



# Evaluation and Management of Abnormal Uterine Bleeding

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## Abstract

Abnormal uterine bleeding (AUB) is a common condition that leads to increased health care costs and decreased quality of life. A systematic approach to AUB evaluation can simplify management and enhance women's well-being. Abnormal uterine bleeding describes any variation from normal bleeding patterns in nonpregnant, reproductive-aged women beyond menarche lasting for at least 6 months. Ambiguous and inconsistent use of terminology and definitions to characterize AUB in the past decades necessitated a new, consensus-based approach to nomenclature and AUB evaluation. This led to the International Federation of Gynecology and Obstetrics (FIGO) System 1 in 2007, which standardized nomenclature, set parameters, and defined normal and abnormal bleeding based on the 5th to 95th percentile data from available large-scale epidemiologic studies. FIGO System 1, endorsed by several national and international societies, improved worldwide communication among educators, clinicians, and researchers. FIGO System 2, published in 2011, focused on classifications of AUB etiology into structural and nonstructural entities using the PALM-COEIN (polyp[s], adenomyosis, leiomyoma, malignancy, coagulopathy, ovulatory dysfunction, endometrial disorders, iatrogenic, and not yet classified) classification system. The PALM-COEIN classification is facilitated by a complete patient history combined with appropriate imaging, histopathologic analysis, or laboratory

evaluation to ensure accurate diagnostic and treatment approaches to AUB. Herein we present the systematic evaluation of AUB.

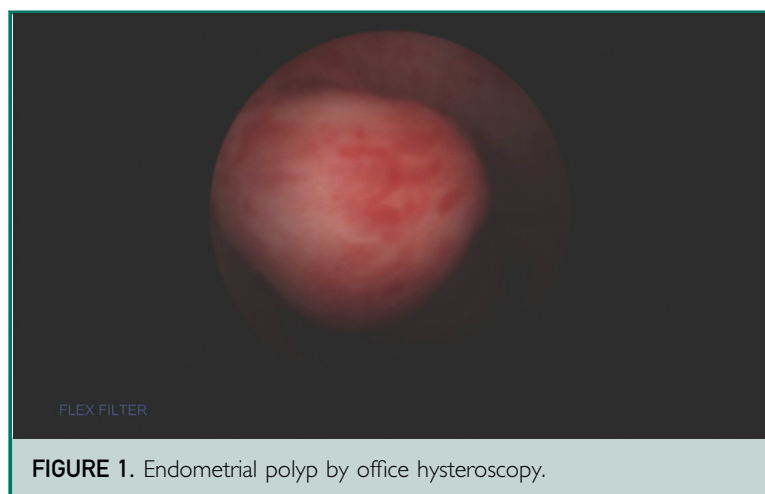
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**A**bnormal uterine bleeding (AUB), a frequent reason for outpatient and emergency department visits in reproductive-aged women, may substantially affect quality of life. Evaluation and management of AUB incurs high health care costs, especially when including the common use of hysterectomy.<sup>1</sup> Fortunately, AUB can often be managed with safe, effective, and noninvasive medical treatments focused on the source of bleeding. Hormonal contraceptives remain a common medical therapy, and the 52-mg levonorgestrel intrauterine system (LNG IUS) is increasingly used to effectively manage troublesome bleeding before a surgical approach. The etiology in reproductive-aged women is almost always benign; however, evaluation and research into AUB was limited by the inconsistent use of terminology and documentation of etiology. The International Federation of Gynecology and Obstetrics (FIGO) Systems 1 and 2 were created to provide clear terminology and nomenclature to globally facilitate the accurate diagnostic and effective treatment approaches to AUB.<sup>2,3</sup> In 2007, FIGO introduced System 1, with standardized definitions and concise terminology for AUB in nonpregnant women.<sup>2</sup> *Menorrhagia*, *metrorrhagia*, and *oligomenorrhea* were replaced with the nomenclature *heavy menstrual bleeding (HMB)*, *intermenstrual bleeding*, and *unscheduled bleeding or breakthrough bleeding (BTB) on hormone medication*.<sup>2</sup> The FIGO System 2 acronym PALM-COEIN (polyp[s], adenomyosis, leiomyoma, malignancy, coagulopathy, ovulatory dysfunction, endometrial disorders, iatrogenic, and not yet classified) systematically defines the most common etiologies for AUB with structural (PALM) and nonstructural (COEIN) causes of AUB.<sup>3</sup>

The FIGO classification for AUB refers to reproductive-aged, nonpregnant women, so the first step is to evaluate for pregnancy and address whether a woman is premenopausal and postmenarche. Bleeding before

menarche, after menopause, and during pregnancy requires different evaluations and is not addressed in this review. In addition, a thorough history will help distinguish gynecologic causes of bleeding from those with urinary or gastrointestinal etiologies.

FIGO System 1 describes the 4 parameters of menstrual bleeding: regularity, frequency, duration, and volume. Normal menstrual bleeding is defined as cycles that occur every 24 to 38 days, with duration of bleeding up to 8 days.<sup>2</sup> Regular menstrual bleeding should be 9 days or less in variation from the beginning of one menses to the beginning of the next one; however, this is age dependent so that women between 26 and 41 years old should have variation of 7 days or less in menstrual cycle length.<sup>4</sup> For frequency terminology, amenorrhea is when menses are absent or a woman experiences no bleeding, frequent menstrual bleeding is when menses occur less than 24 days apart, and infrequent menses is when menses occur more than 38 days apart. For duration, more than 8 days of bleeding is considered prolonged menses. Volume is harder to measure: menses are determined by women to be heavy, normal, or light. Heavy menstrual bleeding is defined as excessive menstrual blood loss that interferes with a woman's physical, social, emotional, or material quality of life.<sup>5</sup> It can occur alone or with other symptoms. Intermenstrual bleeding is bleeding between spontaneous, predictable menses and may occur randomly through the cycle or predictably and cyclically in early, mid, or late cycle. Breakthrough bleeding may occur on hormone medications such as birth control pills/patches/rings or progesterone-only contraceptives.<sup>2</sup> Menstrual history can be assessed using the previously listed criteria to distinguish normal menstrual bleeding from abnormal bleeding. Next, physical examination, including speculum and bimanual examinations, with or without



**FIGURE 1.** Endometrial polyp by office hysteroscopy.

rectal examination, can help isolate the cause of bleeding to the uterus rather than to vulvar, vaginal, cervical, or rectal sources. The PALM-COEIN classification is used herein as a systematic approach to clarifying AUB, focusing on specific evaluation and management strategies.<sup>2,3</sup>

## PALM-COEIN CLASSIFICATION

### Polyps

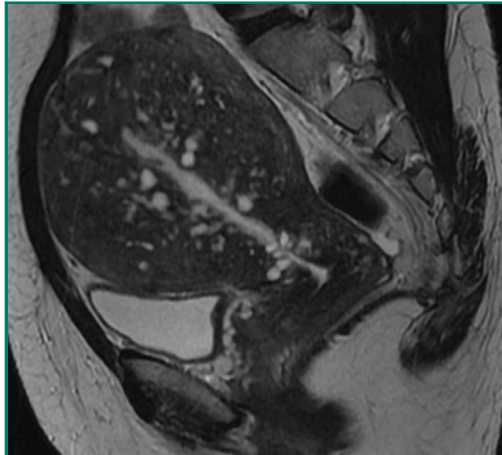
Intermenstrual bleeding or AUB may occur in up to 67% of premenopausal women with endometrial polyps.<sup>6</sup> Polyps may be single or multiple, measuring from a few millimeters to centimeters, and may be sessile or pedunculated.<sup>7</sup> They are localized hyperplastic overgrowths of endometrial glands and stroma around a vascular core forming a projection often from the uterine fundus and extending toward the internal os.<sup>8</sup> The exact cause of polyps is unknown, but possible etiologies include genetic, biochemical, and hormonal factors.<sup>9,10</sup> The prevalence of polyps ranges from 7.8% to 34.9% of women and seems to increase with age.<sup>11</sup> Most endometrial polyps are benign, but a large review of more than 10,000 women suggests that the incidence of malignancy is 1.7% in premenopausal women, whereas the risk in postmenopausal women is 5.4%.<sup>12,13</sup> Risk factors for developing polyps include age, tamoxifen use, increased levels of endogenous or exogenous

estrogen, obesity, and Lynch syndrome (hereditary nonpolyposis colorectal cancer).<sup>14</sup> Endometrial polyps can be accurately diagnosed using transvaginal ultrasound (TVUS) (sensitivity, 91%; specificity, 90%), saline infusion sonohysterography (SIS) (sensitivity, 95%; specificity, 92%), diagnostic hysteroscopy (sensitivity, 90%; specificity, 93%), and hysterosalpingography (sensitivity, 98%; specificity, 35%).<sup>11</sup> The benefits of TVUS or SIS include the ability to visualize the adnexa, whereas polypectomy can be performed with hysteroscopy (Figure 1). Asymptomatic polyps greater than 1.5 cm and symptomatic polyps should be considered for excision and sent for pathologic examination.<sup>13</sup>

Cervical polyps occur most often in the reproductive years, especially after age 40 years.<sup>15</sup> They generally arise from the endocervix potentially from inflammation and hormonal factors. Cervical polyps are rarely larger than 3 cm, are usually nonmalignant, generally are easily removable in the office, and should be sent for pathologic examination. Importantly, cervical polyps may coexist with endometrial intraepithelial neoplasia (EIN) or endometrial hyperplasia and endometrial polyps and may be mistaken for prolapsing leiomyoma.<sup>16</sup>

### Adenomyosis

Adenomyosis is a disorder in which endometrial glands and stroma are present focally or globally through the uterine musculature, causing hypertrophy of the surrounding myometrium. Prevalence is predicted to be 5% to 70% of women.<sup>17</sup> Most cases occur in multiparous women in the fourth to fifth decades of life.<sup>18</sup> Whereas adenomyosis is asymptomatic in one-third of cases, women may present with HMB, irregular bleeding, dysmenorrhea, or dyspareunia. Evidence supports that the pathologic features of adenomyosis are related to abnormal gene expression, increased angiogenesis and proliferation, decreased apoptosis, impaired cytokine expression, local estrogen production, resistance to progesterone, increased nerve density, and immunologic oxidative stress.<sup>19</sup> Definitive diagnosis is by histologic



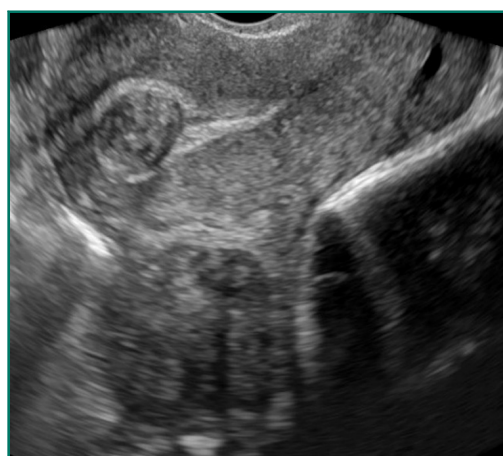
**FIGURE 2.** Adenomyosis of the uterus by magnetic resonance imaging.

examination at hysterectomy; however, specific TVUS and magnetic resonance imaging (MRI) criteria help establish the diagnosis.<sup>20,21</sup> Transvaginal ultrasound may include echogenic striations, myometrial cysts, globular uterus configuration or asymmetrical thickening of the myometrium, and heterogeneity of the myometrium leading to poor definition of the endometrial-myometrial interface (sensitivity, 89%; specificity, 89%).<sup>20</sup> Given that adenomyosis increases uterine vascularity, a pattern of penetrating vessels can be seen at color Doppler ultrasound.<sup>20</sup> T2-weight MRI findings may show diffuse or focal endometrial-myometrial junctional zone widening of 12 mm or more, islands of heterotopic endometrial tissue, cystic dilation of heterotopic glands, and punctate hyperintense foci of hemorrhage (sensitivity, 86%; specificity, 86%)<sup>21</sup> (Figure 2). In a systematic review by Pontis et al,<sup>22</sup> effective medical therapies for adenomyosis include suppressive hormonal treatments such as continuous contraceptive hormones, high-dose progestins, selective estrogen receptor modulators (SERMs), selective progesterone receptor modulators (SPRMs), the 52-mg LNG IUS, aromatase inhibitors, danazol, and temporary use of gonadotropin receptor hormone (GnRH) agonists. The review concluded that if amenorrhea was achieved, there was no statistically significant difference between medical

therapies in terms of pain relief. However, adverse effects and costs vary widely between various treatments. The most promising medical therapy per the authors is the LNG IUS, given its effectiveness and low-profile adverse effects.<sup>22</sup> When endometrial ablation has been performed, adenomyosis is a predictor of treatment failure due to bleeding, with a failure rate of 20%.<sup>23</sup> In nonrandomized studies, uterine artery embolization (UAE) and MRI-guided focused ultrasound (MgFUS) seem to be promising treatments for adenomyosis, although they were approved by the Food and Drug Administration primarily for leiomyoma therapy.<sup>24,25</sup> Taran et al<sup>24</sup> reported improved symptoms in 50% to 90% of women in several small studies undergoing UAE followed for 1 or more years. Use of MgFUS resulted in a 25% to 66% reduction in bleeding over 12 months in women with adenomyosis.<sup>25</sup> Hysterectomy remains definitive therapy for women failing medical treatments.

### Leiomyoma

Leiomyomas (also called myomas or fibroids) are benign monoclonal tumors arising from smooth muscle cells of the myometrium that develop during the reproductive years.<sup>3</sup> They are the most common pelvic tumors, with an estimated lifetime prevalence of 70% in white women and more than 80% in black women.<sup>26</sup> Risk factors for developing leiomyomas include African American race, early menarche, early oral contraceptive use, low parity, obesity, diet (increased consumption of meats, increased glycemic index or load, consumption of alcohol), hypertension, and family history.<sup>27</sup> Symptoms include painful menses or HMB and bulk-related symptoms such as pelvic pressure, urinary frequency, bowel symptoms, or reproductive dysfunction (infertility or obstetrical complications such as adverse outcomes related to leiomyoma location).<sup>26</sup> Clinical diagnosis may be based on results of pelvic examination (although normal findings do not exclude the presence of submucosal leiomyoma as a cause of AUB), with pelvic ultrasound as the standard confirmatory test. The FIGO classification of



**FIGURE 3.** Uterine leiomyoma, intrauterine and subserosal-posterior uterus, by transvaginal pelvic ultrasound.

leiomyoma location helps define the relationship of leiomyomas in reference to the endometrium or the visceral peritoneum (serosal layer)<sup>3</sup> (Figure 3). Submucous (sub-endometrial) or types 0, 1, and 2 leiomyomas can be diagnosed by using either SIS or hysteroscopy.<sup>2,3</sup> In addition, MRI can show the relationship of leiomyomas to both the endometrium and the visceral peritoneum. The use of gadolinium can identify devascularized (degenerated) leiomyomas, and MRI can also be used to determine whether uterine-sparing treatments are an option.<sup>26</sup> Although MRI may demonstrate features concerning for leiomyosarcoma, no preoperative testing can definitively rule out this rare malignancy.<sup>26</sup>

The many treatment options for leiomyomas can help individualize therapy to symptoms. Asymptomatic leiomyomas usually do not need to be treated, except in some cases associated with fertility treatments. When HMB is the only symptom, medical therapies may be highly effective, including tranexamic acid, nonsteroidal anti-inflammatory drugs (NSAIDs), contraceptive hormones, danazol, GnRH agonists, aromatase inhibitors, SERMs, and SPRMs.<sup>26</sup> In a review by Talaulikar,<sup>28</sup> tranexamic acid reduced bleeding by 30% to 60%, and the LNG IUS significantly decreased bleeding while increasing ferritin and hematocrit levels. A uterus with leiomyomas is at

increased risk for expulsion of the LNG IUS, and the LNG IUS may be challenging to place in women with larger leiomyomas. The GnRH agonists can be used preoperatively to reduce leiomyoma volume, correct anemia, and reduce intraoperative blood loss.<sup>26</sup> A review of SPRMs shows them to be beneficial for improving quality of life, decreasing HMB, and creating amenorrhea, but they are not available in the United States currently for leiomyomas.<sup>29</sup> For submucous leiomyomas, hysteroscopic myomectomy may be the best therapeutic option for AUB.<sup>26</sup> Endometrial ablation can be performed in women with leiomyomas who have a normal uterine cavity or in conjunction with hysteroscopic myomectomy to reduce HMB; ablation is reserved for women who have completed childbearing.<sup>30</sup>

For women with bulk symptoms with or without HMB, the goal is to decrease bleeding and shrink leiomyomas. Uterine-sparing options include myomectomy, UAE, MgFUS, or laparoscopic radiofrequency ablation.<sup>26</sup> All of these treatment options have been shown to improve symptoms. In comparing treatments, reintervention risk after 36 months was 1.2% for abdominal myomectomy, 7.4% for UAE, 34.7% for high-intensity focused ultrasound (includes both MRI and ultrasound guided), and 3.2% for hysteroscopic myomectomy.<sup>31</sup> Oral SPRMs seem to be promising as medical therapy that lowers bleeding and decreases leiomyoma size; 1 SPRM is available outside of the United States.<sup>26,29</sup> Additional long-term medical treatments are anticipated in the future. Hysterectomy remains the treatment for leiomyoma symptoms after childbearing is completed and when other options fail.

### Malignancy and Premalignant Conditions

Malignancy of the vagina or uterus (including the cervix) can cause abnormal bleeding. Thus, it is important to discern the etiology of any AUB through examination of the vulva, vagina, and cervix with Pap test screening or tissue sampling, as indicated by the American College of Obstetricians and Gynecologists guidelines.<sup>32</sup> In older premenopausal and menopausal women, AUB may be secondary to EIN



(subtype: simple or benign hyperplasia vs [the more worrisome] subtype: atypical hyperplasia with progression to or concurrent with endometrial malignancy).<sup>33</sup> Women have a 2.8% lifetime risk of developing endometrial cancer, which accounts for 63,000 new cases in the United States yearly.<sup>34</sup> Fortunately, 70% of cases are found at an early stage given that most women (75%-90%) with malignancy present with AUB.<sup>33</sup> Endometrioid (adenocarcinoma) is the most common type of malignancy; papillary serous, clear cell, mucinous, and carcinosarcoma are rarer but more aggressive endometrial cancers. The risks for EIN and malignancy include unopposed estrogen with an intact uterus, obesity, diabetes mellitus, hypertension, nulliparity, and tamoxifen use.<sup>33,34</sup> Women with Lynch syndrome have a 27% to 71% lifetime risk of endometrial cancer and, thus, require close endometrial surveillance until risk-reducing hysterectomy.

The American College of Obstetricians and Gynecologists recommends that all women with AUB older than 45 years and women younger than 45 years who have additional risk factors for EIN undergo endometrial sampling.<sup>35</sup> The sensitivity for endometrial cancer by endometrial sampling using the Pipelle device in premenopausal women is 91%, and the sensitivity for diagnosis of EIN (subtype: atypical endometrial hyperplasia) is 81%.<sup>36</sup> In a systematic review of hysteroscopy for the diagnosis of endometrial cancer, sensitivity was 86% and specificity was 99%; in the diagnosis of EIN, sensitivity was 78% and specificity was 96%.<sup>37</sup> Endometrial intraepithelial neoplasia (subtype: benign hyperplasia without atypia) can be treated with oral progestins or LNG IUS and followed with endometrial surveillance; EIN (subtype: atypical) and endometrial malignancy are best treated with hysterectomy.<sup>33</sup>

### Coagulopathy

Inherited bleeding disorders, especially von Willebrand disease (vWF), are identifiable in 5% to 24% of women with HMB.<sup>38</sup> Coagulopathy should be considered in women with heavy, prolonged menses from an early

reproductive age; a history of frequent bruising, epistaxis, gum/dental bleeding, postpartum hemorrhage, and severe surgical bleeding; and a family history of these issues. Heavy menses may be seen with factor deficiencies (factors VIII and IX are most common, factors VII and XI are less frequent) and platelet disorders.<sup>38,39</sup> An acquired coagulopathy should be considered in the setting of leukemia, aplastic anemia, renal or liver disease/failure, sepsis, and disseminated intravascular coagulopathy and in women taking drugs that affect coagulation or platelet function, such as NSAIDs and herbal remedies, anticoagulants, and chemotherapeutic agents.

Evaluation should begin with a history to assess symptoms and risk factors for a coagulopathy, followed by confirmatory testing.<sup>35,38</sup> Evaluation for a suspected coagulopathy should begin with a complete blood cell count or platelet count for thrombocytopenia, prothrombin (prothrombin time/international normalized ratio), activated partial thromboplastin time followed by, when indicated, plasma vWF antigen, plasma vWF activity (ristocetin cofactor activity, vWF:RCO and vWF collagen binding), factor VIII, and other factor testing.<sup>35,38</sup> Inherited coagulopathies and HMB can be treated with factor replacement and desmopressin acetate as well as hormone therapy as follows.<sup>40</sup> Medical therapy for acquired coagulopathies with HMB may include intravenous (IV) conjugated equine estrogens (Premarin; Pfizer Inc) 25 mg every 4 to 6 hours for 24 hours, combined oral contraceptives (monophasic continuous pills containing 35 µg of ethinyl estradiol) 3 times daily for 7 days (then daily thereafter), or medroxyprogesterone acetate 20 mg orally 3 times daily for 7 days (then daily for 3 weeks).<sup>41,42</sup> Tranexamic acid may be considered for acute AUB using 10 mg/kg IV (maximum of 600 mg per dose) or 1.3 g orally 3 times daily for 5 days.<sup>43,44</sup> Intrauterine tamponade using a 26F Foley catheter infused with 30 mL of saline solution may control bleeding.<sup>44</sup> In women treated with IV Premarin for HMB, 72% had controlled bleeding; in women taking oral contraceptive pills (OCPs) as above, 88% had controlled

**TABLE. Management of Abnormal Uterine Bleeding**

Acute bleeding	Chronic bleeding
Conjugated equine estrogen 25 mg IV every 4-6 h for 24 h with IV antiemetic agents	Ibuprofen 600 mg every 6 h or 800 mg every 8 h; naproxen 500 mg initially and repeat 3-5 h later, then 250-500 mg twice daily; mefenamic acid 500 mg 3 times daily (all with food)
Monophasic 35- $\mu$ g estrogen-containing OCP 3 times daily for 7 d, then 1 daily	Monophasic 30- to 35- $\mu$ g estrogen-containing OCP daily with or without inert pills
Medroxyprogesterone 20 mg or norethindrone 20 mg 3 times daily for 7 d	Medroxyprogesterone 5-10 mg or norethindrone 5-10 mg daily
Tranexamic acid 10 mg/kg IV (maximum, 600 mg per dose) or 1.5 g orally every 8 h for 5 d	Depot medroxyprogesterone 150 mg subcutaneously every 3 mo Levonorgestrel 19.5- to 52-mg intrauterine devices for 5 y (19.5-mg LNG IUS is a slightly smaller device) Etonogestrel subdermal implant for 3 y Tranexamic acid 1.5 g orally every 8 h for 5 d with menses

IV = intravenous; LNG IUS = levonorgestrel intrauterine system; OCP = oral contraceptive pill. Data from Committee on Practice Bulletins—Gynecology. Practice bulletin no. 110: non-contraceptive uses of hormonal contraceptives. *Obstet Gynecol.* 2010; 115(1):206-218; American College of Obstetrics and Gynecology Committee on Practice Bulletins—Gynecology. Practice bulletin no. 136: management of abnormal uterine bleeding associated with ovulatory dysfunction. *Obstet Gynecol.* 2013; 122(1):176-185; and *Obstet Gynecol.*<sup>40</sup>

bleeding compared with 76% using medroxyprogesterone acetate.<sup>41,42</sup> For chronic bleeding, NSAIDs, the 52-mg LNG IUS, combined OCPs (monthly or extended cycle), progestin therapy (oral, intramuscular, or subdermal), or tranexamic acid with menses may be useful.<sup>40</sup> When medical therapies fail for coagulopathies, endometrial ablation or hysterectomy may be warranted after childbearing is completed.

### Ovulatory Dysfunction

Ovulatory dysfunction includes not ovulating on a regular basis or infrequently, which may lead to amenorrhea but more likely results in irregular bleeding. Anovulation occurs most commonly in the early reproductive years and later perimenopausal years. Episodes of bleeding range from light and infrequent for 2 or more months to episodes of unpredictable and extreme HMB requiring intervention.<sup>3,45</sup> When HMB is associated with anovulation, the loss of luteal progesterone results in

persistent proliferative endometrium, which seems to be associated with reduced local levels of prostaglandin F2a, a necessary factor for efficient endometrial hemostasis.<sup>46</sup> A different disorder, generally manifesting in the later reproductive years, can occur in ovulatory women: the luteal-out-of-phase event. These women ovulate but recruit follicles early in the luteal phase, resulting in high circulating estradiol levels and associated HMB.<sup>45</sup> Although there is no identifiable cause, ovulatory dysfunction can occur with polycystic ovarian syndrome, obesity, hypothyroidism, hyperprolactinemia, anorexia, extreme exercise, and significant weight loss.<sup>35</sup>

In women with AUB consistent with ovulatory dysfunction, evaluation should be directed toward identifying treatable causes, which may include thyroid function testing.<sup>35</sup> Human chorionic gonadotropin, prolactin, and follicle-stimulating hormone testing should be considered for prolonged amenorrhea in younger women. Follicle-stimulating hormone levels can fluctuate daily. In obese women, prolonged amenorrhea due to anovulation and exposure to unopposed endogenous estrogen increases the risk of EIN and endometrial cancer; consideration for endometrial sampling/assessment is important.<sup>33,34</sup>

### Endometrial Disorders

Endometrial disorders are due to primary dysfunction of local endometrial hemostasis.<sup>3</sup> Women present with predictable and cyclic menses suggestive of normal ovulation but have HMB. Etiology is not completely defined, but there are likely deficiencies in vasoconstriction (endothelin-1, prostaglandin F2a) and excessive production of plasminogen, leading to accelerated lysis of clot.<sup>47</sup> This latter phenomenon may be improved using tranexamic acid given its antifibrinolytic action.<sup>43</sup> Other therapies for HMB include NSAIDs, oral/ring or patch combined contraceptives (monophasic, monthly, or extended cycle), progestins (oral, intramuscular, subdermal), the 52-mg LNG IUS, and danazol, with surgical interventions such as endometrial ablation or hysterectomy when warranted.<sup>40</sup>

In addition, endometrial inflammation or endometritis may play a role, as seen in

*Chlamydia trachomatis* or ureaplasma infections. Sources of infection are easily treated after cultures with appropriate antibiotic regimens.<sup>35</sup>

### Iatrogenic

The most common iatrogenic causes of AUB are due to hormone therapy such as OCPs or intramuscular, intrauterine, or subdermal contraceptives, which can cause BTB.<sup>3</sup> Corticosteroid-related drugs that may cause BTB are GnRH agonists, aromatase inhibitors, SERMs, and SPRMs. Systemic agents (ie, antidepressants) that contribute to disorders of ovulation, such as those that interfere with dopamine metabolism or cause hyperprolactinemia, may also lead to AUB.<sup>3</sup> Anticoagulants (warfarin, heparin, and direct oral anticoagulants) may cause HMB, prolonged menses, and postmenopausal bleeding. Treatment may not be necessary for minor BTB due to hormones. Breakthrough bleeding may initially be seen when estrogen-containing OCPs are used in a continuous manner without inert pills taken or in the first 4 to 6 months of OCP or LNG IUS use; only reassurance may be required.<sup>3</sup> Use of the subdermal implant has more associated BTB than other hormonal contraceptives and may improve with low-dose estrogen when not contraindicated (oral estradiol 1 mg daily for 10 days), short-course NSAIDs, or doxycycline 100 mg twice daily for 10 days.<sup>48</sup>

### Not Yet Classified

This group of entities causing AUB is poorly defined, inadequately examined, and generally rare.<sup>3</sup> They include arteriovenous malformation, myometrial hypertrophy, and uterine isthmocele secondary to cesarean delivery scar defect. Imaging such as TVUS and MRI may be helpful.

### WHEN TO EVALUATE

Not all AUB needs treatment, but it does require evaluation with a thorough medical history and physical examination. Laboratory testing should include a complete blood cell count and ferritin level measurement when HMB is an issue, with additional studies such as human chorionic gonadotropin,

coagulation tests, hormonal tests, and imaging as indicated. Addressing quality of life and potential anemia as well as discussing that obesity and ovulatory dysfunction may increase the risk of EIN and malignancy are key discussion points for treatment. In premenopausal non-gravid women, menses should occur at least 4 times yearly except in women receiving hormonal contraception.

### MANAGEMENT OF ACUTE AUB

It is important to understand the management of acute AUB (Table). After control of acute AUB, the underlying etiology can be determined using the PALM-COEIN classification. Medical management of acute and life-threatening HMB includes IV Premarin 25 mg every 4 to 6 hours for 24 hours along with antiemetic agents.<sup>41</sup> If bleeding does not lessen significantly within 8 hours, treatment should be changed to a different approach. In addition, caution should be used in giving IV or oral estrogen to women with cardiovascular disease, hypertension, venous thromboembolism, breast cancer, tobacco use after age 35 years, or migraines with aura. Oral treatments for HMB are monophasic 35- $\mu$ g estrogen-containing OCPs given 3 times daily for 7 days, with 1 tablet daily thereafter, or medroxyprogesterone acetate 20 mg 3 times daily for 7 days with 20 mg daily for the next 3 weeks.<sup>42</sup> Tranexamic acid can alternatively be used if no history of venous thromboembolism or cerebral vascular disease as 10 mg/kg IV (maximum of 600 mg per dose) or 1.3 g orally 3 times daily for 5 days.<sup>43</sup> In addition, intrauterine tamponade with a 26F Foley catheter infused with 30 mL of fluid may be used to control acute bleeding.<sup>44</sup>

### SUMMARY

Abnormal uterine bleeding in nongravid reproductive-aged women accounts for frequent visits to primary care and emergency department providers. After a complete history and examination with pregnancy excluded, clinicians can feel comfortable in beginning an assessment of AUB using the PALM-COEIN terminology with management directed toward etiology to improve quality of life. Women with challenging AUB warranting



further evaluation and management should be referred to gynecologists.

**Abbreviations and Acronyms:** **AUB** = abnormal uterine bleeding; **BTB** = breakthrough bleeding; **EIN** = endometrial intraepithelial neoplasia; **FIGO** = International Federation of Gynecology and Obstetrics; **GnRH** = gonadotropin receptor hormone; **HMB** = heavy menstrual bleeding; **IUD** = intrauterine device; **IV** = intravenous; **LNG IUS** = levonorgestrel intrauterine system; **MgFUS** = magnetic resonance imaging—guided focused ultrasound; **MRI** = magnetic resonance imaging; **NSAID** = nonsteroidal anti-inflammatory drug; **OCP** = oral contraceptive pill; **PALM-COEIN** = polyp(s), adenomyosis, leiomyoma, malignancy, coagulopathy, ovulatory dysfunction, endometrial disorders, iatrogenic, and not yet classified; **SERM** = selective estrogen receptor modulators; **SIS** = saline infusion sonohysterography; **SPRM** = selective progesterone receptor modulator; **TVUS** = transvaginal pelvic ultrasound; **UAE** = uterine artery embolization; **vWF** = von Willebrand factor

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