



**NATIONAL HEMOPHILIA FOUNDATION**  
*for all bleeding disorders*

MASAC Document #264  
(Replaces Document #245)

**MASAC RECOMMENDATIONS REGARDING DIAGNOSIS AND MANAGEMENT OF  
INHERITED BLEEDING DISORDERS IN GIRLS AND WOMEN WITH  
PERSONAL AND FAMILY HISTORY OF BLEEDING**

*The following recommendations were approved by the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation (NHF) on February 20, 2021, and adopted by the NHF Board of Directors on March 4, 2021.*

Inherited bleeding disorders are under-recognized as causes of bleeding in girls and women. However, recent data have documented that 50% of girls and women who are carriers for hemophilia A or B have factor VIII or IX levels below 50%, putting them in the category of mild hemophilia and causing them to have an increased risk of bleeding, especially during menstruation and at the time of an accident, surgery, or delivery. Even some genetic carriers of hemophilia with normal factor levels have a bleeding diathesis. Moreover, up to 1% of all girls and women may have laboratory evidence of inherited von Willebrand disease (VWD) and may also have heavy bleeding during menstruation, surgery, or labor and delivery. (1)

Establishing the correct diagnosis of inherited bleeding disorders for women has important implications for management of bleeding, recommendations for invasive procedures, pregnancy and delivery management, and family planning and testing.

With this information in mind, MASAC recommends the following:

**A. Diagnostic Evaluation (2)**

1. Von Willebrand Disease (VWD) and other inherited bleeding disorders should be considered in the differential diagnosis of all girls and women presenting with heavy menstrual bleeding (including all girls and women scheduled for endometrial ablation and/or hysterectomy for heavy menstrual bleeding or abnormal uterine bleeding) and those who have other significant personal or family history of bleeding. Bleeding assessment tools may be utilized in the primary care setting to identify women with significant bleeding tendency who warrant evaluation.
2. Initial testing should include a CBC, PT, PTT, and a TT or fibrinogen. Additional testing specifically for VWD should include factor VIII activity, platelet-dependent VWF activity (VWF: GP1bM, VWF: GP1bR), VWF antigen. This workup should be done in consultation with a hematologist who is well versed in the diagnosis of inherited bleeding disorders. Testing should be completed at a reference laboratory that specializes in coagulation testing and blood samples should be drawn on-site to avoid delays in processing that could alter results. (3) [see also MASAC document #262] Additional testing may be indicated depending on the results to confirm diagnosis of VWD and

distinguish the subtype. If initial testing is negative, then additional evaluation should be considered for platelet function disorders, factor XIII deficiency, fibrinolytic disorders, and connective tissue disorders.

3. If there is a positive family history of a bleeding disorder, girls and women should have the appropriate factor activity level determined as soon as feasible and definitely prior to any planned surgical procedure regardless of age.
4. Girls and women with abnormal uterine bleeding should be regularly evaluated and treated for iron deficiency (anemia).
5. Heavy menstrual bleeding (HMB) can be defined as recommended by Connell et al. (4)
  - Lasting  $\geq 8$  days
  - Consistently soaks through 1 or more sanitary protections every 2 hours on multiple days
  - Requires use of  $>1$  sanitary protection item at a time
  - Requires changing sanitary protection during the night
  - Associated with repeat passing of blood clots
  - Pictorial Blood Assessment Chart (PBAC) score  $> 100$

In clinical practice, HMB is defined as excessive menstrual loss, which interferes with a woman's physical, social, emotional, and/or material quality of life. In terms of blood loss, HMB is defined as a menstrual blood loss of  $>80$  mL per period. This objective assessment can only be obtained by laborious, expensive, and inconvenient measurements involving collection of used sanitary protections. Therefore, simple indirect methods, such as detailed menstrual history or the use of PBAC are used to provide a semiquantitative assessment of the blood loss and its severity as well as monitoring response to treatment.

#### B. Access to Care

1. Girls and women with inherited bleeding disorders should have access to care within a Hemophilia Treatment Center or other clinical program with expertise in bleeding disorders.
2. When indicated girls and women with inherited bleeding disorders should have access to multidisciplinary clinics including hematologists and gynecologists for management of heavy menstrual bleeding and other gynecologic conditions.
3. Girls and women should have access to genetic counseling and genetic testing for diagnostic purposes and family testing and planning.
4. Girls and women with inherited bleeding disorders should have access to the appropriate treatment including antifibrinolytics, DDAVP and factor replacement products when clinically indicated. Cryoprecipitate and fresh frozen plasma should not be used unless the patient is at risk of life-threatening bleeding and a Factor VIII/Von Willebrand Factor concentrate is not rapidly available.

#### C. Management

1. Individualized treatment and emergency plans should be developed depending on the diagnosis, bleeding, and co-morbidities.
2. Perioperative management should be developed for women undergoing invasive procedures.
3. Pregnancy and delivery plans should be in place for pregnant women. See MASAC Document #265.

4. Heavy menstrual bleeding should be managed through a multidisciplinary approach informed by patient preferences. Hormonal therapy (combined hormonal contraception [CHC] or levonorgestrel-releasing intrauterine system) or tranexamic acid over desmopressin is advised to treat women with VWD who do not wish to conceive. (conditional recommendation based on very low certainty in the evidence of effects). This recommendation does not imply that the interventions considered can be prescribed only as monotherapy. In some cases, multiple options can be combined, especially if control of heavy menstrual bleeding is less than optimal with the initial therapy. Desmopressin is not effective in type 3 and many type 2 VWD patients and is contraindicated in type 2B VWD. Women may require additional treatment directed at bleeding symptoms for the first several menstrual cycles after placement of a levonorgestrel-releasing intrauterine system.

#### D. Recommendations

1. Much progress has been made in increasing awareness of girls' and women's bleeding disorders by both the general public and clinicians who are primary care providers for girls and women. Nonetheless, the national outreach and education program should be continued. The target audiences should be health care professionals (e.g. pediatricians, hematologists/oncologists, internists, OB/GYN, family practitioners, emergency department personnel and dentists as well as nurse practitioners in these fields), women's health advocates, and the general public.
2. Multidisciplinary clinics including hematology and gynecology which streamline care should be supported.
3. NHF should continue to work with NHLBI, the American Thrombosis and Hemostasis Network (ATHN), the Foundation for Women and Girls with Blood Disorders, the International Society of Hemostasis and Thrombosis and CDC to develop a national research agenda on women's bleeding disorders.

#### References

1. James AH, Kouides PA, Abdul-Nadir R, et al Evaluation and Management of Acute Menorrhagia in Women with and without underlying bleeding disorders: consensus from an international expert panel, *Eur J Obstet Gynecol Reprod Biol.* 2011 Oct; 158(2): 124-34
2. Connell NT, Flood VH, Brignardello-Petersen R, et al ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease. *Blood Adv.* 2021 Jan 12;5(1): 301-325.
3. Jaffray J, Staber JM, Malvar J, et al. Laboratory misdiagnosis of von Willebrand disease in post-menarchal females: A multi-center study. *Am J Hematol* 2020. 95(9): 1022-1029.
4. Connell NT, James PD, Brignardello-Petersen R, Abdul-Kadir R, Ameer B, Arapshian A, Couper S, Di Paola J, Eikenboom J, Giraud N, Grow JM, Haberichter S, Jacobs-Pratt V, Konkle BA, Kouides P, Laffan M, Lavin M, Leebeek FWG, McLintock C, McRae S, Montgomery R, O'Brien SH, O'Donnell JS, Ozelo MC, Scappe N, Sidonio R, Tosetto A, Weyand AC, Kalot MA, Husainat N, Mustafa RA, Flood VH. von Willebrand disease: proposing definitions for future research. *Blood Adv.* 2021 Jan 26;5(2): 565-569.

*This material is provided for your general information only. NHF does not give medical advice or engage in the practice of medicine. NHF under no circumstances recommends particular treatment for specific individuals and in all cases recommends that you consult your physician or local treatment center before pursuing any course of treatment.*

Copyright 2021 National Hemophilia Foundation. To facilitate the dissemination of these medical recommendations, reproduction of any material in this publication in whole or in part will be permitted provided: 1) a specific reference to the MASAC recommendation number and title is included and 2) the reproduction is not intended for use in connection with the marketing, sale or promotion of any product or service. NHF reserves the right to make the final determination of compliance with this policy. For questions or to obtain a copy of the most recent recommendations, please contact the NHF Director of Communications at 1-800-42-HANDI or visit the NHF website at [www.hemophilia.org](http://www.hemophilia.org).