </ol>
	Malignancy work up (to be guided by hematology consultant): <ol style="list-style-type: none"> <li>Flow cytometry</li> <li>Bone marrow and/or tissue biopsy (to be decided by consulting team)</li> <li>CT c/a/p if unclear</li> </ol>
	Rheumatologic work up: <ol style="list-style-type: none"> <li>ANA</li> <li>HLH has been associated with many rheumatologic conditions in the literature, with SLE and Still's disease being the most common rheumatologic triggers.<sup>3</sup> Additional serologies should be sent in the appropriate clinical context based on symptoms and exam findings.</li> <li>Recommend rheumatology consult to guide appropriate work up.</li> </ol>