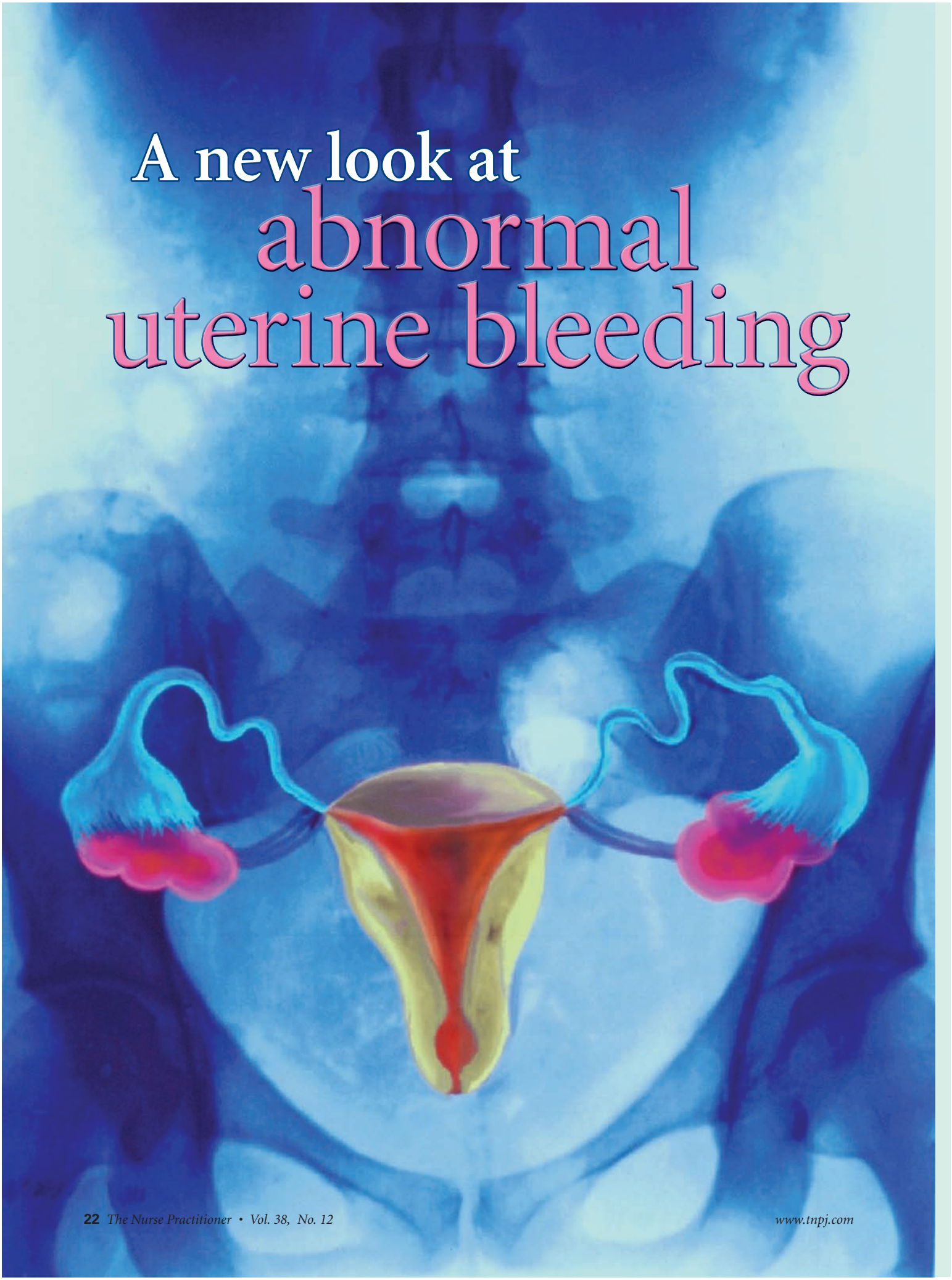
A new look at abnormal uterine bleeding



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Abstract: New universal terminology, classifications, and definitions recommended by the International Federation of Gynecology and Obstetrics and supported by the American College of Obstetricians and Gynecologists to describe abnormal uterine bleeding abnormalities in reproductive women are presented. Identification and management of anovulatory and ovulatory uterine bleeding are explored.

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A 45-year-old female patient presents to a primary care clinic and states to the nurse practitioner (NP) that her periods had begun to become irregular over the past few years with periods every 5 to 6 weeks, lasting 2 days. Two months ago, she began bleeding every 2 to 3 weeks, lasting 7 to 10 days, described as "heavy for the first 4 days." She goes through her pads at night, and on average, uses one pad every 2 hours during the first 3 to 4 days. She has numerous clots and some cramping with her periods, but not anything like it used to be when she was younger. She finds the frequency of the bleeding to be distressful to her, as she never knows when she is going to start bleeding. This scenario or similar episodes of abnormal uterine bleeding (AUB) are present in one out of five women annually.[1] The prevalence of AUB increases with age with 24% of women age 36 to 40 years. The adolescent who is just beginning to menstruate and the perimenopausal-aged woman experience the highest incidence of AUB, which is related to dysfunction within the hypothalamic-pituitary-ovarian axis (HPO) and lack of progesterone secretion. AUB during the menopausal transition (perimenopause) and postmenopausal years account for 70% of gynecologic visits.[2]

Any change within normal menstruation or in the normal menstrual cycle pattern regardless of cause is called AUB, the new umbrella terminology.[3] Women who present with AUB have different perceptions of the degree of bleeding or severity. Some women will present with just a minor deviation from normal and others who experience heavy bleeding for months become frustrated with the bleeding interfering with their quality of life. Fear of embarrassment in soiling clothes will keep a woman from going to work, participating in social events, and engaging in family activities. Prolonged bleeding will impact the woman's sexual functioning and can be a financial burden with the extra expense of sanitary supplies and lost work time.

New terminology

There has not been clarity with the diagnosis for women who present with deviations in uterine bleeding. Cumbersome terminology and confusing research outcome measures have brought forth recommendations from the International Federation of Gynecology and Obstetrics and support from the American College of Obstetricians and Gynecologists (ACOG) for a universal classification system to describe AUB abnormalities in reproductive women.[2,3] The PALM-COEIN classification (polyps, adenomyosis, leiomyoma, malignancy and hyperplasia, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified) identifies uterine bleeding abnormalities by bleeding pattern and etiology.[2,3] The PALM identifies structural etiology that is measureable with diagnostic imaging techniques and/or with histopathologic findings. The classification of AUB is signified by the first letter of the type (AUB-P [polyp]). COEIN group is frequently referred to as the nonstructural etiologies. Three of the categories, coagulopathy, ovulatory dysfunction, and endometrial disorders, are to replace the term "dysfunctional uterine bleeding."[4] Other terminologies, such as metrorrhagia, menometrorrhagia, oligomenorrhea, and menorrhagia, are to be discarded and replaced with new terminology presented. (See *New terminology.*) These new terms are easier to understand and should provide consistency.

The pattern is further defined in regularity, frequency, heaviness, or volume of flow and duration of flow within

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Keywords: abnormal uterine bleeding, anovulatory bleeding, endometrium, ovulatory bleeding

normal limits (between the 5th and 95th percentile).[2-4] Normal parameters would include a menstrual cycle every 24 to 38 days, with regularity from cycle-to-cycle of +/- 2 to 20 days, for duration of 4 to 8 days and 5 to 80 mL of blood loss.[2-5]

Pathophysiology

Although any change in the HPO axis can cause AUB, changes within the endometrium and the ovarian function have the greatest effects on the menstrual cycle. The proliferative phase of the menstrual cycle is under the influence of estrogen secreted from the ovary in the follicular phase. The endometrium grows from 1 to 2 mm in thickness to approximately 12 mm at the time of the luteinizing hormone (LH) surge. The outer layers of the endometrium thicken as the glandular cells proliferate in response to the estrogen secretion.[6,7] Stromal cells become compact. With ovulation, the endometrium secretes a glycogen-rich substance preparing for implantation (secretory phase), which is under the influence of progesterone secreted from the corpus luteum. Glandular tissues become more tortuous, while the stromal cells become edematous. There is an increase and coiling in the spiral arteries that feed the endometrium,[6,7] and a glycogen-rich substance is expelled day 6 postovulation to assist with implantation of a fertilized egg. If fertilization does not occur, the progesterone levels drop and release lytic matrix metalloproteinases, which breakdown the stromal and the thickened, enriched glandular tissue.[6,7] Tissue sloughing occurs with menstruation. Hemostasis is controlled by platelet aggregation and thrombi formation along with mediators that cause vasoconstriction of the vessels.

Ovulatory and anovulatory bleeding

Ovulatory bleeding, the more common AUB and superimposed on regular cyclic menstruation (24 to 35 days), is usually associated with an anatomic (PALM) or functional cause. There is an imbalance in the endometrial prostacyclin and prostaglandin production affecting clotting. Cycles are prolonged (over 8 days) with heavy menses (greater than 80 mL) and occasional clots greater than 1 in (2.5 cm) in diameter.[8] Periods may or may not be characterized by premenstrual symptoms, dysmenorrhea, and midcycle pelvic pain. Changes in cervical mucus should be normal, while biphasic temperature and luteal predictor kits should reflect ovulation. An endometrial biopsy (EMB) will show a secretory phase when done in the last half of the menstrual cycle. Estradiol, follicle stimulating hormone (FSH), and LH are within normal limits as well. Midcycle bleeding may be present that reflects a decreased estrogen production, whereas spotting a few days before menses suggests a deficient progesterone production by the corpus luteum.

AUB with leiomyoma (AUB-L), the most common benign neoplasm, is not dependent on size or location of the fibroid. Endometrial polyps are pedunculated masses of fibrotic stromal and endometrial glands from the endometrial lining of the uterus. Up to 70% of the women with endometrial polyps will experience heavy AUB (AUB-P).[6] Endocervical polyps are an overgrowth of benign stromal tissue contributing to postcoital, intermenstrual bleeding.

AUB associated with coagulopathies (AUB-C) may be inherited or acquired and should be worked up when accompanied by bruising one or more times per month, epistaxis, bleeding from the gums, or heavy bleeding with any surgical or dental intervention. AUB-C is associated with dysfunction of platelet adherence or defects in platelet plug stabilization.[6] Heavy bleeding during the adolescent period may be associated with von Willebrand disease, affecting 11% to 36% of adolescents with AUB-C.[9] Bleeding disorders may be present in 32% of the women who present with AUB. AUB-C can be a concern in adolescent girls and women of all ages and in any gynecologic event, including pregnancy.

New terminology[3,4]

Acute uterine bleeding	Any episode in nonpregnant, reproductive-aged woman, who has sufficient bleeding to require immediate treatment to prevent further blood loss or anemia.
Chronic uterine bleeding	Has been present for 6 months or longer, abnormal in duration, volume, and/or frequency
Heavy menstrual bleeding	Blood loss that interferes with the physical, emotional, social, quality of life, and that can occur alone or in combination with other symptoms.
Prolonged menstrual bleeding	Bleeding longer than 8 days
Shortened menstrual bleeding	Bleeding shorter than 2 days
Light menstrual bleeding	Reduced volume of bleeding from normal
Intermenstrual bleeding	Bleeding that occurs between menstrual cycles. Can be cyclic and predictable or follow no particular pattern.

Anovulatory bleeding

Anovulatory cycles have unpredictable bleeding, which varies in frequency, regularity, duration, and volume. There is a disruption in the HPO axis, resulting in no LH surge and no progesterone secreted from a corpus luteum. In unopposed estrogen, the endometrium proliferates to abnormal heights and becomes fragile. Without progesterone, there is poor stromal support to maintain stability. When the endometrium outgrows the blood supply and nutrients, isolated areas of the endometrium breakdown and slough, repair under the influence of estrogen, while other focal areas breakdown at the epithelial surface. The epithelial repair becomes a patchwork process with focus on the small, localized, broken-down areas, instead of an orderly remodeling of the endometrium.[7] An imbalance with more prostaglandins, causing vasodilatation rather than vasoconstriction, exists. Higher levels of plasminogen activators (enzymes) are released that facilitate dissolution of clots in the endometrium, leading to heavy AUB.[7]

Anovulatory cycles are characterized with frequent spotting to infrequent, heavy bleeding. Dysmenorrhea and premenstrual symptoms are usually not present. There is no change in body temperature, cervical mucus, vaginal pH, and presence of spinnbarkeit or ferning. Serum progesterone would be less than 1 ng/mL around day 20 of the menstrual cycle. An EMB would show the endometrium to be in the proliferative phase at any point in the cycle.

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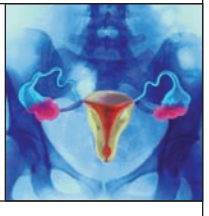


The menopausal transition is associated with anovulatory bleeding and caused by a disruption in HPO axis, as the hormones begin to wax and wane along with the cessation in production of follicles. However, ovulation can occur, is unpredictable, and is referred to as a "luteal out-of-phase" event.[10]

Most ovulatory dysfunctions (AUB-O) are a result of an endocrinopathy (for example, polycystic ovarian syndrome, hypothyroidism, hyperprolactinemia, mental stress, obesity, anorexia, weight loss, or extreme exercise).[10] Iatrogenic causes of ovarian dysfunction (AUB-I) include medications (for example, aspirin, spironolactone, antihistamines, corticosteroids, tricyclic antidepressants, and hormone therapy). Herbal medications such as ginseng, dehydroepiandrosterone (DHEA), black cohosh, red clover, and soy supplements can contribute to ovarian dysfunction.

Presenting symptoms

Women with AUB may present with a small amount of irregular spotting to heavy vaginal bleeding. The frequency, regularity, duration, or volume will vary and may or may not be accompanied with excessive cramping. Excessive blood loss may lead to anemia, exercise-induced fatigue, fainting, increased heart rate, dyspnea, palpitations, and syncope. Onset may be sudden, as the body does not have time to compensate for the acute blood loss.

Assessments

The NP should complete a thorough health history. It should include a complete medical, surgical, and family history to rule out other sources of bleeding. A review of systems should include differential questions to rule out other endocrine and medical problems. Identification of medications should include prescription drugs, over-the-counter medications, and herbal medications. Contraceptive history should include length of time, any change in brands, administration pattern, and change in method. Infertility problems or plans for future childbearing should be addressed. Dieting patterns, weight loss, types of diet aids, excessive exercise, and use of energy drinks or other nutritional stimulants should be included in the nutritional assessment. The social history should include alcohol, drug use, or smoking history. The possibility of trauma should be ruled out by assessing for sexual or physical abuse.

An obstetric and gynecologic history should include number of pregnancies and outcomes, any history of dysmenorrhea, premenstrual symptoms, amenorrhea, infertility, abnormal bleeding patterns, and chronic pelvic pain. Sexual history should focus on number of partners, high-risk sexual behavior, exposure to sexually transmitted infection, and presence of vaginal discharge. (See *Assessment of AUB.*) AUB can affect females of all ages and is not limited to women of reproductive age. Women readily identify when they deviate from their "normal." A diary or calendar can assist the woman in presenting an accurate history of her bleeding along with using visuals to help differentiate heavy, moderate, and light bleeding on a pad or tampon.

Physical assessment

If possible, a complete physical exam should be performed. All exams should evaluate vital signs for postural changes in pulse and BP, assessing for signs of anemia, sallow skin, pale mucous membranes, nail beds, eyelids, slowed capillary filling, and dizziness with standing up. Other quick

assessments for petechiae, ecchymosis, virilization, hirsutism, moon face, buffalo hump, an enlarged thyroid, hair pattern and texture, presence of facial hair, acne, or chloasma may help exclude many possible differentials.

A pelvic exam including both a visual inspection of the external genitalia and perineum and a speculum exam of the vagina should be performed. The amount of blood and clots in the vaginal vault should be noted in addition to whether or not there is an unusual odor. Evidence of trauma on the external genitalia or vaginal wall or of vulvar or vaginal lesions should be assessed. The cervix should be evaluated to determine if it is closed and to rule out pregnancy. Further evaluation should include any motion tenderness, structural abnormalities, polyps, or lesions. A bimanual exam should evaluate the status of the uterus for consistency, tenderness, irregularity in size and shape, position, movability, or evidence of tenderness in the adnexa or presence of an ovarian mass. Pelvic pain should be noted for location and degree of discomfort.

Assessment of AUB[3,4,6,8,12]

Menstrual history
- Last menstrual period
- Length of cycle/days flow
- Heavy/moderate/light
- Cramps/no cramps
- Have periods always been regular
- Age when cycle became regular/irregular
- Age of menarche/menopause
- Mother/sister age of menarche/menopause

Abnormal uterine bleeding history
- When did menstrual bleeding change?
- Frequency, duration, and amount of bleeding now?
- Frequency of flooding or gushing?
- Has cycle lengthened; shortened?
- When does bleeding occur?
- Presence of clots? Passed tissue?
- How frequent change pads/tampons (less than 1-2 hours = abnormal)?
- How many tampons/pads are used per day? Accidents?
- How many tampons/pads are used during a normal period (more than 21 = abnormal)?
- Do you have to wear both a tampon and a pad? Double pads?
- Does bleeding limit your daily activity? For how many days?
- Do you miss school, work, or family events?
- Are you afraid of or have you soiled your clothes in social environment?
- Do you soil clothes at nighttime?
- On a scale of 1 to 4, how does the bleeding affect your quality of life?
- Do you have premenstrual breast tenderness, moodiness, back pain, and pelvic heaviness?

Differential history
- Experiencing any new headaches? Onset? Location?
- Blurring of vision?
- Noticed any voice change?
- Noticed any change in hair texture? Hair loss? Presence of facial, chest, or back hair?
- Any problems swallowing? Pain in the neck?
- Changes in skin texture? Acne? Cystic acne? Location on face, chest, back, buttocks?
- Weight gain? Weight loss?
- Temperature intolerance? Heat? Cold?
- Change in bowel patterns?
- Change in libido?
- Any new illness? Medications? Over-the-counter or herbal medications?

Diagnosis

Pregnancy should always be excluded first in any woman of reproductive age. Initially, a complete blood cell count (CBC) with differential and thyroid-stimulating hormone (TSH) are recommended by ACOG.[2] A CBC with platelets, prothrombin time, and partial thromboplastin time are indicated in adolescents with heavy AUB and women with a history of bleeding disorders. A fibrinogen and thrombin time is optional.[11] According to ACOG, a bleeding time is not indicated, as it is not sensitive or specific.[2] A serum ferritin would be an option if the CBC suggested an iron deficiency anemia. (See *Diagnostic testing for abnormal uterine bleeding.*)

Fasting prolactin levels, drawn in the morning, should be considered in adolescents and repeated if levels are greater than 60 pg/mL to rule out pituitary adenomas.[2,12] Subsequent lab confirmative or differential laboratory testing on day 3 of a regular menstrual cycle should include an FSH, LH, and estradiol, which will help establish an HPO axis problem.[13] Androgen levels of testosterone and dehydroepiandrosterone-sulfate (DHEA-S) may be drawn if signs of virilization or hirsutism are present.

Cultures for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* should be obtained. Vaginal secretions should be evaluated for the presences of Trichomonas vaginalis. Cervicitis may be associated with abnormal bleeding and needs to be ruled out in women with high-risk sexual behaviors. Pap smears may rule out the presence of cervical cancer.

An EMB, a first-line diagnostic test, is sampling of the endometrial lining in women with AUB to identify endometrial hyperplasia or malignancy. This assessment should be done in women over the age of 35 years who are suspected to have anovulatory bleeding or are under the age of 35 years and are morbidly obese, have a history of polycystic ovarian syndrome, chronic anovulation, take tamoxifen, or are at risk for endometrial cancer.[13] Pregnancy should be ruled out prior to performing the pro-

Diagnostic testing for abnormal uterine bleeding[2,6,11-14,16,18]

	Testing	Special considerations
Required lab testing	• Point of care urine pregnancy test (HCG) • CBC with differential • TSH	• Recommended by ACOG for all patients
Optional lab testing	• Platelets • Prothrombin time • Partial thromboplastin time • Fibrinogen • Thrombin time • Liver function • Serum ferritin	• Recommended for adolescents with heavy menstrual bleeding and women with bleeding disorders • Optional based on clinical findings
Confirmative lab testing	• Fasting prolactin • FSH • LH • Estradiol	• Fasting prolactin in the AM; avoid nipple stimulation 1 hour prior to testing • Draw in AM of day 3 of regular menstrual cycle
Specific lab testing	• von Willebrand factor antigen • von Willebrand factor ristocetin cofactor activity • Factor VIII activity	• Suspected von Willebrand disease
Microbiology testing	• *Chlamydia trachomatis* • *Neisseria gonorrhoeae* • *Trichomonas vaginalis* • Bacterial Vaginosis	• Rule out associated cervicitis and metritis
First-line diagnostic testing	• Endometrial biopsy	• Bleeding over age of 35 years
First-line imaging screening	• Transvaginal ultrasonography • SIS	• ACOG recommends >4 mm endometrial stripe followed up with EMB • Done with TVU as first line
Alternative imaging	• Hysteroscopy • MRI	• Computed tomography scan is inappropriate for vaginal bleeding

cedure. The EMB is limited in obtaining an adequate sample with a pipelle but has 84% sensitivity in diagnosing endometrial hyperplasia and cancer.[14] Focal lesions are missed 18% of the time with an EMB.[14]

ACOG recommends transvaginal ultrasonography (TVU) as first-line imaging screening.[2] It should be used when a bimanual exam suggests abnormal findings. If done in conjunction with an EMB or a failed EMB in a postmenopausal woman, ACOG recommends requiring an EMB for anyone having more than a 4 mm endometrial stripe. Duska suggests that an endometrial stripe of less than 3 mm has a greater sensitivity (97.9%) and should be considered the standard; however, it could be debated that it will increase the false-positive rate for EMBs.[15] If a TVU is being performed in a menstruating woman to consider the endometrial stripe and to visualize the uterine lining for focal abnormalities, it should be done between days 4 to 6 of the menstrual cycle.[16] TVU is a good tool to visualize the uterus, endometrium, and adnexa. If the TVU is not adequate or requires further exploration of the uterine architecture, saline-infused sonohysterography (SIS) is performed[2] and, together, they are recommended as first-line diagnostic measures to assess uterine pathology.[13] It is suggested that the SIS is far superior to the EMB in diagnosing pathology in postmenopausal women with AUB.[13] The hysteroscopy, another means of visualizing the endometrial environment, may be used in the office or in outpatient settings in conjunction with treatment of endometrial pathology.[2] The hysteroscopy allows for biopsy or excision of lesions. The magnetic resonance imaging (MRI) is not considered to be a primary diagnostic tool for AUB but reserved for more specific information on size, location, or type of fibroid or presence of adenomyosis. It can be used to guide the treatment for myomectomy or uterine artery embolization.[2,13] Benefits and costs must be evaluated when considering the use of an MRI.

Management

A variety of management options are available when it has been determined that the woman is not at risk for endometrial hyperplasia or is pregnant. It is important to determine

if the bleeding is acute or chronic along with the woman's desire for future reproduction. The goal of treatment in acute AUB is to stop or to decrease the amount of blood flow and to prevent anemia or worsening of anemia. The overall goal of treatment should be to regulate the menstrual cycle, improve the quality of life, and to control the blood loss. A woman's preference should be considered when selecting the best option. (See *Evidence-based management of abnormal uterine bleeding.*)

Hormone therapy is the first line of treatment and may include combined estrogen/progestin hormones in a pill, patch, or vaginal ring. Combined oral contraceptives (COC) have been found to have strong evidence for control of abnormal uterine bleeding.[17] Although off label at this high of a dose,

Evidence-based management of abnormal uterine bleeding

Acute vs Chronic Agent/Dosing	Evidence	Strength of Evidence
Combined Oral Contraceptives (COC) Acute • Oral monophasic estrogen/progestin therapy for 7 days with tapered-down dosing[12,18-20]	• COC have strong evidence for control of AUB[17] • Cessation of bleeding in 88%[25]	• AHRQ systematic review Level I-II[17] • Randomized controlled trial Level II-1[20]
Chronic • Any combined estrogen/progestin product including transdermal patch, vaginal ring, shortened, extended, continuous cycle		• ACOG Committee Opinion[18]
Progestin Acute • Medroxyprogesterone acetate 20 mg orally, three times per day for 7 days[12,18-20]	• Moderate evidence for control of AUB for 21 days. Insufficient evidence for 10 day treatment[17] • 76% cessation of bleeding[25]	• AHRQ systematic review Level I-IIB[17] • Systematic literature review[17] • Level I-1B[22] • Randomized controlled trial Level II-1[20]
Chronic • Medroxyprogesterone acetate 10 mg oral daily dose[12,18-20] • Depo provera 150 mg IM every 3 months • Levonorgestrel-releasing intrauterine system*[23]	• Moderate strength of evidence LNG-IUS had higher approval than COC or other treatment options[17]	• ACOG Committee Opinion[18] • AHRQ systematic review Level I-IIB[17]
NSAIDs Chronic • Mefenamic acid 500 mg initial oral dose, then 250 mg orally every 6 hours* • Ibuprofen 600-800 mg orally, every 6 hours • Meclofenamate sodium 100 mg orally, three times per day • Naproxen sodium 550 mg initial oral dose, then 275 mg orally, every 6 hours.[12]	• Moderate strength of evidence suggests decrease menstrual blood flow[17,24]	• AHRQ systematic review Level I-IIB[17] • Systematic literature review Level I-1B[24]
Antifibrinolytic Agent Chronic • Tranexamic acid 1.3 g orally, three times per day on day 1-5*[12,25]	• Has moderate strength of evidence as being more effective than NSAID or progestin[17,25]	• AHRQ systematic review Level I-IIB[17] • Randomized controlled trial Level II-1[25]

*FDA Approved for AUB

Level or Type of Evidence[2]

I: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Strength of Evidence[2]

Level A: Recommendations are based on good and consistent scientific evidence.

Level B: Recommendations are based on limited or inconsistent scientific evidence.

Level C: Recommendations are based primarily on consensus and expert opinion

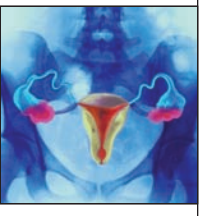
acute bleeding may be managed with an 88% success rate by the use of a 30 to 35 mcg estradiol monophasic/progestin oral pill three to four times a day for a week until bleeding slows or stops.[12,18-20] The pills may be tapered to once a day through one to two continuous pill packs. Conjugated estrogen (Premarin) 1.25 mg for 7 to 10 days, followed by oral medroxyprogesterone acetate (Provera) 5 mg for 5 days, will provide similar results. Normal withdrawal bleeding or slightly heavy menstrual flow should occur following either regimen.[16,21] Treatment should continue for 3 months to provide the most effective results. Once bleeding is stabilized, the use of continuous cycling of monophasic estrogen/progesterone product is an option if the woman desires hormone therapy. When prescribing hormone therapy, the NP must weigh the risks and benefits for the patient and be aware of the patient's medical history. Together, the NP and patient should decide if hormone therapy is right for her, whether it be long term or short term use.

Another option for acute AUB in women who have anovulatory bleeding, do not tolerate estrogen/progestin products, and are over the age of 35 years and smoke is to use oral medroxyprogesterone acetate, norethindrone acetate, or micronized progesterone for 10 days or aqueous progesterone I.M. for 6 to 8 days; however, it is not as effective as other options.[22] Although there is insufficient scientific evidence to support a 10-day course of progestins alone,[20-22] a normal withdrawal bleeding is stimulated, and endometrial hyperplasia is controlled in anovulatory cycles. Short-term use of 21 days of progesterone therapy for ovulatory bleeding has been found to reduce menstrual blood loss.[8,22] Once bleeding is controlled, medroxyprogesterone acetate injectable 150 mg I.M. may be used every 12 weeks, or a levonorgestrel intrauterine contraceptive system (LNG-IUS) may be placed. The LNG-IUS has been shown to decrease blood loss by 90% in AUB, as it is designed to decrease endometrial proliferation.

The Agency for Healthcare Research and Quality (AHRQ) reported a moderate strength of evidence showed the LNG-IUS had a higher approval than COCs or other treatment options.[17] A systematic literature review reported that women who had an LNG-IUS placed before scheduled surgical interventions were likely to cancel the procedure because of the successful response.[23] It is approved by the U.S. FDA for use in AUB[12] and is an excellent option for the obese woman.[16]

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) is recommended in women with ovulatory problems. The NSAIDs block the vasodilator prostaglandins and, therefore, decrease the amount of bleeding with menstruation, should be started as early as 72 hours before the onset of menses, or at the start of menstruation.[12] It is recommended as first-line treatment in women experiencing irregular frequency or duration patterns. Moderate strength of evidence suggests a modest reduction in menstrual blood flow with NSAIDs.[18,24] There is no one NSAID that works more effectively than another. It is a trial, and when one fails, another NSAID should be prescribed.

Further exploration is required if continuation of bleeding with either the estrogen/progestin or the progestin-only methods occurs.



The NP must weigh the risks and benefits for the patient and be aware of the patient's medical history when prescribing NSAIDS. Tranexamic acid (Lysteda) is an antifibrinolytic agent that stabilizes the fibrin matrix and is approved by the FDA to treat AUB.[25] It is only used for 1 to 5 days during menstruation and is ideal for a woman who does not desire birth control or hormone therapy. AHRQ systematic review reports tranexamic acid has moderate strength of evidence as being more effective than an NSAID or progestin alone.[17] Transexamic acid is contraindicated in women with a history of or active thromboembolic disease and those taking combined hormonal contraceptives. It should not be administered in women with renal impairment, disseminated intravascular coagulation, and a thromboembolic or convulsive history. Acquired impaired colored vision has been reported with transexamic acid. It should not be administered concurrently with hormone therapy.[18]

Further exploration is required if continuation of bleeding with either the estrogen/progestin or the progestin-only methods occurs. Surgical options should be explored and choices made based on the woman's desire for further childbearing or quality of life. The NP should refer to a gynecologist to define the best option that may vary from dilatation and curettage, endometrial ablation, uterine artery embolization, myomectomy, or hysterectomy. NP

REFERENCES

1. CDC Centers for Disease Control and Prevention. Blood disorders in women, Heavy menstrual bleeding. 2013. http://www.cdc.gov/ncbddd/blooddisorders/women/menorrhagia.html.
2. Committee on Practice Bulletins—Gynecology. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. ACOG. *Obstet Gynecol*. 2012;120(1):197-206.
3. Fraser IS, Critchley HO, Broder M, Munro MG. The FIGO recommendations on terminologies and definitions for normal and abnormal uterine bleeding. *Semin Reprod Med.* 2011;29(5):383-390.
4. Munro MG, Critchley HO, Fraser IS. The FIGO systems for nomenclature and classification of causes of abnormal uterine bleeding in the reproductive years: who needs them? *Am J Obstet Gynecol*. 2012;207(4):259-265.
5. Evidenced-based practice center (EPC) systematic review protocol. Project title: primary care management of abnormal uterine bleeding (AUB). *AHRQ*. 2011. http://effectivehealthcare.ahrq.gov/ehc/products/340/850/AUB_Protocol_20111121.pdf.

6. Hoffman BL, Schorge JO, Schaffer JI, et al. Chapter 8. Abnormal uterine bleeding. In: Hoffman BL, Schorge JO, Schaffer JI, et al., eds. *Williams Gynecology*. 2nd ed. New York: McGraw-Hill; 2012.
7. Speroff L, Fritz MA. Chapter 15. Dysfunctional bleeding. In: Speroff L, Fritz MA, eds. *Clinical Gynecologic Endocrinology and Infertility*. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2005.
8. Sweet MG, Schmidt-Dalton TA, Weiss PM, Madsen KP. Evaluation and management of abnormal uterine bleeding in premenopausal women. *Am Fam Physician*. 2012;85(1):35-43.
9. James A, Nazzaro A. Bleeding disorders: impact on reproduction. *Contemporary OB/GYN*. 2012;57(7):32-39.
10. Munro MG, Critchley HO, Broder MS, Fraser IS for the 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 Gynecol Obstet*. 2011;113(1):3-13.
11. National Heart, Lung, and Blood Institute. The diagnosis, evaluation, and management of von Willebrand Disease. NIH Publication No. 08-5832. Bethesda (MD): HNLBL; 2007. http://www.nhlbi.nih.gov/guidelines/vwd/vwd.pdf.
12. Ibrahim SA, Smith S. Evaluation amenorrhea. In: Hurt KJ, Guile MW, Bienstock JL, Fox HE, Wallach EE, eds. *The Johns Hopkins Manual of Gynecology and Obstetrics*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.
13. Tsai MC, Goldstein SR. Office diagnosis and management of abnormal uterine bleeding. *Clin Obstet Gynecol*. 2012;55(3):635-650.
14. Null DB, Weiland CM, Camlibel AR. Postmenopausal bleeding-first steps in the workup. *J Fam Pract*. 2012;61(10):597-604.
15. Duska LR. At what thickness is the endometrial stripe cause for concern in a woman who has postmenopausal bleeding? *OBG Management*. 2010;22(10):15-19.
16. Davidson BR, DiPiero CM, Govoni KD, Littleton SS, Neal JL. Abnormal uterine bleeding during the reproductive years. *J Midwifery Womens Health*. 2012;57(3):248-254.
17. Hartmann KE, Jerome RN, Lindegren ML, et al. *Primary Care Management of Abnormal Uterine Bleeding. Comparative Effectiveness Review No. 96*. (Prepared by the Vanderbilt Evidence-based Practice Center under Contract No. 290-2007-10065 I.) AHRQ publication No. 13-EHC025-EF. Rockville, MD: Agency for Healthcare Research and Quality. 2013. www.effectivehealthcare.ahrq.gov/reports/final.cfm.
18. American College of Obstetricians and Gynecologists. ACOG committee opinion no. 557: Committee on Gynecologic Practice. Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Committee Opinion No. 557. *Obstet & Gynecol*., 2013;121(4): 891-896.
19. Pinkerton JV. Pharmacological therapy for abnormal uterine bleeding. *Menopause*. 2011;18(4):453-461.
20. 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(4):924-929.
21. Hickey M, Higham JM, Fraser I. Progestogens with or without oestrogen for irregular uterine bleeding associated with anovulation. *Cochrane Database Syst Rev*. 2012;9:CD001895.
22. Lethaby A, Irvine G, Cameron I. Cyclical progestogens for heavy menstrual bleeding. *Cochrane Database Syst Rev*. 2008;(1):CD001016.
23. Lethaby AE, Cooke I, Rees M. Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. *Cochrane Database Syst Rev*. 2005;(4):CD002126.
24. Lethaby A, Duckitt K, Farquhar C. Non-steroidal anti-inflammatory drugs for heavy menstrual bleeding. *Cochrane Database Syst Rev*. 2013;1:CD000400.
25. Lukes AS, Moore KA, Muse KN, et al. Tranexamic acid treatment for heavy menstrual bleeding: a randomized controlled trial. *Obstet Gynecol*. 2010;116(4):865-875.

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