Suspected hemophagocytic lymphohistiocytosis (HLH) Infection work-up

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)

Minimum 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
  - Other tissues need fresh material for tissue dabs (will clinicians know what it is?), culture and PCR (for?)

For parasitology tests to HTD – if an HTD user, use Winpath user codes. Must provide travel history to ensure correct PCR primers used. Please clarify sample type.

- Tests to ensure no consequences of immunosuppression:
  Depending on travel: Strongyloides serology, Quantiferon-G, Trypanosoma cruzi serology