

FORUM

Living with a “hemophilia-free mind” – The new ambition of hemophilia care?

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Abstract

Despite the numerous and groundbreaking therapeutic advances made in the field of hemophilia over the past decades and particularly in recent years, hemophilia remains a disease that has a major impact on the daily lives of our patients, through the multiple complications and burdensome treatments it imposes. The disease burden is not only physical but also psychological and is difficult to evaluate solely by questionnaires and scores. In this article, we propose to examine the absence of psychological burden and of permanent thoughts about the disease and its complications in people with hemophilia as a new ambition that should guide hemophilia care and research in the future.

KEYWORDS

bleeding, hemophilia, hemostasis, patient outcome, quality of life

Essentials

- Hemophilia has a major impact on the daily lives of our patients, both physically and mentally.
- This impact is potentially reduced by new treatment options.
- The mental burden of people with hemophilia is difficult to measure with current assessment tools.
- The concept of a “hemophilia-free mind” should guide hemophilia care in the future.

Hemophilia is a hereditary bleeding disorder with multiple complications. Health care professionals specializing in hemophilia are confronted with the reality of this disease during regular consultations with each of their patients. These review clinics deliver an important opportunity to ensure the best management of the disease and to assess its diverse consequences. For most people with hemophilia, especially those with moderate and severe hemophilia, their physical and mental well-being are constantly at stake, as the disease impacts their daily activities. This is beautifully summarized in a famous book by Peter Jones entitled “Living With Hemophilia” that was originally published in 1974.¹

Groundbreaking therapeutic advances in hemophilia have been achieved during these past decades; biotechnological advances

have allowed the development of more secure (recombinant factor products) and effective (recombinant factors with extended half-life) therapies for hemophilia² in addition to the establishment of multidisciplinary care in hemophilia reference centers.³ The development of less burdensome treatments (ie, non-replacement therapy) is nonetheless very recent and is only beginning to be available to larger numbers of patients in developed countries. Currently, the available treatments—including the most recent ones—cannot cure the disease, as they only partially compensate the disease’s effects, either in a steady state (emicizumab) or fluctuating mode (factor concentrates). Such treatments are not completely free of limitations, as they require repetitive intravenous or subcutaneous

Evelien Krumb designed the figure.

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administrations. Although their effectiveness has been proven, they do not prevent all bleeding events and do not ease the pains and disabilities, particularly of the joints, which have developed progressively as a result of frequent hemorrhages in the past.

The efficacy of hemophilia treatments is typically determined by measuring the frequency of bleeding events, including those occurring in target joints, by assessing painful symptoms through standardized tools and by assessing joint status clinically or by radiologic imaging. To measure the overall impact of hemophilia and treatment efficacy in people with hemophilia, many other approaches have been integrated and validated. Such approaches attempt to quantify physical activity, evaluate quality of life, and determine the patients' own representations of the disease.⁴⁻⁷ The evaluation is mainly based on questionnaires that seek to explore each patient's mental ecosystem and to determine the multiple consequences of hemophilia on their daily life, a task that is both difficult and ambitious.

Although these questionnaires and tools for assessing quality of life are of major interest, they are not free of limitations.⁸ Their routine implementation is often tedious and time consuming. In this context, having a simple indicator that could integrate the multiple physical and psychological impacts of hemophilia and its management would be a critical step.

The only biological difference between people with and people without hemophilia is a deficiency in one of the clotting factors that results from the presence of a genetic variant at the end of the X chromosome. The consequences of this apparently small difference are substantially enormous, as it influences and shapes the whole life of a person with hemophilia. Every morning, the "hemophilic disease," through its constraining treatments and complications, reminds patients of their vulnerabilities.

Although hemophilia is a hematologic disease with mainly muscular and skeletal consequences, it does not spare each person's mind. In other words, people with hemophilia, even if well treated with current treatment options, rarely have their minds free of hemophilia. The different dimensions of this mental burden, depending on treatment modalities, are summarized in Figure 1. Indeed, people affected by moderate or severe hemophilia are continually confronted with multiple questions that impact their behavior and lead them to adopt more or less automatic coping strategies that they have acquired over the years. Some of these questions are detailed below:

1. Should I treat myself today? When was my previous treatment? When will my next treatment be?
2. Which activities will likely cause pain today? How can I avoid or control the pain?
3. What is the bleeding risk for me today? Will the activity I am considering be dangerous?
4. What will I not be able to do today that I would like to do?
5. Will the fact that I have hemophilia make me feel different from people who are not affected by hemophilia?
6. What skills will I develop and use to cope with the disease today?
7. Will I be able to cope by myself, or will I need help and support?

Drug treatment of hemophilia, optimized management, and ideally a cure should replace these questions with another reality, described in the statements below:

1. I do not have to treat myself today, tomorrow, or the day after tomorrow. I do not have to consider my last treatment.

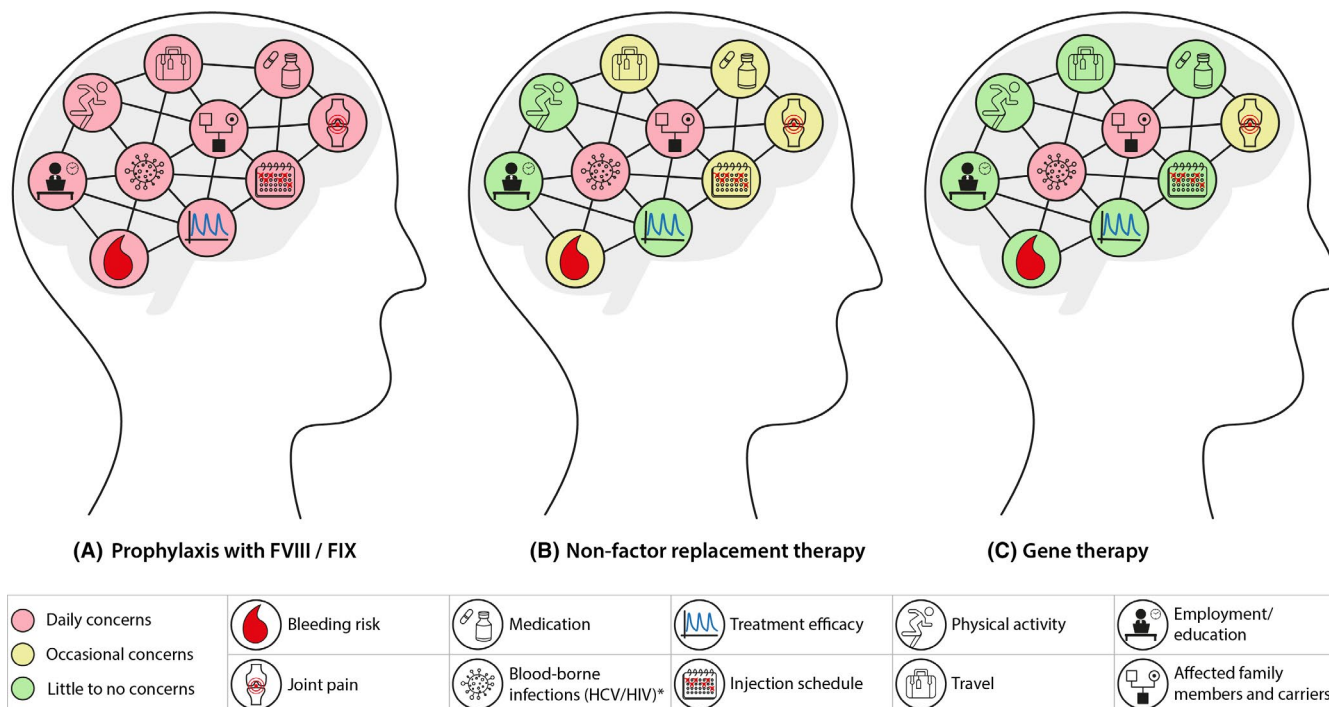


FIGURE 1 Concerns of people with moderate or severe hemophilia according to different treatment modalities. FVIII, coagulation factor VIII; FIX, coagulation factor IX. * In patients born before 1990

2. I am not in pain and should not fear pain.
3. I do not have to worry about being exposed to any particular risk of bleeding.
4. I can do what I want without any real restrictions.
5. I do not have to feel different from people who are not affected by hemophilia.
6. I do not have to find skills and strategies to cope with the disease.
7. I do not need more help or support than another person.
8. I do not even have to consider and ask myself the above questions.

In this hypothesis, the treatment of hemophilia with its pains, fears, frustrations, coping strategies, perceived differences with other people without hemophilia, and frequent lack of independence disappear and no longer engage the person's mind and mental energy. A day without hemophilia on their minds, a day without considering themselves as "bleeders" as opposed to healthy people, is surely the prime aspiration of these people. To free them as much as possible from the biological, physical, and especially mental grasp of hemophilia is what ideal treatments should aim for. This is a difficult goal to achieve, but ideally it should inspire and motivate caregivers and future research.

In routine clinical practice, asking people if they currently experience days when their minds are not preoccupied by hemophilia could be a first step in this process. In our own experience, such "hemophilia-free days" are now possible for some of our patients treated with long half-life factor IX (FIX) concentrates or emicizumab. Some of these patients, for several days a month, seem to be able to live without suffering actively from hemophilia both physically and mentally. This is also true for patients who have been treated with gene therapy, at least for those who, several months after the factor infusion, have achieved sufficient endogenous FIX or factor VIII levels (ideally almost in the normal range) and who are no longer burdened by the gene therapy study protocols.

Lately, we were inspired by the words of a man with hemophilia B who benefited from gene therapy in November 2019 at our hemophilia treatment center in Brussels. He responded very favorably to the treatment and reported feeling free from hemophilia's shackles as his fears and anxiety disappeared from his daily life. Apart from being "bleed free" since the administration of gene therapy and feeling less joint pain, he also felt his mind to be absolved from the constant psychological distress. Whereas before gene therapy, his thoughts had constantly revolved around the disease, the next injection, and the risk of bleeding between two injections, he felt that these days were now mostly over. This case is consistent with observations made by W. Miesbach and R. Klamroth during interviews of three gene therapy study participants in Germany.⁹

Asking patients if life is currently granting them "hemophilia-free days" is a simple, empathetic, and informative question. It allows us to appreciate the overall impact of hemophilia therapies on each patient and their relatives. It also allows us to explore how we can further help our patients on ultimately finding the path of "living without hemophilia."

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RELATIONSHIP DISCLOSURE

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

All authors contributed to and approved the final version of the manuscript.

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