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CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN–GYNECOLOGISTS

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Committee on Practice Bulletins—Gynecology. This Practice Bulletin was developed by the Committee on Practice Bulletins—Gynecology with the assistance of Linda D. Bradley, MD, and Misty Blanchette-Porter, MD. The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

PDF Format

Management of Abnormal Uterine Bleeding Associated With Ovulatory Dysfunction

Abnormal uterine bleeding associated with ovulatory dysfunction (AUB-O) is a condition for which women frequently seek gynecologic care. Anovulatory bleeding is common at the extremes of reproductive age. The choice of treatment of AUB-O depends on several factors, including the woman's age, severity of her bleeding, her medical risk factors, her need for contraception, and her desire for future fertility (1). The purpose of this document is to provide management guidelines for the treatment of patients with AUB-O.

Background

Definition and Nomenclature

Box 1. Causes of Anovulation

Physiologic

Adolescence
Perimenopause
Lactation
Pregnancy

Pathologic

Hyperandrogenic anovulation (eg, polycystic ovary syndrome, congenital adrenal hyperplasia, or androgen-producing tumors)
Hypothalamic dysfunction (eg, secondary to anorexia nervosa)
Hyperprolactinemia
Thyroid disease
Primary pituitary disease
Premature ovarian failure
Iatrogenic (eg, secondary to radiation or chemotherapy)
Medications

Abnormal uterine bleeding associated with ovulatory dysfunction (AUB-O) (ie, oligo-ovulation or anovulation) is a spectrum of disorders most commonly associated with heavy, irregular uterine bleeding. Abnormal uterine bleeding (AUB) occurs in the setting of ovulatory dysfunction because of the effects of chronic unopposed estrogen on the endometrium. Abnormalities at any level of the hypothalamic-pituitary-ovarian axis can result in interruption of the ovulatory cycle. Recognized causes of anovulation are listed in Box 1.

In an effort to create a universally accepted system of nomenclature to describe uterine bleeding abnormalities in reproductive-aged women, an alternative classification system (polyp, adenomyosis, leiomyoma, malignancy and hyperplasia, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified), known by the acronym PALM-COEIN, was published in 2011 by the International Federation of Gynecology and Obstetrics (FIGO) (Box 2) and adopted by the American College of Obstetricians and Gynecologists (2). The PALM-COEIN system classifies uterine bleeding abnormalities by bleeding pattern and etiology. The overarching term AUB is paired with descriptive terms to denote bleeding patterns associated with AUB, such as heavy menstrual bleeding (instead of menorrhagia) and intermenstrual bleeding (instead of metrorrhagia). Abnormal uterine bleeding is further classified by one (or more) letter qualifiers that indicate its etiology (Box 2). The term dysfunctional uterine bleeding—often

used synonymously with AUB in the literature to indicate AUB for which there was no systemic or locally definable structural cause—is not part of the PALM-COEIN system, and discontinuation of its use is recommended (2). The diagnosis of AUB in reproductive-aged women is discussed elsewhere (3).

Ovulatory Cycle

Box 2. PALM-COEIN Classification System for Abnormal Uterine Bleeding in Reproductive-Aged Women

PALM: Structural Causes

Polyp (AUB-P)
Adenomyosis (AUB-A)
Leiomyoma (AUB-L)
    Submucosal myoma (AUB-L_{SM})
    Other myoma (AUB-L_{O})
Malignancy & hyperplasia (AUB-M)

COEIN: Nonstructural Causes

Coagulopathy (AUB-C)
Ovulatory dysfunction (AUB-O)
Endometrial (AUB-E)
Iatrogenic (AUB-I)
Not yet classified (AUB-N)

Each postulated cause of abnormal uterine bleeding is linked with one (or more) letter qualifiers that indicate its etiology or etiologies. The new classification system recommends that the term dysfunctional uterine bleeding be abandoned.

Data from Munro MG, Critchley HOD, Broder MS, Fraser IS. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Int J Gyn Obstet 2011;113:3-13.

Most ovulatory menstrual cycles last between 21 days 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 median age of menarche is 12.43 years with a typical cycle range of 21-45 days, with 7 or fewer days of blood flow in younger females (4). Ovulatory cycles are predictable, but in most women, the length of the cycle can vary by a few

days each month. Overall, the length of the menstrual cycle remains relatively constant throughout the reproductive years, but cycle length varies as a woman approaches menopause (5).

Menstruation results from a complex interaction between the hypothalamus, the anterior pituitary gland, the ovary, and the endometrium. The selection and ovulation of a mature oocyte is the result of the coordinated process that results in the cyclic growth and differentiation of the endometrium. Dysfunction at any level can interfere with ovulation and prevent normal development and sequential shedding of the uterine lining.

During a normal ovulatory cycle—including follicular development, ovulation, corpus luteum development, and luteolysis—the endometrium is sequentially exposed to ovarian production of estrogen alone, followed by a combination of estrogen and progesterone. At the end of the cycle, estrogen and progesterone withdrawal occurs. Follicle development and ovulation are associated with a cyclic pattern of endometrial histology commencing with proliferation followed by secretory change, shedding, and repair. Normal ovarian steroid production is important for nidation and pregnancy. From a clinical perspective, the result is cyclic, predictable, and relatively consistent menstrual blood loss (6).

An intact coagulation pathway is important in regulating menstruation. Menstruation disrupts blood vessels, but with normal hemostasis, the injured blood vessels are rapidly repaired. Restoration of blood vessels requires successful interaction of platelets and clotting factors. Medications, such as warfarin, aspirin, and clopidogrel, can impair the coagulation system and be associated with heavy bleeding.

Pathophysiology

In the absence of ovulation, a corpus luteum does not develop and the ovary fails to secrete progesterone. This results in continual endometrial proliferation without progesterone-withdrawal-induced shedding and bleeding. The clinical result is bleeding that is noncyclic, unpredictable, and inconsistent in volume. The endometrium that develops in the milieu of unopposed estrogen is fragile, vascular, and lacking sufficient stromal support. As one area of bleeding begins to heal, another area begins to slough, which results in erratic bleeding patterns.

Puberty and the perimenopause typically are associated with AUB-O and are considered to be physiologic in these circumstances. In puberty, the immature hypothalamic-pituitary-ovarian axis does not develop the necessary hormonal feedback to result in ovulation and a subsequently stable endometrium. As the perimenopausal transition occurs, progressive oocyte depletion and abnormal follicular development lead to anovulatory cycles.

Establishing the Diagnosis

The evaluation of women with AUB includes a thorough medical history and physical examination, appropriate laboratory and imaging tests, and consideration of age-related factors (3). In order to diagnose AUB-O, structural causes of abnormal bleeding must be excluded. Recognized causes of anovulation are listed in Box 1 and should be considered when evaluating the medical history and physical examination. Patients with AUB-O typically do not experience the breast discomfort, increased mucoid vaginal discharge, or premenstrual cramping and bloating that are characteristic of ovulatory uterine bleeding. In addition, cycles that vary in length by more than 10 days from one cycle to another are likely

anovulatory. If medical therapy fails to resolve bleeding thought to be the result of anovulation, an anatomic cause (including a malignant or premalignant lesion or a coagulopathy) should be reconsidered and the patient re-evaluated. In this document, recommendations are based on the assumption that the diagnosis of AUB-O has been firmly established and endometrial and structural uterine pathology have been ruled out.

A thorough medical history and physical examination will guide the choice of appropriate laboratory studies, diagnostic or imaging tests, and tissue sampling methods. Recommended assessments include the following:

- Pregnancy testing for sexually active women (even those who have had a tubal ligation)
- Sensitive β-hCG level testing to exclude trophoblastic disease in patients who were recently pregnant
- Thyroid-stimulating hormone level assessment to exclude hypothyroidism or hyperthyroidism
- Prolactin level testing (If the level is elevated, the test should be repeated in the fasting state.)
- An endometrial biopsy in women with risk factors for endometrial hyperplasia or malignancy
- Saline infusion sonohysterography, hysteroscopy, or transvaginal ultrasonography may be necessary to rule out an anatomic abnormality

Age-Based Considerations in Evaluation and Management

13-18 Years

Anovulation is the most common etiology of abnormal uterine bleeding during adolescence. During the first 12-18 months after the onset of menstruation, the immaturity of the hypothalamic-pituitary-gonadal axis frequently is the cause of AUB-O. By the third year after menarche, 60-80% of menstrual cycles are 21-34 days long, regardless of age at menarche (7-9). Females with earlier menarche reach regular ovulation sooner than those with delayed menstruation (3). Obesity is becoming an increasingly important contributor to anovulatory cycles in adolescents. Maintaining and achieving ideal body weight are laudable goals during adolescence and may decrease aberrations in menstruation in later life (10). Anovulatory bleeding in teenagers can become excessive, prolonged, and require pharmacologic therapy. Rarely, incessant bleeding can become a medical emergency that requires hospitalization and more intense evaluation and treatment or surgical intervention.

The differential diagnosis of AUB in adolescents is quite similar to that of other age groups, except that the risk of endometrial hyperplasia and malignancy is extremely low. Patients with AUB-O can have a concomitant bleeding disorder. Von Willebrand disease is the most common bleeding disorder in women (11). Adolescents who require hospitalization (ie, those who present with a hemoglobin level of less than 10 g/dL) or require blood transfusion have a 20-30% risk of a coagulopathy (12, 13).

Pregnancy, sexual trauma, and sexually transmitted infections must be ruled out initially, regardless of reported sexual history. Patients also should be evaluated for polycystic ovary syndrome (PCOS) by assessing for signs of hyperandrogenism, such as acne and hirsutism, on physical examination.

Laboratory testing in an adolescent should initially include a measurement of the serum β-hCG level, if the urine pregnancy test result is positive, and a complete blood count with platelets. If the platelets are normal, further testing for a coagulopathy should be considered when significant bleeding or anemia is

present (14). The goals of therapy are to halt abnormal bleeding, prevent its recurrence, avert morbidity, and improve quality of life. For many individuals, the establishment of regular menstruation with a predictable amount of blood flow, duration, and pattern is essential for preserving quality of life. Patients with evidence of iron deficiency should be treated with oral iron therapy. When anemia does not resolve or improve significantly with oral iron therapy, consultation with a blood management team can determine if intravenous iron therapy is needed.

19–39 Years

Polycystic ovary syndrome is one of the most common causes of AUB-O in women of reproductive age. Symptoms may include noncyclic bleeding, hyperandrogenic signs, and characteristic ovarian appearance on ultrasonography (15). Obesity is an important co-morbid condition. Premalignant or malignant endometrial pathology should be considered in these high-risk patients, especially if there is inadequate response to medical therapy.

40 Years to Menopause

Although bleeding changes in women in this age group are largely related to normal menopausal transition, it is important to rule out endometrial hyperplasia and cancer. Perimenopause commences with the onset of cycle irregularity and finishes 1 year after the last menses (16). The mean age of menopause in women in developed countries is 51.4 years. Smokers begin menopause 1.74 years earlier than nonsmokers (17). In North America, the average duration of the menopausal transition is 4 years, and is most often associated with menstrual irregularity.

In perimenopausal women, AUB-O is caused by naturally declining ovarian function. Intermittent anovulation during perimenopause causes recurrent bouts of AUB. Menstrual cycles during menopause can fluctuate between predictable ovulatory bleeding and erratic AUB-O, which can be especially frustrating for the patient.

Pregnancy must be excluded during the evaluation. Pregnancies, although rare, may still occur until 1 full year without menses. Therefore, for women without contraindications, hormonal contraception, rather than hormone therapy, should be used for pregnancy prevention, menstrual control, and alleviation of perimenopausal symptoms in women at risk. Premenopausal use of hormone therapy will not provide menstrual regularity or contraception.

Clinical Considerations and Recommendations

- *When is endometrial evaluation indicated in women of different ages with AUB-O?*

13–18 Years. From 2005 to 2009, the incidence of endometrial cancer in women younger than 20 years was 0.2 per 100,000 women. In the rare case reports of adolescents with endometrial cancer, the clinical history typically includes 2–3 years of abnormal bleeding and obesity (18, 19). Additional endometrial evaluation should be performed if medical treatment has failed after thorough investigation of all potential other causes and co-morbid disorders.

19–39 Years. The incidence of endometrial cancer increases with age. However, the incidence of endometrial carcinoma is still very low in women between the ages of 19 years and 39 years. The risk of endometrial cancer in women aged 20–34 years is 1.6%. In women aged 35–44 years, the rate increases to 6.2%. Among women aged 40 years or younger, risk factors for endometrial cancer include nulliparity, hypertension, body mass index greater than 30, irregular menstruation, and family history (20). Although endometrial carcinoma is rare in women younger than 39 years, patients aged 19–39 years who do not respond to medical therapy or who have prolonged periods of unopposed estrogen stimulation are candidates for endometrial assessment. When endometrial biopsy is nondiagnostic, shows no evidence of hyperplasia or cancer, and the patients fail to respond to medical therapy, office hysteroscopy or saline infusion sonohysterography with further sampling may be appropriate.

40 Years to Menopause. Among women aged 40–50 years, the incidence of endometrial cancer ranges from 13.6 cases to 24 cases per 100,000 women-years and increases to 87.3 cases per 100,000 in women aged 70–74 years (18). Among women younger than 45 years, there is a lower rate of advanced-stage disease, a higher degree of tumor differentiation, and a better prognosis compared with patients older than 45 years (21). Therefore, all women older than 45 years who present with suspected anovulatory uterine bleeding should be evaluated with endometrial biopsy (after pregnancy has been excluded).

- *In women with AUB-O, what is the treatment approach to guide therapy?*

The choice of treatment of AUB-O is guided by the goals of therapy, which may be to stop acute bleeding, avoid future irregular or heavy bleeding, simultaneously provide contraception, and prevent complications, such as anemia, unnecessary surgical intervention, and diminished quality of life. Because AUB-O is an endocrinologic abnormality, the underlying disorder should be treated medically rather than surgically. Surgical therapy is rarely indicated for the treatment of AUB-O, unless medical therapy fails, is contraindicated, is not tolerated by the patient, or the patient has concomitant significant intracavity lesions.

Treatment with exogenous steroids is an important component of medical therapy. Medical treatment options for AUB-O include progestin therapy and combined hormonal contraception. Progestin-only therapies include the levonorgestrel-releasing intrauterine system (levonorgestrel intrauterine device [IUD]), medroxyprogesterone acetate, megestrol acetate, norethindrone acetate, and depot medroxyprogesterone acetate. Combined hormonal contraceptives that include estrogen and progesterone are also effective in the treatment of AUB-O among women without medical contraindications to their use (see *U.S. Medical Eligibility Criteria for Contraceptive Use* available at www.cdc.gov/reproductivehealth/unintendedpregnancy/usmec.htm). Combined hormonal contraceptives include transdermal patches, vaginal rings, and oral contraception. Both approaches offer the benefit of thinning the endometrium and protecting it from hyperplastic transition. In addition, combined hormonal contraceptives, when taken cyclically, induce regular withdrawal bleeding.

A Cochrane review found no randomized trials that evaluated the use of progestins or combined hormonal contraceptives specifically for the treatment of AUB-O (22). However, the levonorgestrel IUD has been shown to be effective in treating AUB and should be considered for all age groups (23, 24). Additionally a study that evaluated 201 women with AUB demonstrated improvements in abnormal menstruation

patterns and physical functioning (eg, exercising, lifting, and self-care) in patients who received oral contraceptives compared with those who received a placebo (25).

- *What medical therapies are most appropriate for each age group?*

13–18 Years. Adolescents with chronic anovulation generally respond well to outpatient medical therapy with exogenous steroids, such as combined hormonal contraceptives. However, if the patient is hemodynamically unstable, has an inability to tolerate an outpatient regimen, or is clinically symptomatic, brief hospitalization (including the use of high-dose estrogen) may be necessary. Evaluation and management of acute uterine bleeding is addressed elsewhere (26).

The interval of menstruation can be extended by administration of continuous combined hormonal contraceptives for several months (avoiding placebo weeks). This regimen permits resolution of anemia, emotional recovery from acute bleeding, and additional imaging studies and consultations if needed. Once the anemia has resolved, a cyclic oral contraceptive or other combined hormonal contraceptive can be prescribed if desired or continuous administration can be maintained. Combined hormonal contraceptives can increase levels of factor VIII and von Willebrand factor, combatting potential underlying coagulopathies. Furthermore, combined hormonal contraceptives suppress ovarian and adrenal androgen production and increase sex hormone–binding globulin, which further reduces bioavailable androgens (27). This ultimately improves symptomatology, such as hirsutism and acne, associated with PCOS. Thus, treatment with a low-dose combination hormonal contraceptive (20–35 micrograms of ethinyl estradiol) remains a mainstay of therapy, especially among anovulatory adolescents with hirsutism and hyperandrogenism.

19–39 Years. Like the adolescent population, women aged 19–39 years also respond to low-dose combined hormonal contraceptive therapy or to progestin therapy, including the levonorgestrel IUD. It is important that contraindications for combined hormonal contraceptives be excluded. Women who present with excessively heavy menstrual cycles and are hemodynamically unstable may benefit from high-dose estrogen therapy (26).

Weight loss and increased exercise are strongly advised in overweight anovulatory women. Several studies have demonstrated a return to ovulatory cycles with sustained weight reduction. It is thought that weight loss leads to a decrease in serum testosterone concentration and resumption of ovulation (28).

40 Years to Menopause. Late perimenopausal patients may be treated with cyclic progestin therapy, low-dose oral contraceptive pills, the levonorgestrel IUD, or cyclic hormone therapy. Each of these therapies offers advantages of menstrual control and endometrial protection. Although only the contraceptive pill and the levonorgestrel IUD provide contraception, the others provide relief from perimenopausal symptoms, such as hot flashes, night sweats, and vaginal atrophy. The choice of therapy often is guided by the patient's priorities in combination with a consideration of safety. In 120 perimenopausal women who were given continuous estrogen and cyclic progestin or cyclic progestin alone, 86% of women in the combined treatment group experienced cyclic menstrual bleeding, as well as a reduction in vasomotor symptoms. In addition, 76% of these women rated their bleeding as normal in amount and duration (29).

The efficacy of the levonorgestrel IUD was evaluated in 56 obese perimenopausal women with AUB. The mean age was 42 years and the mean body mass index was greater than 30. At the 48-month follow-up, the satisfaction rate was 75%; amenorrhea and hypomenorrhea were noted with longer use (30).

- *In patients with AUB-O who have completed childbearing, what are the potential concerns of endometrial ablation treatment?*

  Medical therapy should be considered before surgical therapy. For women who choose a surgical approach, endometrial ablation or hysterectomy should be considered. Patients who choose endometrial ablation therapy should be counseled about the risks regarding the future ability to detect and diagnose endometrial cancer. Furthermore, patients should be educated that endometrial ablation does not provide contraception.

  Endometrial ablation is not recommended as first-line therapy for AUB-O. Physicians must provide thorough informed consent and adequate counseling to women with AUB-O who desire endometrial ablation. When satisfactory endometrial evaluation cannot be reliably performed after endometrial ablation (which is necessary to rule out the possible endometrial cancer) hysterectomy may need to be considered. Women who have completed childbearing, in whom medical therapy has failed, or who have contraindications to medical therapy are candidates for hysterectomy without cervical preservation. In studies not specifically designed for women with anovulatory AUB, a significant improvement in quality of life resulted after hysterectomy compared with medical management (31–34) but the results were equivalent to those women who were treated with the levonorgestrel IUD (34).

  Women with AUB-O treated solely with endometrial ablation are theoretically at risk of the development of endometrial cancer. Endometrial abnormalities that may impede the future evaluation of the endometrial cavity have been documented after ablation (35). Retrospective case series and case reports highlight the difficulty in the evaluation of the endometrium after endometrial ablation (36). Long-term complications that are now being recognized include postablation Asherman syndrome, synechiae, cervical stenosis, contracture of the endometrium, strictures, endometrial distortion, and delay in the detection of endometrial cancer (37). Traditional methods of endometrial surveillance, including endometrial biopsy, hysteroscopy, transvaginal ultrasonography, and saline infusion sonohysterography, may be compromised after endometrial ablation (38, 39). Attempting these procedures after ablation is fraught with patient discomfort, which may preclude thorough assessment (40). Ultrasound-guided operative hysteroscopy also may be impossible because of the presence of dense uterine synechiae.

  No prospective trials have tabulated incidence or risk factors for the development of endometrial cancer after endometrial ablation. Women with AUB-O may have numerous risk factors for endometrial cancer. Endometrial ablation alone does not address any of these underlying risk factors, which leaves the patient at risk of the development of cancer in areas of the endometrium that were not fully ablated. Long-term chronic anovulation treated with endometrial ablation may place a woman at increased risk of the development of endometrial cancer compared with women who are treated with medical therapy (41). A systematic review of the literature to detect cases of endometrial cancer after endometrial ablation, found 22 cases of endometrial cancer (42). Most cases (76.5%) were stage I at diagnosis. The interval from endometrial ablation to endometrial cancer ranged from 2 weeks to 10 years. All but three cases involved patients with known risk factors for endometrial cancer.

- *Can office endometrial biopsy be offered to patients with AUB-O?*

  Office endometrial biopsy for the diagnosis of endometrial hyperplasia or cancer is preferred over dilation and curettage because it is less invasive, safer, and less expensive. However, the sensitivity of office endometrial biopsy is influenced by the type of lesion that is present (focal or diffuse), pathologic diagnosis (intracavitary leiomyoma or polyp), size of the lesion, presence of uterine malformation, volume of pathology, surface area of the endometrial cavity, and number of lesions. The biopsy also may provide information about the hormonal status of the endometrium.

  A meta-analysis noted that the sensitivity of endometrial biopsy was 68% in studies that used hysterectomy and 78% in studies that used dilation and curettage as the reference (43). Additionally, the meta-analysis concluded that there was a 0–54% rate of sampling failure.

  An important limitation of office endometrial biopsy is that it samples an average of 4% of the endometrium with a reported range of 0–12% (44). The failure of office endometrial biopsy in postmenopausal women is particularly concerning. In postmenopausal women in whom the result of the office endometrial sampling was determined to be insufficient, 20% had uterine pathology after a secondary investigation, and 3% of the patients had malignant disease (45).

  A classic study in 1995 demonstrated that endometrial cancer may be focal but that the Pipelle had a reported 83% sensitivity in detecting endometrial cancer (46). A retrospective study of 375 patients found that office-based endometrial biopsy had a low sensitivity for detecting polyps and leiomyomas, only 0.10 compared with 0.33 for diagnosing hyperplasia (47). Lesions that are focal or encompass a small surface area may be missed with office endometrial biopsy.

- *What is the suggested further investigation of women with AUB-O who have failed medical management?*

  Failure of medical management requires further investigation, including imaging or hysteroscopy.

  Hysteroscopy. Hysteroscopy permits full visualization of the endometrial cavity and endocervix and is extremely helpful in diagnosing focal lesions that may be missed with endometrial sampling. Performing hysteroscopy in the office is quick and less expensive than performing it in an operating room setting. Rapid visual inspection permits targeted biopsy and accurate diagnosis of atrophy, endometrial hyperplasia, polyps, leiomyomas, and endometrial cancer. The likelihood of endometrial cancer diagnosis after a negative hysteroscopy result is 0.4–0.5% (48).

  Transvaginal Ultrasonography. Transvaginal ultrasonography is generally not recommended in the virginal patient, and transabdominal imaging is less sensitive and of limited value in the evaluation of the endometrium, but can be used to evaluate other structural abnormalities.

  In premenopausal women, transvaginal ultrasonography ideally should be scheduled between days 4–6 of the menstrual cycle, when the endometrium is the thinnest. In anovulatory women who have no cycle, endometrial thickness alone is not considered a clinically robust observation that can be used to determine management. Endometrial thickness varies during the proliferative phase (4–8 mm), whereas the endometrial echo during the secretory phase ranges from 8 mm to 14 mm (49). One study demonstrated that endometrial thickness alone should not be used to exclude benign endometrial

pathology in premenopausal women because this would miss one out of six intracavitary lesions (50). The study authors advocate the use of saline infusion sonohysterography or hysteroscopy to further evaluate the endometrium in premenopausal women with abnormal bleeding and normal endometrial thickness.

Saline Infusion Sonohysterography. Saline infusion sonohysterography is an office-based imaging procedure that infuses saline into the endometrial cavity during transvaginal ultrasonography to enhance the visualization of intracavitary polyps and myomas (51). Saline infusion sonohysterography has a high sensitivity (ranging from 96% to 100%) and a high negative predictive value (ranging from 94% to 100%) in evaluating the uterus and endometrium for pathology (52, 53).

Saline infusion sonohysterography can determine the presence or absence of intracavitary lesions and depth of myometrial involvement with leiomyomas, and it more accurately evaluates the endometrium compared with transvaginal ultrasonography alone. There are several reasons why transvaginal ultrasonography may miss intracavitary lesions otherwise detected by saline infusion sonohysterography. Small abnormalities may not be visualized on conventional ultrasonography because of a collapsed endometrial cavity. It has been speculated that endometrial polyps may be missed on conventional ultrasonography because the mass conforms to the shape of the endometrial cavity (54).

Saline infusion sonohysterography coupled with endometrial biopsy is a good predictor of the type of surgical or medical intervention that can be offered (55). That is, when the results of saline infusion sonohysterography and endometrial biopsy are both negative, the likelihood of identifying endometrial pathology is low, and conservative options can be offered. This streamlined approach facilitates patient care and minimizes unnecessary surgical intervention. Hysteroscopic surgery is recommended for focal intracavitary or endocervical lesions.

Summary of Recommendations and Conclusions

The following recommendations and conclusions are based on limited or inconsistent scientific evidence (Level B):

- The levonorgestrel IUD has been shown to be effective in treating AUB and should be considered for all age groups.
- Medical treatment options for AUB-O include progestin therapy and combined hormonal contraception.
- Women who have completed childbearing, in whom medical therapy has failed, or who have contra-indications to medical therapy are candidates for hysterectomy without cervical preservation.
- Because AUB-O is an endocrinologic abnormality, the underlying disorder should be treated medically rather than surgically. Surgical therapy is rarely indicated for the treatment of AUB-O, unless medical therapy fails, is contraindicated, is not tolerated by the patient, or the patient has concomitant significant intracavitary lesions.

The following recommendations and conclusions are based primarily on consensus and expert opinion (Level C)

- Failure of medical management requires further investigation, including imaging or hysteroscopy.

- The choice of treatment of AUB-O is guided by the goals of therapy, which may be to stop acute bleeding, avoid future irregular or heavy bleeding, simultaneously provide contraception, and prevent complications, such as anemia, unnecessary surgical intervention, and diminished quality of life.
- Endometrial ablation is not recommended as a first-line therapy for AUB-O. Physicians must provide thorough informed consent and adequate counseling to women with AUB-O who desire endometrial ablation.

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The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1990–January 2013. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician-gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

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.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

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.