Jessica Manson and Rachel Tattersall Co-Chairs HiHASC
Ratified at annual meeting 18.11.20 – for review Novemeber 2022
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Hyperinflammation and HLH Across Speciality Collaboration (HiHASC) Terms of Reference

Remit

Haemophagocytic lymphohistiocytosis (HLH) is a condition of hyperinflammation leading to cytokine storm due to immune system dysregulation. HLH can cause tissue damage, multi-organ failure and has a very high mortality rate. While HLH is rare, it is also under-recognised and may present to almost any medical speciality.

Primary HLH (pHLH) is a genetic disorder of the immune system, presenting mainly in childhood. There are clear evidence based protocols and diagnostic criteria for pHLH and definitive treatment is bone marrow transplant [i].

Secondary HLH (sHLH) usually occurs in previously immunocompetent people and may be triggered by rheumatic disease (when it is termed MAS - Macrophage Activation Syndrome), malignancy (especially haematological malignancy), as a sequelae of immune therapy eg CART therapy (termed cytokine release syndrome) and most commonly infection (sometimes termed macrophage activation like syndrome – MALS – in sepsis) [ii].

Diagnosis of sHLH is not yet evidence based or standardized. Different criteria exist for different subsets and clinical features often mimic the underlying disease. Diagnosis of sHLH is extrapolated from criteria for pHLH and the use of biomarkers including serum ferritin (often highly elevated)[iii] and the H-score [iv] a weighted composite which helps to calculate the probability of sHLH being present. Diagnosis of sHLH is often on the basis of serial assessments of these parameters and patterns of results rather than absolute values and may ultimately be made by expert MDT assessment of these various factors, the clinical phenotype and consensus diagnosis. Treatment of sHLH requires both treatment of the hyperinflammation with immune suppression (modalities extrapolated from treatemtn of pHLH and including steroids, etoposide, anakinra and intravenous immunoglobulin-IVIG) and treatment of the triggering illness.

The HLH Across Speciality Collaboration (HiHASC) was set up in 2018 by Dr Jessica Manson (University College London Hospitals) and Dr Rachel Tattersall (Sheffield Teaching Hospitals and Sheffield Childrens' Hospitals) as a professional network for HLH and hyperinflammatory medicine.

Terms of reference

The purpose of HiHASC is

- to formalise and provide a digital presence for a network of professionals in the UK with a common interest in HLH and hyperinflammation
- To ensure diverse medical speciality representation across professionals working with all age groups to enable cross boundary, multi-disciplinary working to improve awareness of HLH
- To promote and facilitate formal multidisciplinary group working in regions and across the UK

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- To raise awareness of HLH and hyperinflammation and facilitate education
- To facilitate research and thereby improve the evidence base for HLH
- To liaise with medicines regulation agencies to ensure equitable access to relevant medicines to treat HLH
- To support Histio UK in providing patient resources and to support advocacy for people with HLH and their families. HiHASC does not have direct patient engagement but the close relationship with Histio UK enables patient perspectives to be key in the HiHASC professional network.

Membership

Membership of HiHASC is open to any healthcare professional working subject to a written expression of interest to the co-chairs of HiHASC

Meetings are called and coordinated by the co-chairs. The leadership team set up HiHASC in 2018 and recognise formal leadership arrangements and processes are necessary going forward. A proposal for these arrangements is contained in appendix A and was agreed at the annual HiHASC meeting 18.11.20

HiHASC is unable to financially support individual meeting attendance

Meetings

HiHASC has at least two meetings per year

Relationship with HistioUK

HistioUK is a charity (https://www.histiouk.org) whose aim is:

The relief of sickness and preservation of good health among patients affected by histiocytic diseases their families and carers, in particular but not exclusively by:

(i) the promotion and furtherance of scientific research into the physiology and pathology of histiocytes and the aetiology of histiocytocytic diseases, the useful results of which will be disseminated for the public benefit;

(ii) the development of more accurate means of diagnosis, improved protocols for management of patients and ultimately measures for prevention of histiocytic diseases;

(iii) the provision and dissemination of information, education and knowledge in support of patients and families affected by the disease to include the medical professions and general public;

(iv) collaboration with interested individuals and organisations.

HiHASC collaborates with HistioUK as per the terms of reference above. HistioUK provides a web based platform via their website for HiHASC and support to organise HiHASC meetings.

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APPENDIX A

The leadership team of HiHASC comprises two co-Chairs – their term will be 3 years from ratification of this terms of reference

Responsibilities
Attend biannual meetings and other events/functions (as requested). Review agenda and supporting materials prior to board meetings.
Share developments in the field and identify best practice standards
Provide support and advice to HiHASC members.
Serve as an ambassador and advocate to HiHASC providing a connection to and ongoing exchange of information and ideas with practitioners in the field and other external contacts.
Assist in identification and acquisition (when appropriate) of external funding and resources to support HiHASC
Assist in the identification and recruitment of new members.

Personal Characteristics
Ability to: listen, analyse, think clearly and creatively, work well with people individually and in a group, and provide constructive feedback.
Willing to: prepare for and attend board meetings, ask questions, share ideas, opinions, and experiences, and open doors in the field.
Possess: honesty, openness to differing views, a friendly, responsive, and patient approach, engagement skills, personal integrity, a developed sense of values, and concern for and interest in the program's development.

Membership
Elections

- Any member of HiHASC may propose candidates as Chair or deputy chair by sending in writing the name of each such candidate supported by the endorsement of another HiHASC member and consent of the candidate to the nominated election manager to arrive not less than four weeks before the scheduled date of the annual general meeting. Proposals received after this date will be declared invalid.
- If no nominations are received by this date, the deadline for nominations may be extended at the discretion of the leadership team.
- If candidates for office are nominated in excess of the number of vacancies available, the election manager shall send a ballot paper to each Voting Member on a one member-one-vote basis not less than fourteen days before the scheduled date of the annual general meeting. Voting Members shall record their votes and return the ballot paper to the election manager no later than seven clear days before the annual general meeting. Voting papers returned after this date shall be invalid. Scrutineers shall be appointed by the leadership team to count the votes and the results shall be announced at the meeting, the candidates securing the largest number of votes being elected to the vacancies that exist.

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[i] Henter JI, Horne A, Arico M, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer* 2007; **48**(2): 124-31.
[ii] Carter SJ, Tattersall RS, Ramanan AV. Macrophage activation syndrome in adults: recent advances in pathophysiology, diagnosis and treatment. *Rheumatology (Oxford, England)* 2019; **58**(1): 5-17.
[iii] La Rosee P, Horne A, Hines M, et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. *Blood* 2019; **133**(23): 2465-77.
[iv] Fardet L, Galicier L, Lambotte O, et al. Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. *Arthritis Rheumatol* 2014; **66**(9): 2613-20.