

## **Suspected hemophagocytic lymphohistiocytosis (HLH): Comprehensive infection work-up**

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Patients should have an infectious diseases /- tropical consult where possible, which would focus on:

- Full travel history including to Mediterranean
- Contact & sexual history and environmental exposures.
- Vaccines/meds/family history
- Careful examination including rash, murmurs, oral and genital ulcers, urine analysis, and particular focus on areas not visualised well in cross-sectional imaging
- Consideration of need for presumptive antibiotics eg for difficult-to-culture organisms eg doxycycline if relevant history
- For all patients: cross-sectional imaging (+/- PET) to look for focus of infection
- Laboratory investigations to look for an infectious cause (please see below)

### General notes

- Ideally send geographical panel with one sample to the reference lab (less expensive than multiple requests)
- Interpretation of serology unreliable following SCT/chemo/IVIg and in babies: have a low threshold for requesting PCR

### Comprehensive infection laboratory dataset to find underlying diagnosis

- Microbiology: 3 sets of blood cultures, ideally before starting antibiotic
- Parasitology
  - Malaria film or RDT
  - Toxoplasma serology
  - Leishmania serology (HTD will do rk39 & DAT 0.5 mls separated serum required)
  - Paediatrics: add EDTA whole blood to parasitology for Leishmania PCR on buffy coat
- Virology
  - Blood for
    - SAVE (pre blood products transfusion!)
    - HBsAg
    - HAV IgM
    - HCV serology

- HEV serology (IgM and IgG)
- HIV serology
- EBV and CMV serology
- EBV, CMV PCR
- Parvovirus B19 PCR
- In children: add HHV6 PCR and adenovirus PCR
- Combined nose/throat swab for respiratory PCR viral screen

### Additional laboratory investigation

- *According to ID consult / history, consider adding:*
  - Syphilis serology
  - Coxiella serology
  - Brucella serology
  - Serology for endemic mycoses
  - Other serology: geographical panel to send to the “Rare and Imported Pathogens Laboratory (RIPL) (including Rickettsia serology).
  - Add QuantiFERON-TB in paediatrics
- *In immunocompromised patients*
  - Add
    - Hepatitis C PCR
    - HHV6 PCR (in allogenic stem cell recipients)
    - Adenovirus PCR
    - Hepatitis E PCR
  - Consider adding:
    - HHV8 PCR (on EDTA whole blood)
    - Cryptococcal antigen
    - Beta-D glucan
    - Strongyloides serology
    - Microscopy for OCP (stool)
- *Investigations on bone marrow*
  - Bone marrow trephine biopsy
    - Send to histopathology/haematopathology specifying “please look for amastigotes”
  - Bone marrow aspirate film and fresh aliquot (unfixed, fresh or in EDTA)
    - Send to HTD parasitology lab for stains/PCR/culture

*If no fresh material saved, curls from formalin-fixed tissue for PCR can be sent but this will delay the diagnosis by 48 hours*

  - Send to microbiology for AFB smear and culture. Consider 16S PCR
- *Investigations on other tissues eg spleen*

- Splenic aspirate
  - Send smear to parasitology for microscopy
  - Send fresh splenic aspirate to parasitology for culture and PCR
  - Send smear to microbiology for AFB microscopy/culture/GenXpert/16S PCR
- *Tests to ensure no consequences of immunosuppression*  
Depending on travel: Strongyloides serology, Quantiferon-G, Trypanosoma cruzi serology