

Abnormal Uterine Bleeding in Reproductive-aged Women



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KEYWORDS

- Menorrhagia • Menstrual bleeding • Sonohysterography • Uterine bleeding
- Anovulation

KEY POINTS

- Abnormal uterine bleeding (AUB) is one of the most common gynecologic complaints in reproductive-aged women.
- The new International Federation of Gynecology and Obstetrics classification system should be used to classify all forms of AUB.
- Anovulatory bleeding is the most common nonanatomic cause of AUB and is most often observed in adolescents and perimenopausal patients as well as in some women with other pathologic conditions (eg, obesity, polycystic ovarian syndrome).
- Most AUB unrelated to uterine structural abnormalities is amenable to medical management, including hormonal treatments, antifibrinolytics, and nonsteroidal antiinflammatories.
- Uterine structural abnormalities that cause AUB (ie, polyps, fibroids, adenomyosis) generally require surgical management.

INTRODUCTION

Abnormal uterine bleeding (AUB) is one of the most common gynecologic conditions experienced by women of reproductive age. AUB is the cause of approximately one-third of all visits to gynecologists among premenopausal women and more than 70% of office visits among perimenopausal and postmenopausal women. The estimated annual direct cost of AUB in 2007 was approximately \$1 billion, with indirect economic costs of \$12 billion.¹ These figures do not account for intangible costs and productivity loss. Health care providers should be aware of the most common causes and treatment options for AUB given the high prevalence of the condition.

The term AUB has traditionally described all forms of abnormal vaginal bleeding. The use of other terms for vaginal bleeding, such as dysfunctional uterine bleeding,

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polymenorrhea, menorrhagia, metrorrhagia, and hypermenorrhea, has caused confusion for many health care providers. In addition, the terminology used in other countries for the various gynecologic causes of vaginal bleeding has not been congruent with the medical definitions used in the United States. In response to these concerns, the International Federation of Gynecology and Obstetrics (FIGO) published a new nomenclature system in 2011 to create an internationally accepted classification system.² This system allows for consistent terminology in describing AUB and facilitates communication between health care providers, and also provides a format to accurately analyze effective medical and surgical treatments. The system classifies AUB by bleeding pattern as well as cause and includes 9 main categories. The system was recently accepted by the American College of Obstetricians and Gynecologists (ACOG) and an update to the AUB 2000 practice bulletin was published in 2013.³ This article reviews the FIGO classification system as well as evaluation and management options.

NORMAL VERSUS ABNORMAL UTERINE BLEEDING

Normal Menstrual Bleeding

Most ovulatory menstrual cycles last between 21 and 35 days. The duration of normal menstrual flow is generally 5 days, with most blood loss occurring within the first 3 days.⁴ The average amount of bleeding during the menstrual cycle is 30 to 40 mL. Only 10% of women have more than 80 mL, which is considered abnormal. Approximately 65% of patients have anemia when menstrual blood loss exceeds 80 mL per month.⁵ Approximately 25% of patients with measured blood loss of less than 60 mL consider their menstrual cycles to be heavy. Therefore, research supports that it is difficult for most women to accurately estimate menstrual blood loss and differentiate between normal and heavy menstrual bleeding.

Menstrual cycles are predictable in most women, but the length of the cycle can vary by a few days each month and is more unpredictable during puberty and perimenopause. The menstrual cycle comprises the follicular phase and the luteal phase. These phases are controlled through complex interactions between the ovary, hypothalamus, pituitary gland, and uterus. The follicular phase is initiated by recruitment of an oocyte in response to ovarian stimulation from the pituitary. The follicular phase is marked by estrogen dominance, and is typically of a variable length secondary to hormonal fluctuations during oocyte selection and maturation. These fluctuations are most prominent during the pubertal and perimenopausal transitions.

The luteal phase is marked by progesterone dominance after ovulation and is generally a more fixed length of 12 to 14 days. Menstruation occurs as estrogen and progesterone levels decline at the end of the luteal phase if pregnancy does not occur. Dysfunction at the level of the hypothalamus, pituitary, or ovary can interfere with ovulation and prevent routine shedding of the endometrium, which may result in heavy menstrual bleeding, intermenstrual spotting/bleeding, or both.

Abnormal Uterine Bleeding

AUB has been defined by FIGO as bleeding from the uterine corpus that is abnormal in regularity, volume, frequency, or duration and occurs in the absence of pregnancy.² The causes of AUB are classified as “related to uterine structural abnormalities” and “unrelated to uterine structural abnormalities.” AUB is classified by one or more letters that indicate the cause. These are categorized by the acronym PALM-CO EIN (polyp, adenomyosis, leiomyoma, malignancy, and hyperplasia; coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not otherwise classified). In addition,

patterns of AUB are described as either heavy menstrual bleeding (previously referred to as menorrhagia), or intermenstrual bleeding (instead of metrorrhagia). Leiomyomas may be subclassified as either submucosal or those that do not affect the uterine cavity (Fig. 1). Abnormal bleeding associated with the use of exogenous steroids (ie, hormonal treatments), intrauterine systems (IUSs) or devices, or other systemic or local agents are classified as iatrogenic, whereas the remainder of rare or ill-defined causes are categorized as not yet classified.

AUB may be acute or chronic. Acute AUB refers to an episode of heavy bleeding that is of sufficient quantity to require immediate intervention to prevent further blood loss. The amount of bleeding may be subjectively excessive as determined by the health care provider and/or associated with other signs of significant blood loss, such as hemodynamic instability or anemia. Patients should be assessed to determine the level of acuity and the most likely cause of the bleeding to tailor appropriate treatment.⁶ Acute AUB may be an isolated event or occur in a background of chronic AUB. The evaluation of acute AUB is similar to evaluation of chronic AUB after assessment of hemodynamic status and assuring stability of the patient. Although this article focuses primarily on chronic AUB, medical treatments for acute AUB are discussed.

EVALUATION

History and Physical Examination

It is important to have an organized and evidence-based approach to evaluation and management of AUB. The evaluation of women with AUB includes a thorough medical history and physical examination, appropriate laboratory and imaging tests, and

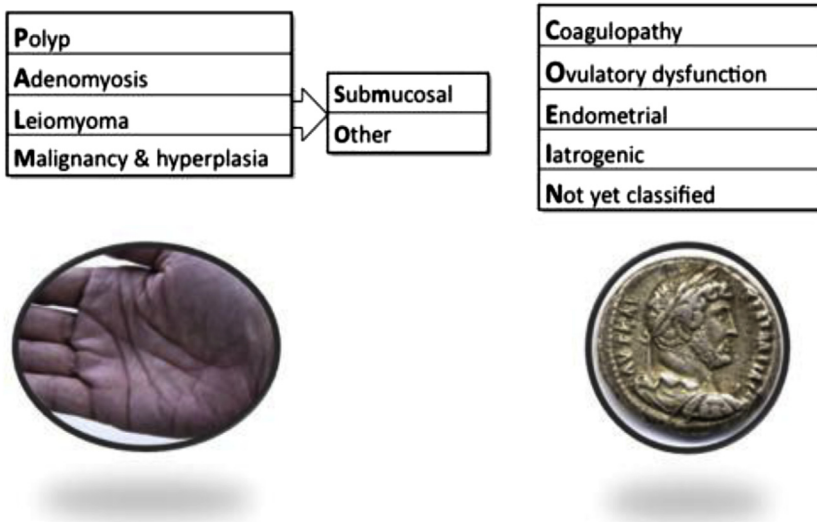


Fig. 1. Basic classification system. The leiomyoma category (L) is subdivided into patients with at least 1 submucosal myoma (L_{sm}) and those with myomas that do not affect the endometrial cavity (L_0). (From Munro MG, Critchley HO, Broder MS, et al. FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COIN) for causes of abnormal uterine bleeding in nonpregnant women of reproductive age. *Int J Gynaecol Obstet* 2011;113:5; with permission.)

consideration of age-related factors that may help to focus the differential diagnosis. The medical history should include a patient description of her bleeding patterns as well as any recent changes in amount, duration, frequency, and associated pain. The history should also include questions about other bleeding problems (eg, epistaxis, bleeding gums, frequent bruising), particularly in adolescents presenting with acute bleeding and adults with chronic heavy menstrual bleeding and anemia. Pertinent medical conditions should also be elicited (eg, thyroid disease, hypertension, renal disease, anorexia/bulimia, psychiatric conditions, and other chronic medical conditions) because these may contribute to ovulatory dysfunction. Any pertinent family history should be discussed (ie, bleeding disorders/coagulopathies) as well as other gynecologic and obstetric history. A list of medications should also be obtained because some may contribute to AUB (ie, hormones, anticoagulants/fibrinolytics, psychotropics).

The physical examination may also reveal findings that contribute to AUB. Any signs of thyroid disease (nodule, goiter), hyperprolactinemia (galactorrhea), polycystic ovarian syndrome (PCOS) (acne, hirsutism), should be documented. Signs of a bleeding disorder may include petechiae, epistaxis, and ecchymoses. A pelvic examination, including a speculum and bimanual examination, should evaluate for any signs of trauma, external or internal vaginal/cervical lesions, infection, and uterine enlargement.

Laboratory Testing

Laboratory testing depends on the patient history and physical examination. Initial evaluation may include a complete blood count (CBC), thyroid-stimulating hormone (TSH), prolactin, and pregnancy test. Other testing may be indicated based on the pelvic examination, including a pap smear and cultures as well as wet mount of discharge if an infection is suspected. A summary of recommended tests is provided in **Box 1**. Patients with a history of AUB involving heavy menstrual bleeding (AUB-HMB) since

Box 1

Recommended assessment for AUB

Complete blood count (if patient reports heavy menstrual bleeding).

Pregnancy testing (for sexually active women).

TSH.

Prolactin level testing (repeat in the fasting state if increased and in the follicular phase when possible).

Pap smear if indicated.

Cervical cultures (if vaginal discharge or signs of infection are present).

Pelvic ultrasonography (saline infusion sonohysterography or hysteroscopy if ultrasonography is inconclusive or further evaluation is warranted).

Screening for bleeding disorders (when indicated in adolescents with heavy menstrual bleeding or adults with chronic menstrual bleeding and a positive screening history).

Endometrial biopsy in women more than 45 years old. Obtain if younger than 45 years if patient has risk factors for endometrial hyperplasia or malignancy.

Data from American College of Obstetricians and Gynecologists. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. Obstet Gynecol 2012;120:197–206.

menarche or with either postpartum hemorrhage or surgery-related bleeding, including dental procedures, should be screened for bleeding disorders. Other indications for bleeding disorder testing include frequent bleeding from the gums, epistaxis or easy bruising (1 or more times per month), or a family history of a bleeding disorder. Initial evaluation should include a CBC and platelets, prothrombin time, partial thromboplastin time, fibrinogen, or thrombin time (optional). If these tests are abnormal the patient should be evaluated more thoroughly for an underlying bleeding disorder such as von Willebrand disease, which is the most common of the inherited bleeding disorders in women.⁷

Uterine Evaluation

Uterine evaluation for AUB should include imaging studies and an endometrial biopsy when indicated. The risk of endometrial cancer is 6.2% in women aged 35 to 44 years but increases more significantly to 13.6 to 24 per 1 million woman-years for women aged 40 to 50 years. Endometrial biopsy should be performed as a first-line test in patients more than 45 years of age. An endometrial biopsy should also be obtained in patients younger than 45 years with a history of exposure to unopposed estrogen (ie, PCOS, obesity), those who fail medical management and have persistent AUB, or those who have any irregularity in the appearance of the endometrium on ultrasonography.⁸ Endometrial biopsies are most often performed with a endometrial suction device, which has a sensitivity of 81% and specificity of more than 98% as long as a sufficient sample is obtained.⁹ However, this is a blinded procedure and may miss small lesions. Therefore, patients with a normal endometrial biopsy (ie, no hyperplasia or cancer) should have additional endometrial assessment with ultrasonography if not already performed, as well as possible dilation and curettage and hysteroscopy if symptoms persist.

Evaluation of the uterus for anatomic causes of bleeding should include imaging studies. Visualization of the uterine architecture with either transabdominal or transvaginal ultrasonography is a valuable tool to assess anatomic causes of bleeding. Transvaginal ultrasonography generally provides better visualization of the uterus and ovaries; however, it may not be the preferred method for patients uncomfortable with the vaginal probe. A full bladder improves visualization of the uterus during transabdominal ultrasonography. Ultrasonography may reveal either endometrial or myometrial abnormalities. Myometrial abnormalities most commonly include uterine leiomyomas or adenomyosis. Uterine leiomyomas (fibroids) are overgrowths of smooth muscle cells and are generally visualized as homogeneous, well-circumscribed lesions. Adenomyosis results from invagination of endometrial tissue into the myometrium and is typically more diffuse in appearance than leiomyomas. It is generally visualized on ultrasonography as a heterogeneous-appearing area with small cystic areas.

Ultrasonography ideally should be scheduled between days 4 and 6 of the menstrual cycle, when the endometrium is the thinnest. Endometrial thickness varies during the menstrual cycle. It is typically 4 to 8 mm during the follicular phase, and 8 to 14 mm during the luteal phase.¹⁰ Ultrasonography performed during the follicular phase may be more likely to detect subtle abnormalities within the endometrium, such as small polyps or intracavitary fibroids. The size and location of all abnormalities should be noted. Further evaluation is warranted by either saline infusion sonohysterography or hysteroscopy if an endometrial or intracavitary abnormality is suspected.

Saline infusion sonohysterography can determine the presence or absence of intracavitary lesions and the depth of myometrial involvement with leiomyomas. Saline infusion sonohysterography is an office-based imaging procedure that infuses saline

into the endometrial cavity during transvaginal ultrasonography. The saline distends the uterine cavity to enhance the visualization of intracavitary polyps and myomas, which may otherwise be obscured by adjacent endometrial tissue (**Fig. 2**).

Saline infusion sonohysterography has a high sensitivity (96%–100%) and a high negative predictive value (94%–100%) in evaluating the uterus and endometrium for disorders.^{11,12} Saline infusion sonohysterography should be performed in the follicular phase of the cycle after menstruation has ended but before ovulation to ensure that the patient is not pregnant and to optimize image quality. Saline infusion sonography has similar diagnostic accuracy to office hysteroscopy (81.3% vs 87.5%, respectively) but is generally less painful.¹³

Hysteroscopy is a technique that allows direct visualization of the uterine cavity by placing a thin telescopic instrument through the cervix into the uterus. It permits full visualization of the endometrial cavity and endocervix and may be performed either in an operating room or office setting. It is helpful in diagnosing and treating focal or diffuse lesions. It may be performed diagnostically instead of saline infusion sonography, or operatively to confirm and treat any visualized abnormality. Hysteroscopy can assist in the diagnosis of atrophy, endometrial polyps, leiomyomas, and other endometrial abnormalities. Tissue samples may be sent for pathologic evaluation to confirm the diagnosis and rule out endometrial hyperplasia and cancer. An algorithm for uterine evaluation is provided in **Fig. 3**.

MANAGEMENT (SURGICAL AND NONSURGICAL)

Medical Management

The goals of medical management for patients with AUB are regulation of menstrual cycles for patients with AUB involving intermenstrual bleeding (AUB-IMB), and decreased menstrual blood loss for patients with AUB-HMB. Medications to reduce menstrual blood loss include hormonal treatments, antifibrinolytics, and prostaglandin synthetase inhibitors. The choice of treatment depends on its appropriateness considering other medical conditions and the preference of, and tolerability by, the patient. A summary of medical treatment options is provided in **Box 2**.

Medical management is preferred to surgical treatment of most patients unless an anatomic cause for bleeding is identified (ie, polyp, fibroid, hyperplasia, cancer). Medical management with hormones is often recommended for patients with AUB not related to an anatomic cause because the cause in these patients is often anovulation. Correction of the underlying hormonal imbalance for patients with anovulation frequently results in improvement in AUB-HMB and AUB-IMB.

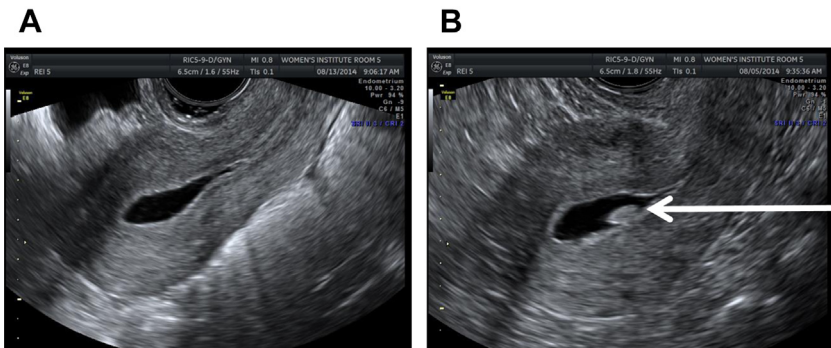


Fig. 2. Sonohysterography. (A) Normal intrauterine cavity. (B) Uterine filling defect (arrow).

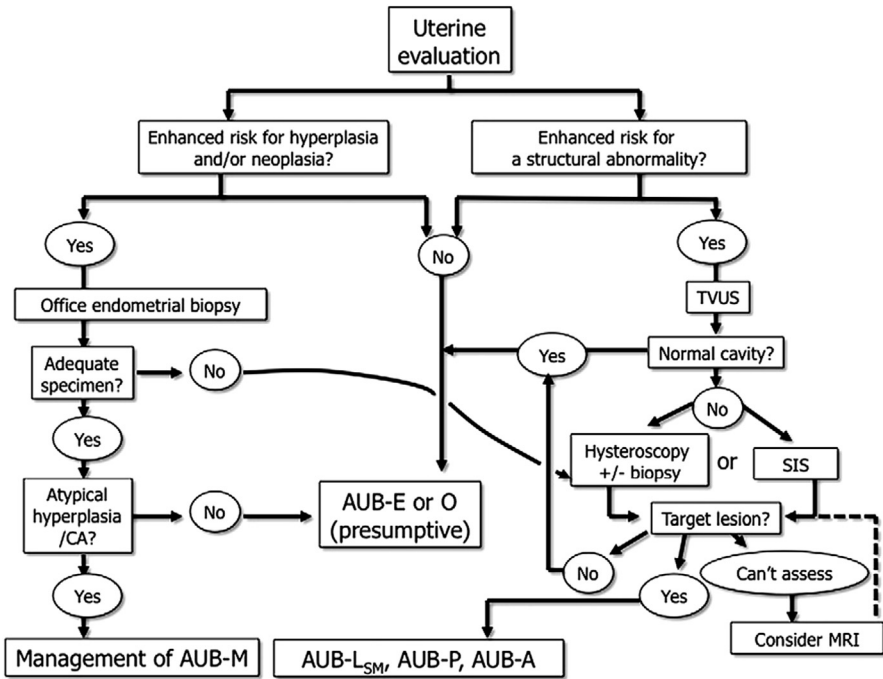


Fig. 3. Uterine evaluation of AUB. AUB-A, abnormal uterine bleeding-adenomyosis; AUB-E, abnormal uterine bleeding-endometrial or AUB-O, abnormal uterine bleeding-ovulatory dysfunction; AUB-L_{SM}, abnormal uterine bleeding-submucosal leiomyoma; AUB-M, abnormal uterine bleeding-malignancy or hyperplasia; AUB-P, abnormal uterine bleeding-polyp; CA, carcinoma; SIS, saline instilled sonography; TVUS, transvaginal ultrasonography. (From Munro MG, Critchley HO, Broder MS, et al. FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet* 2011;113:3-13; with permission.)

Hormonal therapies

Hormonal treatments for AUB include estrogens or progestins, given either independently or in combination (ie, combined oral contraceptive pills [OCPs]). The goal of hormonal therapy is to restore the sequence of synchronized growth of the endometrium with estrogen and stabilization with progesterone before endometrial shedding at menstruation. Estrogens stimulate endometrial tissue growth over the surface of the denuded endometrium to stop menstrual bleeding. There is also evidence that estrogens stimulate clotting at the capillary level, which contributes to cessation of menstruation.¹⁴ Most forms of hormonal treatment are effective for both acute and chronic bleeding but the dosing is adjusted according to the acuity of the bleeding. In addition, most forms of hormonal treatment are approved for contraceptive indications, but are often used for medical management of AUB.

Estrogens are the most effective hormonal treatment of acute bleeding. Intravenous conjugated equine estrogens stop bleeding in 70% of patients within 4 to 8 hours compared with 30% with placebo.¹⁵ Bleeding also stops for almost 90% of patients with acute bleeding by administration of combined OCPs 3 times daily for 1 week.¹⁶ Only intravenous conjugated equine estrogen is approved for treatment of acute AUB requiring hospitalization, although other routes and doses of administration of estrogens may be effective. Estrogen therapy should be continued for at least 3 weeks

Box 2**Medical management of acute or chronic heavy menstrual bleeding**

Nonsteroidal antiinflammatory drugs

Mefenamic acid 500 mg twice a day for 4 to 5 days

Naproxen 250 to 500 mg twice a day for 4 to 5 days

Ibuprofen 600 to 1200 mg daily for 4 to 5 days

Antifibrinolytics^a

Tranexamic acid (650 mg) 3 tabs (1.3 g) 3 times a day for 5 days

Acute bleeding: 10 mg/kg intravenously (IV) if available (maximum 600 mg/dose)

Hormonal treatments

Conjugated estrogens

Acute bleeding: 25 mg IV every 4 to 6 hours for 24 hours (follow with combined oral contraceptive pills [OCs])

Combined OCPs

Ethinyl estradiol combination pill (35 µg)^b

Acute bleeding: 1 tablet 3 times a day for up to 7 days until bleeding decreases, then taper

Progestins

Medroxyprogesterone acetate 5 to 10 mg daily for 12 to 14 days^a

Acute bleeding: 10 mg every 4 hours (up to 80 mg/d for acute bleeding) then every 6 hours for 4 days, then every 8 hours for 3 days, then every 12 hours for 2 days to 2 weeks, then daily

Norethindrone 5 mg daily for 5–10 days^a

Acute bleeding: 5 to 10 mg every 4 hours until bleeding stops, then every 6 hours for 4 days, then every 8 hours for 3 days, then every 12 hours for 2 days to 2 weeks, then daily

Levonorgestrel intrauterine system (approved for use for 5 years)

^aData from James AH, Kouides PA, Abdul-Kadir 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;158:124–34.

^bData from American College of Obstetricians and Gynecologists. ACOG committee opinion no. 557: management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. *Obstet Gynecol* 2013;121(4):891–6.

to prevent immediate subsequent bleeding episodes. Care should be taken when prescribing higher dose estrogen therapy for extended periods because of a possible increased risk of thromboembolic events. Standard doses of estrogens are typically sufficient to control bleeding once the acute bleeding event has been treated. Estrogen therapy should be followed by a progestin for 10 days each month to schedule a synchronized withdrawal bleed. A scheduled program of an estrogen followed by progestin should be continued monthly for most patients to regulate further AUB.

There are several progestin-only treatments, including medroxyprogesterone acetate, megestrol acetate, norethindrone acetate, depomedroxyprogesterone acetate, the etonogestrel implant, and the levonorgestrel IUS (ie, intrauterine system). Progestins induce secretory changes in an estrogen-primed endometrium. Therefore, it is important to remember that progestins do not provide benefit to women with bleeding

secondary to low estrogen levels with a thin endometrium on ultrasonography. They are most likely to be effective in patients with anovulatory bleeding and adequate estrogen (ie, PCOS). Contraindications include known or suspected pregnancy, undiagnosed vaginal bleeding, known or suspected breast cancer, active deep vein thrombosis, pulmonary embolism, or history of these conditions; active or recent stroke or myocardial infarction; and impaired liver function. Side effects are generally nausea, weight gain and fluid retention, mood changes, edema, as well as irregular bleeding.

Progestins may be given continuously or cyclically. Cyclic progestin therapy once per month for 10 to 14 days allows for a synchronized withdrawal bleed. Progestins antagonize estrogen and are effective to stop endometrial growth during the luteal phase. This treatment prevents excessive amounts of endometrium from developing during each menstrual cycle. Progestins cause endometrial atrophy when given continuously and are used effectively in higher dosages for patients with endometrial hyperplasia. Oral progestins given in a cyclic fashion do not prevent ovulation. Patients should be advised to use alternate forms of contraception if they are not actively trying to conceive.

There are no studies comparing progestins with placebo for treatment of heavy menstrual bleeding. A review of published studies reported that oral progestins offered no advantage compared with nonhormonal treatment with tranexamic acid or nonsteroidal antiinflammatory drugs (NSAIDs). However, there was a benefit of the levonorgestrel IUS compared with oral progestins for women with ovulatory cycles. The levonorgestrel IUS was also better tolerated than oral progestin.¹⁷ This effect is likely secondary to its local effect on the endometrium without the systemic side effects of oral administration. Although effective for treating heavy menstrual bleeding, approximately 36% of patients have the IUS removed at 2 years because of lack of effectiveness.¹⁸ Advantages of the levonorgestrel IUS include its efficacy for contraception and that it may remain in place for 5 years. However, the levonorgestrel IUS is not cost-effective for short-term use.

Combined hormonal contraceptives are available in oral, patch, and vaginal ring forms. Combined hormonal contraceptives work well for most patients with bleeding because they contain both the estrogen and progestin agents. They are also well suited for patients requesting contraception or who are not actively trying to conceive. Highly significant reductions in menstrual blood loss have been reported with oral contraceptives (43%); however, there have been no well-designed placebo-controlled trials.¹⁹ There have not been any large trials evaluating the oral route compared with other routes of administration of combined hormonal contraception. However, all routes should be similarly effective for control of heavy menstrual bleeding.

There are many other advantages of combined oral contraceptives for certain patient populations. Perimenopausal patients may note improvement in hot flashes as well as other menopausal symptoms related to low estrogen levels. Adolescents may experience improvement of acne. Patients with polycystic ovarian syndrome may have decreases in acne and hirsutism, and have a decreased risk of endometrial cancer. Combined hormonal contraceptives can increase levels of factor VIII and von Willebrand factor, which may benefit patients with underlying coagulopathies.

Nonsteroidal antiinflammatory drugs

Nonsteroidal antiinflammatories are a category of medications that reduce prostaglandin levels by inhibiting the enzyme cyclooxygenase. Several NSAIDs have been evaluated for patients with AUB-HMB, including mefenamic acid (MFA), naproxen,

ibuprofen, meclofenamic acid, diclofenac, indomethacin, and acetylsalicylic acid. However, the most commonly used are MFA, naproxen, and ibuprofen. The endometrium of women with heavy menstrual bleeding has been shown to have higher levels of the prostaglandins E2 and F2 α and inhibition of prostaglandin is the presumed mechanism for reduced blood loss.²⁰ They are contraindicated in patients with platelet disorders or on anticoagulants. They are generally not recommended for people with kidney disease, heart failure, or cirrhosis, or for people who take diuretics. The most common side effect is gastrointestinal upset.

Menstrual blood loss is reduced with NSAIDs by up to 35% for about 75% of patients with heavy menstrual bleeding.²¹ There are also limited data directly comparing OCPs with NSAIDs. A large meta-analysis of NSAIDs compared with other medical management for control of menstrual blood loss found that NSAIDs are effective but that tranexamic acid or the levonorgestrel IUS are more effective. The data comparing the effectiveness of different NSAIDs are limited, but suggest that there is no significant difference between MFA and naproxen. However, side effects may be less common with MFA.²²

Antifibrinolytics

Plasminogen activators have been found at higher than expected concentrations in the endometrium of women with heavy menstrual bleeding.²³ Plasminogen activators are enzymes that result in fibrinolysis and degradation of blood clots. Plasminogen activator inhibitors decrease fibrinolysis and promote clot formation, which decreases menstrual blood loss. Tranexamic acid is an antifibrinolytic therapy approved for medical treatment of menorrhagia. It reversibly binds to lysine binding sites on plasminogen molecules. It is associated with a significant reduction in mean blood loss (40%–50%) in women with heavy menstrual bleeding compared with placebo. It was found to be more effective than oral progestin or MFA.²⁴ Tranexamic acid may be prescribed to decrease menstrual blood loss for patients with bleeding disorders such as von Willebrand disease, but is not approved for use in patients less than 18 years of age. It is available over the counter in many countries, but requires a prescription in the United States. It is generally well tolerated with few side effects. The most common side effects reported are nausea and dizziness. It is contraindicated in patients with active thromboembolic disease, disseminated intravascular coagulation, macroscopic hematuria, and color blindness. It should be used with caution with patients at risk of clotting; however, long-term use has not been associated with a higher risk of thrombosis compared with the risk of spontaneous thrombosis in untreated women.²⁵

Surgical Treatment

Surgical treatment of AUB may also be considered for patients who do not improve with medical management or have anatomic causes for bleeding. Several surgical options exist. However, definitive treatment with hysterectomy should only be considered for patients who have completed childbearing or have contraindications from, or are unresponsive to, medical management. Surgery is generally recommended for patients with anatomic causes of bleeding, whereas medical management is the mainstay of treatment of nonanatomic causes. However, approximately 80% of patients with heavy menstrual bleeding treated with surgery have no anatomic disorder.²⁶

Surgical treatment of fibroids typically includes myomectomy (removal of fibroids) by hysteroscopy, laparoscopy, or laparotomy. Other nonmedical treatments for fibroids include embolization, cryomyolysis, and magnetic resonance–guided focal ultrasonography ablation. Embolization is generally not recommended for patients

who are still interested in childbearing because it may decrease uterine and subsequent placental blood flow. There are also limited pregnancy outcome data on other treatments besides myomectomy for patients interested in fertility. Surgical treatment of polyps is typically hysteroscopic resection. Adenomyosis is often difficult to treat surgically because of its diffuse growth into the myometrium. However, it may be resected in a similar fashion to a myomectomy, although the borders are most difficult to identify. Surgical treatments for AUB in patients who have completed childbearing include endometrial resection/ablation and hysterectomy.

Endometrial ablation techniques were developed in the 1980s. The first method was hysteroscopic ablation with laser photovaporization.²⁷ Subsequent techniques involved either ablating the endometrium with a rollerball, or resecting it with a cautery loop under direct observation with hysteroscopy. The newer second-generation techniques for ablation use either microwave energy, thermal balloon, radiofrequency, cryotherapy, or heated water. The second-generation modalities are quicker, some may be performed in the office, are generally less expensive, and do not require hysteroscopy. They seem to have similar results for treatment of heavy menstrual bleeding, with similar patient satisfaction.²⁸

Endometrial ablation is often preferred by patients compared with definitive surgical hysterectomy because of quicker return to normal function and avoidance of major surgery. Vaginal discharge is the most commonly reported side effect as the endometrium undergoes necrosis. Patients having endometrial ablation generally experience immediate decreases in bleeding; however, many patients need subsequent hysterectomy. The probability of a woman requiring a repeat procedure is higher than with a definitive hysterectomy. The relative risk at 1 year is 14.9 (95% confidence interval [CI], 5.2–42.6) and increases to 36.4 (95% CI, 5.1–259.2) at 4 years.²⁹

Definitive surgical treatment of AUB is hysterectomy. Approximately 600,000 hysterectomies are performed annually in the United States, and approximately 20 million American women have had a hysterectomy.³⁰ Hysterectomy is efficacious for the management of AUB because it removes the source of bleeding. It treats bleeding from both anatomic and nonanatomic causes. However, a hysterectomy has risks, including urinary incontinence, sexual dysfunction, and other signs of estrogen deprivation if the ovaries also removed. Other immediate risks include infection, bleeding, and mortality of 1 to 6 per 1000 women when performed for benign causes.³¹

SUMMARY/DISCUSSION

AUB is a common problem in reproductive-aged women and has many causes. There is a new international classification system developed by FIGO that has been supported by ACOG. Health care providers should have an evidence-based approach to evaluation and management. Medical management is effective to control most AUB related to nonanatomic causes. Medical management may include hormonal and/or nonhormonal treatments and should be tailored to the patient depending on side effect profiles and contraindications. Hormonal therapies decrease bleeding for most patients. Nonhormonal treatments such as NSAIDs and antifibrinolytics are also effective and may be used in conjunction with or instead of hormonal treatments. Patients with anatomic causes for bleeding may benefit from medical management, but may require surgical treatment of the underlying abnormality (ie, polyp, myomas, adenomyosis). Surgical treatment of patients who have completed childbearing may include endometrial ablation or hysterectomy.

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