

Normal menstrual cycle

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Menstruation

- Menstruation is a woman's monthly bleeding from her reproductive tract induced by hormonal changes of the menstrual cycle.

For menstruation to occur:

- Coordinated HPO axis
- Responsive endometrium
- Patent outflow

Normal menstrual cycle

- The menstrual cycle (as well as AUB) should be described according to four specific symptomatic components (cycle frequency, duration, volume, regularity of cycle).

Normal Menstrual Cycle

- **Frequency of menses (or length of menstrual cycle)**

Mean is 28 days +/- 7 days

menstrual cycle tends to shorten with age

initially irregular

- **Duration of menstruation**

Normal 4.5–8.0 days; prolonged >8 days, shortened <4.5 days.

Mean is 5 days

As age increases, the duration of menstruation decreases

- **Volume of monthly menstrual blood loss (ml)**

Range 20 – 50 ml, mean 40 ml; heavy is >80 ml; light is <5 ml.

In women with no pre-existing menstrual problems, the normal amount of monthly menstrual blood loss (MBL) is 25–50 ml.

- **Regularity of menstrual cycle (cycle to cycle variation over 12 months, measured in days)**

Ovarian Cycle

❑ Follicular phase(preovulatory)

- Recruitment
- Selection of a dominant follicle
- Increasing levels of estradiol & inhibin B

❑ Ovulatory phase

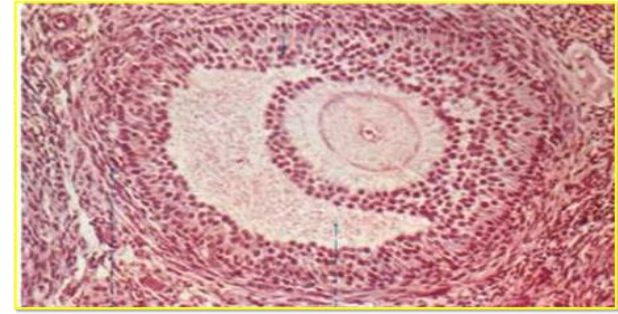
- LH surge
- Rupture of preovulatory follicle wall
- Release of viable ovum

❑ Luteal phase(postovulatory)

- Corpus luteum
- Increasing levels of progesterone
- Secretory changes in endometrium

Follicular Phase

- A group of the most mature follicles
- (called “**antral follicles**”) are recruited.
- Only the follicles **most sensitive to FSH** undergo a further development.
- The follicle most sensitive to FSH continue to develop and produce a large amount of **estradiol and inhibin B**.
- The remaining follicles become **atretic**.(99%)



Ovulation

- Event in the menstrual cycle by which a selected mature follicle breaks and **releases a viable oocyte from the ovary.**
- Each month, one egg is released in humans; but occasionally, two or more can erupt during the menstrual cycle.
- If pregnancy does not occur, the menstruation appears after **exactly two weeks**

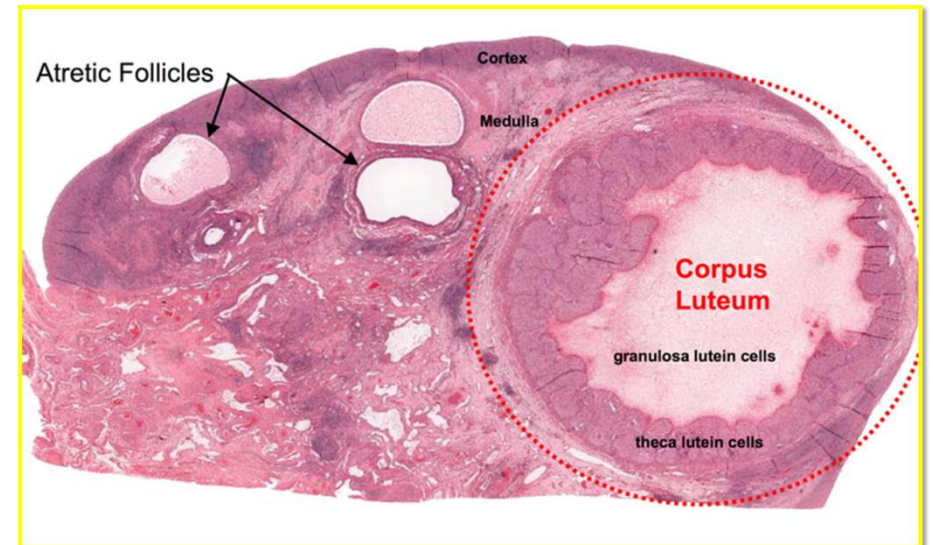
Ovulation

- The onset of the LH surge occurs **34-36 hours** before ovulation & reliably indicates the timing of ovulation



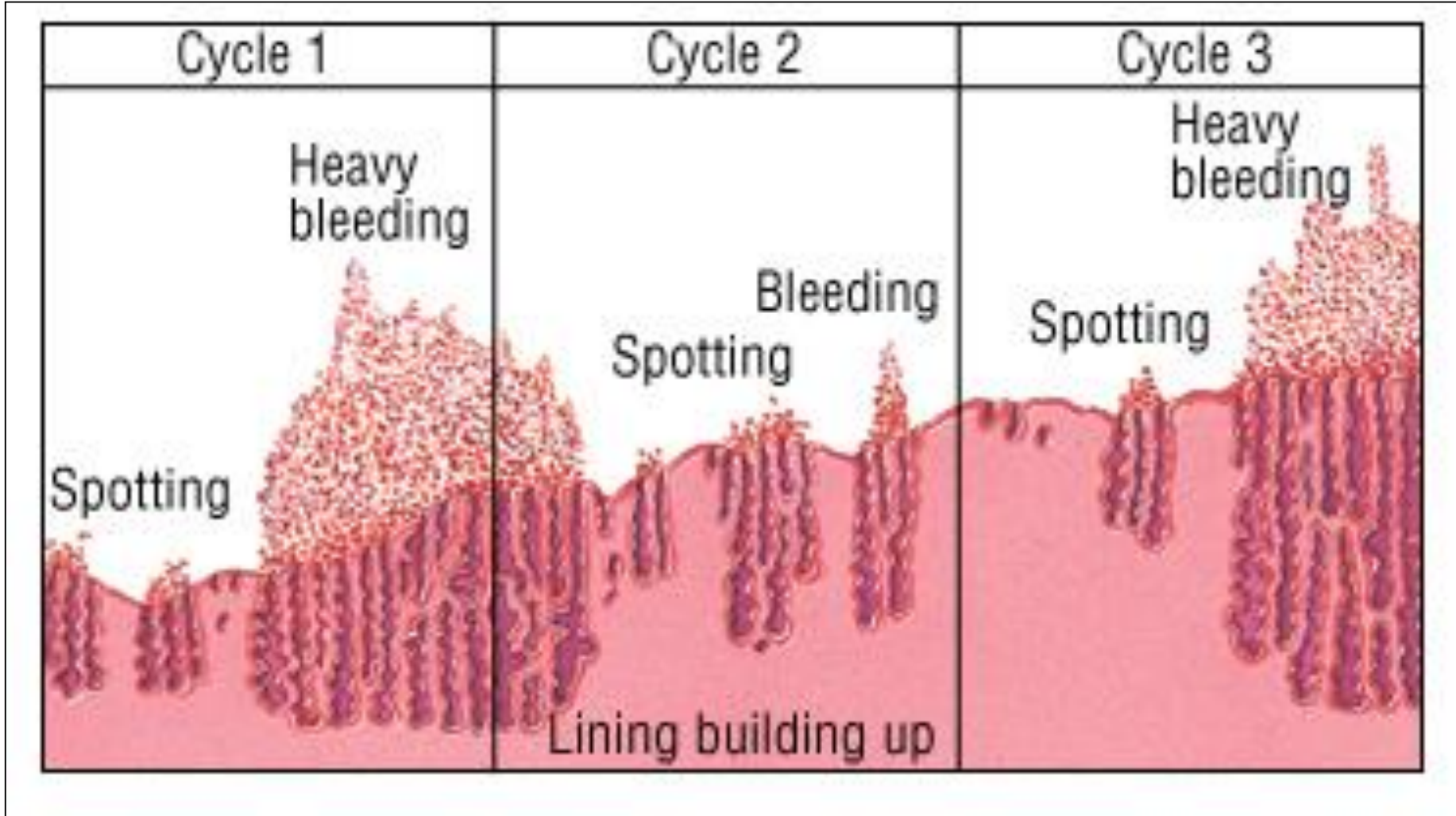
Luteal phase

- Peak levels of progesterone are attained 7 days after ovulation which approximates the time of implantation of the embryo
- In early pregnancy, hCG maintains luteal function with secretion of progesterone until placental steroidogenesis is established



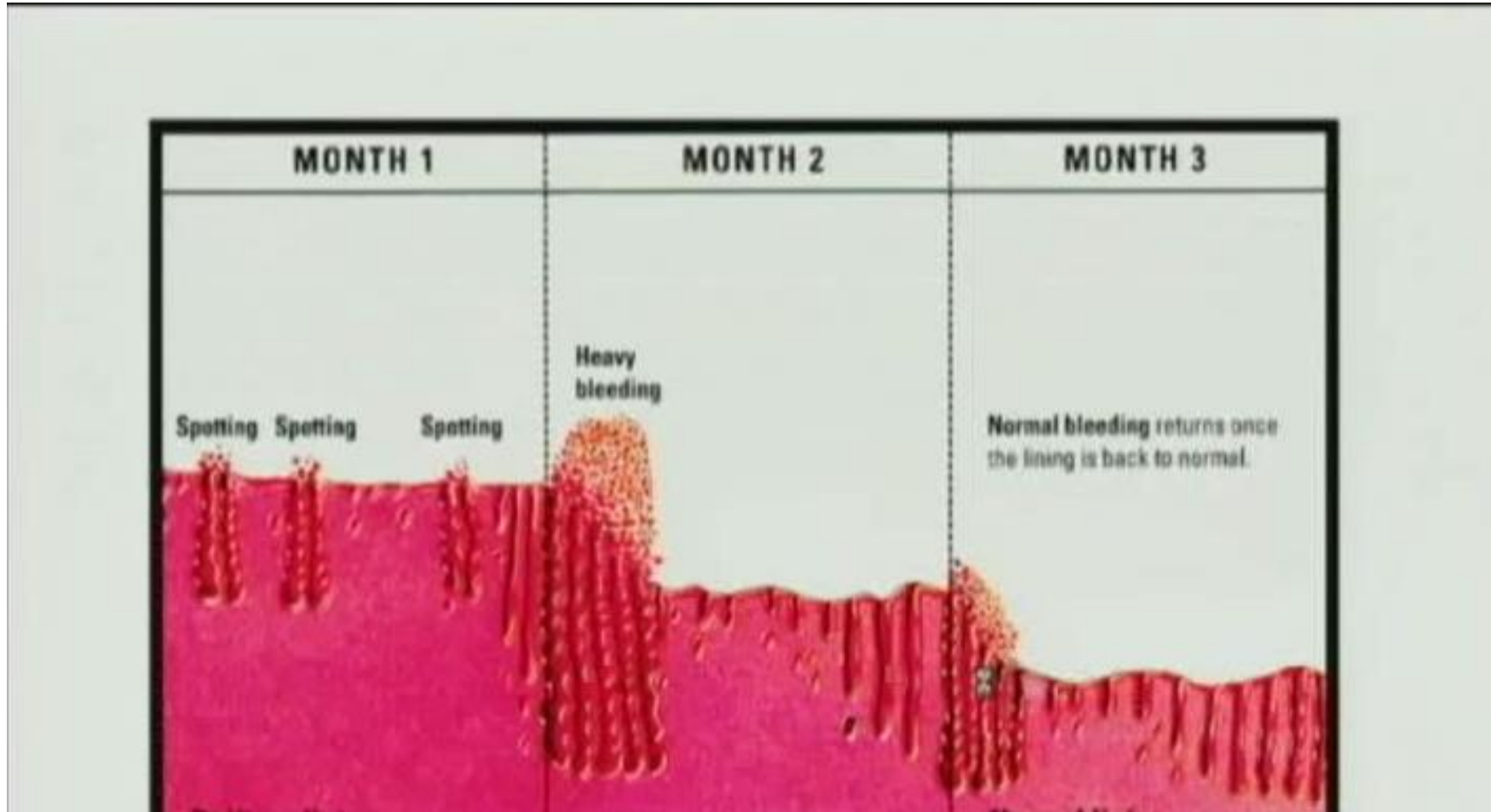
E  **proliferative changes**

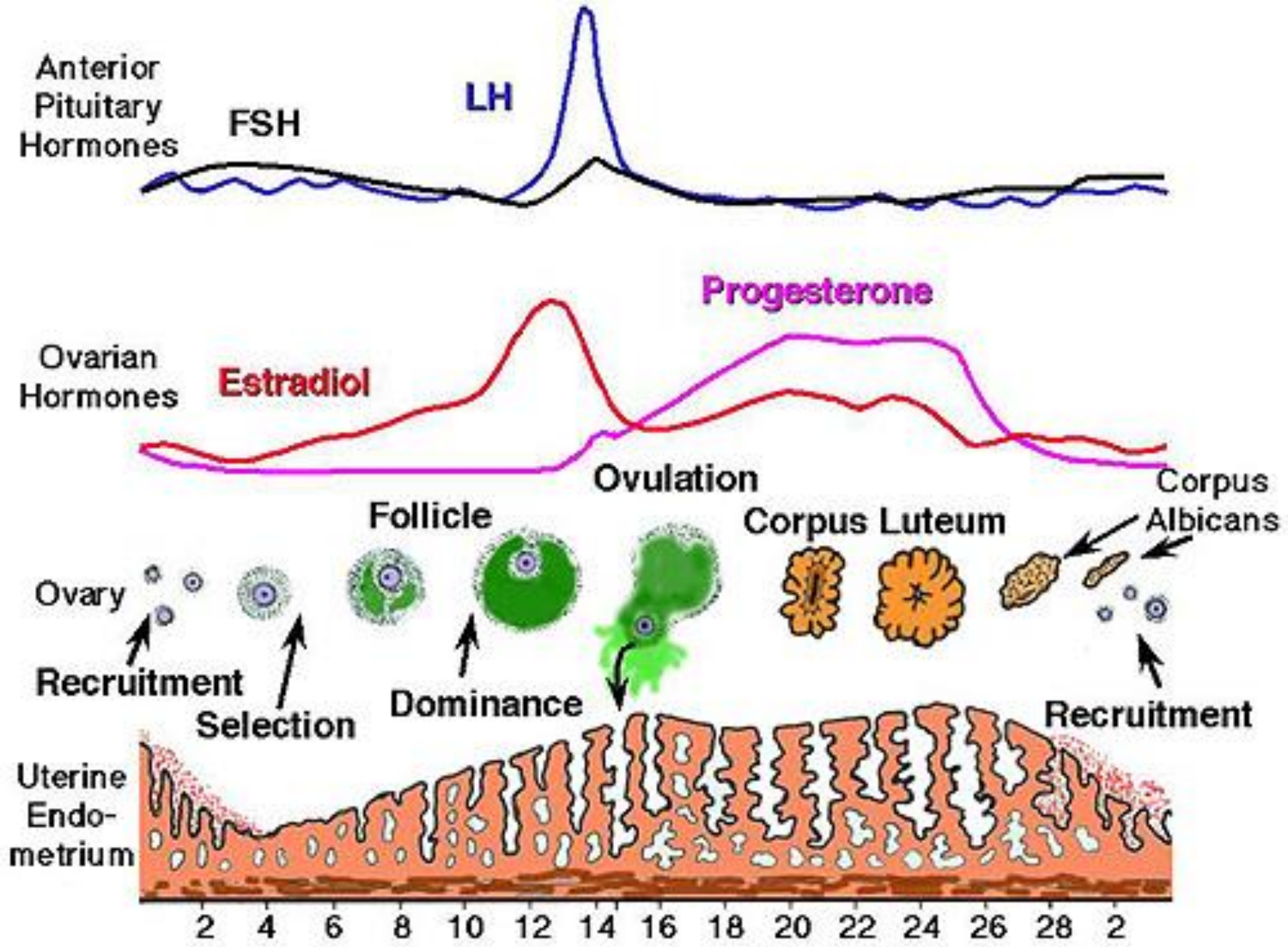
E dominant endometrium is UNSTABLE



P  **Secretory changes**

P dominant endometrium is STABLE





AUB

Definition

- Vaginal bleeding from the uterus with a variable pattern to the normal cycle.
- It can be any of these forms:
 1. Abnormal frequency
 2. Lasting longer than usual
 3. Heavier bleeding than usual
 4. Irregular pattern
- it is a highly prevalent symptom of an underlying condition/s experienced by one in three women of reproductive age.

Chronic vs acute

- **Acute:** Excessive AUB bleeding that requires immediate intervention to prevent further blood loss.
- **Chronic:** AUB that is present for the majority of the past 6 months.
- Note: acute AUB may present in the context of existing chronic AUB or might occur without such a history

Traditionally used terminology

1. **Polymenorrhea**: Abnormally frequent menses at intervals of less than 24 days
2. **Oligomenorrhea**: infrequent cycles >35 days
3. **Menorrhagia (hypermenorrhea)**: Excessive and/or prolonged menses (>80 mL and >7 days) occurring at normal intervals
4. **Metrorrhagia**: Irregular episodes of uterine bleeding
5. **Menometrorrhagia**: Heavy and irregular uterine bleeding
6. **Polymenorrhagia**: a combination of polymenorrhea (frequent menstrual bleeding) and menorrhagia (heavy menstrual bleeding).
7. **Dysfunctional uterine bleeding**: Bleeding caused by ovulatory dysfunction

Updated terminology

- **Heavy menstrual bleeding (HMB):** menstrual blood loss (MBL) that is subjectively considered to be excessive by the woman and interferes with her quality of life previously known as menorrhagia.
- **Intermenstrual bleeding (IMB):** Uterine bleeding that occurs between clearly defined cyclic and predictable menses.
- **Postcoital bleeding (PCB):** Non-menstrual genital tract bleeding immediately (or shortly after) intercourse
- **Postmenopausal bleeding (PMB):** Genital tract bleeding that recurs in a menopausal woman at least one year after cessation of cycles
- **Dysfunctional uterine bleeding:** Abnormal bleeding in the absence of organic pelvic pathology, systemic disease or pregnancy (diagnosis of exclusion)

Causes & their classification

- We use the International Federation of Obstetrics and Gynaecology (FIGO) classification with acronym '**PALM-COEIN**' to classify the causes of AUB in **Structural (PALM)** and **Non-structural (COEIN)**
- Structural causes (PALM):
 1. **P**olyp (AUB-P) – an abnormal but benign growth of tissue
 2. **A**denomyosis (AUB-A) – a condition where the type of cells that normally line the uterus are found in the muscle layer of the uterus
 3. **L**eiomyoma (AUB-L) – a fibroid; a benign growth in the muscle of the uterus
 4. **M**alignancy (AUB-M) – a cancerous growth

Causes & their classification

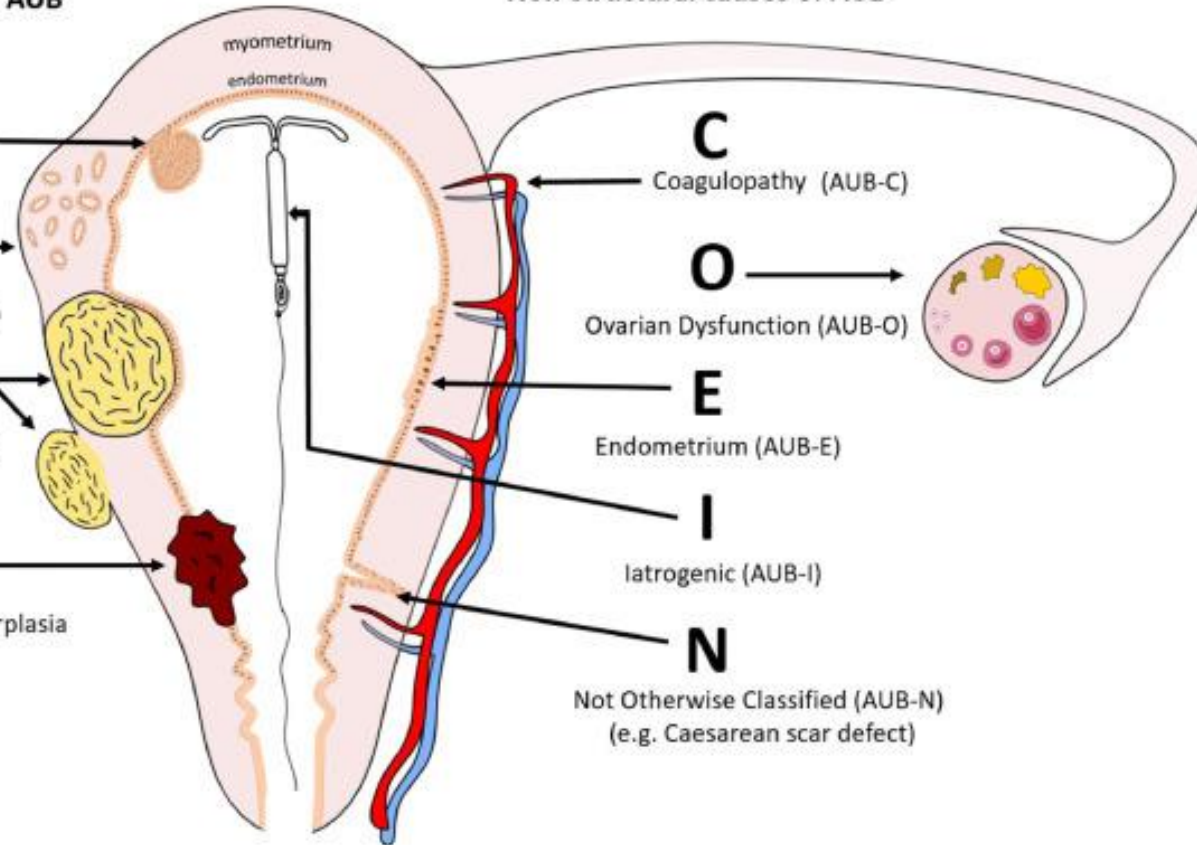
- Non-structural causes (COEIN):
 1. **C**oagulopathy (AUB-C): Von Willbrand and thrombocytopenia are common causes. Also, blood thinners intake like warfarin.
 2. **O**vulation disorders (AUB-O): like PCOS, CAH, hypothyroidism, Cushing's disease, hyperprolactinemia
 3. **E**ndometrial disorders (primary)(AUB-E): like Disturbances of local endometrial haemostasis, vasculogenesis or inflammatory response (chronic endometritis)
 4. **I**atrogenic (AUB-I): due to an accidental injury in a procedure like IUCD placement or medications like COCP, Tamoxifen and progestins.
 5. **N**ot yet classified (AUB-N): such as chronic endometritis, arteriovenous malformations, and myometrial hypertrophy

"PALM"
Structural causes of AUB

- P** Polyp (AUB-P)
- A** Adenomyosis (AUB-A)
- L** Leiomyoma (AUB-L)
- M** Malignancy and Hyperplasia (AUB-M)

"COEIN"
Non-structural causes of AUB

- C** Coagulopathy (AUB-C)
- O** Ovarian Dysfunction (AUB-O)
- E** Endometrium (AUB-E)
- I** Iatrogenic (AUB-I)
- N** Not Otherwise Classified (AUB-N)
(e.g. Caesarean scar defect)



History

- Detailed history can help narrow down the diagnosis.
- Focused questions about:
 1. Frequency
 2. Duration
 3. Volume- through number of pads used.
 4. Regularity

History

- Symptoms that are important to recognize:
 1. HMB at a young age especially around the menarche, is highly suggestive of coagulopathy such as Von willbrand disease.
 2. Increased urine frequency, constipation and lower back pain suggest fibroids.
 3. Dyspareunia - endometriosis or PID
 4. Pressure symptoms – mass
 5. Hirsutism – PCOS
 6. Galactorrhoea – hyperprolactinemia
 7. Offensive vaginal discharge - pelvic infections.
 8. Weight gain, constipation, and hair loss suggest thyroid disorder.

History

- Detailed past gynecological history contraception(&fertility plan), pap smear ..
- Obstetric history
- Past medical history: Pre-existing bleeding tendencies/FHx
- Drug Hx: Anticoagulant medications/ Tamoxifen
- Past surgical history may influence the treatment.
- Risk of STI
- Family history of gynecological history
- Finally ask about the impact on the patient quality of life.

Physical exam

General examination

- Signs of anemia:
SOB, chest pain, pallor
- Bleeding tendency:
bruises or gum bleeding
- Signs of hypothyroidism:
wt gain, cold intolerance, fatigue.

Abdominal examination

- look for any tenderness or masses
- Tenderness - endometriosis or pelvic infection
- Large fibroids, endometriotic cysts, and tumours could present as abdominal masses.

- Speculum:
- 1-look for any local cervical or vaginal lesions
- 2-Assess the severity of the blood loss
- Bimanual examination:
- uterine size, shape, tenderness & mobility.
- Enlarged uterus -fibroids , adenomyosis, Restricted mobility, endometriosis and PID

Imaging

- Pelvic ultrasound:
- First-line imaging choice for AUB
- Indications:
 - 1-Any abnormalities on bimanual examination
 - 2-symptoms that persist after initial treatment
- Can help in identifying structural causes that cause AUB like adenomyosis and leiomyomas.

- Hysteroscopy:
- Allows for direct visualization of endometrial cavity that helps in detecting polyps and small fibroids.
- Also allows endometrial biopsy
- Saline infusion sonography (sonohysterography)
- Saline injected into uterus during TVUS.
- Better at detecting small fibroids than TVUS alone.

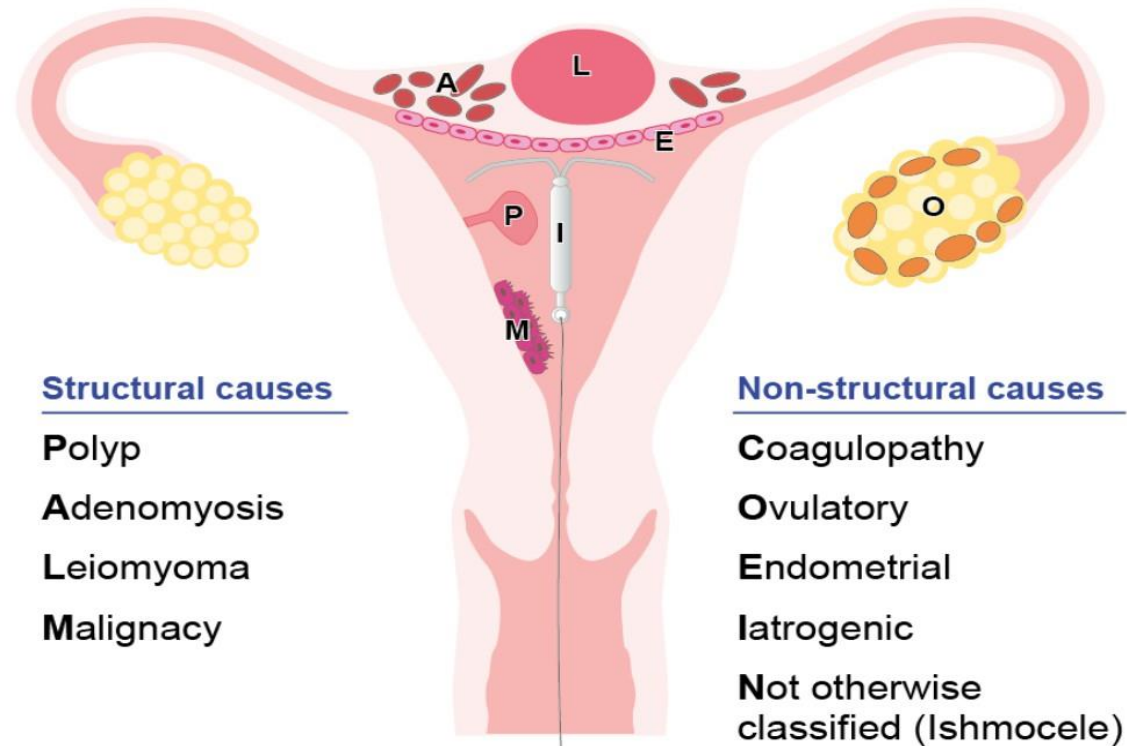
- Endometrial biopsy indications:
- Anovulatory cycles
- Obesity
- Nulliparity
- Older age
- Abnormal US lining thickness

Investigations

- BHCG
- TSH
- Prolactin
- FSH
- Estradiol
- LH
- Coagulation
- Pap smear
- Complete blood count

Management

- The management of AUB is largely dependent on the underlying cause, however, many options are available, including medical and surgical options.



Management of AUB

- 1-Medical treatment
 - -Hormonal
 - -Non Hormonal
- 2-Surgical Treatment
 - -Endometrial ablation
 - -Hysterectomy

Management of AUB

	<20 yrs	20-40 yrs	>40 yrs
Medical	Always	First option after endometrial biopsy	Temporizing & if surgery is refused or imminent menopause
Surgical	Never	Seldom, only if medical treatment fail	First opinion if bleeding is recurrent

Medical Treatment- Hormonal

- **Including:**

1-Estrogen progesterone contraceptives

Combined Oral contraceptives (OCs)

- Mechanism of action: endometrial suppression
- The advantage of estrogen-progesterone contraceptives are that they make bleeding more regular,lighter and reduce dysmenorrhea
- Reduce blood loss by 35 to 69%

2- Miriema IUS

- Levonorgestrel
- induce suppression of the endometrium
- Its main advantages are relief of dysmenorrhea, effective contraception, and long term control of menorrhagia following insertion
- long use (up to 5 years)
- May be an alternative to hysterectomy in some



Medical Treatment- Hormonal

3-Progesterone

- Progestin (Oral Medroxyprogesterone Acetate or Norethindrone).
- Promotes endometrial suppression
- 5 mg tablets one to three tablets daily
- Can be given from day (5 - 26) in a cyclical manner, or from day (15/19 - 26).
- Provides lighter and predictable bleeding patterns

4 Transdermal patch's

5 Vaginal Rings

Medical Treatment- Non Hormonal

- **Including**

- 1 Anti-fibrinolytics: Tranexemic acid**

- is an antifibrinolytic agent that competitively blocks the conversion of plasminogen to plasmin, thereby reducing fibrinolysis.

- 1g taken Orally 3 times a day from the start of menses up to 5 days

- Reduces menstrual blood loss by 50%

- Tranexamic acid is effective in treating menorrhagia associated with IUCD.

- NSAIDs: Mefenamic acid** “alongside helping with dysmenorrhea, it reduced bleeding up to 40%”

- NSAIDs reduce the volume of menstrual blood loss by causing a decline in the rate of prostaglandin synthesis in the endometrium, leading to vasoconstriction and reduced bleeding.

- Mefenamic acid 500mg taken orally 3times from day 1-5 in the cycle



Surgical Treatment

- Although not considered 1st line, they are helpful in patients who have completed their families, or who are not responsive to medical management
- **Including:**
 - 1 Endometrial ablation
 - 2 Uterine artery embolization
 - 3-Hysterectomy

Surgical Treatment

1-Endometrial ablation

is a minimally invasive surgical alternative to medical treatment or hysterectomy, targeting the destruction or removal of the endothelial surface of the uterine cavity for treatment of heavy menstrual bleeding of benign origin.

-The endometrium can be ablated by: Heating, Freezing, or Ultrasonic Energy.

-Consider endometrial ablation in patients with:

excessive uterine bleeding that is unresponsive to medical treatment and in whom doesn't desire for future fertility

Surgical Treatment

2-Uterine artery embolization

-Uterine artery embolization is an option for patients with uterine leiomyomas.

-Women wishing to retain their fertility should be counseled carefully before undergoing UAE as the effects on subsequent reproductive function are uncertain.



3-Hysterectomy

Hysterectomy represents definitive treatment for uterine bleeding. This procedure has a high rate of patient satisfaction because it is curative,

Summary of Medical Treatments For Abnormal Uterine Bleeding

Treatment	Drugs & regimen	Efficacy	Contraception
Combined hormonal contraceptives	<ol style="list-style-type: none"> cOCP for 21 days each month Continuous or extended regimen Contraceptive ring or patch cyclic or continuous 	Menstrual regularity, 20% to 50% reduction in MBL, reduction in dysmenorrhea and PMS	Yes
LNG-IUS	20mcg/24hrs local LNG one IUS for up to 5 years	70% to 97% reduction in MBL, amenorrhea in up to 80% at 1 year, reduced dysmenorrhea	Yes
Cyclic oral progesterone	<p>MPA 5-10mg po for 10-14d (luteal, anovulatory)</p> <p>NETA 5mg tid day 5-26 (long phase, ovulatory)</p>	Bleeding reduced by up to 87% with long phase regimen	No
Injected progesterone	DMPA 150 mg IM q90days	60% amenorrhea at 12 months, 68% at 24 months	Yes
Danazol	100-400mg po daily	80% reduction MBL, 20% amenorrhea, 70% oligomenorrhea	No
GnRH agonists	Leuprolide acetate. IM Monthly, 3 to 6 months	Bleeding stopped in 89% by 3 to 4 weeks	No
NSAIDS	<ul style="list-style-type: none"> Naprosyn 500mg od-bid ibuprofen 600-1200mg Mefenamic acid 500mg od starting day or day before menses for 3 to 5 days until ceases 	20% to 50% reduction MBL, reduction in dysmenorrhea in 70%	No