

GYNECOLOGY

Von Willebrand disease and other bleeding disorders in women: Consensus on diagnosis and management from an international expert panel

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Bleeding from the reproductive tract in women is a naturally occurring event, generally the result of menstruation and childbirth, and is not associated with a bleeding disorder in most cases. In those women who do have a bleeding disorder such as von Willebrand disease (VWD), there is an increased incidence of pathologic bleeding. Menstruation and childbirth may lead thereby to unacceptable blood loss. The lack of a clinical tool for the objective assessment of abnormal reproductive tract bleeding and the lack of awareness of the potential of bleeding disorders to exacerbate or even cause abnormal bleeding¹ leads to the underdiagnosis and suboptimal treatment of women with bleeding disorders.

To highlight the significance of this problem and to provide an expert consensus on how to specifically identify and manage bleeding disorders in obstetrics

Reproductive tract bleeding in women is a naturally occurring event during menstruation and childbirth. In those women with menorrhagia or postpartum hemorrhage, however, historically there has been an underdiagnosis of congenital bleeding disorders, which is presumably because of a lower awareness among obstetricians and gynecologists. To increase the awareness of bleeding disorders such as von Willebrand disease, a group of experts that included obstetrician-gynecologists and hematologists came together to discuss the diagnosis and management of menorrhagia and postpartum hemorrhage in affected women. This consensus is intended to allow physicians to better recognize bleeding disorders as a cause of menorrhagia and postpartum hemorrhage so that effective disease-specific therapies can be offered.

Key words: coagulation factor, menorrhagia, postpartum hemorrhage, von Willebrand disease, von Willebrand factor

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and gynecology, specialists in the care of women with bleeding disorders met on September 20, 2007, for a consensus conference. The specialists represented a

diverse group of experts in the fields of obstetrics and gynecology and hematology. The meeting participants were from a variety of institutions in North America, Europe, and New Zealand. CSL Behring (Marburg, Germany) provided financial support to allow the participants to convene.

The meeting was structured as a series of presentations on menorrhagia, bleeding disorders that included VWD, diagnosis and treatment of women with both conditions, management of postpartum hemorrhage (PPH) in women with bleeding disorders, and reproductive tract bleeding in women with rare bleeding disorders (RBDs). Six central questions were addressed by the meeting's discussion, which are used as section headings herein, and a consensus was sought for each question. The consensus is meant to provide clinical information to obstetricians and gynecologists and recommend strategies for the identification and confirmation of a bleeding disorder that could underlie reproductive

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TABLE
Levels of evidence²

Grade	Level	Evidence obtained from
A	1a	Metaanalysis of randomized controlled trials
	1b	At least 1 randomized controlled trial
B	2a	At least 1 well-designed controlled study without randomization
	2b	At least 1 other type of well-designed quasiexperimental study
	3	Well-designed nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
C	4	Expert committee reports or opinions and/or clinical experiences of respected authorities

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tract bleeding and offer potential management strategies. Where no consensus could be reached, no advice is given. VWD is the bleeding disorder of main concern for this consensus. Recommendations have been assigned a grade and level of evidence; the use of the United States Agency for Health Care Policy and Research Criteria is summarized in the Table.²

Before the meeting, members of the group reviewed pertinent references from their own searches, databases, and publications. In addition, Dr Andra James served on the expert panel that authored the US National Heart Lung and Blood Institute's guidelines, The Diagnosis, Evaluation and Management of von Willebrand Disease. She reviewed the guidelines in their entirety and reviewed all of the references that pertained to women's health issues and VWD that were compiled for that document. A description of that literature search, which covered the years 1990-2006, is described elsewhere.³ Dr Augusto Federici coauthored and reviewed the Italian Guidelines for the Diagnosis and Management of von Willebrand Disease.⁴ Dr Rezan Abdul-Kadir coauthored and reviewed the United Kingdom Haemophilia Doctors' Organization guidelines for the treatment of women with inherited bleeding disorders.⁵

Background

The prevalence of menorrhagia in women with VWD is 74-92%.⁶⁻⁸ The

prevalence increases according to severity of VWD type, with a higher percentage in VWD type 3 than in types 1 and 2.⁹ Conversely, the prevalence of VWD in women with menorrhagia is 5-24%, with an overall prevalence of 13% (95% confidence interval [CI], 11-16%) based on a systematic review of 11 studies comprising 988 women with menorrhagia.¹⁰ Bleeding disorders, especially VWD with an incidence of approximately 1% in the general population,¹¹⁻¹³ are therefore of notable concern in women with menorrhagia. VWD is an inherited disease, and although it affects male and female with equal frequency, women are more likely to manifest the disorder clinically because of the bleeding challenges that are associated with menstruation and childbirth.¹⁴

Unlike in menorrhagia, there are no studies that document an increased prevalence of bleeding disorders among women with PPH.^{15,16} Nonetheless, PPH is an anticipated problem in women with bleeding disorders, particularly delayed or secondary PPH, that occurs > 24 hours after delivery. There are multiple case reports and case series that document the increased risk of PPH in women with VWD,¹⁷⁻²⁵ but only 4 case control studies have compared the rate of PPH in women with VWD with the rate in women without PPH^{7,26-28}; there is only 1 study in which ascertainment was not retrospective.²⁶ That study did show a statistically significant differ-

ence between the rate of PPH in women with VWD (6%) and the rate in women without VWD (4%). Unlike PPH in the general population, which occurs overwhelmingly in the immediate postpartum period,^{29,30} in women with VWD, PPH may be delayed.^{23,25} In a review of published cases,³¹ the average day of examination was 15 days after delivery.

VWD is caused by a deficiency in, or a dysfunction of, von Willebrand factor (VWF). VWF is a multimeric protein synthesized in megakaryocytes and endothelial cells. It has 2 main hemostatic functions. In primary hemostasis at the site of injured vessel walls, it facilitates platelet adhesion to subendothelial structures (such as exposed collagen fibers) and supports platelet aggregation and thrombus formation. As part of secondary hemostasis, VWF acts as a carrier protein for coagulation factor VIII (FVIII), stabilizing and protecting FVIII procoagulant activity. Type 1 VWD results from a deficiency of VWF. Type 2 VWD results from abnormal VWF. There are 4 subtypes: type 2A is characterized by a deficiency of normal multimers of VWF; type 2B is characterized by VWF with enhanced platelet binding and can result in thrombocytopenia; type 2M is characterized by VWF with reduced platelet binding; and type 2N is characterized by VWF with reduced binding to FVIII, which allows FVIII to be proteolyzed.

Type 3 VWD results from the absence or near absence of VWF. With the exception of type 3, which is rare and severe; cases of type 2N VWD is generally inherited by autosomal dominant transmission.³

Individuals with VWD are at an increased risk for mucocutaneous bleeding that includes epistaxis, easy bruising, prolonged bleeding after trivial cuts, excessive bleeding with dental procedures, excessive bleeding from the oral cavity, gastrointestinal bleeding, excessive postoperative bleeding, and reproductive tract bleeding.^{32,33} The signs and symptoms of VWD depend on the type and severity of the disease. Most people with type 1 disease have bleeding that is mild-to-moderate in severity, does not require routine transfusions or other treatments, and is not life-threatening. Life-threat-

ening bleeding that involves the brain or gastrointestinal tract can occur in individuals with type 3 disease, in some individuals with type 2 disease, and, rarely, in individuals with type 1 disease. Bleeding within deep tissues, such as muscles and joints, may occur in individuals with type 3 disease.³ The most common symptom that women with VWD experience is menorrhagia.³

What is menorrhagia?

Menorrhagia is, in general, a loosely defined term that is given to heavy menstrual bleeding. Meeting participants discussed how menorrhagia could be diagnosed and what associated factors might support a diagnosis of menorrhagia. Participants believed that a specific definition of menorrhagia would provide a structured benchmark by which a gynecologist could diagnose menorrhagia more readily. With the acceptance that menorrhagia is generally defined as > 80 mL of blood loss per menstrual cycle,³⁴ the following associations were agreed on as being indicative of women with menorrhagia: soaking through a pad or tampon within 1 hour³⁵; soaking through bed clothes³⁵; below normal ferritin³⁵; anemia; and pictorial blood assessment chart score > 100 ("Appendix of Selected Terms").³⁶

Although quality of life (QoL) impairment was also mentioned as an associated factor, meeting participants decided that it was problematic to define a quantitative cut-off of when QoL impairment is due to menorrhagia. QoL is therefore included in this consensus only as a measure of therapeutic response.

When should a gynecologist suspect a bleeding disorder and pursue a diagnosis?

Most women with menorrhagia do not have a bleeding disorder, and gynecologic evaluation is required to evaluate other causes of bleeding, even in women with a known bleeding disorder. Because menorrhagia is often the first clinical manifestation that women with bleeding disorders encounter, many affected patients initially visit their gynecologist, often at menarche.³⁷ A recent study of adolescents with menorrhagia cites a 33%

prevalence of VWD in this patient group.³⁸ Meeting participants discussed a list of other symptoms that should raise the clinical suspicion of a bleeding disorder. Although some data indicate that the degree of menorrhagia is not necessarily predictive of a bleeding disorder, there appears to be a positive correlation between the severity of the bleeding disorder and the prevalence of menorrhagia.

An underlying bleeding disorder should be considered if any of the following indicators are present (especially before any invasive procedures are undertaken): menorrhagia since menarche (grade B, level IIB^{39,40}); family history of a bleeding disorder (grade B, level IIB⁴⁰); personal history of 1, but usually several, of the following symptoms: (1) epistaxis (generally bilateral epistaxis, > 10 minute duration, once in the last year possibly necessitating packing or cautery; grade B, level IIB⁴⁰); (2) notable bruising without injury (and > 2 cm in diameter; grade B, level IIB⁴⁰); (3) minor wound bleeding (ie, from trivial cuts lasting for > 5 minutes; grade B, level IIB⁴⁰); (4) bleeding of oral cavity or gastrointestinal tract without an obvious anatomic lesion; grade B, level IIB⁴⁰); (5) prolonged or excessive bleeding after dental extraction; grade B, level IIB⁴⁰); (6) unexpected postsurgical bleeding; grade B, level IIB⁴⁰); (7) hemorrhage from ovarian cysts or corpus luteum, possibly with accompanying pain during ovulation (termed *Mittelschmerz*; grade C, level IV); (8) hemorrhage that required blood transfusion (grade B, level IIB⁴⁰); and (9) PPH, especially delayed PPH (after 24 hours; grade C, level IV; failure of response to conventional management of menorrhagia (grade C, level IV).

Meeting participants agreed that a bleeding disorder may be a contributing factor to menorrhagia, even in the presence of gynecologic disease. Previous studies have confirmed that coexistent VWD and uterine fibroid tumors can lead to menorrhagia.^{6,7,27}

What hematologic evaluations should be ordered and when should they be repeated?

Hematologic evaluation appears to be most sensitive when coagulation factor

levels, most notably VWF and FVIII, are at their lowest. This occurs during menstruation when estrogen and progesterone are also at their lowest.⁴¹⁻⁴³ A consensus was reached that a patient's platelet number and function and specific coagulation factor profile should be assessed in collaboration with a hematologist. Evaluations should include complete blood cell count (grade C, level IV), activated partial thromboplastin time (grade C, level IV), prothrombin time (grade C, level IV), VWF (measured with ristocetin cofactor activity and antigen; grade B, level III⁴⁴⁻⁴⁶), FVIII (grade B, level III^{45,47,48}), and fibrinogen (grade C, level IV).

Participants also agreed on the following conclusions: (1) Evaluations should not be delayed to coincide with menstruation (but repeat testing during menses should be considered if the first set of VWF levels are at the lower limit of normal; grade C, level IV); (2) Patients should not be removed from hormonal contraception to permit testing. Nonetheless, it should be remembered that women with mild type 1 VWD may have normal results when hormonal contraceptives are used; when estrogens are sometimes, but not always,⁴¹ associated with the cessation of spontaneous bleeding episodes; and when there is normalization of coagulation test results⁴⁹ (grade C, level IV); (3) If the aforementioned panel of tests is normal, studies of platelet aggregation and platelet release should be arranged because emerging data suggest that defects in platelet aggregation and/or release may be associated with menorrhagia (grade B, level IIB).⁵⁰

Although it is well documented that blood group affects plasma VWF levels,⁵¹ most meeting participants agreed that identification of blood group is not essential. Bleeding symptoms in VWD are determined by VWF levels, independent of blood group. Knowledge of blood group therefore would not change the treatment strategy for patients who experience menorrhagia (grade C, level IV).

Meeting participants agreed that hematologic evaluations should be repeated to confirm the diagnosis of a

bleeding disorder. Given the known fluctuations of VWF that occur in individuals, it must be emphasized that borderline-normal VWF levels do not necessarily exclude a diagnosis of VWD. VWF levels in the lowest quartile of the normal range (40-60 IU/dL) and other borderline coagulation values should be retested, ideally during menses as noted earlier (grade C, level IV).

The role of point-of-care instruments in the diagnosis of a bleeding disorder was not discussed in depth. The general consensus was that, by the time the diagnosis of a bleeding disorder is considered, full hematologic evaluation is indicated. Collaboration with a hematologist would also be required, and the role of instruments (such as PFA-100; "Appendix of Selected Terms") for an obstetrician or gynecologist would be of limited value (grade C, level IV).

How should menorrhagia be managed in women with bleeding disorders?

Meeting participants discussed management of menorrhagia, both in the context of a confirmed diagnosis of a bleeding disorder and when no such diagnosis is as yet available. Although management is optimally implemented after a diagnosis, meeting participants agreed that tranexamic acid (1-1.5 g, 3-4 times/day; "Appendix of Selected Terms") may be given to women before hematologic evaluation (grade C, level IV). Participants agreed that nonsteroidal antiinflammatory drugs should not be used as first-line therapy for menorrhagia in general, because they affect platelet function and may further increase menstrual loss in those women with undiagnosed bleeding disorders. Nonsteroidal antiinflammatory drugs should be avoided altogether in women with diagnosed VWD and menorrhagia (grade C, level IV). Cyclooxygenase-2 inhibitors were also discussed as possible alternatives for the management of menstrual pain in women with bleeding disorders, although no consensus was reached given the lack of studies specifically in this population.

Meeting participants then focused on different management strategies in the context of a desire for future fertility

(Figure). If the answer is "yes" to future fertility with a desire to become pregnant soon, then conservative medical management should be used. Therapy should include nonhormonal hemostatic agents (ie, antifibrinolytics such as tranexamic acid and aminocaproic acid or desmopressin (DDAVP; Stimate; grade A, level Ib⁵²; "Appendix of Selected Terms"). In cases refractory to antifibrinolytics and unresponsive to DDAVP, for example in severe VWD, coagulation factor replacement is required. VWF/FVIII replacement therapy can be considered the definitive therapy, particularly in those severe cases such as massive hemorrhage (grade C, level IV).

If future fertility is desired, but pregnancy is not wanted in the near future, conservative medical management should also be used, with combined, possibly continuous, hormonal contraception as first-line therapy (grade C, level IV). Combined hormonal contraception will play multiple roles (eg, reducing menstrual blood flow, suppressing ovulation, and preventing hemorrhagic ovarian cysts, and possibly raising coagulation factor [eg, VWF and FVIII] levels).⁴⁹ The levonorgestrel intrauterine system (grade B, level IIb)⁵³ and injectable medroxyprogesterone acetate are also viable options. Hormonal therapy may also be used in conjunction with nonhormonal treatments such as tranexamic acid or aminocaproic acid, DDAVP, and coagulation factor replacement (grade C, level IV).

If the answer is "no" to future fertility, therapeutic options can include invasive procedures such as endometrial ablation or hysterectomy, which is an option to be considered especially in the presence of a pelvic disease, such as uterine fibroid tumors). Of course, these invasive options should be avoided in adolescents, and these young women should be reassured that menstruation can be suppressed without having to undergo procedures that impact their future fertility.

A combination of therapies is often required to treat menorrhagia in women with bleeding disorders. Therefore, consultation with a hematologist is essential. DDAVP, for example, is appropriate only for certain patients. Most patients with type 1 VWD will have a ≥ 2 -fold

increase in VWF levels,⁸ but DDAVP is only partially effective in most patients with type 2 VWD, may cause thrombocytopenia in patients with type 2B VWD, and is not effective in patients with type 3 VWD. DDAVP may actually be contraindicated in patients with type 2B VWD, because its use could worsen thrombocytopenia and precipitate thrombosis.⁹ In addition, DDAVP should not be administered at $> 300 \mu\text{g}$ daily (1 puff to each nostril in the patient who weighs $> 50 \text{ kg}$) for 2-3 days because tachyphylaxis and fluid retention can develop. Fluid intake should also be carefully monitored. Coagulation factor replacements are, in turn, specific to the blood disorder being treated (eg, plasma-derived VWF-containing FVIII concentrate for patients whose condition is unresponsive to DDAVP). Cryoprecipitate administration should be avoided because of the risk of viral or other antigenic contamination. VWF-containing FVIII concentrates that are available for the replacement of VWF in VWD include Humate-P (licensed in the United States to replace VWF), Alphanate S/D (licensed in the United States to replace VWF), Koate DVI (not licensed in the United States to replace VWF); Wilate (not currently available in the United States), Wilfactin (not available in the United States).

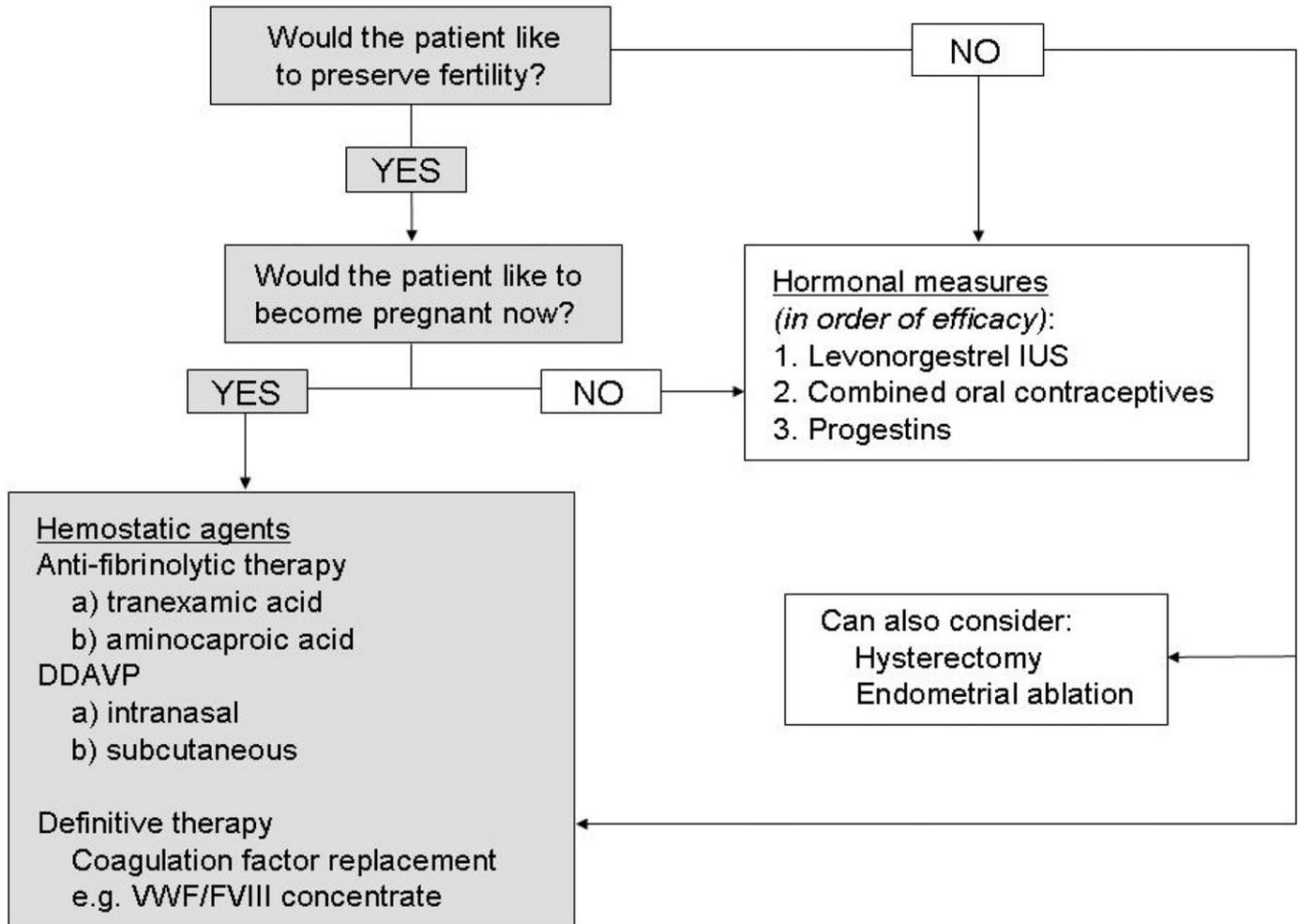
Meeting participants agreed that hemostatic therapy should start on the first or second day of menses, with the specific therapeutic choice, dose, duration of therapy, and therapeutic monitoring to be tailored to the individual patient and clinical situation. Ideally, the pictorial blood assessment chart should be used to assess menstrual blood loss. Monitoring of therapeutic response may also include evaluations of ferritin, hemoglobin, and possibly coagulation factor levels as advised by a hematologist. QoL instruments may be used to assess the patient's day-to-day activities, which would include work and school performance.

How can PPH be prevented in women with bleeding disorders?

Participants agreed on the following recommendation to reduce the risk of PPH

FIGURE

Algorithm for management of VWD-related menorrhagia



Decision tree that outlines the algorithm for the determination of the best management strategy of von Willebrand disease-related menorrhagia that is based on future fertility. Hemostatic agents and hormonal measures can be combined as needed.

DDAVP, desmopressin; FVIII, coagulation factor VIII; IUS, intra-uterine system; VWD, von Willebrand disease; VWF, von Willebrand factor. James. VWD and other bleeding disorders in women. *Am J Obstet Gynecol* 2009.

in women with diagnosed bleeding disorders:

Women in the third trimester should be treated in consultation with a hematologist to ensure an adequate hemostatic condition for delivery. VWF levels should be determined then because most women with type 1 VWD will have normalization of their subnormal VWF levels by this time (grade B, level IIb).^{25,54,55}

Women should deliver at a specialized center if their coagulation factor profile is not in the normal range by the third trimester. Of particular note here are women with RBDs or bleeding disorders with coagulation factor levels < 50 IU/

dL, type 3 or type 2 VWD, or type 1 VWD with a history of hemorrhage (grade C, level IV).

Although VWF and FVIII levels rise during pregnancy and delivery,^{54,55} there was consensus that the levels may still not rise to the same levels that are observed in women with a normal pregnancy; thus, the risk of PPH is likely increased. During a normal pregnancy, concentrations of various coagulation factors change to support an overall prothrombotic state, thereby providing a level of protection against bleeding during parturition.⁵⁶ FVII and FX levels tend to increase mod-

estly, and FVIII and fibrinogen levels increase by approximately 2-fold, although VWF levels increase approximately 3-fold. Coagulation factors remain elevated for a period after delivery, although there may be considerable interpatient variability. Assuming that third-trimester VWF levels are at least 50 IU/dL, epidural analgesia/anesthesia may be considered safe at the time of delivery³; otherwise, epidurals should be considered only under appropriate hemostatic cover (grade C, level IV).

Meeting participants also agreed to the following recommendations:

1. PPH should be anticipated and prepared for in women with diagnosed bleeding disorders (grade C, level IV).
2. An experienced clinical team must be available during pregnancy and at delivery. Ideally, such a team should include, but is not necessarily limited to, an obstetrician, hematologist, anesthesiologist, nurse and/or midwife, and appropriate laboratory technicians (grade C, level IV).
3. Women should be delivered at a center with a blood bank onsite (grade C, level IV).
4. Women should have adequate venous access during labor with perhaps 2 large-bore cannulae (grade C, level IV).
5. The third stage of labor should be actively managed (grade A, level Ib⁵⁷).
6. Obstetric risk factors for PPH should be assessed before delivery (grade C, level IV).

VWF concentrate can be used to raise VWF levels at the time of delivery in women whose levels are < 50 IU/dL. Tranexamic acid (1 g immediately and then every 6 hours as needed) is an additional option for the prevention of PPH in women with bleeding disorders. The use of DDAVP to raise VWF levels before delivery warrants extreme caution, given the risk of hyponatremia. Women who are given DDAVP at any stage should be monitored for fluid overload and hyponatremia because maternal seizures have been reported.¹⁹ It is also important to note that, especially in women with bleeding disorders, the risk of PPH persists for as long as 1 month after delivery. Therefore, clinical monitoring and appropriate therapies should be continued after birth.

Menorrhagia and RBDs: what do we know?

Meeting participants discussed RBDs and how they could affect the treatment of menorrhagia. RBDs are inherited autosomally, with prevalences that range from approximately 1 in 2 million for FII and FXIII deficiency to 1 in 500,000 for FXI and FVII deficiency. According to 2 recent global surveys,^{58,59} patients who are affected by RBDs around the world seem to reach approximately 7000. The

most frequent of these bleeding disorders is FXI deficiency, but others include deficiencies in FV, FVII, FVIII, FIX, FX, FXIII, and fibrinogen.

Regarding the prevalence of menorrhagia among women with the different RBDs, an analysis was published from an international registry of 101 Iranian women of reproductive age with severe RBDs.⁶⁰ Menorrhagia was reported in 50% of women who were affected by FV, FVII, and FX deficiencies, in addition to afibrinogenemia and combined FV/FVIII deficiency. Other reports have indicated prevalences of menorrhagia in women with RBDs; however, all the reported prevalences were variable because of the small numbers of women who were analyzed. A more extensive analysis of a larger group of affected women is required to evaluate the real prevalence of menorrhagia and other gynecologic problems.⁶¹

A consensus was reached: Among RBDs, DDAVP is useful for the treatment of menorrhagia in combined FV/FVIII deficiency. Further studies are required to elucidate its role in other RBDs (grade C, level IV). Diagnosed patients should be treated with antifibrinolytic therapy and appropriate factor replacement, when available (grade C, level IV).

Available factor concentrates for the treatment of RBDs include fibrinogen (Clottagen, Fibrinogen HT, Fibrinogen, FIBRORAAS, Haemocomplettan P); FVII (Provertin, Factor VII, FACTEUR VII) and recombinant FVIIa (NovoSeven); FXI (Factor XI, HEMOLEVEN); and FXIII (Fibrogammin P).

There is currently no specific FV replacement. Also, with the exception of recombinant FVIIa, none of the aforementioned factor concentrates for RBDs is currently available in the United States. Therefore, patients may have to receive allogeneic blood products (eg, fresh frozen plasma and platelets) in the case of severe bleeding.

Comment

An awareness of bleeding disorders (such as VWD, RBDs, and platelet disorders) is an important asset for obstetricians and gynecologists. These disorders remain underdiagnosed in women with

menorrhagia and potentially in other cases of abnormal bleeding (such as PPH). Clues that include a family or personal history of bleeding events should provoke suspicion of an underlying bleeding disorder. Responding to these clues facilitates collaboration among obstetrician-gynecologists and hematologists that could lead to a decrease in the diagnosis of "idiopathic" menorrhagia and allow more effective management of bleeding events. This, in turn, should lead to improved QoL and school and work performance indicators in these women. The authors of this consensus believe that these recommendations will aid obstetricians and gynecologists to better anticipate, prepare for, and manage cases of abnormal reproductive tract bleeding in women with bleeding disorders. ■

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Appendix: of Selected Terms

Aminocaproic acid (Amicar): an antifibrinolytic medication that is administered intravenously or orally as a solution (syrup) or tablet.

Desmopressin acetate (DDAVP): a synthetic analogue of the hormone arginine vasopressin that is administered intravenously. It is only appropriate for the treatment of bleeding disorders that involve deficiency or dysfunction of von Willebrand factor or coagulation factor VIII. Fluid intake should be restricted carefully during administration of DDAVP acetate so as not to augment its existing side-effect profile (eg, fluid retention). Especially during parturition, when administration of fluids is combined routinely with that of oxytocin, fluid retention should be monitored to avoid potential water intoxication.

Levonorgestrel intrauterine system (Mirena): made of plastic, shaped like the letter T, and contains a synthetic female hormone levonorgestrel. The hor-

mone acts like the natural hormone progesterone is released into the uterus over time and prevents pregnancy.

Medroxyprogesterone acetate (Amen, Curretab, Cytrin, Depo-Provera, and Provera): inhibits the secretion of pituitary gonadotropins and prevents follicular maturation and ovulation. It is administered intravenously or orally as a tablet.

Pictorial blood assessment chart (PBAC): a semiquantitative evaluation of menstrual blood loss; women fill in the number and appearance of their sanitary protection and size of blood clots on a pictorial chart. A derived score of ≥ 100 represents menstrual blood loss of ≥ 80 mL.

PFA-100: a test of platelet function (adhesion and aggregation) that measures the time taken for blood to clot and thereby block an artificial membrane. The membrane is coated with collagen plus either epinephrine or adenosine diphosphate. The result is referred to as the closure time and is measured in seconds.

Tranexamic acid (Cyclokapron): an antifibrinolytic medication that is administered intravenously or orally as a tablet.