

Hemophilia-free mind: a call to action

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Dear Editor,

Over the last few decades, therapeutic goals for people with hemophilia (PwH) -particularly moderate and severe forms- have undergone a remarkable transformation. We moved from merely ensuring and improving survival to reducing frequency and severity of bleeding episodes, and ultimately to striving for a quality of life comparable to that of the general population. This progress is further bolstered by advancements in multidisciplinary management, which addresses not only hematological aspects but also physiatric/orthopedic care, pain management, and psychological support. Consequently, we can now offer to newborns a life largely unloaded by the burden of hemophilia. This includes achieving optimal control over joint bleeds and other hemorrhages (aiming for the “Annualized Bleeding Rate 0”), preserving joint integrity, and reducing disease impact on social and professional life through the use of extended half-life products or non-replacement therapies. The arrival of gene therapy, particularly for Hemophilia B, now offers the possibility of “forgetting” the disease in daily life for several years.¹⁻⁵ Thus, in recent years, the adjective “free” has increasingly characterized the world of hemophilia:

pain-free, bleeding-free, arthropathy-free, and treatment-free. This trajectory led toward the concept of a “Hemophilia-free mind” (HFM) - a state where patients live their daily life without the constant thought about the disease, its effects, or its treatment. Krumb and Hermans⁶ highlighted how PwH adopt coping strategies to face the impact of hemophilia on their lives, moving from some questions that they pose themselves daily (e.g., which activities will cause pain today? what is the risk of bleeding today?): a day free from these intrusive thoughts is the first aspiration for PwH and should be the aim of clinicians. A more complete definition of HFM was subsequently given as freedom from joint and muscle bleeding, joint damage and disabling arthropathy, from pain and the constraints of treatment. Ultimately, freedom to partially or totally free brain, mind and consciousness from the constraints, fears and restrictions of haemophilia.⁷

Assuming that the overarching goals of HFM are universally shareable among clinicians, it remains essential to acknowledge the potential drawbacks associated with this concept. Attention should be paid to the risk of misinterpretations, overextension, or distortions that may arise when translating an aspirational framework into clinical practice. A central issue is, in our opinion, that while alleviating the biological, physical, and psychological burden of the disease is paramount, we could hesitate in the creation of a generation of PwH so “free” from the past struggles to lose the awareness of the condition itself. For instance, PwH undergoing gene therapy show varying results in terms of achieved through levels and duration of effect, necessitating continuous monitoring and contact with the Hemophilia Center; moreover, the certainty for transmitting the affected gene to their daughters remains. Patients on gene therapy or non-replacement therapies must remain aware that replacement therapy maybe still required for invasive procedures or breakthrough bleeds, always in consultation with their treating physician. Furthermore, for many PwH on non-replacement therapy the risk of losing their abilities of self-treatment by intravenous route could be a concern during emergency situations far from the center. Regarding replacement therapy, even the latest generation products with significantly extended half-lives (e.g., efanesoctocog alfa) do not consistently provide complete coverage in the most distant days from the infusion.

Does it remain crucial that PwH understand the importance and implications of their treatments and know how to manage specific scenarios or must these challenges be managed exclusively by the clinician?

Our concern is that the (indisputable) will of removal of a load that creates fears, anxiety and health inequities could lead to the disappearance of hemophilia awareness, that means also the abil-

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ity of critically judging daily life several scenarios (e.g., physical activity, risk of trauma, *etc.*) and the acknowledgement of the need to maintain a connection with the Hemophilia center lifelong.

In our opinion, if HFM could be a legitimate ambition by patients, clinicians target should be a “limitation free Hemophilia” namely a condition in which hemophilia is present but is not able to create limits and obstacles to the full realization of patient’s life. Through this framework it is not an overstatement to say that intense activities need additional replacement treatment (e.g., sport), and that a central role is played by patient education to a lifestyle consistent with the current therapeutic model.

At last, to further investigate how HFM concept is interpreted in clinical practice, the perspectives of physicians involved in the care of people with hemophilia will be explored through an online survey jointly promoted by AICE (Italian Association of Hemophilia Centers) and Siset (Hemostasis and Thrombosis Study Italian Society). This survey, which we hope will engage a broad participation of colleagues, aims to capture the diversity of views across hemophilia treatment centers and within different regional settings, as well as the individual nuances shaped by each clinician’s personal experience.

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