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Screening and Management of Bleeding Disorders in Adolescents With Heavy Menstrual Bleeding

ABSTRACT: *Heavy menstrual bleeding* is defined as excessive menstrual blood loss that interferes with a woman's physical, social, emotional, or material quality of life. If obstetrician–gynecologists suspect that a patient has a bleeding disorder, they should work in coordination with a hematologist for laboratory evaluation and medical management. Evaluation of adolescent girls who present with heavy menstrual bleeding should include assessment for anemia from blood loss, including serum ferritin, the presence of an endocrine disorder leading to anovulation, and evaluation for the presence of a bleeding disorder. Physical examination of the patient who presents with acute heavy menstrual bleeding should include assessment of hemodynamic stability, including orthostatic blood pressure and pulse measurements. The first-line approach to acute bleeding in the adolescent is medical management; surgery should be reserved for those who do not respond to medical therapy. Use of antifibrinolytics such as tranexamic acid or aminocaproic acid in oral and intravenous form may be used to stop bleeding. Nonmedical procedures should be considered when there is a lack of response to medical therapy, if the patient is clinically unstable despite initial measures, or when severe heavy bleeding warrants further investigation, such as an examination under anesthesia. After correction of acute heavy menstrual bleeding, maintenance hormonal therapy can include combined hormonal contraceptives, oral and injectable progestins, and levonorgestrel-releasing intrauterine devices. Obstetrician–gynecologists can provide important guidance to premenarchal and postmenarchal girls and their families about issues related to menses and should counsel all adolescent patients with a bleeding disorder about safe medication use and future surgical considerations.

Recommendations and Conclusions

The American College of Obstetricians and Gynecologists makes the following recommendations and conclusions regarding bleeding disorders in adolescents:

- Heavy menstrual bleeding at menarche and in adolescence may be an important sentinel for an underlying bleeding disorder.
- If obstetrician–gynecologists suspect that a patient has a bleeding disorder, they should work in coordination with a hematologist for laboratory evaluation and medical management.
- When obtaining a medical history, it is important to identify risk factors for bleeding disorders as well as medical conditions that would alter management.
- Physical examination of the patient who presents with acute heavy menstrual bleeding should include assessment of hemodynamic stability, including orthostatic blood pressure and pulse measurements.
- In adolescent girls with heavy menstrual bleeding, speculum examination typically is not required.
- Evaluation of adolescent girls who present with heavy menstrual bleeding should include assessment for anemia from blood loss, including serum ferritin, the presence of an endocrine disorder leading to anovulation, and evaluation for the presence of a bleeding disorder.
- Routine ultrasonography should not be obtained solely for the workup of heavy menstrual bleeding in

adolescents; however, it can be considered for patients who do not respond to initial management.

- The first-line approach to acute bleeding in the adolescent is medical management; surgery should be reserved for those who do not respond to medical therapy.
- Adolescents who are hemodynamically unstable or actively bleeding heavily should be hospitalized for management.
- In the absence of contraindications to estrogen, hormonal therapy for acute heavy menstrual bleeding can consist of intravenous conjugated estrogen every 4–6 hours; alternatively, monophasic combined oral contraceptive pills (OCPs) (in 30–50 microgram ethinyl estradiol formulation) can be used every 6–8 hours until cessation of bleeding.
- Use of antifibrinolytics such as tranexamic acid or aminocaproic acid in oral and intravenous form may be used to stop bleeding.
- After correction of acute heavy menstrual bleeding, maintenance hormonal therapy can include combined hormonal contraceptives, oral and injectable progestins, and levonorgestrel-releasing intrauterine devices (LNG-IUDs).
- Iron replacement therapy should be provided for all reproductive-aged women with anemia due to bleeding.
- Nonmedical procedures should be considered when there is a lack of response to medical therapy, if the patient is clinically unstable despite initial measures, or when severe heavy bleeding warrants further investigation, such as an examination under anesthesia.
- Obstetrician–gynecologists can provide important guidance to premenarchal and postmenarchal girls and their families about issues related to menses and should counsel all adolescent patients with a bleeding disorder about safe medication use and future surgical considerations.
- Adolescents in whom a bleeding disorder has been diagnosed should be reminded that products that prevent platelet adhesion, such as aspirin or nonsteroidal antiinflammatory drugs, should be used only with the recommendation of a hematologist.
- In adolescents with known bleeding disorders, preoperative surgical evaluation, choice of hemostatic agents for control of intraoperative blood loss, and need for blood products should be determined in conjunction with a hematologist and an anesthesiologist.

Introduction

Although menstruation in adolescence can be irregular because of anovulation and immaturity of the hypothalamic–pituitary–ovary axis, cycles typically occur every 21–45 days and last 7 days or fewer. *Heavy menstrual bleeding* is defined as excessive menstrual blood loss that interferes with a woman's physical, social, emotional, or material quality of life. It can occur alone or in combination with other symptoms (1). Heavy menstrual bleeding should be classified according to the PALM–COEIN system: Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia, Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, and Not otherwise classified (2). In adolescents, structural causes of heavy menstrual bleeding are less common; an underlying bleeding disorder is second only to anovulation as a cause of heavy menstrual bleeding in adolescent girls. Heavy menstrual bleeding at menarche and in adolescence may be an important sentinel for an underlying bleeding disorder. The frequency of bleeding disorders in the general population is approximately 1–2%, but bleeding disorders are found in approximately 20% of adolescent girls who present for evaluation of heavy menstrual bleeding and in 33% of adolescent girls hospitalized for heavy menstrual bleeding (3–5). If obstetrician–gynecologists suspect that a patient has a bleeding disorder, they should work in coordination with a hematologist for laboratory evaluation and medical management.

Common Bleeding Disorders in Adolescents

The most common bleeding disorders in adolescent girls who present with heavy menstrual bleeding are von Willebrand disease, platelet function defects, thrombocytopenia, and clotting factor deficiencies. Thrombocytopenia can be congenital or acquired; heavy menses can be the presenting symptom of immune thrombocytopenic purpura or thrombotic thrombocytopenic purpura (6). See Table 1 for common bleeding disorders in adolescents who present with heavy menstrual bleeding.

Presenting Symptoms and Signs

Approximately one half of adolescent girls with bleeding disorders present with heavy menstrual bleeding at menarche; others may not present until cycles become ovulatory (7). Of adolescent girls and women with an inherited bleeding disorder, 75–80% report having heavy menses as the most commonly cited clinical manifestation of their disorder (8, 9). Although classically regular heavy menses are associated with bleeding disorders, adolescent girls may have prolonged menses or irregular menses due to anovulation superimposed on the bleeding disorder. Of children and adolescents with a bleeding disorder, 70% report passage of clots and bleeding through clothes and sheets (10). Recurrent hemorrhagic corpus luteum, with or without rupture, or hemoperitoneum with ovulation also can be gynecologic indications of a bleeding disorder (3). Anemia that results from bleeding can cause associated symptoms of headaches and fatigue. Low iron stores in adolescents with heavy menstrual bleeding, reflected by a low ferritin level, even without anemia, are associated with fatigue and decreased cognition

Table 1. Common Bleeding Disorders in Adolescents Who Present With Heavy Menstrual Bleeding

Bleeding Disorder	Physiologic Description	Recommended Laboratory Tests
Platelet Function Disorders (Defects of platelet adhesion, aggregation, or secretion)		
von Willebrand Disease		aPTT, von Willebrand antigen, von Willebrand activity, vWF:RCo, factor VIII level
Type 1	Quantitative deficiency of vWF, autosomal dominant inheritance	
Type 2 (multiple subtypes)	Qualitative defect in vWF activity in platelet adhesion or binding factor VIII, most commonly autosomal dominant inheritance	
Type 3	Absent vWF, autosomal recessive	
Glanzmann thrombasthenia	Abnormalities of the platelet membrane glycoproteins IIb or IIIa (GPIIb/IIIa) that mediate binding to fibrinogen, resulting in reduced platelet aggregation or clumping	Platelet aggregation studies
Bernard–Soulier syndrome	Inherited deficiency in platelet membrane glycoprotein complex Ib-IX causing defective adhesion of the platelets to subendothelial matrix	Platelet aggregation studies
Delta storage pool disorders	Disorder of platelet secretion due to defects in platelet activation factors	Platelet aggregation and secretion studies
Other Disorders		
Clotting factor deficiencies	Deficiencies of any major clotting factor, factor VIII deficiency (hemophilia A) and factor IX deficiency (hemophilia B) are symptomatic carriers due to X-linked inheritance, but can occur due to inactivation of the X chromosome carrying the normal gene	Isolated prolonged PT detects factor VII deficiency; Isolated prolonged aPTT detects VIII, IX, XII deficiencies; Combined prolonged PT or aPTT detects deficiencies in factors II, V, X, fibrinogen
Thrombocytopenia	Low platelet count. Can be associated with idiopathic thrombocytopenia, or immune-mediated thrombocytopenic purpura	Platelet count
Fibrinolytic pathway defects	Dysfibrinogenemia or plasminogen deficiency	Fibrinogen or thrombin time

Abbreviations: aPTT, activated partial thromboplastin time; PT, prothrombin time; vWF, von Willebrand factor; vWF:RCo, von Willebrand factor ristocetin cofactor.

specifically affecting verbal learning and memory (11–13). Adolescents with heavy bleeding may have impaired school attendance and performance, decreased participation in sports, and may present with symptoms of depressed mood or anxiety (4).

Evaluation and Diagnosis

The evaluation of an adolescent with a bleeding disorder includes a thorough medical history and physical examination, as well as appropriate laboratory and imaging tests. The obstetrician–gynecologist should be aware of risk factors and comorbidities associated with bleeding disorders.

Medical History

When obtaining a medical history, it is important to identify risk factors for bleeding disorders as well as medical conditions that would alter management. See Box 1 for a recommended screening tool for adolescent patients who report heavy menstrual bleeding. Adolescents who meet the criteria detailed in Box 1 should undergo laboratory screening for a bleeding disorder. Adolescents may not be able to accurately describe their menstrual bleeding, and it may be helpful to ask a caregiver about quantity of pads or tampons used and bleeding through hygiene products that soils clothing and sheets. In adolescents with known bleeding disorders, the pictorial blood assessment chart (Fig. 1) may help to assess response to treatment, although it may not be predictive of bleeding disorders (14). If a patient is using a mobile app to chart her menstrual cycle, reviewing that data may be helpful.

Physical Examination

Physical examination of the patient who presents with acute heavy menstrual bleeding should include assessment of hemodynamic stability, including orthostatic blood pressure and pulse measurements. Dermatologic

Box 1. Screening Tool to Identify Adolescents With Heavy Menstrual Bleeding for Testing and Evaluation for Underlying Bleeding*

1. How many days did your period usually last, from the time bleeding began until it completely stopped?
   i. Less than 7 days
   ii. Greater than or equal to 7 days
   iii. Don't know
2. How often did you experience a sensation of "flooding" or "gushing" during your period?
   i. Never, rarely, or some periods
   ii. Every or most periods
   iii. Don't know
3. During your period did you ever have bleeding where you would bleed through a tampon or napkin in 2 hours or less?
   i. Never, rarely, or some periods
   ii. Every or most periods
   iii. Don't know
4. Have you ever been treated for anemia?
   i. No
   ii. Yes
   iii. Don't know
5. Has anyone in your family ever been diagnosed with a bleeding disorder?
   i. No
   ii. Yes
   iii. Don't know
6. Have you ever had a tooth extracted or had dental surgery?
   i. No (If no, go to question 7)
   ii. Yes
   iii. Don't know
   6a. Did you have a problem with bleeding after tooth extraction or dental surgery?
      i. No
      ii. Yes
      iii. Don't know
7. Have you ever had surgery other than dental surgery?
   i. No (If no, go to question 8)
   ii. Yes
   iii. Don't know
   7a. Did you have bleeding problems after surgery?
      i. No
      ii. Yes
      iii. Don't know

(*continued*)

Box 1. Screening Tool to Identify Adolescents With Heavy Menstrual Bleeding for Testing and Evaluation for Underlying Bleeding* (*continued*)

8. Have you ever been pregnant?
   i. No
   ii. Yes
   iii. Don't know
   8a. Have you ever had a bleeding problem following delivery or after a miscarriage?
      i. No
      ii. Yes
      iii. Don't know

How to Use the Screening Tool

The screening tool is considered to be positive if 1 of the following 4 criteria were met:

1. The duration of menses was greater than or equal to 7 days and the woman reported either "flooding" or bleeding through a tampon or napkin in 2 hours or less with most periods;
2. A history of treatment of anemia;
3. A family history of a diagnosed bleeding disorder; or
4. A history of excessive bleeding with tooth extraction, delivery or miscarriage, or surgery

Adapted from Philipp CS, Faiz A, Dowling NF, Beckman M, Owens S, Ayers C, et al. Development of a screening tool for identifying women with menorrhagia for hemostatic evaluation. Am J Obstet Gynecol 2008;198:163.e1–8; Philipp CS, Faiz A, Heit JA, Kouides PA, Lukes A, Stein SF, et al. Evaluation of a screening tool for bleeding disorders in a US multisite cohort of women with menorrhagia. Am J Obstet Gynecol 2011;204:209.e1–7.

signs of anemia and bleeding disorders include pallor and presence of bruises and petechiae. An abdominal examination should be done to assess for distention, hepatosplenomegaly, or masses. If a patient has vaginal bleeding, make sure this is appropriate with sexual maturity level (Sexual Maturity Rating, Tanner staging III and above) and not due to other sources (eg, trauma). In adolescent girls with heavy menstrual bleeding, speculum examination typically is not required (4).

Laboratory Evaluation

Evaluation of adolescent girls who present with heavy menstrual bleeding should include assessment for anemia from blood loss, including serum ferritin, the presence of an endocrine disorder leading to anovulation, and evaluation for the presence of a bleeding disorder. See Figure 2 for a recommended approach to testing and Table 1 for recommended laboratory tests for selected bleeding disorders. In the setting of acute heavy menstrual bleeding in a patient who is hemodynamically

unstable, a blood type and crossmatch should be included.

Serum ferritin level also should be routinely obtained in young women who present with heavy menstrual bleeding (13, 15). Although a low ferritin level always indicates low iron stores, a normal or high ferritin level does not rule out iron deficiency anemia given that the ferritin level may be elevated in inflammatory states (16). Additionally, obstetrician–gynecologists should follow guidelines on sexually transmitted infection screening based on age and risk factors (17).

Imaging Recommendations

Structural causes of acute abnormal uterine bleeding (AUB) in adolescents are rare, thus, the use of imaging in this age group may not be helpful in diagnosis (18). Routine ultrasonography should not be obtained solely for the workup of heavy menstrual bleeding in adolescents; however, it can be considered for patients who do not respond to initial management (Fig. 2). The decision to perform an imaging examination should be based on the clinical judgment of the obstetrician–gynecologist or other gynecologic care provider and, if deemed necessary, transabdominal ultrasonography may be more appropriate than transvaginal ultrasonography in adolescent patients (2, 19).

Acute Management

The first-line approach to acute bleeding in the adolescent is medical management; surgery should be reserved for those who do not respond to medical therapy. The choice of treatment for acute management is dependent on clinical stability, overall acuity, suspected etiology of the bleeding, and underlying medical problems. Adolescents who are hemodynamically unstable or actively bleeding heavily should be hospitalized for management. Volume expansion with crystalloid, hormonal therapy, and iron replacement should be initiated. See Figure 2 for an algorithm that incorporates testing and management. For guidance on medical management applicable to postmenarchal adolescents, see ACOG Committee Opinion No. 557, *Management of Acute Abnormal Uterine Bleeding in Nonpregnant Reproductive-aged Women* (2).

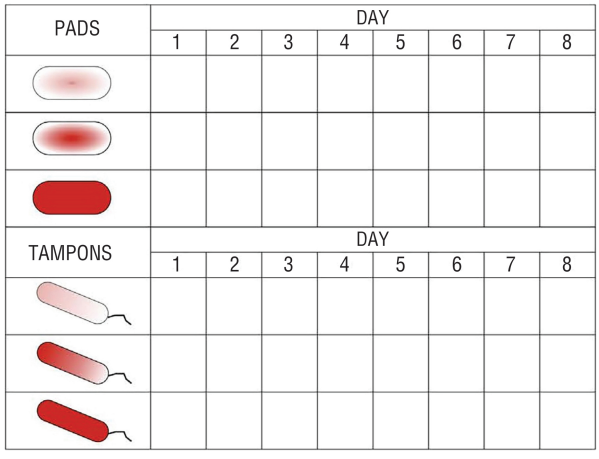

Figure 1. Pictorial Blood Loss Assessment Chart. Each woman fills in on the chart how many pads or tampons she uses each day and to which degree they are soiled with blood according to the 3 alternative pictures on the diagram. A score is calculated by multiplying the number of pads and tampons by a factor of 1 for lightly soiled items, 5 for medium soiled items, 10 for totally soaked tampons, and 20 for totally soaked pads. (Reprinted from Hald K, Lieng M. Assessment of periodic blood loss: interindividual and intraindividual variations of pictorial blood loss assessment chart registrations. J Minim Invasive Gynecol 2014;21:662–8.)

Hormonal Medical Therapy

Most girls have completed 95% of their growth by menarche, so concern about the use of estrogen and closure of epiphyseal plates should not preclude hormone use for the treatment of heavy menstrual bleeding (3). See Table 2 for medical and hormonal therapies for acute heavy menstrual bleeding. In the absence of contraindications to estrogen, hormonal therapy for acute heavy menstrual bleeding can consist of intravenous conjugated estrogen every 4–6 hours; alternatively, monophasic combined OCPs (in 30–50 microgram ethinyl estradiol formulation) can be used every 6–8 hours until cessation of bleeding. Once bleeding has stopped (typically within 24–48 hours), a combined OCP tapering regimen should be initiated. If bleeding has not stopped or significantly improved within 24–48 hours, a hematologist should be contacted if not yet involved. Tapering regimens vary and doses of combined OCs should be maintained at the level needed to prevent bleeding until the hemoglobin has increased to a level adequate for the patient to tolerate a potentially heavy withdrawal bleed. High-dose estrogen therapy in the form of intravenous conjugated estrogens or combined OC tapering regimens often induces nausea and vomiting, which can be exacerbated by oral iron therapy; thus, antiemetics also should be prescribed. In girls and adolescents with underlying bleeding disorders, continuous use of combined OCs may be optimal. Progesterone-only therapy is effective for cessation of bleeding for girls and adolescents in whom estrogens are contraindicated or not tolerated. Oral medroxyprogesterone 10–20 mg every 6–12 hours or norethindrone acetate 5–10 mg every 6 hours can be used. Depot medroxyprogesterone acetate is not a first-line therapy because of the difficulty to titrate to effect or to discontinue if there are adverse effects.

Nonhormonal Therapy

Use of antifibrinolytics such as tranexamic acid or aminocaproic acid in oral and intravenous form may be used to stop bleeding. The prescribing information for tranexamic acid lists concurrent use of OCs as a contraindication because of theoretical risks of thrombosis (20). Estrogen influences hemostasis by increasing the levels of

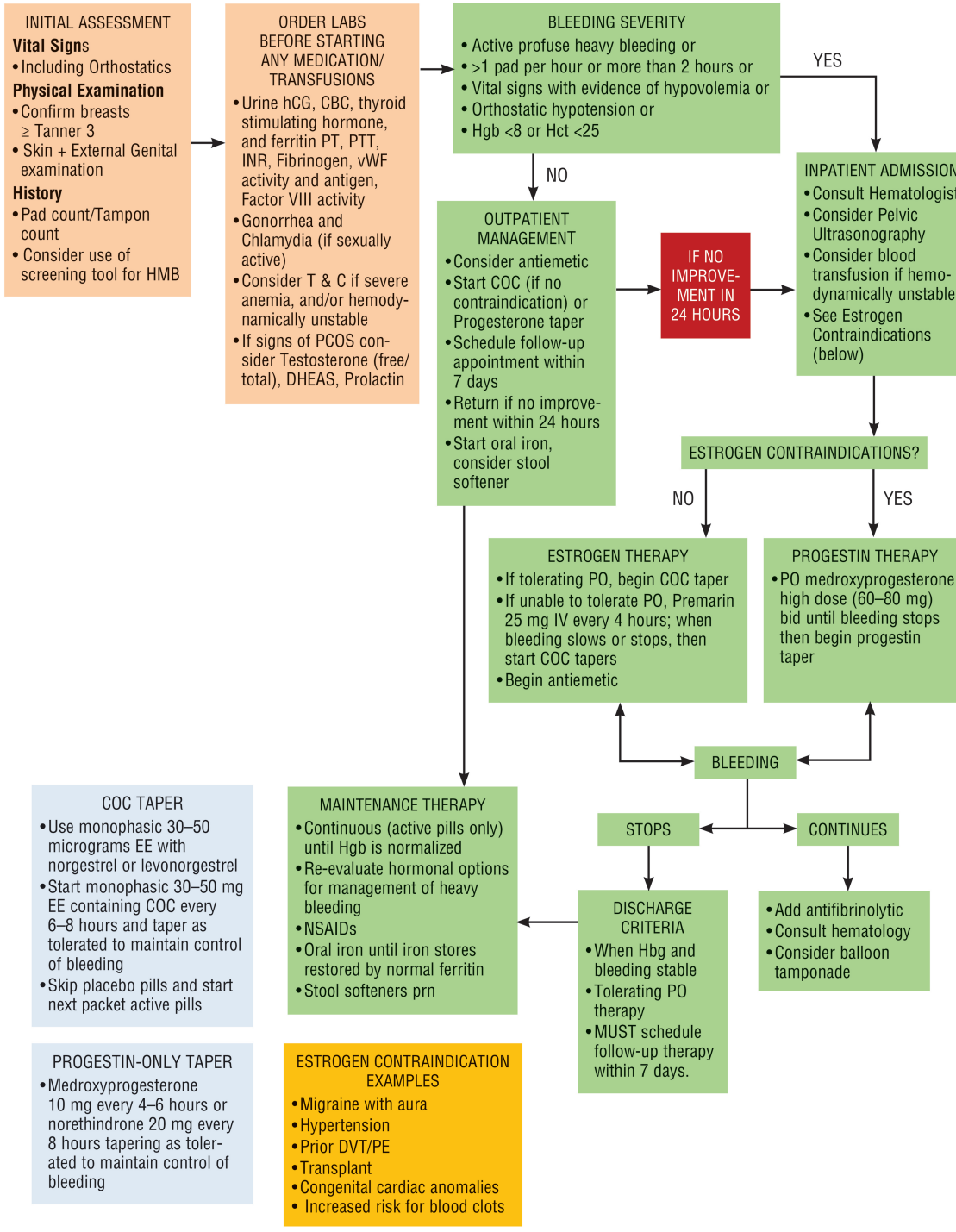

Figure 2. Approaches to Testing and Management. (Adapted from Ely JW, Kennedy CM, Clark EC, Bowdler NC. Abnormal uterine bleeding: a management algorithm. J Am Board Fam Med 2006;19:590–602.). Abbreviations: bid, two times a day; CBC, complete blood cell count; COC, combined oral contraceptive; DHEAS, dehydroepiandrosterone sulfate; DVT, deep vein thrombosis; EE, ethinyl estradiol; hCG, human chorionic gonadotropin; Hct, hematocrit; Hgb, hemoglobin; HMB, heavy menstrual bleeding; INR, international normalized ratio; IV, intravenously; NSAIDs, nonsteroidal antiinflammatory drugs; PCOS, polycystic ovary syndrome; PE, pulmonary embolism; PO, orally; prn, as needed; PT, prothrombin time; PTT, partial thromboplastin time; T & C, type and cross; vWF; von Willebrand factor.

Table 2. Medical Treatment Regimens for Acute Heavy Menstrual Bleeding*

Drug	Suggested Dose	Dose Schedule
Conjugated equine estrogen[†]	25 mg IV	Every 4–6 hours for 24 hours
Combined oral contraceptives[‡§]	Monophasic combined oral contraceptive pills that contain 30–50 micrograms of ethinyl estradiol	Every 6–8 hours until cessation of bleeding
Medroxyprogesterone acetate[‖¶]	20 mg orally	Three times per day for 7 days
Tranexamic acid[‡]	1.3 g orally[#] or 10 mg/kg IV (maximum 600 mg/dose)	Three times per day for 5 days (every 8 hours)

Abbreviations: FDA, U.S. Food and Drug Administration; IV, intravenously.

*The U.S. Food and Drug Administration's labeling contains exhaustive lists of contraindications for each of these therapies. In treating women with acute abnormal uterine bleeding, physicians often must weigh the relative risks of treatment against the risk of continued bleeding in the context of the patient's medical history and risk factors. These decisions must be made on a case-by-case basis by the treating health care provider. See also the Centers for Disease Control and Prevention's U.S. Medical Eligibility Criteria for Contraceptive Use for additional information, available at https://www.cdc.gov/reproductivehealth/contraception/mmwr/mec/.

[†]DeVore GR, Owens O, Kase N. Use of intravenous Premarin in the treatment of dysfunctional uterine bleeding—a double-blind randomized control study. Obstet Gynecol 1982;59:285–91.

[‡]James AH, Kouides PA, Abdul-Kadir R, Dietrich JE, Edlund M, Federici AB, 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;158:124–34.

[§]Other combined oral contraceptive formulations, dosages, and schedules also may be effective.

[‖]Munro MG, Mainor N, Basu R, Brisinger M, Barreda L. Oral medroxyprogesterone acetate and combination oral contraceptives for acute uterine bleeding: a randomized controlled trial. Obstet Gynecol 2006;108:924–9.

[¶]Other progestins (such as norethindrone acetate), dosages, and schedules also may be effective.

[#]Other dosages and schedules also may be effective.

clotting factors (VII, VIII, X, fibrinogen) and plasminogen, lowering antithrombin III and protein S levels, and altering activated protein C resistance. Tranexamic acid inhibits fibrinolysis. Although there is a theoretical risk of thrombosis, the concomitant administration of tranexamic acid and OCs has been used when monotherapy has failed; review of the existing literature has not identified an increased risk of venous thromboembolism in this setting, although studies are very limited (21, 22). It is an important treatment option to control bleeding in this population and a reasonable approach to management when other options have failed.

The Role of Transfusion

Because the majority of adolescents with a bleeding disorder who present with heavy menstrual bleeding are otherwise healthy, often it is possible to avoid blood transfusion; exceptions include hemodynamically unstable patients or those with severe symptoms of anemia (eg, tachycardia, lethargy, syncope tachypnea). In general, adolescents respond to hormonal management and iron therapy quickly and tolerate anemia better than do adult patients. Theoretically, avoiding exposure to red blood cell antigens may reduce the risk of hemolytic disease of the newborn in any future pregnancy. Transfusion guidelines developed by the Eastern Association for Surgery of Trauma, the American College of Critical Care Medicine, and the Society of Critical Care Medicine advocate for restrictive red blood cell transfusion practices and transfusion only for a hemoglobin of 7 g/dL or less to limit complications of allogenic transfusions (23). Studies of restrictive transfusion practices in critically ill children as well as a 2016 Cochrane review found no increase in adverse events using this approach (24, 25). Based on expert opinion, if a blood transfusion is medically necessary based on hemodynamic status, transfusion of one unit of packed red cells and reassessment of hemodynamic status are preferred to the historic automatic transfusion of two units. Otherwise healthy adolescents may tolerate hemoglobin levels less than 7 g/dL, and a decision to transfuse should be based on hemodynamic status and presence of active bleeding, not only the hemoglobin level. It still is important to initiate iron therapy because iron packaged in transfused red cells is not immediately available for erythropoiesis (16). When a patient's adherence to an oral medication regimen at discharge is a concern, the use of intravenous iron during hospitalization may be considered. Consultation with a hematologist may be useful.

Nonmedical Management

Procedural interventions in adolescents usually are considered second-line treatment given the presumed desire for future fertility. Nonmedical procedures should be considered when there is a lack of response to medical therapy, if the patient is clinically unstable despite initial measures, or when severe heavy bleeding warrants

further investigation, such as an examination under anesthesia. Ultrasonography can help guide procedural management. In cases when a thickened endometrium is suggestive of a clot or decidual cast, the obstetrician–gynecologist can consider suction curettage. Endometrial ablation, uterine artery embolization, and hysterectomy are invasive measures that can cause infertility and should not be considered in the adolescent population unless absolutely necessary, such as in life-threatening situations. Surgical options that spare fertility include intrauterine balloon tamponade and suction evacuation or suction curettage (machine or manual).

Intrauterine Balloon

Intrauterine balloon placement is an effective, low-cost, readily available, accessible modality that does not require special training for insertion and can help avoid further invasive procedures. Most studies on intrauterine balloons have focused on women with postpartum hemorrhage and have demonstrated reduction in bleeding in an emergent setting (26, 27). Intrauterine balloons designed for obstetric use in adult women are not appropriately sized for the adolescent patient. Instead, a Foley catheter should be placed with a 30-cc balloon that can be inserted easily through the cervix and inflated with saline until resistance of the myometrium is felt (4, 28, 29). The amount of saline needed to feel resistance varies depending on uterine size and can be as little as 10 cc.

Often it is not necessary to dilate the cervix before placement of the balloon, and ultrasonography can be used simultaneously to confirm proper placement of the pediatric catheter. The balloon usually can be kept in place for 12–24 hours while other medical therapies are being administered (29). Gradual deflation of the balloon by removing 5 mL of saline at a time can be performed once bleeding has ceased, or the balloon can be removed after 24 hours with observation for bleeding. An advantage of the balloon is the ability to simultaneously monitor for uterine bleeding; a leg bag can be attached to record output. There are no dedicated studies specifically analyzing the use of the intrauterine balloon in nonpregnant reproductive-aged adolescents and women with AUB. The procedure may carry substantial risks (eg, endometrial infection), and although there are not good data on the use of antibiotics, they may be considered for the duration the balloon is in place. Other risks of the procedure include uterine perforation and damage to the endometrial lining (29).

Uterine Evacuation

Sharp curettage can result in additional blood loss for patients with a bleeding disorder and should be avoided in this population. However, suction evacuation or suction curettage (machine or manual) may be appropriate if ultrasonography identifies a clot or decidual cast. The therapeutic effect of dilation and curettage for the management of AUB is thought to be its facilitation of the removal of structurally fragile bleeding endometrium, allowing for restoration of normal hemostatic events with regeneration of the integrity of the endometrium and restoration of the normal proliferation response (30). Concomitant hysteroscopy may be of value for those patients in whom intrauterine pathology is suspected or if a tissue sampling is desired (2). Additionally, concomitant placement of a levonorgestrel-releasing intrauterine device (LNG-IUD) for long-term management should be considered in this setting. In these cases of heavy menstrual bleeding, patients should be counseled about the higher risk of expulsion.

Long-Term Management

After correction of acute heavy menstrual bleeding, maintenance hormonal therapy can include combined hormonal contraceptives, oral and injectable progestins, and LNG-IUDs. Nonhormonal treatment for anemia may include oral iron supplementation and dietary optimization.

Systemic Hormonal Management

Adolescent girls with bleeding disorders may require a combination of hormonal and nonhormonal therapy to control heavy menstrual bleeding. Combined OCs, the transdermal contraceptive patch, the vaginal contraceptive ring, and the LNG-IUD all have been shown to reduce menstrual blood loss (31). Continuous or extended-cycle use of hormonal contraception (pills, patch, or ring) should be considered to reduce heavy withdrawal bleeding in adolescents with bleeding disorders. When selecting a combined OC, monophasic pills that contain 30–50 micrograms of ethinyl estradiol with a second-generation progesterone should be chosen as first-line therapy because they are more likely to stabilize the endometrium than lower dose formulations. If there is breakthrough bleeding, doubling the dose of the combined OC until the bleeding stops may be preferable to allowing a withdrawal bleed in this population. Some patients who experience breakthrough bleeding while taking a 30–35-microgram ethinyl estradiol-containing combined OCP may have decreased bleeding with the continuous use of a 50-microgram ethinyl estradiol-containing OCP.

Progestin therapy is another option for adolescents and women who cannot tolerate estrogen-containing therapy or in whom estrogen is contraindicated. Norethindrone (norethisterone) is available as a progesterone-only contraceptive pill (0.35 mg daily). Its short half-life can lead to breakthrough bleeding and decreased contraceptive efficacy in adolescents. Norethindrone in 5-mg tablets is not indicated for contraceptive use but can be titrated in doses of 5–15 mg daily for menstrual suppression. A small proportion of norethindrone is metabolized to ethinyl estradiol, approximately equivalent to 4 micrograms of ethinyl estradiol per 5 mg of norethindrone (32). It is still classified as a progestin in

terms of thrombotic risk. Breakthrough bleeding may occur. Subcutaneous formulations of medroxyprogesterone acetate are available for girls and adolescents in whom intramuscular injection is contraindicated because of the increased risk of intramuscular hematoma. Although highly effective for contraception, the etonogestrel contraceptive implant is not recommended for first-line therapy for heavy menstrual bleeding in girls and adolescents with a bleeding disorder because breakthrough bleeding is a common adverse effect.

Intrauterine Devices

Adherence to daily, weekly, or monthly medication may be challenging for adolescents. The use of a long-acting reversible contraceptive method, such as the LNG-IUD may be a good choice for the adolescent patient. Copper IUDs may exacerbate bleeding and should be avoided in adolescents with a bleeding disorder. Although there are LNG-IUDs of varying size, cost, dose, and suggested duration of use on the market, data on use in women with bleeding disorders currently exist only for 52-mg LNG-IUDs, not for lower-dose devices. There are concerns with efficacy of lower-dose IUDs to treat bleeding. The LNG-IUD has been demonstrated to reduce heavy menstrual bleeding in all women and is an effective treatment when compared with usual medical and surgical therapies (33–37). Although there are limited data on the efficacy of the LNG-IUD in controlling menstrual bleeding in adult women with heavy menstrual bleeding due to a bleeding disorder (38–41), data on its use in adolescents with bleeding disorders are even more sparse. However, case reports of adolescents with bleeding disorders have reported significant improvement in heavy menstrual bleeding after placement of the LNG-IUD (21, 42, 43). Although research is limited, the LNG-IUD appears to be an effective therapeutic option for adolescents with bleeding disorders, with minimal complications, high rates of adherence, and improvement in heavy menstrual bleeding and anemia. Notably, LNG-IUD use includes the added benefit of highly effective contraception with higher efficacy, higher continuation rates, and higher satisfaction rates compared with short-acting contraceptives (44).

Although there are concerns about the potential for LNG-IUDs to increase the risk of bleeding at the time of insertion in adolescents with bleeding disorders, studies of IUD placement in this population do not report bleeding insertion complications (21, 38–41, 45). However, most, if not all, patients in these studies received prophylactic hemostatic coverage. Co-management with a hematologist is recommended to optimize periprocedural hemostasis and decrease the potential risk of bleeding. Perioperative hemostatic agents include desmopressin acetate and antifibrinolytic medications (eg, aminocaproic acid, tranexamic acid). Currently, no standardized protocol exists for operative placement of the LNG-IUD in the patient with a bleeding disorder. In-office placement of an IUD versus placement in the operating room will depend on the severity of the bleeding disorder and judgment of the gynecologist in consultation with a hematologist. A patient's cognitive status and ability to tolerate necessary speculum placement should be considered when choosing the optimal placement setting.

Nonhormonal Treatments for Anemia

The World Health Organization defines *anemia in females 12 years and older* as a hemoglobin threshold of 12 g/dL (46). Iron deficiency generally is identified by a serum ferritin concentration below 15 micrograms/L. Adolescents with heavy menstrual bleeding are at an even higher risk of iron deficiency, with 0.4–0.5 mg of iron lost with every 1 mL of blood. The incidence of iron deficiency among these adolescents is 9%, increasing to 15–20% when iron deficiency without anemia is included (16, 47).

Despite known adverse effects, there remains a paucity of data regarding optimal screening, diagnosis, and treatment of anemia for adolescents. This lack of evidence on which to base clinical decision making leads to variability in practice and suboptimal management (48, 49). The Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics recommend annual screening for adolescents who are at high risk of iron deficiency; however, no single test is accepted for diagnosing iron deficiency (50, 51). The American College of Obstetricians and Gynecologists recommends obtaining a complete blood count and iron studies, when possible.

First-line therapy for iron deficiency anemia includes oral iron supplementation along with dietary counseling to increase iron intake. The CDC recommends that adolescent girls and women who have anemia receive an oral dose of 60–120 mg per day of iron (51, 52). There is emerging data that once-a-day to every-other-day dose scheduling is more efficient than multiple doses because increased levels of released hepcidin can decrease iron absorption (53, 54).

Duration of therapy should be directed by the severity of anemia and the patient's response to treatment. If interventions to decrease menstrual flow are successful, then a 3- to 6-month course of iron supplementation is sufficient. A ferritin level should be obtained to confirm the complete resolution of iron deficiency (13, 16).

Other Gynecologic Considerations in Adolescents With Bleeding Disorders

In addition to diagnosis and management of uterine bleeding, management of hemorrhagic ovarian cysts and dysmenorrhea can be a challenge in adolescents with bleeding disorders. Obstetrician–gynecologists can provide important guidance to premenarchal and

postmenarchal girls and their families about issues related to menses and should counsel all adolescent patients with a bleeding disorder about safe medication use and future surgical considerations.

Hemorrhagic Ovarian Cysts

Increased incidence of hemorrhagic ovarian cysts has been reported in women with bleeding disorders (55–57). In a CDC-conducted survey of 102 women aged 18–70 years with von Willebrand disease compared with 88 controls, 52% of those with von Willebrand disease reported a history of ovarian cysts compared with 22% of the control group ($P<.0001$) (58). The cysts occur as a result of excessive bleeding into the corpus luteum at the time of ovulation, and rupture of these cysts may result in hematoperitoneum (56). Systemic hormones potentially are an option for patients with recurrent hemorrhagic cysts and can be used in combination with an LNG-IUD.

Preparing the Prepubertal Girl With a Bleeding Disorder and Her Family for Menarche

With puberty and menarche come reproductive concerns related to heavy menstrual bleeding, hemorrhagic ovarian cysts, dysmenorrhea, and onset of sexual activity. In the setting of known bleeding disorders, puberty may increase anxiety about bleeding and risk of menstrual hygiene accidents at school for patients and their families. Adolescents with known bleeding disorders should be counseled before menarche and have a plan in place for the possibility of heavy menstrual bleeding with menarche. The patient and her family should develop a plan in conjunction with the patient's gynecologist and hematologist (59). Although the American College of Obstetricians and Gynecologists recommends that adolescents have their first reproductive health visit between the ages of 13 years and 15 years (60), if reproductive concerns present before 13 years of age, an earlier visit to the gynecologist or other gynecologic care provider may be warranted (3, 61).

Use of Nonsteroidal Antiinflammatory Drugs

Nonsteroidal antiinflammatory drugs are commonly used for dysmenorrhea. Adolescents in whom a bleeding disorder has been diagnosed should be reminded that products that prevent platelet adhesion, such as aspirin or nonsteroidal antiinflammatory drugs, should be used only with the recommendation of a hematologist (62).

Future Gynecologic and Reproductive Health Concerns

In adolescents with known bleeding disorders, preoperative surgical evaluation, choice of hemostatic agents for control of intraoperative blood loss, and need for blood products should be determined in conjunction with a hematologist and an anesthesiologist. Vulvovaginal trauma, including straddle injury and coital injury, may be associated with increased bleeding in girls with bleeding disorders; such events may require hemostatic agents and factor replacement, in addition to surgical management. A hematologist also should be consulted before surgery for possible egg retrieval for use in a future pregnancy.

Resources for Patients and Families

Obstetrician–gynecologists should encourage the use of medical alert bracelets and should work with families to ensure adequate access to care. Patients and families should be informed that accidental trauma is a common cause of bleeding in adolescents with bleeding disorders. There are a large number of apps available for use on smartphones; see For More Information for patient resources. Supportive therapy can help adolescent girls manage the emotional effects of having a bleeding disorder. Many resources on bleeding disorders exist for patients and health care providers through the National Heart, Lung, and Blood Institute (63), National Hemophilia Foundation (64), Hemophilia Federation of America (65), the Foundation for Women and Girls with Blood Disorders (66), and the American Society of Hematology (67). When available, patients should be referred to multidisciplinary clinics for women and girls with bleeding disorders, which incorporate single-site consultation with gynecology, hematology, and social work, and provide comprehensive care that is convenient for patients and their families.

Conclusion

Proportionally, adolescent girls are more likely than women to have an underlying bleeding disorder as a cause of heavy menstrual bleeding. Screening for bleeding disorders and iron deficiency anemia should be included in the initial evaluation of girls with heavy menstrual bleeding. Hormonal therapy can include combined hormonal contraceptives, oral and injectable progestins, and LNG-IUDs. Iron replacement therapy should be provided for all reproductive-aged women with anemia due to bleeding. Control of heavy menstrual bleeding in girls with a bleeding disorder may require combined therapy with hemostatic agents. Care of girls and adolescents with bleeding disorders should be in consultation with a hematologist, ideally at a multidisciplinary clinic site.

For More Information

The American College of Obstetricians and Gynecologists has identified additional resources on topics related to this document that may be helpful for ob-gyns, other health care providers, and patients. You may view these resources at https://www.acog.org/More-Info/HeavyMenstrualBleeding.

These resources are for information only and are not meant to be comprehensive. Referral to these resources does not imply the American College of Obstetricians and Gynecologists' endorsement of the organization, the

organization's website, or the content of the resource. The resources may change without notice.

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