



437 Team: Obstetrics and Gynecology

Abnormal Uterine Bleeding

Objectives:

- Describe the physiology of normal 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 .

References:

- Kaplan USMLE step 2 CK - Obstetrics and Gynecology
- Online Meded videos
- Team 435

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*We advise you to review : Menstrual Cycle Physiology lecture

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 exclude **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 Normal Infrequent Absent	<24 24-38 24-38 ----
Regularity of menses, cycle-to-cycle variation over 12 months	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 5-80

Abnormal Vaginal Bleeding, Causes:

Pregnancy

- In a patient who has abnormal bleeding during the reproductive age group, pregnancy or a complication must first be considered.
- **Complication** of early pregnancy that are associated with bleeding include:
 - incomplet abortion,
 - threatened abortion,
 - ectopic pregnancy,
 - hydatidiform mole.
- **Diagnosis:** urine/serum beta-hCG required to confirm pregnancy. If pregnancy identified vaginal ultrasound will help sort out which pregnancy complication is operative.
- **Management:** varies with the individual diagnosis.

Anatomic Lesion

- If pregnancy test is negative, then an anatomic causes should be considered.
- **The classic history** is unpredictable bleeding (without cramping) occurring between normal, predictable menstrual periods (with cramping)
- **Causes:**
 - Vaginal (lacerations, varicosities, tumors),
 - Cervical (polyps, cervicitis, tumors),
 - Endometrial (submucosal leiomyomas, polyps*, hyperplasia, cancer),
 - Myometrial (adenomyosis).
- **Diagnosis:**
 - Lower genital tract > pelvic and speculum exam,
 - Upper genital tract > saline sonogram, endometrial biopsy, or hysteroscopy.
- **Management:** Varies according to the individual diagnosis.

* Endometrial Polyp or Submucosal Leiomyoma: Predictable vaginal bleeding with intermenstrual bleeding, 33-year-old woman, Normal height and weight

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. The three types can vary in severity. 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.
- **Diagnosis:** Positive 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).
- **Management:** consultation with hematology specialist

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**, results in *unopposed estrogen* (there is 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:** The most cause of AUB in adolescence is anovulatory bleeding from immaturity of the HPO axis. Regular periods will be established within 2-3 years of menarche.
- For women of reproductive age ovulatory dysfunction is caused by: **PCOS** (most common cause of ovulatory dysfunction), pregnancy, STD (Gonorrhea and Chlamydia).
- Ovulatory dysfunction is also the cause of AUB in peri-menopausal women secondary to declining ovarian function.

Diagnosis:

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

- Bleeding is usually **without cramping** since there is no PG release to cause myometrial contractions.
- Cervical mucus will be clear, thin, and watery, reflecting the estrogen dominant environment.
- Basal-body temperature (BBT) chart will not show a **midcycle temperature rise** due to the absence of the thermogenic effect of progesterone.
- Endometrial biopsy will show a proliferative endometrium.

Management:

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**.
- 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** is 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.

Management Cont:

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.

Other managements:

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.
 - **NSAID is Antiplatelets** but actually it can hold off bleeding because it has **effect in uterus (prostaglandins) much effect than platelets**
- **Tranexamic acid (Lysteda)**
 - 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**)
- **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.

Management summary (Meded):

- **Lifestyle modifies:** ↓ stress , ↓ anxiety & lose weight
- **Medical therapy:** OCP, IUD & NSAID
- **Surgical therapy:** Ablation & hysterectomy

Evaluation of AUB



History: ask about heaviness and pattern of bleeding.

- ❑ If the period is irregular and not predictable : ovulatory dysfunction
- ❑ If there is bleeding between the periods : structural cause
- ❑ Heavy periods : coagulopathy

Physical 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

Investigation:

1. **Labs :**
 - **Pregnancy test**
 - CBC: looking for anemia
 - Serum iron and iron-binding capacity
 - Thyroid function test
 - Coagulation tests (PT, PTT, and INR) to exclude any coagulopathy
 - Liver function test
2. **Endometrial biopsy :** to rule out hyperplasia and cancer in high risk women > 40, diabetic or obese women
3. **Imaging tests,** if indicated: Pelvic ultrasonography or MRI

History

1. Age
2. Parity
3. Medical history(bleeding disorders)
4. Surgical history
5. Medications (contraception?which type?)
6. Family history
7. Age of menarche
8. Describe her period is it regular or not ,the amount,interval (how long does it last?)
9. Ask if there is any clots? Is there any bleeding between the periods?
10. Look for symptoms of hypothyroidism
11. Look for symptoms of anemia

Examination

1. General (vital signs in case of bleeding the patient will have tachycardia and hypotension)
2. Look for signs of anemia
3. Look for other signs such as weight gain/acne/ hirsutism/ecchymosis
4. Abdominal & pelvic examination

Abnormal Uterine Bleeding

PALM-COEIN Classification (FIGO 2011)

Visualizable by inspection or imaging:

- ◀ **P**: Polyps (AUB-P)
- ◀ **A**: Adenomyosis (AUB-A)
- ◀ **L**: Leiomyoma (AUB-L)
- ◀ **M**: Malignancy (AUB-M)

Needs further workup:

- ◀ **C**: Coagulopathy (AUB-C)
- ◀ **O**: Ovulatory disorders (AUB-O)
- ◀ **E**: Endometrial (AUB-E)
- ◀ **I**: Iatrogenic (AUB-I)
- ◀ **N**: Not yet classified (AUB-N)

Treatment



Depends on the etiology of AUB.

- **Anovulatory bleeding:**
 - 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 (Video 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.



Questions

1. What are the parameters of a normal menstrual cycle?

- Interval 21-35 days (Mean: 28 days)
- Duration: 2-7 days (Mean: 5 days)
- Volume: <80ml (Mean 35 ml)
- Composition: Non-clotting blood, endometrial debris

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

The menstrual cycle can be divided into two portions:

- From the **perspective of the endometrium**, the menstrual cycle consists of the proliferative phase and the secretory phase.
- From the **perspective of the ovary**, the cycle is composed of the follicular phase and the luteal phase. The two phases are demarcated by ovulation.
- Thus, the proliferative phase corresponds to the follicular phase and the secretory phase corresponds to the luteal phase.
- Day 1 is the first day of bleeding. In a 28 day cycle, ovulation occurs on Day 14.
- During the early follicular phase, increasing FSH drive the growth of a cohort of follicles. The increase in follicles drives a corresponding increase in estradiol. As estradiol increases, the endometrium proliferates and hypertrophies in response. FSH decreases in response to the negative inhibitory effect of estradiol. As a result the follicle, which is most sensitive to FSH, becomes dominant, continuing to secrete estradiol. This is the follicle destined for ovulation. The massive amount of estradiol causes the LH surge which signals ovulation or the release of the oocyte.
- The corpus luteum is formed at the ovulation site and produces progesterone. This progesterone trans- forms the endometrium to make it receptive to implantation. If pregnancy does not occur, then the corpus luteum undergoes atresia with a consequent fall in progesterone. This progesterone withdrawal causes the endometrium to shed. The fall in progesterone also allows FSH to rise and a new cohort of follicles to develop, and a new cycle

3. 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.

4. What possible etiologies could cause this patient's bleeding?

PALM-COEIN is an acronym that was published in 2011 by the International Federation of Gynecology and Obstetrics that was created for the purpose of establishing a universally accepted nomenclature to describe (approach) uterine bleeding abnormalities.

PALM-Structure Causes

- Polyp **usually normal examination**
- Adenomyosis **On examination there will be Symmetrical growth /boggy flaccid uterus**
- Leiomyoma
- Malignancy and Hyperplasia
- Fibroids On examination asymmetrical growths or nodules**

COEIN-functional Causes

- Coagulopathy
- Ovulatory Dysfunction
- Endometrial **hyperplasia**
- Iatrogenic
- Not Yet Classified

5. 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 excessively exercising with low BMI**)
- Hyperprolactinemia
- Thyroid disorder **symptoms of hypothyroidism**
- Primary pituitary disease
- Premature ovarian failure
- Iatrogenic (due to radiation or chemotherapy)
- **Medications**

6. 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.**

7. How can you tell if this patient is having ovulatory cycles?

- History consistent with ovulatory cycles (**painful**, regular, presence of menses).
- 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.**

8. 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.**
- Pelvic Ultrasound

9. 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?

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

10. Describe potential treatment options for this patient

- 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 or a hysterectomy (if she does not desire childbearing and desires definitive treatment).

Medical options include the following:

1. Oral contraceptive pills
 2. Cyclic progestin to cause shedding of the endometrium
 3. GnRH agonist
 4. High dose NSAIDs pain control
 5. Tranexamic acid
 6. 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.

11. 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.
- **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.