Reviewed By
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Video Case

Abnormal Uterine Bleeding

Objectives:

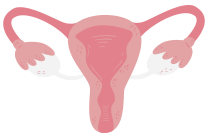
- → Define/Describe the physiology of normal/endocrinology menstrual cycle.
- → Define abnormal uterine bleeding AUB.
- → Describe the pathophysiology and identify etiologies of AUB.
- → Describe the steps in the evaluation and the management of AUB.
- → Summarize medical and surgical options for AUB.

- → Slides
- → Important
- → Golden notes
- → Extra
- → 439 Doctor's notes
- → 441 Doctor's notes
- → 441 Female Presentation
- → Reference

Video Case | Editing File

Abnormal uterine bleeding

Introduction:



Abnormal uterine bleeding: is menstrual flow outside of normal **regularity**, **frequency**, **volume** or **duration**. Common and can range from complete absence of bleeding (amenorrhea) to life-threatening hemorrhage. Normal uterine bleeding in menarche & menses

The etiology of the bleeding irregularities includes benign or malignant growths, systemic disease, coagulation defects, and hormonal imbalance.

AUB accounts for more than 70% of all gynecological consults for peri-menopausal and post-menopausal women.

Early pregnancy and its complications should always be ruled out as the cause of AUB in women of reproductive age.

- Abnormal uterine bleeding = Diagnosis of exclusion (**DOE**) by excluding **coagulopathy**, **thyroid** & **prolactin diseases.** Imaging (**US & MRI**) **ONLY** if you suspect any disease to exclude.

Clinical Dimensions	Descriptive Terms	Normal Limits (5th to 95th Percentiles)
Frequency of menses (days)	Frequent	<24
	Normal	24-38
	Infrequent	24-38
	Absent	----
Regularity of menses, cycle-to-cycle variation over 12 months	Regular	Variation +/- 2-20 days
	Irregular	Variation >20 days
Duration of flow (days)	Prolonged	>8.0
	Normal	4.5-8.0
	Shortened	<4.5
Volume of monthly blood loss (mL)	Heavy	>80
	Normal	5-80
	Light	<5

Abnormal vaginal bleeding

Causes of abnormal vaginal bleeding:

	Overview	Causes	Diagnosis	Management
Pregnancy	In a patient who has abnormal bleeding during the reproductive age group, **pregnancy must first be considered.**	**Early pregnancy** associated **with bleeding** can include several ***complications*** such as **Incomplete abortion, threatened abortion, ectopic pregnancy and hydatidiform mole**.	**Urine/serum beta-hCG required to confirm pregnancy** If it's positive, identified vaginal ultrasound will help sort out which pregnancy complication is operative.	**Varies with the individual diagnosis**
Anatomic lesions	If pregnancy test is -ve, then an anatomic causes should be considered. The classic history is **unpredictable** bleeding (without cramping) occurring between normal, **predictable** menstrual periods (with cramping).	**Vaginal** (lacerations, varicosities, tumors). **Cervical** (polyps, cervicitis, tumors). **Endometrial** (submucosal leiomyomas, polyps, hyperplasia, cancer). **Endometrial Polyp or Submucosal Leiomyoma**: Predictable vaginal bleeding **Myometrial** (adenomyosis).	**Lower genital tract** → pelvic and speculum exam. **Upper genital tract** → saline sonogram, endometrial biopsy, or hysteroscopy.	
Inherited Coagulopathy	**Up to 15%** of patients with abnormal vaginal bleeding (**especially in the adolescent age group**) have **coagulopathies**. Review of systems may be positive for other bleeding symptoms including **epistaxis, gingival bleeding, and ecchymoses**.	**Von Willebrand disease** is the **most common hereditary coagulation abnormality.** Coagulopathies can be due to vessel wall, platelets, coagulation, fibrinolytics disorders. Von Willebrand disease arises from a deficiency of vWF, a protein required for platelets adhesion.	**+ve family history**/review of systems helpful for screening. Initial lab **tests include (CBC, platelet count, PT, PTT) and screening for Von Willebrand factor antigen (vWF).** Platelet bleeding: superficial + evaluated by platelet count. Factor bleeding: deep + evaluated by coagulation studies (PT,PTT,INR). It is important to ask about Rx that affect coagulation (**Aspirin**).	**consultation with hematology specialist**

Dysfunctional Uterine Bleeding

Causes of abnormal vaginal bleeding:

Dysfunctional Uterine Bleeding

- → If pregnancy, anatomical, coagulopathy causes ruled out, then the diagnosis of **hormonal imbalance** should be considered.
- → The classic history is bleeding which is **unpredictable in amount, duration and frequency (without cramping).**
- → The most common cause of DUB is **anovulation** *(unopposed estrogen: continuous stimulation of the endometrium with no secretory phase).*
  - → An estrogen-dominant endometrium is structurally unstable as it increasingly thickens, with inadequate structural support, it eventually undergoes random, disorderly, and unpredictable breakdown resulting in estrogen breakthrough bleeding.
  - → **Ovulatory Dysfunction**:
    - → **Adolescence**: the most common cause of AUB in adolescence is **anovulatory** bleeding from immaturity of the HPO axis.
    - → **Reproductive age**: most common cause is is **PCOS**, pregnancy, STIs (Gonorrhea and Chlamydia), hyperprolactinemia, thyroid disorders and stress.
    - → **Perimenopausal**: ovulatory dysfunction secondary to **declining ovarian function.**

Diagnosis of DUB

- → **Anovulatory cycles** can usually be diagnosed from a history of irregular, unpredictable bleeding.

01 **Bleeding**

- → Bleeding is usually **without cramping** since there is no PG release to cause it.

02 **Cervical mucus**

- → Cervical mucus will be **clear, thin**, and **watery**, reflecting the estrogen dominant environment.

03 **Basal-body temperature**

- → Basal-body temperature (BBT) chart will not show a **midcycle temperature rise** due to the absence of the thermogenic effect of progesterone.

04 **Endometrial biopsy**

- → Endometrial biopsy will show a **proliferative** endometrium.

Dysfunctional Uterine Bleeding

Management of Dysfunctional Uterine Bleeding:

	Management of DUB
Progesterone	→ **Progesterone:** trial involves administering progestin to stabilize the endometrium, stop the bleeding, and prevent random breakdown. When the progestin is stopped, spiral arteriolar spasm results in PG release, necrosis, and an orderly shedding of the endometrium. → A **positive** progesterone trial confirms a clinical diagnosis of **anovulation** and a negative progesterone trial rules out anovulation. → Anovulation can be ***secondary*** to other medical conditions. It's important to identify and correct a reversible cause of anovulation if present. → **Hypothyroidism:** a common cause of anovulation, diagnosed by a high TSH and treated with **thyroid replacement**. → **Hyperprolactinemia**: diagnosed by a serum prolactin test, an elevated prolactin inhibits GnRH by increasing dopamine. Treatment depends on the cause of elevated prolactin. → **Progestin management:** Replacement of the hormone that is lacking (progesterone or progestin). → These methods help regulate the menstrual flow and prevent endometrial hyperplasia, but do not reestablish normal ovulation. → **Cyclic MPA Medroxyprogesterone acetate** can be administered for the last 7–10 days of each cycle. → **Oral contraceptive pills (OCs)**. Estrogen-progestin oral contraceptives are often used for convenience. The important ingredient, however, is the progestin—not the estrogen. → **Progestin intrauterine system (LNG-IUS)**. The levonorgestrel IUS (Mirena or Skyla) delivers the progestin directly to the endometrium. This treatment can significantly decreasing menstrual blood loss.
If **progestin management is not successful** at controlling blood loss, the following generic methods have been successful:	
NSAIDs	→ Can decrease dysmenorrhea, improve clotting, and reduce menstrual blood loss. → They are administered for only five days of the cycle and can be used and can be combined with OCs. → **NSAIDs** are **antiplatelets** but actually they can hold off bleeding because of the uterine effect (**prostaglandins) being stronger than the platelets effect.**
Tranexamic acid (Lysteda)	→ It is **antifibrinolytic**, it can be used to stabilize clots in uterine arterioles or capillaries of women who may have excessive fibrinolytic activity and can reduce blood loss by about 40%. → Works by inhibiting fibrinolysis by plasmin. → It is contraindicated with history of DVT, PE, or CVA, and not recommended with E+P steroids.
If patient not tolerate to medical therapy or continuous to bleed **surgical intervention is required** (they are going to **remove ability to have kids** but **bleeding will stop**).	
surgical intervention	→ **Endometrial ablation procedure:** destroys the endometrium by heat, cold, or microwaves. It leads to an iatrogenic Asherman syndrome and minimal or no menstrual blood loss. Fertility will be affected. → **Hysterectomy** (removal of the uterus) is a last resort and performed only after all other therapies have been unsuccessful.

Abnormal uterine bleeding

Abnormal uterine bleeding PALM-COEIN classification (FIGO 2011)

Structural causes

Visualizable by inspection or imaging:

- → **P:Polyps (AUB-P):** have characteristic type of bleeding "intermenses bleeding".
- → **A: Adenomyosis (AUB-A):** gland cells in the endometrium go to myometrium and bleed and the muscle is disturbed by glands, can't contract and stop bleeding. Causing heavy periods.
- → **L: Leiomyoma (AUB-L): Leiomyoma** or fibroid is a benign tumor of smooth muscle ,it has NO malignant potential and the most common presenting symptom is bleeding in submucosal or intra mural spaces.
- → **M:Malignancy (AUB-M)** Needs further workup:
  - → **Endometrial cancer:** can be diagnosed early by **PIelle (**that's make negative pressure to take biopsy or hysteroscopy), pap-smear is not enough.

Non-structural causes

No Needs further workup:

- → **C: Coagulopathy (AUB-C)**
- → **O: Ovulatory disorders (AUB-O)**
- → **E: Endometrial (AUB-E)**
- → **I:Iatrogenic (AU B-1):** Copper IUD (worsen or cause heavy menstrual bleeding), antiplatelets, warfarin, NOACs, COC.
- → **N: Not yet classified (AUB-N):** Hypothyroid, hyperprolactinemia (adenoma) menorrhea or oligoovulation lead to bleeding, sleeve gastrectomy, depression, lifestyle stress that lead to hypothalamic dysfunction.

Evaluation of AUB

- → **History**:
  - → If the period is irregular and not predictable : ovulatory dysfunction
  - → If there is bleeding between the periods : structural cause
  - → Heavy periods : coagulopathy
- → **Physical examination:**
  - → General (vital signs in case of bleeding the patient will have tachycardia and hypotension)
  - → Look for signs of anemia
  - → Look for other signs such as weight gain/acne/ hirsutism/ecchymosis
  - → Abdominal & pelvic examination
  - → PCOS: sign of weight gain, acne, hirsutism, evidence of insulin resistance
  - → Coagulopathy: petechiae, ecchymosis, skin pallor or swollen joints
  - → Signs of thyroid disease
  - → Pelvic exam: including bimanual exam to assess the size and contour of the uterus
- → **Investigations:**
  - → **Labs**:
    - → **Pregnancy test**
    - → CBC: looking for anemia
    - → Prolactin level
    - → Serum iron and iron-binding capacity
    - → Liver function test
    - → Coagulation tests (PT, PTT, and INR) to exclude any coagulopathy
  - → **Endometrial biopsy** : to rule out hyperplasia and cancer in high risk women > 40, diabetic or obese women
  - → **Imaging tests**, if indicated: Pelvic ultrasonography or MRI

Abnormal uterine bleeding

Treatment

Depends on the etiology of AUB:

- → **Anovulatory bleeding:**
  - → If Oral contraceptives
  - → Cyclic progesterone
  - → Levonorgestrel IUD
  - → Endometrial ablation (after ruling out endometrial hyperplasia by biopsy)
- → **Coagulopathy:**
  - → Antifibrinolytic therapy (Tranexamic acid)
- → **Structural source (polyps and fibroid)**
  - → Surgical: Polypectomy / Myomectomy / Hysterectomy

Teaching Case

A 45 year-old G2P0020 woman, with LMP 21 days ago, presents with heavy menstrual bleeding. Prior to 6 months ago her cycles occurred every 28-30 days, lasted for 6 days, and were associated with cramps that were relieved by Ibuprofen. In the last 6 months there has been a change with menses occurring every 25-32 days, lasting 7-10 days and associated with cramps not relieved by ibuprofen, passing clots and using two boxes of maxi pads each cycle. She is worried about losing her job if the bleeding is not better controlled. She denies dizziness, but complains of feeling weak and fatigued. Her weight has not changed in the last year. She denies any bleeding disorders or reproductive cancers in the family. She uses condoms for contraception. She takes no daily medications and has no other medical problems. She is married and works in a factory. On physical exam, her weight is 150 pounds, height is 5 feet, 6 inches, BP 130/88, P 100. She appears pale. Pelvic exam : shows normal vulva, vagina and cervix; normal sized, non-tender, mobile uterus; non-tender adnexa without palpable masses.

Q1: What are the parameters of a normal menstrual cycle?

Normal compared to her period numbers are not fixed

- → Interval : 21-35 days (Mean: 28 days) + or - 5 days
- → Duration: 2-7 days (Mean: 5 days)
- → Volume: <80ml (Mean 35 ml) How many pads does she change during the day and are they full of blood ?
- → Composition: Non-clotting blood, endometrial debris

Teaching Case

Q2: Describe the normal endocrinologic and physiologic events that make the menstrual cycle possible.

A	→ Hormones coming from the anterior pituitary gland **FSH & LH** under the stimulation of GnRH from the hypothalamus. → **FSH** (Follicular Stimulating Hormone): responsible for the initial stimulation & maturation of the follicles in the beginning of the cycle (first day of menstruation). → **LH**: surge in the middle of the cycle, responsible for ovulation. → The follicle which reaches maximum growth will ovulate. Both LH & FSH will be very low at the end of the cycle through the negative feedback effect of elevated circulating estradiol and progesterone.
B	→ The granulosa cells of the growing follicles releases estrogen creating a +ve feedback on LH. After 50 hours of high estrogen levels (200pg) positive feedback on the release of gonadotropins is created, resulting in LH surge. → LH surge takes 36 hours, 24 hours to reach the peak and 10-12 hours to ovulates. At the peak of LH the follicle will rupture and the ovum will be released the ovum will be converted to corpus luteum which will release large amounts of **progesterone**: which inhibits the estrogen proliferation, causes secretion, enlarges the increased number of endometrial glands, increases the secretions of the vacuoles & spiral vessels will be more coiled to prepare the endometrium for pregnancy. → Progesterone will be responsible for protecting the pregnancy, corpus luteum will survive for 3 months (till the placenta forms) with the help of HCG. HCG supports corpus luteum which will provide progesterone for ovum and endometrium supporting the pregnancy and creating a cycle. When a pregnancy occurs, the serum β-human chorionic gonadotropin (β-hCG) becomes positive at day 22–23 of the cycle. The β-hCG becomes positive when the zygote implants into the endometrium, usually 7–8 days after ovulation. Therefore, the serum β-hCG becomes positive before the missed period. → If there was no pregnancy, progesterone will luteinize the endometrium and corpus luteum will be converted to corpus albicans by day 23 causing sharp decrease in the level of the progesterone causing menses.
C	→ Follicles will release a great amount of **estrogen** at the beginning of the cycle, which will decrease at the time of ovulation. progesterone, on the other hand, will increase with ovulation.
D	→ The **functional layer** of the endometrium is the layer that changes with the ministerial cycle while no changes occur at the basal layer. → Estrogen is responsible for the growth in the functional layer at the beginning of the cycle (increase in the depth from 0.5 mm to 8 mm, stroma & number of cells converting the single layer of low columnar epithelium into pseudostratified). In the later half of the cycle estrogen will decrease and progesterone will increase changing the grown endometrium into luteinized endometrium progesterone can't act on the endometrium without the preparation of estrogen. if there was no pregnancy estrogen and progesterone levels will fall which can't support the endometrium leading it to shed out. → Progesterone in **early pregnancy** it induces endometrial secretory changes favorable for blastocyst implantation. → Progesterone in **later pregnancy** its function is to induce immune tolerance for the pregnancy and prevent myometrial contractions.

Or Click **Here** to revise "Physiology of Menstrual cycle" lecture

Q3: What is the definition of abnormal uterine bleeding?

→ Menstrual bleeding which falls outside the normal parameters is considered abnormal.
→ **Menorrhagia** is prolonged **excessive bleeding**.
→ **Metrorrhagia** is irregular or **intermenstrual bleeding**.
→ The combination of these is **menometrorrhagia**.
→ Bleeding that occurs after menopause has occurred is also considered abnormal uterine bleeding.

Q4: What possible etiologies could cause this patient's bleeding?

→ **PALM-Structure Causes**
  → Polyp usually normal examination, abnormal growth of endometrial gland and growth damage the ability of uterus to stop bleeding (intermenses bleeding)
  → Adenomyosis On examination there will be Symmetrical growth /boggy flaccid uterus
  → Leiomyoma fibroid
  → Malignancy and Hyperplasia Fibroids On examination

→ **COEIN-functional Causes**
  → Coagulopathy
  → Ovulatory Dysfunction
  → Endometrial hyperplasia
  → Iatrogenic

→ **Not Yet Classified**

Teaching Case

Q5: Which are the potential etiologies of ovulatory dysfunction?

→ Hyperandrogenic anovulation (polycystic ovary syndrome) (main complain irregular menstrual period), congenital adrenal hyperplasia (triads of: Irregular menstruation, hirsutism & Virilization), or androgen- producing tumors (same previous triads but they occur suddenly in this case)
→ Hypothalamic dysfunction (i.e. due to anorexia nervosa the patient is not eating and excessive exercising with low BMI)
→ Hyperprolactinemia
→ Thyroid disorder symptoms of hypothyroidism
→ Primary pituitary disease
→ Premature ovarian failure
→ Iatrogenic (due to radiation or chemotherapy)
→ Medications

Q6: Discuss the mechanism for anovulatory bleeding

→ Progesterone withdrawal signals the endometrium to shed in a uniform way by causing spiral artery spasm.
→ Women who do not ovulate do not experience progesterone withdrawal because they do not form a corpus luteum and usually have bleeding due to unopposed estrogen with either estrogen withdrawal or estrogen excess.
→ Neither of these mechanisms causes spiral artery spasm, and therefore can result in non-uniform shedding of the lining at irregular intervals. Unopposed estrogen will lead to continuous proliferation of the endometrial tissue the patient suddenly will have bleeding.

Q7: How can you tell if this patient is having ovulatory cycles?

→ History consistent with ovulatory cycles (painful, regular, presence of molimina).
→ Timed (luteal phase) endometrial biopsy is it secretory?
→ LH surge kits (ovulation prediction kits) detect LH surge in urine which follows LH surge in serum but occurs before ovulation.
→ Basal body temperature chart with small temperature increase (0.5 degrees) after ovulation.
→ Day 21 serum progesterone level.

Q8: What are the appropriate lab tests that should be ordered in this patient?

→ CBC, Hemoglobin levels, TSH, Prolactin
→ Pregnancy Test
→ Endometrial Biopsy Last choice
  → Done to look for dysplasia or cancer in women above 40
  → Done before 40 if the patient has high risk factors such as DM, polycystic ovary syndrome and obesity.
  → Regardless of her age we should not disregard biopsy
→ Pelvic Ultrasound

Q9: Labs show Hgb: 9.0, HCT: 27%, HCG: negative, TSH and Prolactin are within normal limits. Endometrial biopsy shows normal secretory endometrium, Pelvic ultrasound shows a normal sized uterus with a heterogeneous myometrium, the endometrial lining is 1.4 cm and irregular consistent with endometrial polyp, normal ovaries. What further tests would you order based on the following results? **Dr said we treat the polyp since we know the problem these are other option if the US was normal**

→ Fluid-enhanced sonohysterogram injection of uterus with contrast will show a filling defect
→ Hysterosalpingogram
→ Diagnostic hysteroscopy it can be therapeutic

Q10: Describe potential treatment options for this patient

A polyp in someone who is 45 is different than in someone who is 25 in older patients the risk of malignancy is higher. They remove it in younger patients because it decreases the chance of pregnancy.

→ Certain etiologies will respond better to certain therapies.
→ Ablation is most effective when there is no structural lesion.
→ In this patient's case, because she likely has an anatomic abnormality, one may consider offering a hysteroscopy "polypectomy" or a hysterectomy (if she does not desire childbearing and desires definitive treatment).

Medical options include the following:

→ Oral contraceptive pills
→ Cyclic progestin to cause shedding of the endometrium
→ GnRH agonist
→ High dose NSAIDs pain control
→ Tranexamic acid
→ Levonorgestrel IUD (Mirena) it contains progesterone which will cause shedding of the endometrium and improve the symptoms.

→ If a patient came with heavy menstrual period we don't do copper IUD because it will make it worse.
→ However, since the etiology of her abnormal uterine bleeding is likely an endometrial polyp, medical management is really only an option as temporizing measures if she is not a surgical candidate.

Q11: What are important considerations when counseling the patient and helping her choose the best option for her?

→ **Fertility:** The patient's desire for future childbearing should be assessed
→ **Therapeutic goals:** The patient should consider how permanent a solution she desires. The various possible therapies are associated with a failure rate and a recurrence risk.
→ **Operative risks:** Patients who have significant comorbidities or who are severely anemic should approach surgical therapies carefully.Comorbidities increase the risk of anesthesia .
→ **Time to menopause:** The length of time until likely menopause should be discussed with patient and should be taken into consideration in the patient who might be hesitant to pursue surgical therapy.
→ You should discuss all the management options with your patient.
→ If she is young and she still wants to have children you shouldn't offer hysterectomy.

441 Dr's Notes

→ Other non structural causes of bleeding: physical or emotional stress drugs (psychiatric medications) will affect GnRH and FSH.

→ Endometrial Biopsy is very simple procedure that can be done without anesthesia. always keep in mind endometrial evaluation and biopsy especially with women over 40 presenting with bleeding or less than 40 and US showing fibroid.

→ **Fibroid** risk is almost 70% very common and important does not carry cancer risk infertility cause heavy bleeding or pressure symptoms. management options:
  → **surgical** {myomectomy- hysterectomy for older pt eliminate the risk of dissemination- uterine artery ligation}
  → **medical** {OCP GnRH agonist..}
  → **Ablation is contraindicated** in **fibroid**.
→ In GYN : **OCP progesterone only IUD GnRH** all these can treat any kind of abnormal bleeding by any case.
→ **Polyp**: has easy management can do it in office setting with a hysteroscope
→ **Adenomyosis:** one of the toughest disorders do not respond to treatment options. it's not common present with heavy bleeding severe dysmenorrhea. it's usually diffuse throughout the myometrium there is not much surgical options. it also has infertility issues and the treatment will jeopardize their fertility.
  → Dx:can not be diagnosed with endometrial biopsy since the mass is in the myometrium only found in **MRI** or US where There is loss of endometrial / myometrial definition line.
  → Tx: hysterectomy.

→ Only 30% of patients with leiomyosarcoma show positive endometrial biopsy

→ **PCOS**
  → **three pillars:**
    → Hyperandrogenism : acne- abnormal hair growth-abnormal hair pattern- male pattern balding severe {voice change- fat distribution}
    → Insulin resistance: obesity- difficulty losing weight.
    → Cycle irregularity
  → Dx: Rotterdam 3 criteria of diagnosis you need 2 of 3 :
    → Abnormal uterine bleeding
    → Abnormal labs with high androgen or symptoms
    → US finding of PCOS
  → Tx: lifestyle modification **Exercise** and resistance exercises are most important number one way to improve insulin resistance make muscles require more insulin

439 Dr's Notes

Progesterone - OCP - GnRH agonist can be used for most bleedings but they interfere with pregnancy
Cyclosporine agent can control bleeding

PALM COEIN

Polyps:
→ Have low chance of becoming malignant but the chance is higher if the patient is more than 40
→ Bleeding pattern **"intermenstrual bleeding"**
→ Can cause malignancy, bleeding and infertility (interfere with sperm)

Adenomyosis : "intrauterine endometriosis" endometrial tissue inside the myometrium
→ Toughest to treat, usually affect the whole myometrium.
→ Severe cyclic pain, bleeding (endometrial tissue stimulated by hormones)
→ Tx: treat as endometriosis GnRH agonist OCP.

Leiomyoma :
→ Very common 70-80% accidental microscopic fibroid.
→ Abnormal proliferation of smooth muscle fiber with no malignant potential.
→ Most common symptom: **Bleeding**, compression symptoms *presentation might differ depending on the location (serosa, mucosa, laden..)
→ Tx: Myomectomy, progesterone, OCP, GnRH agonist. GnRH is Secreted by pulsatile pattern from the hypothalamus when we give injection will not stimulate FSH, this shuts down the ovaries and it can't be used for more than 6 months.

Malignancy:
→ cervical cancer : post coital bleeding
→ uterine malignancy : obese menopause women present with bleeding
→ Most common gynecological cancer is endometrial then ovarian then cervical

Coagulation :
→ Ask about Aspirin in history

Coagulopathy

Ovulatory dysfunction:
→ **PCOS**
  → Triad: hyperandrogenism- insulin resistance- cyclic irregularity secondary amenorrhea
  → Dx: you have to have 2 out of 3 criteria:
    → US finding of polycystic ovaries (more than 20 follicles in one ovary and the follicle has to be more than one cm)
    → hyperandrogenism (acne - hirsutism - lab high free testosterone)
    → cyclic irregularity: "anovulatory cycle" happen because effect of androgen on the ovary can be oligomenorrhea or bleeding
    → Presentation other than the above: difficulty losing weight- acanthosis nigricans
  → Tx: lifestyle modification- Symptom control (OCP for cycle irregularity- metformin for insulin resistance- sleeve gastrectomy - Diane ocp that has antiandrogenic effect)
→ Other causes :**Hyper- or hypothyroidism**- **Hyperprolactinemia**- **Stress**- **Premature ovarian failure** losing the ovarian function before 35 can be genetic or acquired with radiotherapy - **Meds** antipsychotics, antidepressants.

Endometrial: any women above the age of 40 with uterine bleeding should have endometrial biopsy
Iatrogenic
Not yet classified

Reference

Abnormal Uterine Bleeding

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CLINICAL KEYS FOR THIS CHAPTER

- During the reproductive years (puberty to menopause), menstrual bleeding normally occurs every 24 to 38 days, except during the first few years of menstruation, during and for a short time after pregnancy and lactation, and in the perimenopausal period. The normal duration of bleeding is 4.5 to 8 days, and the amount of normal flow is less than 80 mL of blood. Brief deviations from normal bleeding patterns occur in many women. Once pregnancy and malignancy are ruled out, short episodes of abnormal uterine bleeding (AUB) resolve spontaneously with little or no treatment.
- Some women may experience heavy irregular AUB during their reproductive years. The causes of most cases of heavy bleeding are benign, and symptoms are often effectively managed with hormonal treatment alone. Up to 20% of women experience debilitating symptoms caused by heavy bleeding at some point during their reproductive years. Heavy menstrual bleeding may result from systemic disorders, coagulation defects, or diseases of the reproductive system.
- Traditional terminology for AUB has been replaced by more accurate descriptions of the frequency, regularity, duration, and amount of menstrual flow. A newer system for categorizing the causes of AUB (PALM-COEIN) helps to organize the evaluation and treatment of women with bleeding disorders.
- After first determining that the source of vaginal bleeding is the uterus, a series of tests is recommended to determine the cause of the AUB. Except in extreme cases, the initial therapy is medical, with a variety of hormonal and nonhormonal regimens available to control the bleeding.
- Surgical therapy is reserved for those women for whom medical management fails or for those who have obviously significant pathology (e.g., polyps) or life-threatening hemorrhage when they first present with AUB.

Abnormal uterine bleeding (AUB) patterns (unrelated to pregnancy) are common and can range from complete absence of bleeding (amenorrhea) to life-threatening hemorrhage. The etiology of the bleeding irregularities includes benign or malignant growths, systemic disease, coagulation defects, and hormonal imbalance. Bleeding pattern disruptions caused by imbalance of hormones were previously termed *dysfunctional uterine bleeding* (DUB). Newer terminology has been introduced to more accurately describe most abnormal bleeding patterns, and a new, more inclusive classification system has been adopted to categorize the various causes of AUB.

Diagnosis

Initially, abnormal vaginal bleeding is assumed to emanate from the uterus. A pelvic examination, including the insertion of a vaginal speculum, is essential to eliminate the possibility that the vulva, vagina, exocervix (or ectocervix), or even the rectum or bladder is actually the source of the bleeding. **Early pregnancy and its complications should always be ruled out as the cause of AUB in women of reproductive age.**

The newer terminology for menstrual bleeding provides information about four dimensions of a woman's cycle: (1) frequency, (2) regularity, (3) duration, and (4) blood loss. Table 26-1 outlines the normal and abnormal values for each of these dimensions and provides the newer terms to describe the abnormalities. As an example, the assessment of abnormal bleeding in a woman with complaints of "irregular menstruation" can be categorized as follows: If her cycle length (first day of menses to the first day of the next menses) is 23 days, she bleeds for 10 days during each cycle, and she loses 100 mL of blood, this would

amenorrhea. Chapters 35 and 41 address perimenopausal and postmenopausal bleeding. This chapter is focused on the etiology, differential diagnosis, evaluation, and treatments for both acute and chronic heavy menstrual bleeding.

Heavy menstrual bleeding occurs in 9-14% of healthy women of reproductive age and is the reason for up to 20% of outpatient clinic visits by women. Heavy menstrual bleeding can cause severe anemia, but less significant blood loss can diminish a woman's quality of life and even her income when workplace activity is adversely affected.

Acute Excessive Bleeding in Nonpregnant Women of Reproductive Age

The etiologies, workups, and therapies of excessive bleeding can differ for acute heavy bleeding compared with chronic heavy bleeding, although often there is considerable overlap. A woman who presents with heavy bleeding needs to be assessed for hemodynamic stability, anemia, and always the possibility of pregnancy. She should be asked about symptoms of dizziness, shortness of breath, or loss of consciousness. Her vital signs must be assessed for hemodynamic stability. It is helpful to get a description of her current bleeding episode as well as her recent and usual bleeding patterns, along with any previous evaluations or treatments. A complete history, including medication history, can provide insight into which of the PALM-COIEN categories is more likely, but a broad differential should be developed. It is quite possible for a woman to have more than one problem as the cause of her abnormal bleeding. Obvious causes requiring immediate surgeries should be ruled out, such as vaginal trauma or bleeding lacerations, as well as aborting fibroids (leiomyomata).

Hospitalization and transfusion are generally recommended for women who have severe anemia (hemoglobin ≤7 g/dL) and those who are hemodynamically unstable. Outpatient transfusion is an option for women with borderline presentations. Patients who decline blood transfusions or blood products in spite of severe anemia should be cared for by a team experienced with other treatment options. Before a transfusion is started, blood tests should be performed. Box 26-2 lists the tests that should be considered for the workup of AUB.

Baseline hemoglobin is mandatory, and a complete blood count (with red blood cell indices) is performed to determine the chronicity of the problem, to rule out thrombocytopenia, and to identify possible hematologic malignancies. Coagulation factors should be obtained, as well as serum iron, iron-binding capacity, and serum ferritin levels. Following these initial assessments, liver, renal, and thyroid function tests may help to identify other systemic causes of excessive uterine bleeding.

BOX 26-2

INITIAL DIAGNOSTIC TESTS FOR ACUTE EXCESSIVE BLEEDING IN WOMEN OF REPRODUCTIVE AGE

- Urine tests
  - Pregnancy test
- Blood tests
  - Blood count with reticulocyte count and differential
  - Serum iron and iron-binding capacity
  - Serum ferritin
  - Coagulation tests (PT, PTT, and INR)
  - Thyroid function tests
  - Liver function tests
  - Creatinine, BUN
- Imaging tests, if indicated
  - Pelvic ultrasonography
  - Saline infusion sonography
- Biopsies as necessary
  - Cervical biopsy
  - Endocervical biopsy
  - Endometrial biopsy

BUN, Blood urea nitrogen; *INR,* international normalized ratio; *PT,* prothrombin time; *PTT,* partial thromboplastin time.

Many of the test results may not be available for days, but the heavy bleeding needs to be promptly controlled. First-line therapy is generally medical. **Surgical approaches are usually reserved for women whose condition does not respond to medical therapies and for those who are bleeding so heavily that there is insufficient time to consider medical treatments.** First-line medical therapy usually involves hormonal manipulations (Box 26-3).

In the past, it was believed that high doses of estrogen were needed to induce cell proliferation over the denuded areas of endometrium that were thought to be actively bleeding. Both high-dose intravenous estrogen and high doses of combined oral contraceptive pills were recommended. **More recently, it has been recognized that high doses of estrogen may not be necessary to control the bleeding.** Furthermore, hemorrhage is known to induce a hypercoagulable state, and the addition of high-dose estrogen may increase the risk of dangerous clotting, especially in women with reactive thrombocytosis. As a result, the doses used in these estrogen-based therapies have been significantly reduced, and **high-dose progestin-only therapies have been recommended as first-line treatment for acute heavy menstrual bleeding, particularly in the outpatient setting.**

Although many hormonal regimes have been used in clinical practice, prospective clinical trials have shown that only three therapies are reliably effective for the treatment of acute excessive bleeding in

be described as "frequent, prolonged, and heavy menses." Other important traditional terms include *amenorrhea,* which refers to the absence of any menstrual bleeding or spotting for at least 3 months; *intermenstrual bleeding,* which refers to bleeding between normally spaced menses; and *postcoital bleeding,* which refers to bleeding after vaginal intercourse.

This newer, more descriptive terminology for patterns of AUB replaces the older, less precise terms listed in Box 26-1. However, it is important to become familiar with these older terms, because they have been used for decades in clinical practice and in the medical literature and are still used for diagnostic coding purposes.

The newer classification system, called *PALM-COEIN,* is depicted in Figure 26-1. Appropriate testing is needed to differentiate the various causes of AUB. The classification system takes into account that there are two different influences on AUB. On the one hand, a woman may have structural abnormalities of her uterus that are the likely causes of her bleeding, with the PALM elements standing for ***p***olyps, ***a***denomyosis, ***l***eiomyomas (fibroids), and ***m***alignancies. Rare problems such as imperforate hymen or transverse vaginal septum are more likely to present with primary amenorrhea and not with chronic bleeding problems. The COEIN portion of the classification system refers to important functional disorders such as ***c***oagulation defects, ***o***varian dysfunction (formerly DUB), ***e***ndometrial (uterine cavity lining) causes, and ***i***atrogenic. A "***n***ot yet classified" category completes the acronym and is available for a cause of bleeding that is not currently included or idiopathic.

Chapter 33 covers the causes of infrequent menses (oligomenorrhea) and both primary and secondary

TABLE 26-1

TERMINOLOGY USED TO DESCRIBE BLEEDING PATTERNS

Clinical Dimensions	Descriptive Terms	Normal Limits (5th to 95th Percentiles)
Frequency of menses (days)	Frequent Normal Infrequent Absent	<24 24-38 >38 —
Regularity of menses, cycle-to-cycle variation over 12 mo	Regular Irregular	Variation ± 2-20 days Variation >20 days
Duration of flow (days)	Prolonged Normal Shortened	>8.0 4.5-8.0 <4.5
Volume of monthly blood loss (mL)	Heavy Normal Light	>80 5-80 <5

BOX 26-1

TRADITIONAL TERMINOLOGY FOR ABNORMAL UTERINE BLEEDING

- *Polymenorrhea:* Abnormally frequent menses at intervals of less than 24 days
- *Menorrhagia* (hypermenorrhea): Excessive and/or prolonged menses (>80 mL and >7 days) occurring at normal intervals
- *Metrorrhagia:* Irregular episodes of uterine bleeding
- *Menometrorrhagia:* Heavy and irregular uterine bleeding
- *Dysfunctional uterine bleeding:* Bleeding caused by ovulatory dysfunction

*Less descriptive terms that are no longer recommended.

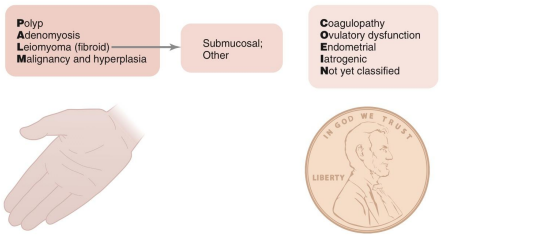

FIGURE 26-1 PALM-COEIN classification system for abnormal uterine bleeding that has been approved by the International Federation of Gynecology and Obstetrics. (Modified from Munro MG, Critchley HO, Fraser IS: The FIGO classification of causes of abnormal uterine bleeding in the reproductive years. *Fertil Steril* 95:2204–2208, 2011.)

BOX 26-3

MEDICAL THERAPEUTIC OPTIONS FOR ACUTE HEAVY UTERINE BLEEDING

Older Estrogen-Based, High-Dose Treatments

Conjugated equine estrogen 30 mg intravenously every 3 hr for up to 24 hr
OR
50 µg of ethinyl estradiol (EE), 0.15 mg of levonorgestrel, one tablet orally every 6 hr for 5 days

Newer Therapies Prospectively Studied and Validated in Outpatient Settings

Medroxyprogesterone acetate 20 mg orally every 8 hr for 7 days, then once daily for 21 days
OR
Oral contraceptive pills with 35 µg of EE, 1.0 mg of norethindrone acetate, one tablet orally every 8 hr for 7 days, then 20 µg of EE, 1.0 mg of norethindrone acetate pills, one tablet orally once daily for 21 days
OR
Medroxyprogesterone acetate 20 mg orally every 8 hr for 3 days with intramuscular injection of depot medroxyprogesterone acetate 150 mg

Lower-Dose Oral Contraceptive Pill Treatment Proposed

Any 35-µg EE oral contraceptive pill for 1 day, then one tablet orally every 12 hr for two doses, then one tablet orally once daily for 19 days

BOX 26-4

MEDICAL TREATMENT OPTIONS FOR CHRONIC HEAVY MENSTRUAL BLEEDING

Normalize Prostaglandins

Ibuprofen 800 mg orally every 8 hr from start of menses through last days of heavy bleeding (<5 days)
Naproxen 500 mg orally every 12 hr from the start of menses through the last day of heavy bleeding (<5 days)

Antifibrinolytic Therapy

Tranexamic acid 650 mg, two tablets orally every 8 hr from start of menses for up to 5 days

Coordinate Endometrial Sloughing (Best for Anovulation)

MPA 10-mg tablet orally each day for last 10 days of cycle
Estrogen-containing oral contraceptive pills, transdermal patches, or vaginal rings

Endometrial Suppression (Lighter Bleeding or to Create Amenorrhea)

Progestin-only oral contraceptive or implant, MPA or NETA daily
Extended-cycle oral contraceptives, vaginal rings
DMPA 150-mg intramuscular injection every 11-13 wk
LNG-IUS 20 µg/24 hr
May be combined with hormonal therapies
Do not use with estrogen-containing products

DMPA, Depot medroxyprogesterone acetate; *LNG-IUS,* levonorgestrel intrauterine system; *MPA,* medroxyprogesterone acetate; *NETA,* norethisterone acetate.

women of reproductive age. This is true regardless of the underlying etiology of the heavy bleeding or the status of the endometrium (e.g., hyperplastic or atrophic).

Imaging studies can usually be delayed until the heavy bleeding is controlled. More urgent imaging may be needed if there are other symptoms, such as significant pain. In a woman with suspicious ultrasonic findings or increased risk factors for cancer, biopsy is indicated once the bleeding has been stabilized and her hemoglobin level is normal. Biopsies in women of reproductive age seldom reveal problems missed by the other tests. In fact, outpatient biopsies often miss the more common causes, such as endometrial polyps and fibroids.

When a woman with heavy uterine bleeding does not respond to the initial therapy within 12 to 24 hours, surgery is indicated. A dilation and curettage is performed to remove the remaining endometrium. When needed, **a balloon may be placed within the uterine cavity** to tamponade bleeding vessels. **Selective embolization of uterine blood vessels** can be done by an interventional radiologist if persistent active bleeding continues. **As a last resort, and only rarely, hysterectomy is indicated.**

After the initial episode has been resolved, efforts should be made to prevent a recurrence of the uterine bleeding. This usually involves correcting any specific causes identified in the workup (e.g., providing thyroxine when hypothyroidism is diagnosed) and using therapies listed in Box 26-3 for ongoing treatment of chronic heavy bleeding. Short-term treatments to suppress the endometrium may be needed after hospital discharge while awaiting test results. This can be hormonal (continuation of the initial therapy) or may involve longer-acting medications, such as gonadotropin-releasing hormone analogues.

Chronic Heavy Menstrual Bleeding

Therapies should be targeted to the underlying structural or medical problems that are detected in the workup (e.g., endometrial polypectomy, thyroid hormone replacement, desmopressin treatment). All medical therapies are intended to control bleeding from the endometrium. They can be organized as summarized in Box 26-4. The following steps should be considered: (1) normalize prostaglandins, (2) antifibrinolytic therapy, (3) coordinate endometrial sloughing, and (4) endometrial suppression. Each of these is discussed in turn in the following sections.

NORMALIZE PROSTAGLANDINS

Nonsteroidal antiinflammatory agents (NSAIDs) may be used to normalize prostaglandins. **Many women**

Reference

with heavy bleeding have an imbalance of prostaglandins. For example, levels of vasodilating prostaglandin E_2 (PGE_2) may exceed levels of vasoconstricting $PGF_{2\alpha}$, or there may be excessive numbers of receptors for PGE_2 compared with those for $PGF_{2\alpha}$. An increased $PGE_2/PGF_{2\alpha}$ ratio is more common among anovulatory women. NSAIDs taken in higher doses alter the prostaglandin ratios, but correct dosing and timing is needed to avoid interfering with platelet function. This therapy reduces blood loss by 20-30% and can be combined with hormonal therapies.

ANTIFIBRINOLYTIC THERAPY

Antifibrinolytic agents can be used to stabilize clots in uterine arterioles or capillaries of women who may have excessive fibrinolytic activity. Successive clots formed in the vessels feeding the endometrium are lysed in these women, and antifibrinolytic therapy can reduce blood loss by about 40%. These agents should not be combined with estrogen-containing medications.

COORDINATE ENDOMETRIAL SLOUGHING

Lack of ovulation results in very low progesterone levels. To prevent unopposed estrogenic stimulation of the endometrium that is usually seen in women with anovulatory cycles, a progestin such as oral medroxyprogesterone acetate or norethindrone can be added to emulate a luteal phase. Another approach is to prescribe additional progestin daily with conventional cycling with estrogen-progestin contraceptive pills or with patches or vaginal rings. This limits endometrial growth and provides lighter, predictable bleeding patterns. **One oral contraceptive pill has been approved by the Food and Drug Administration as treatment for heavy menstrual bleeding (a product containing estradiol valerate and dienogest),** but this benefit has been reported clinically for all combined hormonal contraceptives.

ENDOMETRIAL SUPPRESSION

Progestin-only pills and the contraceptive implant have modest but measurable impacts on blood loss, but the **levonorgestrel intrauterine system (LNG-IUS)** 20 µg/24 hours and depot medroxyprogesterone acetate injections induce complete amenorrhea in a significant percentage of women with longer use.

The higher-dose LNG-IUS is the most effective medical treatment for idiopathic heavy menstrual bleeding and **treats excessive bleeding at least as well as endometrial ablation.** It can prevent one-half of women from undergoing hysterectomy. Extended-cycle use of oral contraceptives or uninterrupted use of vaginal contraceptive rings for 3 to 12 months can also prevent scheduled bleeding for substantial periods of time.

If a woman does not respond appropriately to treatment, her evaluation must be reinitiated. Hysteroscopy can provide direct visualization of the endometrium to identify previously undetected causes of bleeding in about 25% of women whose bleeding persists despite appropriate therapy.

SURGICAL TREATMENT

Surgery is generally reserved for women whose medical therapy fails or for those in whom significant pathology has been identified in the initial evaluation. Commonly indicated procedures include polypectomy and myomectomy (see Chapter 19). After malignancy or premalignancy has been excluded, endometrial ablation is an option if the woman does not desire to become pregnant again and has not sufficiently responded to medical therapies. The endometrium can be ablated by a variety of destructive methods, such as freezing, heating, or applying ultrasonic energy. Over 70% of women who are treated with ablation have satisfactory bleeding patterns, including some with amenorrhea. Twenty percent of these women will need a second ablation, and 10% will ultimately undergo hysterectomy. Following ablation, women must be given effective contraception. Ablation causes significant damage to the endometrium, so spontaneous abortion rates are high, and there is a significant risk of abnormal placentation, such as placenta percreta.

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