Evaluation and Management of Abnormal Uterine Bleeding

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Abnormal uterine bleeding (AUB): focus on women of reproductive age; urine pregnancy test in office or at home usually adequate; causes of AUB frequently hormonal and anatomic; blood dyscrasia and infectious causes rare; AUB refers to any change from normal in volume, duration, regularity, or frequency of uterine bleeding; AUB common reason for patients to visit gynecologist; dysfunctional uterine bleeding related to signals to ovaries from hypothalamus or pituitary, and most commonly caused by anovulatory bleeding from polycystic ovary syndrome (PCOS); other causes midcycle spotting, short follicular phase, and long luteal phase

Menstrual history: document changes in amount, duration, frequency, and regularity of bleeding as perceived by patient; asking whether bleeding heavy or light yields little information; normal cycle 25 to 35 days; change in length of cycle more important than duration of cycle

Menstrual cycle: follicle grows in response to follicle-stimulating hormone (FSH); ovulation typically occurs at day 14 in 28-day cycle; ovulation accompanied by spike in luteinizing hormone (LH) in response to rise in estrogen on approximately day 12; level of progesterone (P) low (<3 ng/dL) in first half of cycle, and peaks near time of ovulation, when embryo may implant; in absence of pregnancy, P falls; if pregnancy occurs, P level remains high and rises; withdrawal of P triggers shedding of endometrium; women who do not ovulate do not make P, and have no fall in P to stimulate menses; irregular cycles normal in women ≤19 yr of age before hypothalamic-pituitary axis established; can treat with oral contraceptives (OC); during perimenopausal transition, which can last 6 yr, irregular cycles normal as oocytes depleted

History and examination: assess activities of daily living, pain, other medical conditions, and coagulopathy; evaluate general health; examine breast to rule out galactorrhea or hyperprolactinemia; on pelvic examination, look for vaginal atrophy, confirm site of bleeding, do Papanicolaou test as indicated, and look for increased uterine size due to fibroids or adenomyosis

Laboratory tests: obtain complete blood cell count (CBC); disorders of thyroid and prolactin can cause ovulatory dysfunction; like FSH and LH, thyrotropin (TSH) and prolactin from anterior pituitary; problem in brain can cause abnormalities of production in hypothalamus and pituitary that affect TSH and prolactin; correcting abnormal TSH or prolactin might resolve uterine bleeding; perform cervical cultures if concerned about infection; can screen for bleeding disorders

Imaging: hysteroscopy best way to view inside of uterus; can also do saline infusion sonohysterography to look for polyp or intracavitary fibroid; magnetic resonance imaging of pelvis not indicated (except to look for adenomyosis or fibroids in preparation for surgery)

Tissue sampling: if concerned about cancer or precancerous condition, perform endometrial biopsy

Diagnosis: PALM-COEIN (polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified) classification system for AUB from International Federation of Gynecology and Obstetrics (FIGO); PALM refers to structural causes of AUB visible on imaging or histopathology

Polyps: inflamed, hypertrophic overgrowths of endometrium; typical findings regular menses with spotting after intercourse or at irregular intervals; polyps not always apparent on ultrasonography (US), but visible on sonohysterography in which sterile saline injected into cavity before performing vaginal US; hysteroscopy best method for detecting and treating polyps

Adenomyosis: endometriosis within myometrium; painful because endometrial glands shed into muscle; common in premenopausal period; often improves at menopause; patients typically have cyclic bleeding; uterus enlarged and tender; patients can have painful intercourse; rarely causes bleeding between periods; visible on US; OC effective because progesterin-dominant OC shrink endometrium; can also treat with levonorgestrel-releasing intrauterine device (LNG-IUD); hysterectomy only effective surgical treatment

Leiomyoma: benign in 99.9% of cases; more common in blacks than whites; patients can have regular, cyclic bleeding, but menses heavy or increased in duration; intramural and subserosal fibroids less likely to cause AUB than submucous and intracavitary fibroids; saline infusion sonohysterography or hysteroscopy superior to US; OC good treatment for intracavitary fibroids because they cause atrophy of endometrium; nonsteroidal anti-inflammatory drugs used for pain; uterus artery embolization (UAE) useful for poor surgical candidates; UAE causes atrophy of entire uterus, so avoid in women who desire future childbearing; can remove intracavitary fibroids during outpatient hysteroscopy, or perform myomectomy or hysterectomy; after removal, growth of some fibroids likely to continue, and new fibroids can grow

Malignancy and endometrial hyperplasia: requires tissue diagnosis; rare in young women except in cases of chronic anovulation (eg, PCOS); condition more common in perimenopausal

Educational Objectives

The goal of this program is to improve diagnosis and treatment of abnormal uterine bleeding (AUB) and breast disease. After hearing and assimilating this program, the clinician will be better able to:

1. Diagram the changes in pituitary and ovarian hormones throughout the menstrual cycle.
2. Select imaging modalities for patients with AUB based on historical features and findings on physical examination.
3. Create a chart of causes of AUB and accompanying treatments.
4. List the differential diagnosis of a breast mass.

5. Discuss the relationship between lactation and breast cancer.

Faculty Disclosure

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women; no guidelines on when to biopsy, but consider in women >35 yr of age with AUB or >1 episode of postmenopausal bleeding; do biopsy or US of endometrial lining; biopsy if lining >5 mm in thickness; no clear guidelines on whether to do biopsy or US; treat hyperplasia with 3- to 6-mo of P using 10 mg daily medroxyprogesterone (Provera), or LNG-IUD

**Coagulopathy:** history helpful; usually diagnosed in younger women; patients have regular menses, but bleeding heavy or prolonged; can use validated clinical questionnaire to assess whether more testing needed; ask about history of bleeding with dental procedures, nosebleeds, bruising, bleeding from gums, and family history of bleeding; if history suggests hemorrhagic diathesis, check CBC, prothrombin time, partial thromboplastin time, and ristocetin cofactor; tests for coagulopathy changing and improving, so consider referral to hematologist if coagulopathy suspected; treat with continuous OC, LNG-IUD, desmopressin, or tranexamic acid (procoagulant; do not administer with OC)

**Ovulatory dysfunction:** PCOS most important disorder; other causes include disorders of thyroid hormones and prolactin, premature ovarian failure, other diseases of pituitary, and medications; **prolactin** — slightly high prolactin levels cause short luteal phase and more frequent periods; higher levels cause anovulation and irregular bleeding; with extremely high levels, amenorrhea likely; look for galactorrhea; even if prolactin level normal, if patient has ovulatory dysfunction and galactorrhea, treat with bromocriptine; **diagnosis of PCOS** — per Rotterdam criteria, PCOS diagnosed if 2 of 3 criteria present; criteria include irregular or no periods, hyperandrogenism (eg, hirsutism), and polycystic ovaries on US; using these criteria, ≤15% of population has PCOS; 6% to 10% probably more accurate estimate when criteria for US used less frequently, as in United States; 90% of patients with PCOS have abnormal menses and 70% have hirsutism; acne and alopecia less useful as predictors; if diagnosis in doubt, can measure testosterone (T) to look for hyperandrogenism; **US** — many normal women have polycystic-appearing ovaries but no other features of PCOS; US not needed to diagnose woman with irregular periods and hirsutism; **hormone levels** — women with PCOS have low P levels; endometrium grows without shedding and becomes hyperplastic; levels of FSH do not vary; levels of estrogen in high to normal range; levels of LH do not vary; T normal or high; in ethnic groups with few hair follicles, measuring T may aid in diagnosis of PCOS primarily clinical diagnosis; diagnostic criteria; ratio of LH to FSH not needed for diagnosis; **tests other than hormone levels** — PCOS ovarian ultrasound; check glucose tolerance test or hemoglobin A1c, and lipids in patient with PCOS; perform endometrial biopsy if concerned about hyperplasia; **congenital adrenal hyperplasia (CAH)** — 1% to 4% of whites in United States have CAH; measure 17-hydroxyprogesterone only if patient Hispanic, Mediterranean, Slavic, or Ashkenazi Jewish and has severe hirsutism, or had hirsutism at time of menarche or before menarche; **Cushing syndrome** — rare; patient likely to also have moon facies, buffalo hump, hypertension, and diabetes; **treatment** — depends on goal of patient; to correct menstrual abnormalities, treat with OC or cyclic P; to treat hyperandrogenism, decrease levels of T with OC and add spironolactone 200 mg daily for 6 mo if needed; refer for infertility issues; metformin helps with diabetes and cardiovascular disease; reducing weight by 2% to 5% and eating low-carbohydrate diet improves metabolic and reproductive function

**Endometrial causes:** rare; includes postpartum endometritis and endometritis after abortion; in teenagers, pelvic inflammatory disease can present as abnormal bleeding; obtain cultures, assess pain on examination, and check white blood cell count if necessary

**Iatrogenic causes:** some antidepressants alter ovarian function via effects on serotonin or dopamine; therapeutic doses of warfarin and heparin usually do not cause AUB; **Ginkgo biloba**, ginseng, and motherwort can cause ovulatory dysfunction and AUB

**Not yet classified:** rare cause of AUB

**Summary:** when cause of AUB structural (ie, PALM), frequency of bleeding normal; intermenstrual bleeding possible if polyp or hyperplasia present; consider US in patients with heavy but regular menses who may have adenomyosis or leiomyoma; if regularity of cycles in question, chart basal body temperature or menstrual calendar for 2 mo; **OC** — patients with benign breast disease and varicose veins may take OC, but avoid in patients with severe problems of liver or heart; well-controlled diabetes not contraindication to OC; migraine with aura (but not regular headaches) contraindication to OC; antibiotics could decrease effectiveness of OC

### Diagnosing and Managing Fibrocystic Breast Disease

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**Evaluation:** describe breast mass and its location thoroughly using clock position and distance from nipple; determine whether mass superficial or deep, denote size, and describe as diffuse or well circumscribed, fixed or mobile, fluctuant, uniform, or tender; note nipple discharge and lymphadenopathy

**Fibrocystic change:** imprecise term describing heterogeneous group of benign, nonproliferative lesions; masses often not discrete; typically fibroglandular (nodular), symmetric, and tender to palpation; can present with pain (often cyclic and worse before menses); best time to examine 5 days after onset of menses, when breasts least influenced by hormones; typical location, upper outer quadrant, but can occur anywhere in breast

**Cyst:** most common nonproliferative mass; usually occur in women 35 to 50 yr of age; uncommon in younger women and postmenopausal women; recurrent problems most common in perimenopausal women, and usually resolve after menopause; in younger women, microcysts may be seen on US or mammography; cysts visible on US using musculoskeletal or superficial soft tissue setting; clear area without septation or solid components confirms simple, benign cyst; alternatively, aspiration of clear yellow to straw-colored fluid with no blood and resolution of mass after aspiration confirms simple cyst; for complex cyst with septations or other unusual appearance, refer patient for diagnostic imaging to rule out malignancy

**Galactoceles:** milk-filled cyst associated with lactation; have patient pump, nurse, and use warm compresses; aspiration introduces risk for milk fistula

**Fat necrosis:** benign mass after blunt trauma, surgery, injection, or radiation; mass irregular, hard, and granular

**Other nonproliferative masses:** treat lipoma and sebaceous cyst as for other areas of body; if removing lipoma, consider surgical consultation to minimize scarring; **breast abscess** — usually occurs in lactating women; treat with drainage and antibiotics, or aspirate, then follow carefully

**Fibroadenoma (FA):** solid with fibrous and glandular components; most FAs simple and do not require removal; usually occur in younger women; can grow with exposure to estrogen from use of oral contraceptives (OC) or during pregnancy; FA not contraindication to OC; no risk for breast cancer if FA not complex and no adjacent proliferative disease; despite classic features on imaging, most biopsies to confirm diagnosis; excise complex tumors; juvenile FA — occurs at 10 to 18 yr of age; tumors have increased glandularity and cellularity compared with simple FA; remove, but avoid damage to developing breast

**Adenoma:** epithelial tumor similar to FA but without fibrous component; does not increase risk for breast cancer; lactating adenoma — occurs in lactating women; confirm diagnosis with core biopsy; however, biopsy can result in milk fistula
Steroids: Suggested Reading


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1. Dysfunctional uterine bleeding is most closely related to _______ and thus distinguished from abnormal uterine bleeding.
   (A) Change in volume of uterine bleeding
   (B) Change in duration of uterine bleeding
   (C) Change in regularity or frequency of uterine bleeding
   (D) Signaling from hypothalamus or pituitary to ovaries

2. Which of the following is the best way to view the inside of the uterus?
   (A) Ultrasonography
   (B) Saline infusion sonohysterography
   (C) Hysteroscopy
   (D) Magnetic resonance imaging

3. Regular menses with spotting between periods suggests:
   (A) Adenomyosis
   (B) Leiomyoma
   (C) Endometrial hyperplasia
   (D) Endometrial polyp

4. All the following are considered treatment options for adenomyosis, except:
   (A) Myomectomy
   (B) Hysterectomy
   (C) Levonorgestrel-releasing intrauterine device
   (D) Oral contraceptives

5. Benign in 99.9% of cases, _______ is more common in blacks than whites, and affected patients can have regular, cyclic bleeding with heavy menses.
   (A) Adenomyosis
   (B) Leiomyoma
   (C) Endometrial hyperplasia
   (D) Endometrial polyp

6. A patient with extremely high prolactin levels is most likely to present with:
   (A) Short luteal phase
   (B) Frequent menses
   (C) Irregular bleeding
   (D) Amenorrhea

7. Which of the following is the most common nonproliferative mass of the breast?
   (A) Fibrocystic change
   (B) Cyst
   (C) Fat necrosis
   (D) Galactocele

8. On ultrasonography of the breast, a clear area without septation or solid components is adequate to confirm the presence of a benign cyst.
   (A) True
   (B) False

9. Which of the following is the correct treatment for a phyllodes tumor of the breast?
   (A) Aspiration
   (B) Core biopsy, followed by close observation
   (C) Wide local excision
   (D) Incision and drainage

10. Lactation and breast-feeding _______ the risk for breast cancer later in life.
    (A) Increase
    (B) Decrease
    (C) Do not change