

## Dr. Degar et al reply

*To the Editor:*


We thank Drs. Rousset and Ray for their comment<sup>1</sup> on our manuscript and for highlighting the importance of a consensus-driven, multidisciplinary approach to the management of patients with hemophagocytic lymphohistiocytosis (HLH) and macrophage activation syndrome (MAS).<sup>2</sup>

As Rousset and Ray note,<sup>1</sup> the nature of MAS-HLH lends itself to the need for input from many subspecialties and a predetermined approach to the diagnosis and treatment of affected patients. The presentation of MAS-HLH can be pleomorphic, ranging from the classic presentation of multisystem dysfunction to organ-specific manifestations such as central nervous system (CNS)-isolated HLH.<sup>3,4</sup> It can occur in the setting of a genetic condition (familial HLH) or secondary to an infection, rheumatologic condition, or malignancy. Thus, multiple stakeholders need to be engaged to recognize MAS-HLH in its various forms and to treat the resulting multiorgan involvement. The hyperinflammation that is characteristic of MAS-HLH is often easier to manage earlier in the disease course and will progress at a relentless pace until sufficient immunosuppression is implemented. Thus, timely recognition and prompt treatment of MAS-HLH is paramount. Yet, treatment approaches for MAS-HLH include chemotherapy-based protocols and/or cytokine-directed therapies with almost no comparative studies to evaluate these approaches.<sup>5-8</sup> It can therefore be difficult for providers from different subspecialties to agree upon an initial therapeutic strategy given the lack of data in the field. It is for these reasons that multidisciplinary teams and an agreed-upon management approach are particularly important in MAS-HLH.

Rousset and Ray note several features of their multidisciplinary team for MAS-HLH that were also important for success at our institution.<sup>2,9</sup> The first is continued engagement of a group of pediatric subspecialties with an interest and expertise in MAS-HLH. Second, this MAS-HLH workgroup developed consensus on a diagnostic and treatment approach for patients with MAS-HLH that was workable at their institution. Finally, infrastructure was put in place to facilitate communication (email list servers, newsletters) and implementation of the MAS-HLH guideline (electronic order sets). It is likely that implementing these fundamentals will be helpful for other clinicians who are seeking to create similar multidisciplinary teams.

Our experience, coupled with that of Rousset and Ray, emphasizes the importance of multidisciplinary teams in the management of children with immune dysregulation. Swigart et al recently reported on the successful development of a multidisciplinary, inpatient consult service for children with sepsis and multiorgan dysfunction syndrome.<sup>10</sup> During the coronavirus disease 2019 (COVID-19) pandemic, many pediatric institutions developed a similar multisubspecialty approach to

the management of children with multisystem inflammatory syndrome. The development, structure, and scope of these types of collaborative and multidisciplinary teams vary across institutions. Some teams address a single syndrome, like MAS-HLH, whereas others encompass the broader phenotype of immune dysfunction. The approach to such a team can be semiformal or highly structured. At certain hospitals, there is strong institutional support and resources whereas others, as noted by Rousset and Ray, do not enjoy this luxury. There is no one-size-fits-all approach that will work. Instead, the secret to success seems to be the willingness of a group of motivated clinicians to improve care for children with complex immune conditions through ongoing communication, organization, and guideline development. Once formed, these groups can provide the foundations needed to track outcomes, establish research initiatives, create educational opportunities, and offer long-term follow-up for patients. Although there is a continued need to demonstrate that multidisciplinary teams improve outcomes, there is increasing evidence that this approach benefits patients and providers alike and should be the standard of care.

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