

32nd Annual Charleston APRN Conference

Case Based Approach to Abnormal Uterine Bleeding

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Learning Objectives

- Implement current diagnostic recommendations for endometrial cancer in women who present with postmenopausal bleeding
- Formulate a treatment plan for women with abnormal uterine bleeding including heavy menstrual bleeding and amenorrhea
- Evaluate patients based on their treatment choice, tolerance, and clinical risk profile when selecting a therapeutic intervention for the management of heavy menstrual bleeding

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How Each Case Will Work

- Step 1: Case set-up
- Step 2: Case questions and discussion
 - Write down your answers
- Step 3: Closure/Wrap-up/Q&A
- Note – Some answers may vary



Courtesy of Wikimedia and Aryanaslami

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FIGO AUB Definitions of AUB Symptoms

Frequency	Amenorrhea - absent
	Infrequent (>38 days)
	Normal
	Frequent (<24 days)
Duration	Normal (≤8 days)
	Prolonged: (>8 days)
Regularity	Normal (Shortest to longest cycle variation ≤7-9 days)
	Irregular (Shortest to longest cycle variation >8-10 days)
Flow Volume	Light
	Normal
	Heavy
Intermenstrual bleeding	None
	Random
	Cyclic - early cycle
	Cyclic - mid cycle
	Cyclic - late cycle

Munro, M.G., et al. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. Int J Gynecol Obstet. 2018 143: 393-406.

Menorrhagia and metrorrhagia were replaced with the nomenclature heavy menstrual bleeding (HMB)

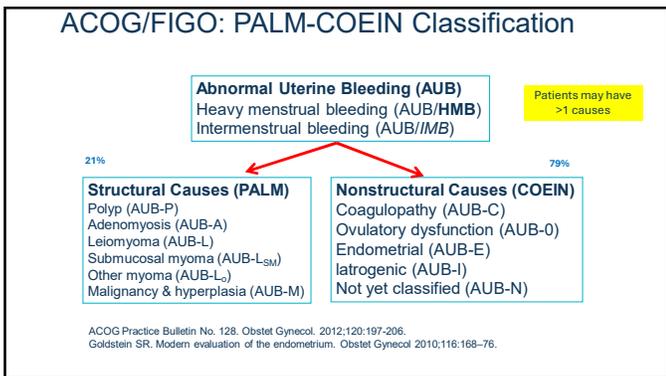
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ACOG/FIGO: PALM-COEIN Classification

- Introduced in 2011 by the International Federation of Gynecology and Obstetrics (FIGO)
- PALM – structural etiologies
 - Polyp, adenomyosis, leiomyoma, malignancy and hyperplasia
- COEIN - nonstructural etiologies
 - Coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, not otherwise classified
- ACOG supports the PALM-COEIN nomenclature system

Wouk N, Helton M. Abnormal Uterine Bleeding in Premenopausal Women. Am Fam Physician. 2019 Apr 1;99(7):435-443.

5



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ARS Question 1

An 18-year-old female presents to establish care after moving from Colorado. She has a 3-month history of amenorrhea. She had normal periods until this time, with menarche at age 12 years. She denies any voice changes, excess body hair, cold or heat intolerance, unusual fatigue or weakness. Pregnancy test negative. What is your next step?

- A. TSH and prolactin levels
- B. MRI of the brain
- C. Progesterone challenge test
- D. Estrogen and progesterone challenge test



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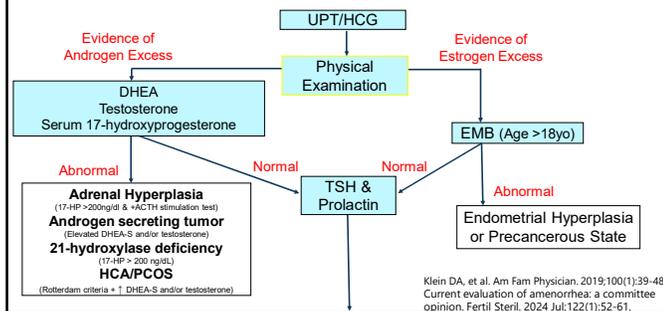
Causes of Amenorrhea

- List of potential causes of amenorrhea is long
- Most cases are accounted for by six conditions
 - Polycystic ovary syndrome (PCOS)
 - Hyperprolactinemia
 - Thyroid dysfunction
 - Hypogonadotropic and hypergonadotropic hypogonadism
 - Anatomic abnormalities

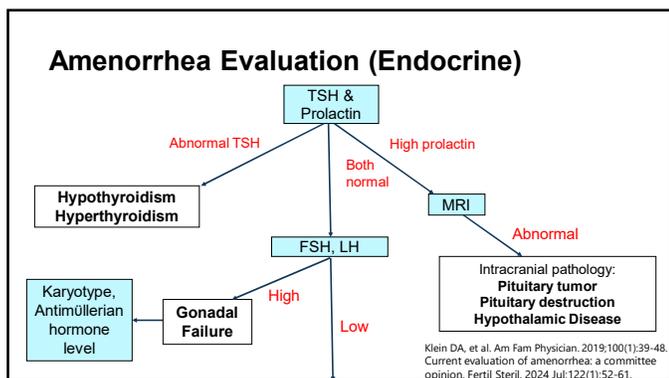
Lebduska E, et al. Abnormal Uterine Bleeding. Med Clin North Am. 2023;107(2):235-246.

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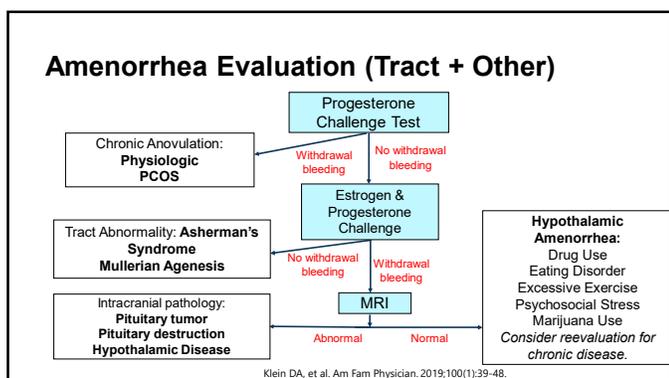
Amenorrhea Evaluation



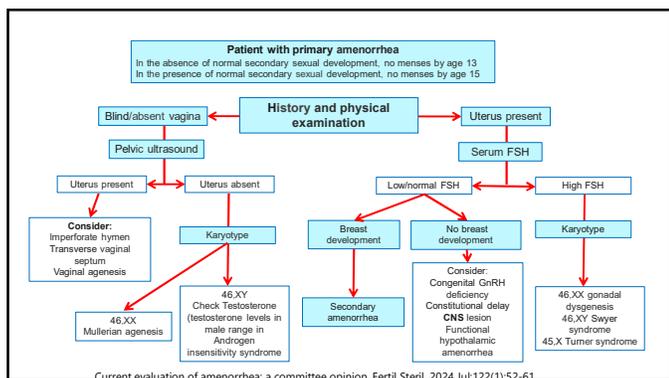
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Interpretation of Laboratory Studies for Amenorrhea										
	17-HP	anti-Müllerian hormone	DHEA-S	Estradiol	LH (IU per L)	LH/ FSH	FSH (IU per L)	Prolactin	Testosterone	TSH
Congenital adrenal hyperplasia	High	Normal	High normal	Low	< 15	> 1	< 10	Normal	High	Normal
Functional hypothalamic amenorrhea	Normal	High	Normal	Low	< 10	~ 1	< 10	Low normal	Low normal	Low normal
Hyperprolactinemia	Normal	Normal	Normal /sl. high	Low	< 10	> 1	< 10	High	Normal	High or normal
Menopause	Normal	Low	Normal	Low	> 15	< 1	> 15	Normal	Low normal	Normal
Polycystic ovary syndrome	Normal	Normal or high	High normal	Low	< 15	> 1	< 10	High normal	High or high normal	Normal
1° ovarian insufficiency	Normal	Low	Normal	Low	> 15	< 1	> 15	Normal	Low normal	Normal

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ARS Question 2

26-year-old female presents with a 3-month history of "spotting." She previously had normal periods. Bleeding is irregular, for a few days at a time, ~2x per month. She has no other complaints. Screening is up to date. After a negative pregnancy test, the next action should be:

- A. EMB
- B. Start treatment
- C. Perform uterine ultrasound



Courtesy of Wikimedia Commons/Wjbalubadubdub

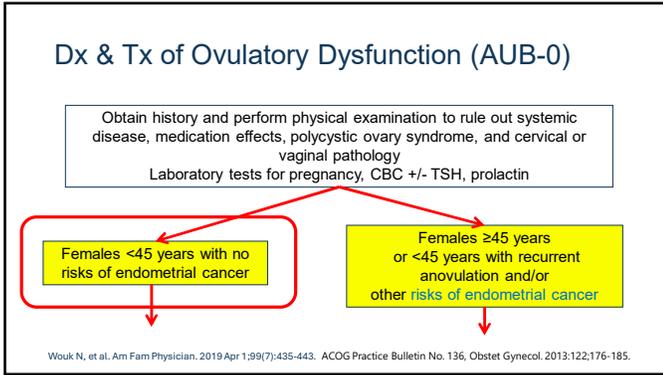
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Determination of Ovulatory Status

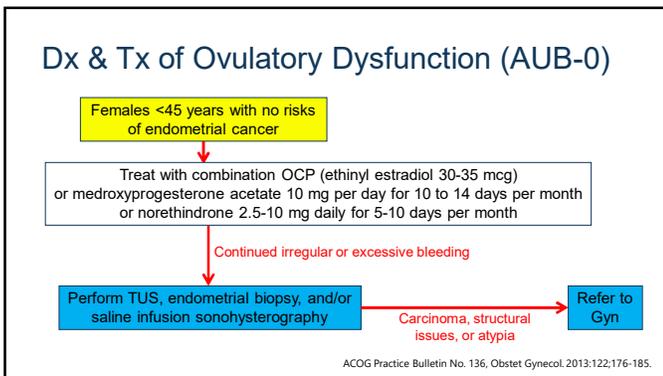
- Ovulation - predictable cyclic menses every 24–38 days
- **Ovulatory disorder bleeding** is typically irregular in timing & flow
 - Often interspersed with episodes of amenorrhea
 - AUB related to an ovulatory disorder categorized as **AUB-O**
- If uncertain, measurement of serum progesterone timed to the best estimate of mid-luteal phase
- **Endometrial biopsy** used to evaluate for the presence of hyperplasia, premalignant or malignant endometrial change
 - Not recommended as a diagnostic method for ovulatory status

Munro, M.G., et al. Int J Gynecol Obstet, 2018 143: 393-408.

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- ### Contraindications to COCP
- Previous Stroke
 - Current or history of ischemic heart disease
 - Migraine with aura
 - Smoking >15 cigarettes/day or are smokers >35 years old.
 - Severe cirrhosis or liver tumor
 - Uncontrolled hypertension (>160/100 mmHg)
 - <21 days post-natal
 - Current breast cancer or breast cancer <5 years ago
 - History of deep vein thrombosis
 - Major surgery with prolonged immobilization - should stop estrogen containing contraceptives before 4-6 weeks
 - Anticonvulsants including phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine and lamotrigine
- Jewson M, et al. Progesterone and abnormal uterine bleeding/menstrual disorders. Best Pract Res Clin Obstet Gynaecol. 2020;69:62-73

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ARS Question 1

63-year-old female presents with an episode of vaginal bleeding. Menopause at age 56. She complains of "abdominal bloating," but otherwise feels normal. Screening is up to date. She denies postcoital bleeding. Which of the following is NOT an appropriate next step?

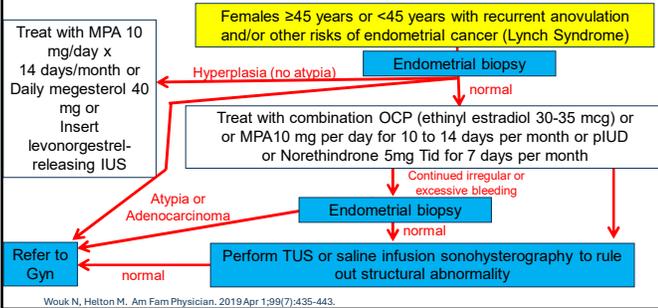
- A. EMB
- B. Start treatment
- C. Perform uterine ultrasound
- D. Perform uterine hysteroscopy



Courtesy of Wikimedia & Christopher Michel

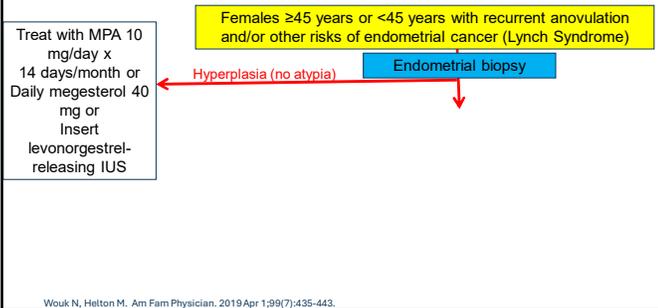
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Dx & Tx of Endometrial (AUB-E) Bleeding

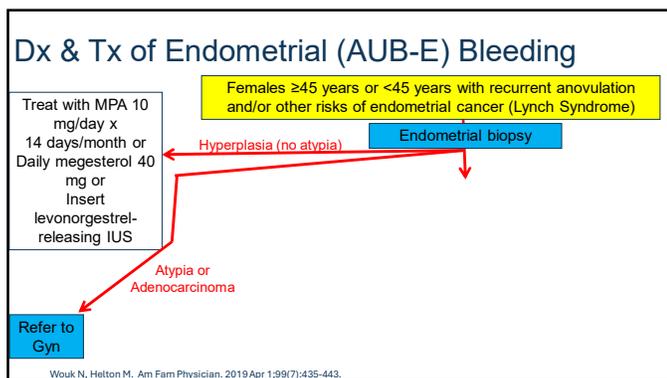


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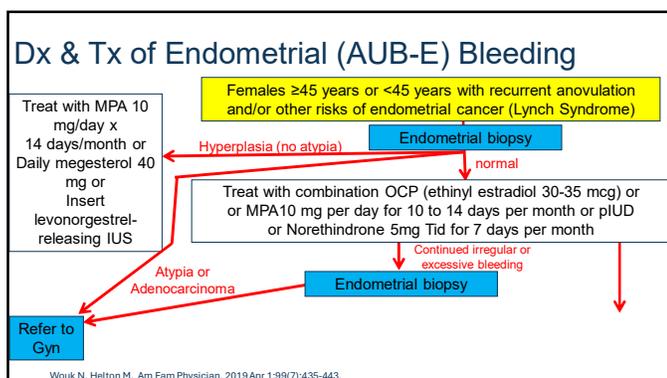
Dx & Tx of Endometrial (AUB-E) Bleeding



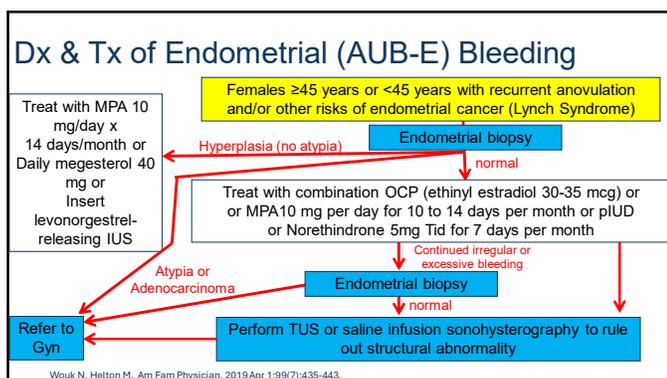
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Comparison of Imaging/Tissue Sampling for Endometrial Pathology

Test	Effectiveness
Endometrial biopsy	91% sensitive and 98% specific for detecting cancer 82.3% sensitive and 98% specific for detecting hyperplasia with atypia
Office hysteroscopy	94% sensitive and 89% specific for intracavitary abnormality
Saline infusion sonohysterography	88-99% sensitive and 72-95% specific for detecting intracavitary abnormality in premenopausal women
Transvaginal ultrasonography	Less sensitive and specific than saline infusion sonohysterography 60-92% sensitive and 62-93% specific for intracavitary abnormality in premenopausal women

ACOG PB 128. Obstet Gynecol 2012;120:197-206.

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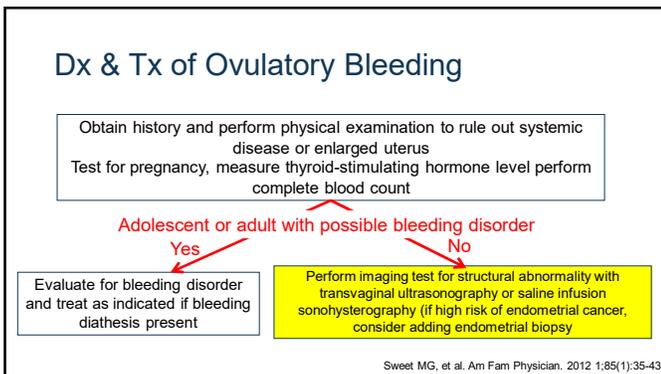
Endometrial Biopsy for Adolescents

- Rarely required
- Should be reserved for adolescents with **unresponsive** uterine bleeding
- AUB histology = disordered proliferative pattern without secretory activity (no progesterone effect)
- EMB with hormonal therapy = hormonal effects and may interfere with biopsy interpretation

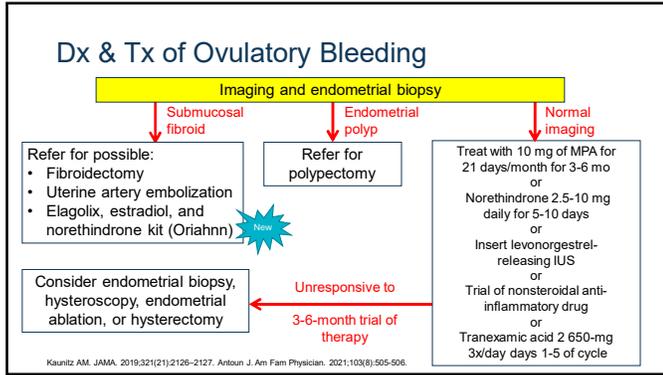


Courtesy of Dr. E.J. Mayeaux, Jr.

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AUB type	Pattern	Potential causes	Treatment options
Cyclical or ovulatory (Predictable)	Heavy menstrual bleeding	Adenomyosis, fibroids, copper intrauterine device, coagulation disorders	Hormone therapy (oral or intrauterine), NSAIDs, tranexamic acid, iron supplements, endometrial ablation, uterine artery embolization, hysterectomy
Nonscyclical (Unpredictable)	Ovulatory dysfunction	Polycystic ovarian syndrome	Hormonal therapy
	Iatrogenic	Hormonal contraceptives	Expectant management, try alternative contraceptive
	Intermenstrual	Endometrial polyp, submucosal fibroid, Infection (endometritis)	Hysteroscopy Antibiotics
	Postcoital	Cervical polyp Cervicitis Malignancy	Polyp removal Antibiotics Refer to specialist

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Etiology of HMB in Adolescents

Etiologies	n	Percent
Indeterminate	1030	45.9
Ovarian Uterine Disorders	532	23.7
Coagulation Disorders	436	19.4
Platelet Disorders	140	6.23
Unspecified Bleeding Disorder	46	2.05
Drug Induced Bleeding	16	0.712
Bleeding Secondary Renal Disease	11	0.49
Infection	10	0.445
Isolated Increased Bleeding Time	8	0.356
Chemotherapy Recipient	5	0.223
Exon 28 Polymorphism	4	0.178
Fanconi Anemia	3	0.134
Aplastic Anemia	2	0.089
Ehlers Danlos Syndrome	2	0.089
VWD and Platelet Dysfunction	1	0.0445

Hall EM, et al. BMC Womens Health. 2024 Feb 20;24(1):136.

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Adult Heavy Menstrual Bleeding Etiology

Meta-analyses with 53 studies and 41,541 patients

Overall bleeding disorders prevalence	30% (95% CI, 14-46)
von Willebrand disease	8% (95% CI, 7-10)
Platelet function defect	9% (95% CI, 7-12)
Abnormal thyroid	3% (95% CI, 0-6)
Polycystic ovarian syndrome	8% (95% CI, 4-12)
Bleeding disorders in adults	16% (95% CI, -8 to 41)
Bleeding disorders in adolescents	39% (95% CI 18-60)

Comishen KJ, et al. Etiology and diagnosis of heavy menstrual bleeding among adolescent and adult patients: a systematic review and meta-analysis of the literature. J Thromb Haemost. 2025 Mar;23(3):863-876.

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Screening for Systemic Hemostasis Disorders

1. Heavy menstrual bleeding since menarche
2. One of the following:
a Postpartum hemorrhage
b Surgical related bleeding
c Bleeding associated with dental work
3. Two or more of the following symptoms:
a Bruising 1–2 times per month
b Epistaxis 1–2 times per month
c Frequent gum bleeding
d Family history of bleeding symptoms

- 90% sensitivity for detection of common coagulopathies
- If positive
 - Hematologist consult
 - Test for von Willebrand factor, Ristocetin cofactor, partial thromboplastin time (PTT)
 - Categorized as having AUB-C
- AUB + anticoagulant = AUB-I

Munro, M.G., et al. Int J Gynecol Obstet, 2018 143: 393-408. Kouides PA, et al. Fertil Steril. 2005;84:1345-1351.

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Screening for Systemic Hemostasis Disorders

- Tool demonstrated to have 90% sensitivity for the detection of coagulopathies
- For those with a positive screening result, further testing is necessary, often following consultation with a hematologist
- von Willebrand factor, Ristocetin cofactor, partial thromboplastin time (PTT) and other measures
- If the results are positive, the woman with AUB would be being categorized as having AUB-C
- Previously, by convention, individuals with AUB associated with the use of anticoagulant are included in the AUB-I category

Munro, M.G., et al. Int J Gynecol Obstet, 2018 143: 393-408.

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Testing for Specific Coagulopathies

Initial Testing for Coagulopathies:

1. Complete blood count
2. PT, PTT
3. Fibrinogen
4. Von Willebrand panel (von Willebrand factor antigen level, Ristocetin cofactor, factor VIII level)

For rare bleeding disorders:

1. Alpha-2-antiplasmin activity
2. Euglobulin clot lysis time
3. Tissue plasminogen activator level
4. Plasminogen activator inhibitor-1

Additional specific tests:

1. Peripheral blood smear
2. Platelet aggregation study (adenosine diphosphate, epinephrine collagen)
3. Platelet aggregometry
4. Coagulation factor assays
5. Clot solubility testing
6. Tests of fibrinogen function (Fibrin Split Products, D-dimer level)

Bacon JL. *Obstet Gynecol Clin North Am.* 2017;44(2):179-193.

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Observe vs. Treat with HRT

- Decision for adolescents depends upon ¹
 - Severity and chronicity of the DUB
 - Patient considerations
 - Guardian considerations
- The primary purpose of hormonal treatment is to stabilize endometrial proliferation and promote cyclic shedding
- > 90% of adolescents respond to hormonal treatment ²

1. Slap GB. *Best Pract Res Clin Obstet Gynaecol.* 2003; 17:75. 2. Strickland JL. *Obstet Gynecol Clin North Am.* 2003; 30:321.

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AUB: Urgent Management

- Conjugated equine estrogen
 - 25 mg intravenously every 4 to 6 hours for up to 24 hours
 - 2.5 mg orally every 6 hours for 21 days
- Estrogen-progestin oral contraceptives
 - 1 35 mcg of ethinyl estradiol monophasic pill orally TiD for 7 days
- Norethindrone, 5 mg orally TiD for 7 days
- Tranexamic acid 10 mg per kg IV every 8 hours or 20 to 25 mg per kg orally every 8 hours

Wouk N, Helton M. *Abnormal Uterine Bleeding in Premenopausal Women.* *Am Fam Physician.* 2019;99(7):435-443.

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Chronic Bleeding Management

- Depot medroxyprogesterone (Depo-Provera) 150 mg intramuscularly or 104 mg subcutaneously every 13 weeks
- Estrogen-progestin oral contraceptives 1 monophasic pill containing 35 mcg of ethinyl estradiol daily
- Levonorgestrel 52-mg (20-mcg-per-day) intrauterine device (Mirena)
- Naproxen, naproxen 500-1000mg / day starting at the onset of bleeding
- Norethindrone 2.5 to 5 mg orally once daily
- Tranexamic acid (Lysteda) 1,000 to 1,500 mg orally 3 times daily

Wouk N, et al. Abnormal Uterine Bleeding in Premenopausal Women. Am Fam Physician. 2019;99(7):435-443.

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AUB With Hormonal Contraception

- LNG IUDs: Counsel patients most will experience a reduction in bleeding within 12 months
- LNG IUDs: Prescribe naproxen 500 mg twice per day for 5 days
- LNG IUDs: estradiol (2 mg/day for 6 weeks)
- DMPA: Counsel patients most will experience amenorrhea or lighter menses with continued use after six to 12 months
- Progestin implant/DMPA: Consider prescribing daily OCPs
- CHC: Increase dose of ethinyl estradiol
- Continuous use CHC: Add a 4- or 5-day hormone-free interval

Schrager S, et al. Abnormal Uterine Bleeding Associated With Hormonal Contraception. Am Fam Physician. 2024;109(2):161-166.

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Patients with Increased Thrombosis Risk

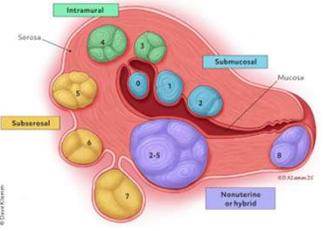
- Levonorgestrel-releasing intrauterine device [LNG 52 mg IUD, Mirena or Liletta] first-line method
 - Results in a low level of systemic progestin absorption but has not been associated with an elevated risk of venous thromboembolism (VTE)^{1, 2}
- Estrogen-containing therapies are generally avoided³
- The US Medical Eligibility Criteria for Contraceptive Use classifies progestin-only methods as having "advantages that generally outweigh the theoretical or proven risks" with a history of VTE³
 - Package labeling for norethindrone acetate, medroxyprogesterone acetate, and depot medroxyprogesterone acetate list a history of VTE as a contraindication
- TXA is contraindicated in some patients with increased risk of thrombosis.

1. Lukes AS, et al. Fertil Steril 2008; 90:673. 2. Cockrum RH, et al. Obstet Gynecol 2022; 140:477. 3. Nguyen AT, et al. 2024. MMWR Recomm Rep 2024; 73:1.

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FIGO Uterine Fibroids Classification

0: Pedunculated, completely inside the mucosal cavity
 1: < 50% intramural
 2: ≥ 50% intramural
 3: 100% intramural, but still contacting the mucosa
 4: Completely intramural
 5: Subserosal ≥ 50% intramural
 6: Subserosal < 50% intramural
 7: Pedunculated subserosal
 8: Nonuterine



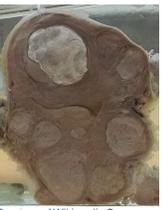
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 © 2015 KlineCorporation

Keating MK, et al. Uterine Fibroids: Rapid Evidence Review. Am Fam Physician. 2025 Oct;112(4):393-400.

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Medical Treatment of Uterine Myomas

- GnRH agonists (buserelin, goserelin, leuprolide, nafarelin)
- GnRH antagonists (elagolix [Orilissa], relugolix [Orgovyx])
- Hormonal contraceptives
- 52-mg levonorgestrel-releasing intrauterine device
- Nonsteroidal anti-inflammatory drugs
- Selective progesterone receptor modulators (mifepristone, ulipristal [Ella])
- Tranexamic acid



Courtesy of Wikimedia Commons

Keating MK, et al. Uterine Fibroids: Rapid Evidence Review. Am Fam Physician. 2025 Oct;112(4):393-400.

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Uterine Fibroid Surgical Therapies

- Myomectomy
- Embolization
- MR-guided ultrasound surgery
- Hysterectomy
- Endometrial ablation
- MR-guided ultrasound surgery
- Radiofrequency ablation
- Hysterectomy



Courtesy of Wikimedia Commons

Keating MK, et al. Uterine Fibroids: Rapid Evidence Review. Am Fam Physician. 2025 Oct;112(4):393-400.

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Surgery vs. Medical Therapy for Heavy Menstrual Bleeding

- Surgery, especially hysterectomy, reduces menstrual bleeding more than medical treatment at one year
- No conclusive evidence of satisfaction difference between LNG-IUS and surgery, although adverse effects (bleeding and spotting) are more likely
- Oral medication suits a minority of women in the long term, and the LNG-IUS device provides a better alternative to surgery in most cases
- Hysterectomy is a definitive treatment but can cause serious complications for a minority of women
 - Most women are well-advised to try a less radical treatment first-line
- LNG-IUS and surgery appear to be safe, acceptable and effective

Marjoribanks J, et al. Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD003855.

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The Cost of AUB Workup

- 90-day median cost for AUB workup and management was \$2279 (IQR \$512–4828)
- Among patients with a diagnostic biopsy, median 90-day costs:
 - \$2203 (IQR \$499–3604) for benign or disordered proliferative endometrium (DPE) diagnosis
 - \$21,039 (IQR \$19,084-24,536) for a diagnosis of EC
- Costs were standardized and inflation-adjusted to 2017 US Dollars (USD)

Warring SK, et al. The cost of diagnosing endometrial cancer: Quantifying the healthcare cost of an abnormal uterine bleeding workup. Gynecol Oncol. 2022 Jan;164(1):93-97

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Evaluation of Patient with AUB

- | | |
|---|---|
| <p>1. Assessment of bleeding:</p> <ul style="list-style-type: none"> a. Acute or chronic? b. Pattern: Regular, irregular bleeding or unscheduled bleeding c. Amount: <ul style="list-style-type: none"> i. Compared with prior periods ii. Presence of blood clots and menstrual accidents iii. Pictorial blood loss <p>2. Assessment of bleeding:</p> <ul style="list-style-type: none"> a. Document change in health-related quality of life b. Document patient interest in contraception and future fertility <p>3. Review medication to detect any iatrogenic causes of abnormal uterine bleeding</p> <p>4. Screen for coagulopathy using a validated questionnaire¹⁴: positive screen if</p> <ul style="list-style-type: none"> a. Excessive menstrual bleeding since menarche, or b. History of postpartum hemorrhage, surgery-related bleeding, or bleeding associated with dental work, or c. History of 2 or more: bruising >5 cm once or twice/month, epistaxis once or twice/month, frequent gum bleeding, family history of bleeding symptoms. | <p>5. Focused physical examination with emphasis on possible causes using the PALM-COEIN classification along with the signs of coagulopathy</p> <p>6. Perform endometrial biopsy if high risk for endometrial cancer:</p> <ul style="list-style-type: none"> a. Age >45 years b. Any of the following condition irrespective of age: <ul style="list-style-type: none"> i. Body mass index >30 kg/m² ii. History of unopposed estrogen use or state iii. Tamoxifen iv. Family history of endometrial or colon cancer <p>7. Laboratory tests:</p> <ul style="list-style-type: none"> a. Pregnancy test b. Complete blood counts c. Coagulopathy laboratory testing if screening + d. Thyroid-stimulating hormone e. Cervical culture f. Cervical cytology if indicated per guidelines |
|---|---|

Bilow MR, El-Nashar SA. Obstet Gynecol Clin North Am. 2016; 43(3):415-30.

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Practice Recommendations

- When looking for an unusual cause of amenorrhea, don't forget to consider an eating disorder, marijuana use, and psychosocial stressors.
- In females < 45 years of age with no risks of endometrial cancer, a short trial of therapy may be attempted before diagnostic work-up.
- When considering a bleeding disorder, use a tool demonstrated to have 90% sensitivity for the detection of coagulopathies

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Answers

- 1. A
- 2. B
- 3. B

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