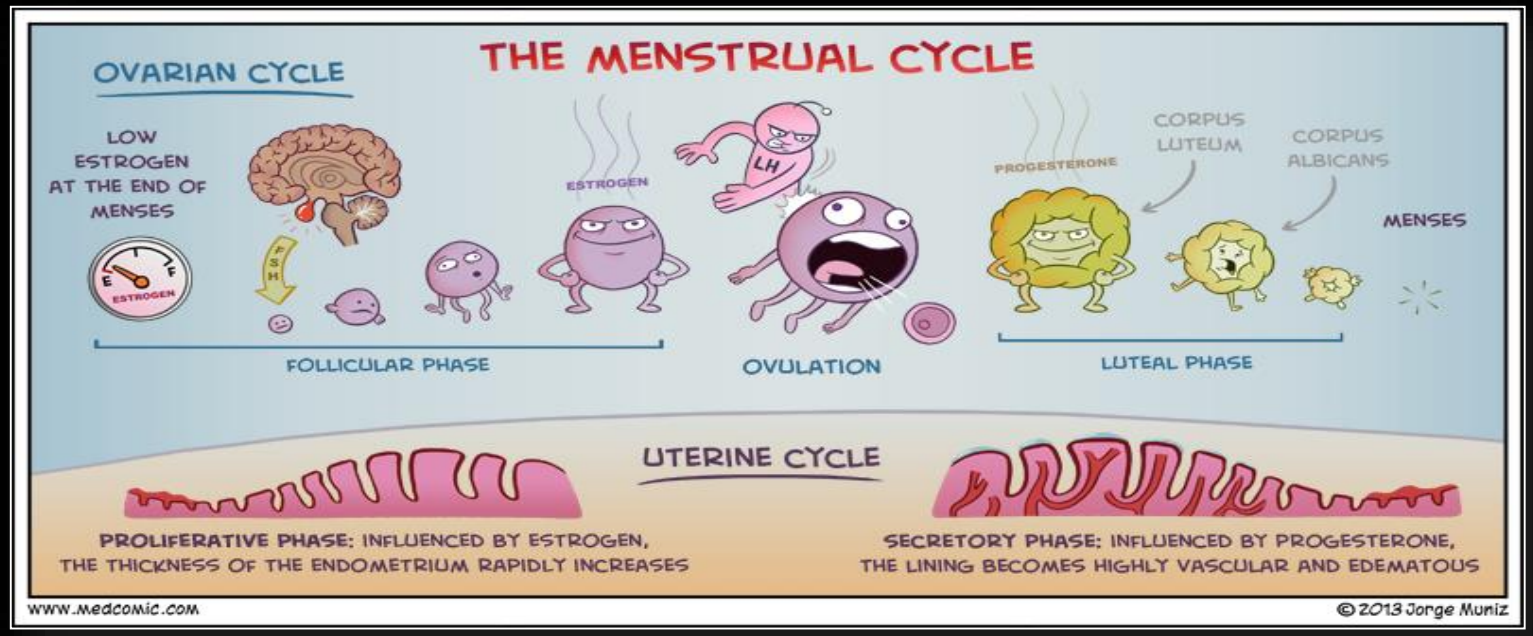


Menstrual cycle and its disorders

Dr Fida Al-Asali

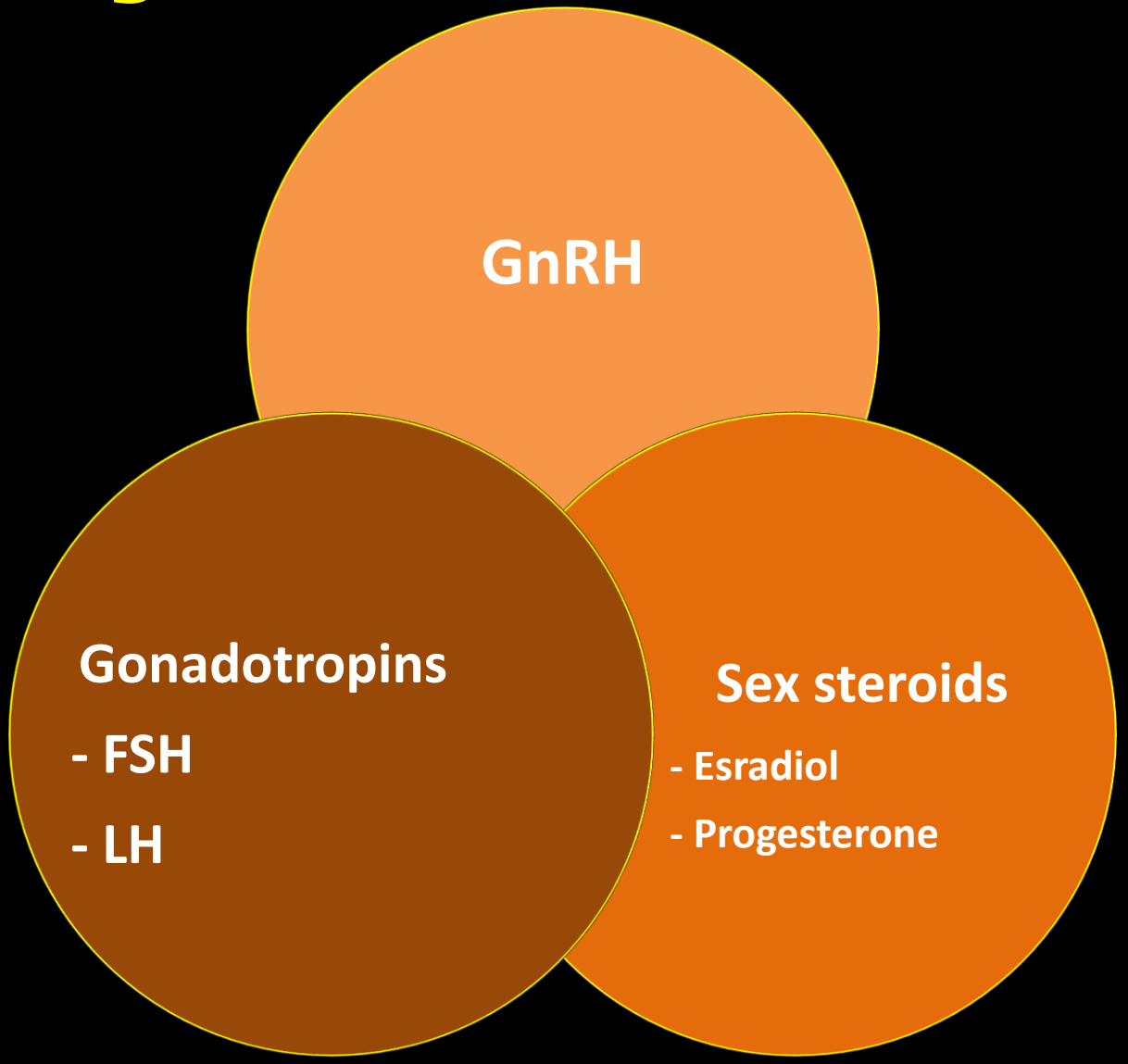
Menstruation

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

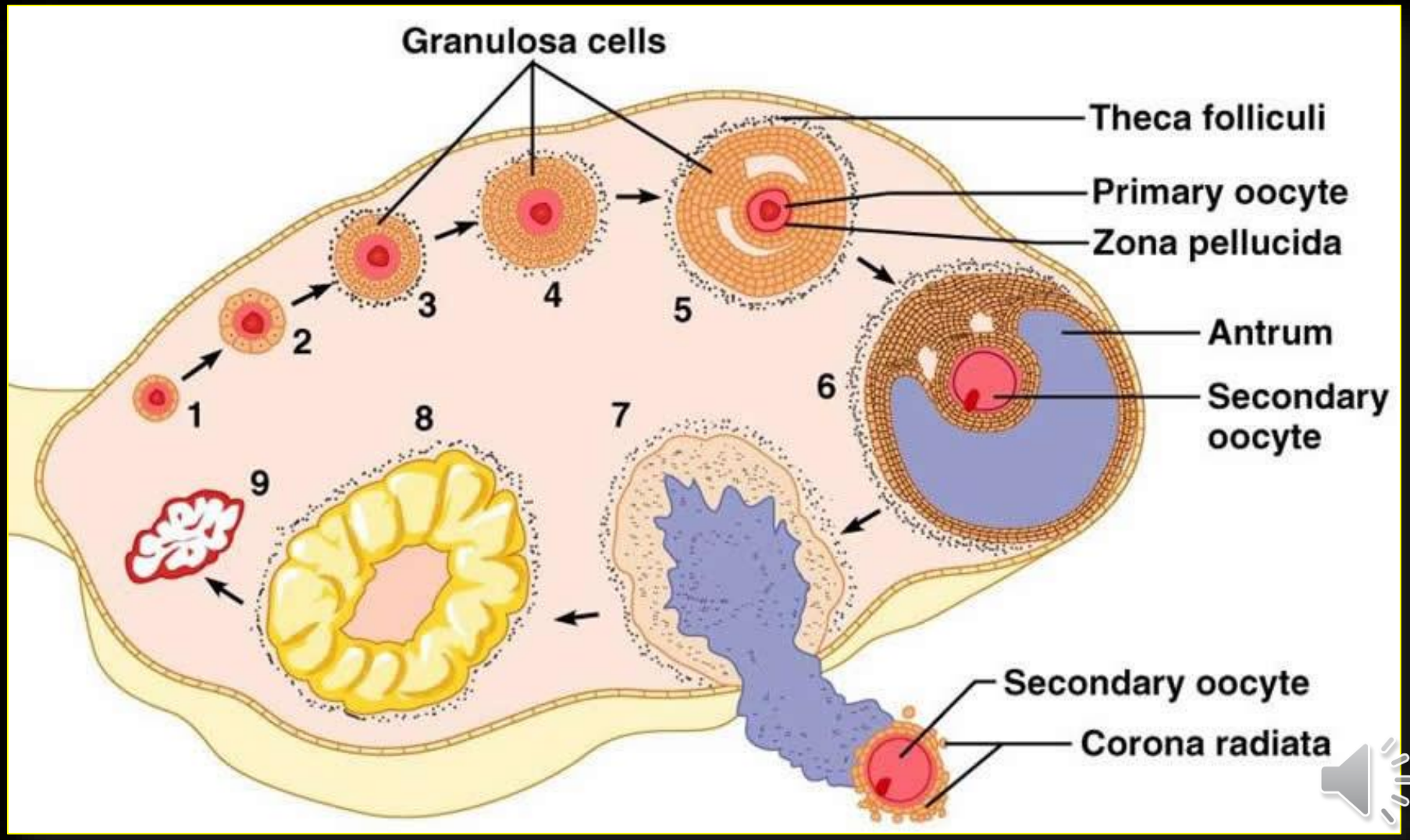
For menstruation to occur:

- Coordinated HPO axis
- Responsive endometrium
- Patent outflow

Cycle interaction



Dominant follicle



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

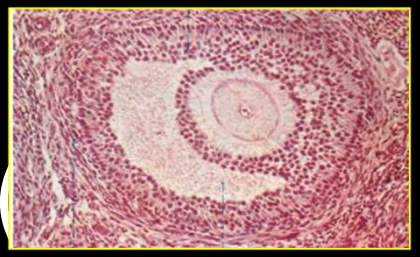
Ovulation

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

Follicular Phase



A group of the most mature follicles (“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%)

Mechanism of follicle rupture

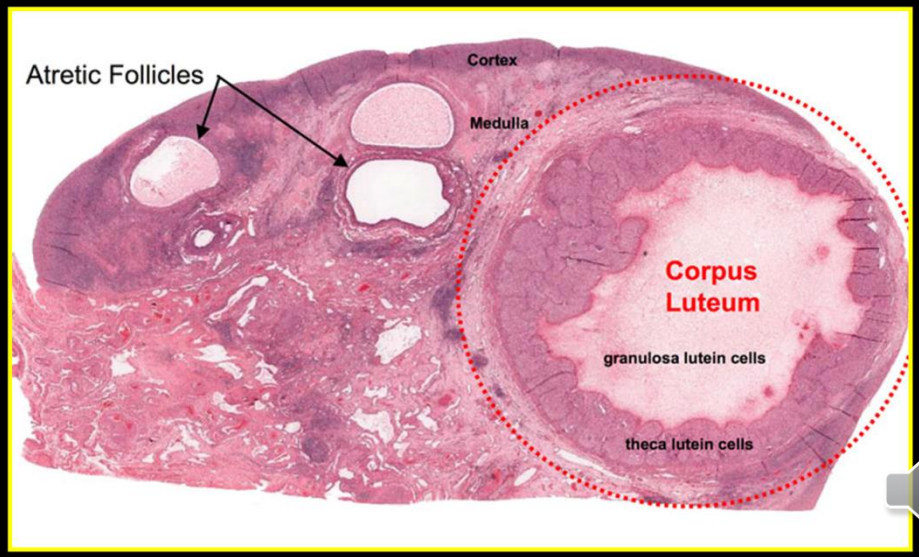
- An increase of intrafollicular pressure
- Perifollicular ovarian smooth muscle contractions
- Vascular alterations in the perifollicular vessels.
- **Prostaglandins and proteolytic enzymes are responsible for the digestion and rupture of the follicle wall**
- Some factors, such as cytokines, O2 free-radicals, nitric oxide and angiotensin II could contribute to these actions, but this issue is still unclear (Homburg 2005).

Ovulation

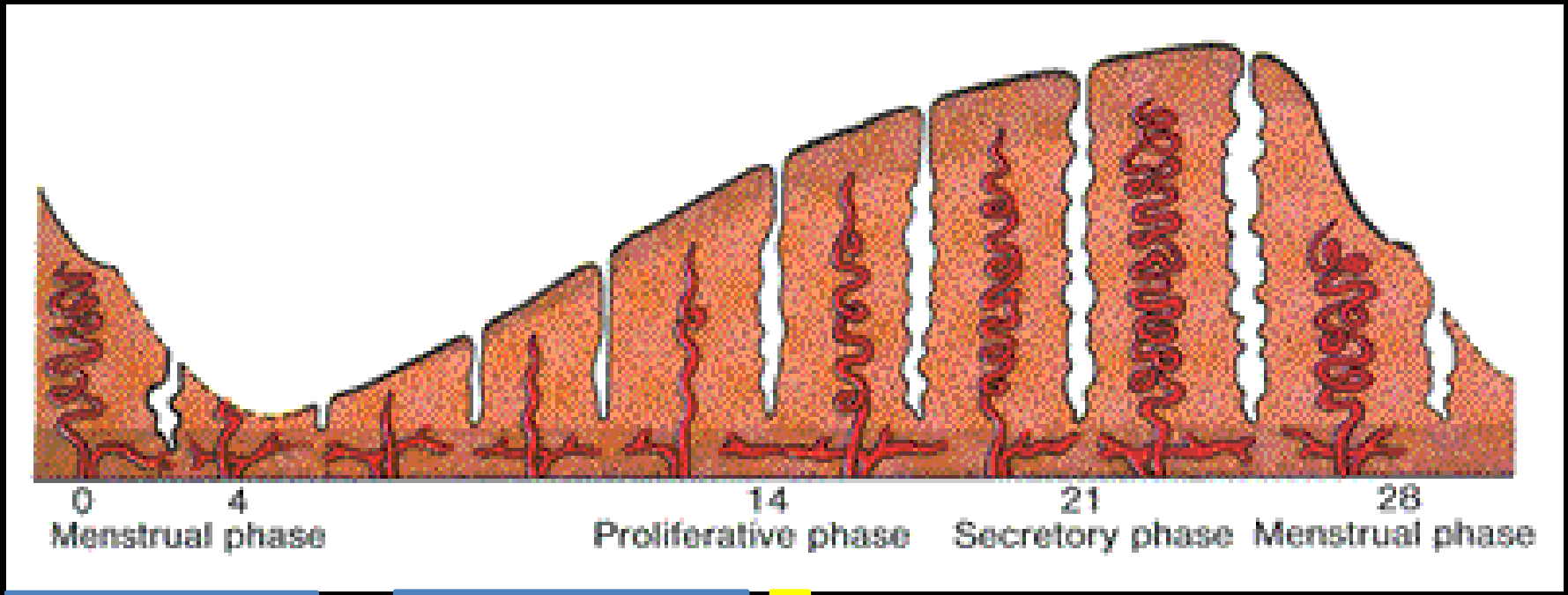
- The onset of the LH surge occurs 34-36 hours before ovulation & reliably indicates the timing of ovulation

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



Phases of the endometrium



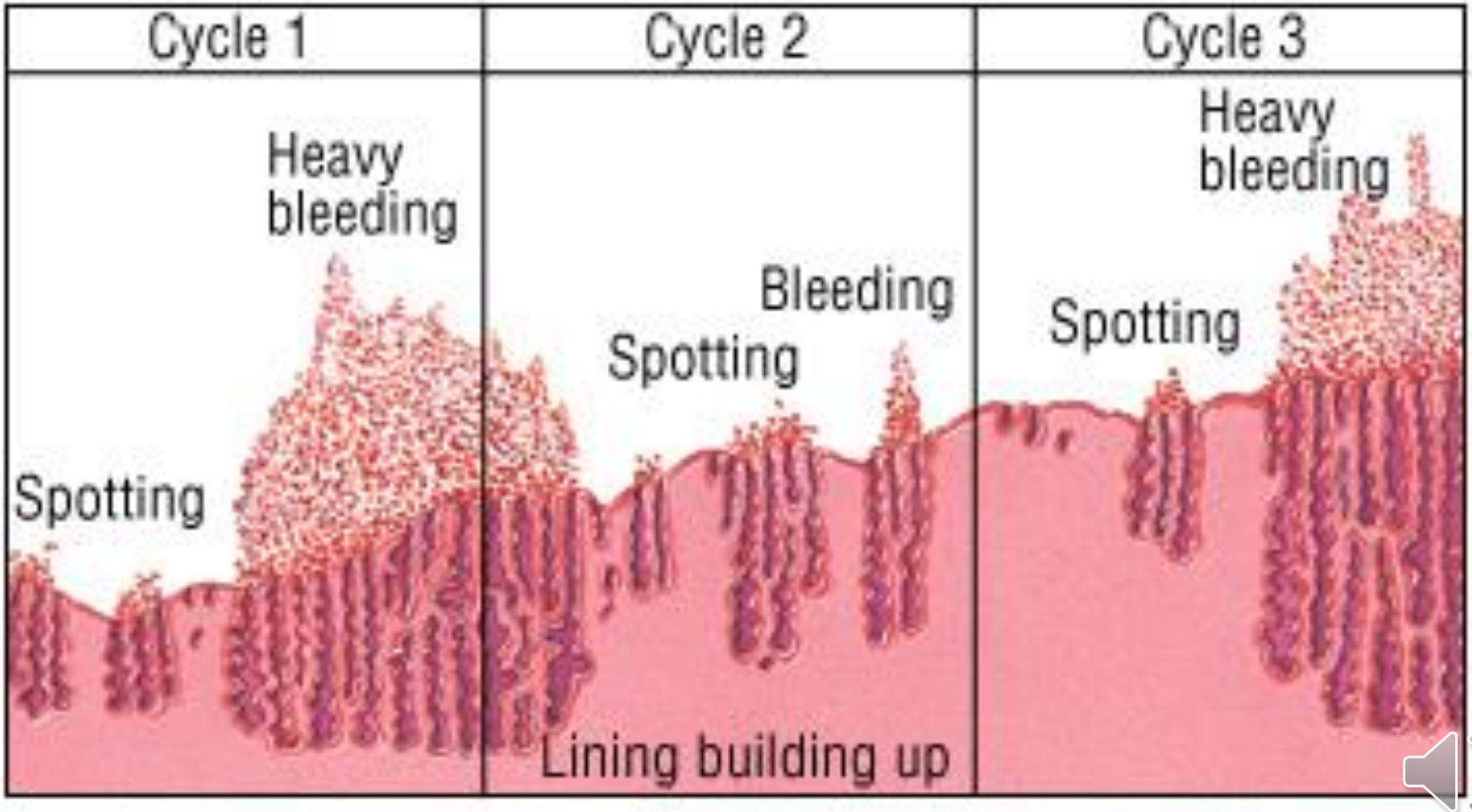
Duration	Estrogen	Progesterone
• 2-8 days	• variable • Vascular growth	• **Fixed 14 days** • **gland tortuosity & secretion, stromal oedema ,decidual reaction of the endometrium**

Cervical changes

Follicular phase	Luteal phase
Internal os- funnel shape	Tightly closed
Mucus- thin &watery	Thick & viscid
Stretchabilty- increased	lost

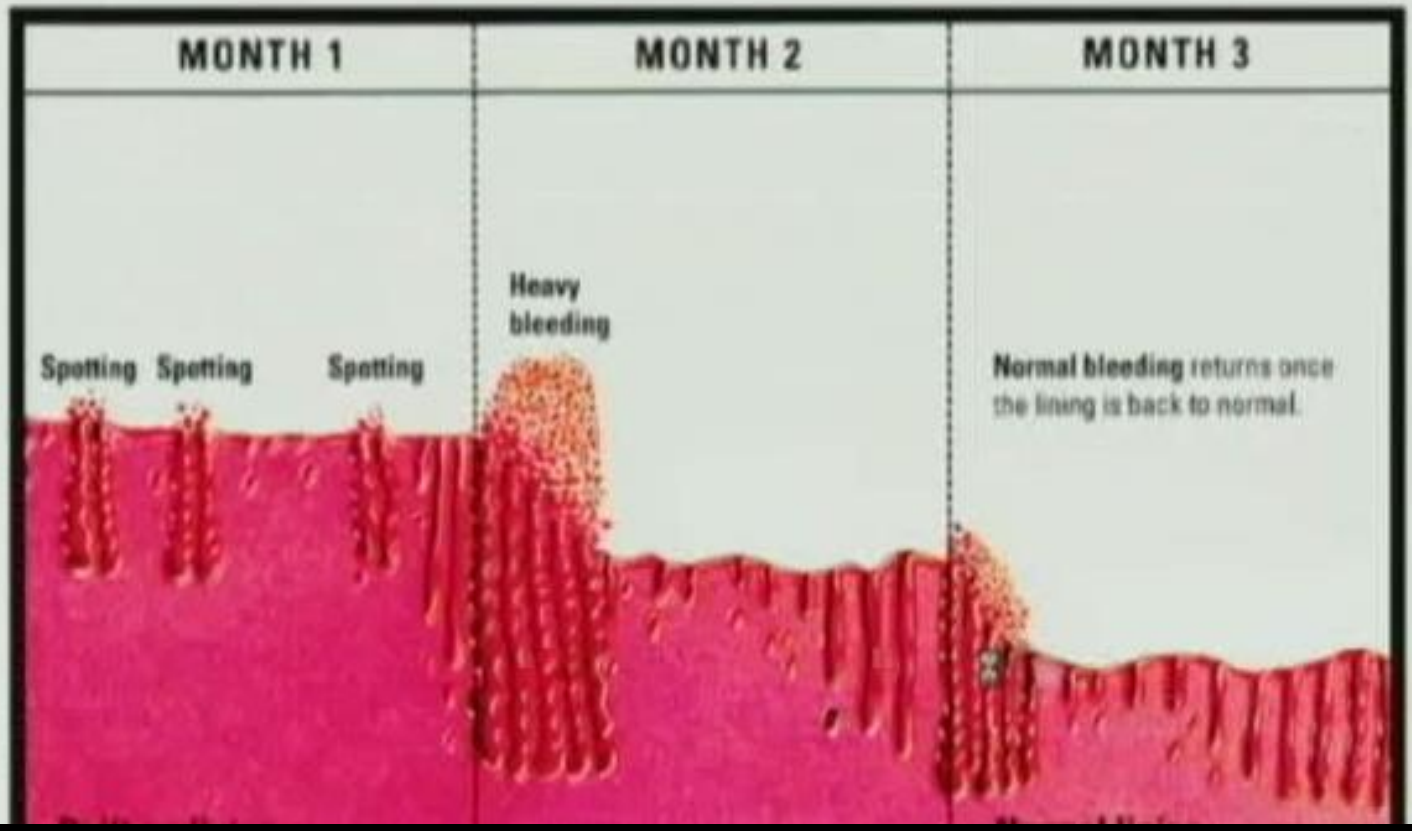
E → proliferative changes

E dominant endometrium is UNSTABLE



P → Secretory changes

P dominant endometrium is STABLE



Menstrual phase

- Rapid ↓ in steroids → shedding of the unused endometrium.
- Inflammatory mediators (PGs, ILs, and TNF) → vasospasm in spiral end arteries → hypoxia and endometrial devitalization.
- Complex vascular changes controlled by above secondary messengers, also → natural haemostatic mechanisms including platelet plugs, coagulation cascade, and fibrinolysis.
- Endometrium lost down to basalis layer

Endometrial breakdown

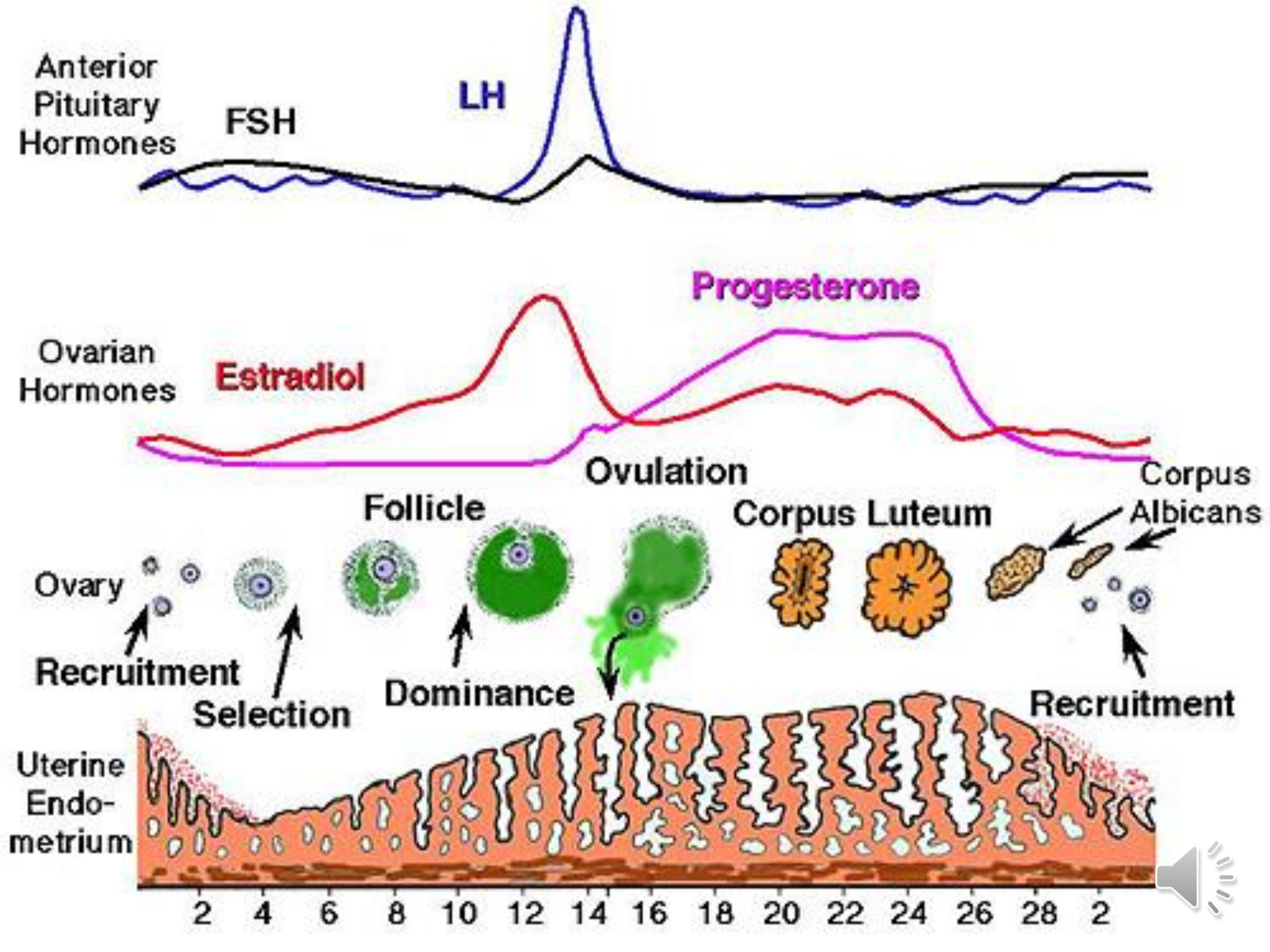
Basalis layer remains → **repair**

The endometrium is protected from the lytic enzymes in the menstrual fluid by mucinous layer of carbohydrate products discharged from glands and stromal cells

Menstrual Fluid

- Autolysed functionalis
- Inflammatory exudate
- RBC
- Proteolytic enzymes (mainly plasmin)

If rate and flow is high clots are formed


Anterior Pituitary Hormones
FSH
LH
Ovarian Hormones
Estradiol
Progesterone
Ovulation
Follicle
Corpus Luteum
Corpus Albicans
Ovary
Recruitment
Selection
Dominance
Recruitment
Uterine Endo-metrium
2 4 6 8 10 12 14 16 18 20 22 24 26 28 2

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)

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)

Menstrual Disorders

Dysmenorrhea: painful menses

Primary Dysmenorrhoea

Intrinsic, essential, Idiopathic

Usually begins with ovulatory menstrual periods

Most common medical problem in young women

Pathophysiology

Theories:

- Uterine contraction and vasoconstriction
- Modulation and stimulation of pain fibres
- Psychological and behavioural causes

Clinical picture

- **Pain**
- Typically presents 6–12 months after menarche.
- Pain is usually cramping in nature and occurs in the lower abdomen or pelvis but may radiate to the back or down the thighs.
- It may commence before the onset of bleeding and usually lasts 8–72 hours.
- Associated symptoms include nausea and vomiting, fatigue and headache.

Secondary dysmenorrhoea

- **Due to organic or psycho-sexual causes**
- **Usually occurs years after the menarche & pain may occur throughout the luteal phase as well as during menstruation.**
- **Deep dyspareunia may also be present**

- **Causes**
  - Endometriosis
  - Adenomyosis
  - PID
  - IUCD in utero
  - Pelvic adhesions
  - Fibroids (though not always causal)
  - Cervical stenosis (iatrogenic LLETZ/instrumentation)
  - Congenital abnormalities causing genital tract obstruction, e.g. non-communicating cornua

Management

Appropriate **reassurance and analgesia**

Symptom control:

- **PGSI**

- mefenamic acid 500mg tds with each period is effective
- COX-1, COX-2

- COCP to abolish ovulation
- data on Mirena IUS demonstrate benefit
- Paracetamol, hot-water bottles, etc., may be helpful for some

Treat any underlying causes:

- Endometriosis—COCP, progestagens, GnRH analogues
- antibiotics for PID
- relief of obstruction (usually surgical)
- *Therapeutic laparoscopy:* gold standard for diagnosis + management of endometriosis/adhesions/ PID

dominal Pain

Trouble Sleeping

Back Pain

Fain

sea

Suicidal Thoughts

Joint/Muscle Pain

Flu Like Symptoms

Depression

Mental"Fog"

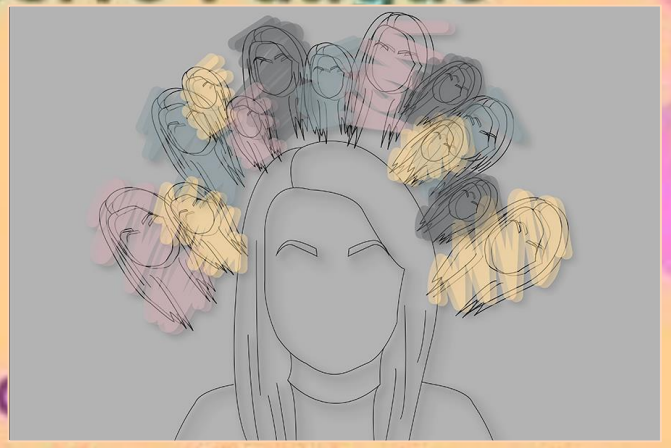
adaches

PMDD

art Palpitations

Excessive Fatigue

Attacks



Mood Swings

Chills

Hives

ficulty Concentrating

Feelings

Isolating/Withdrawing

Dizziness

Depression

Breast Tendern

Premenstrual disorders

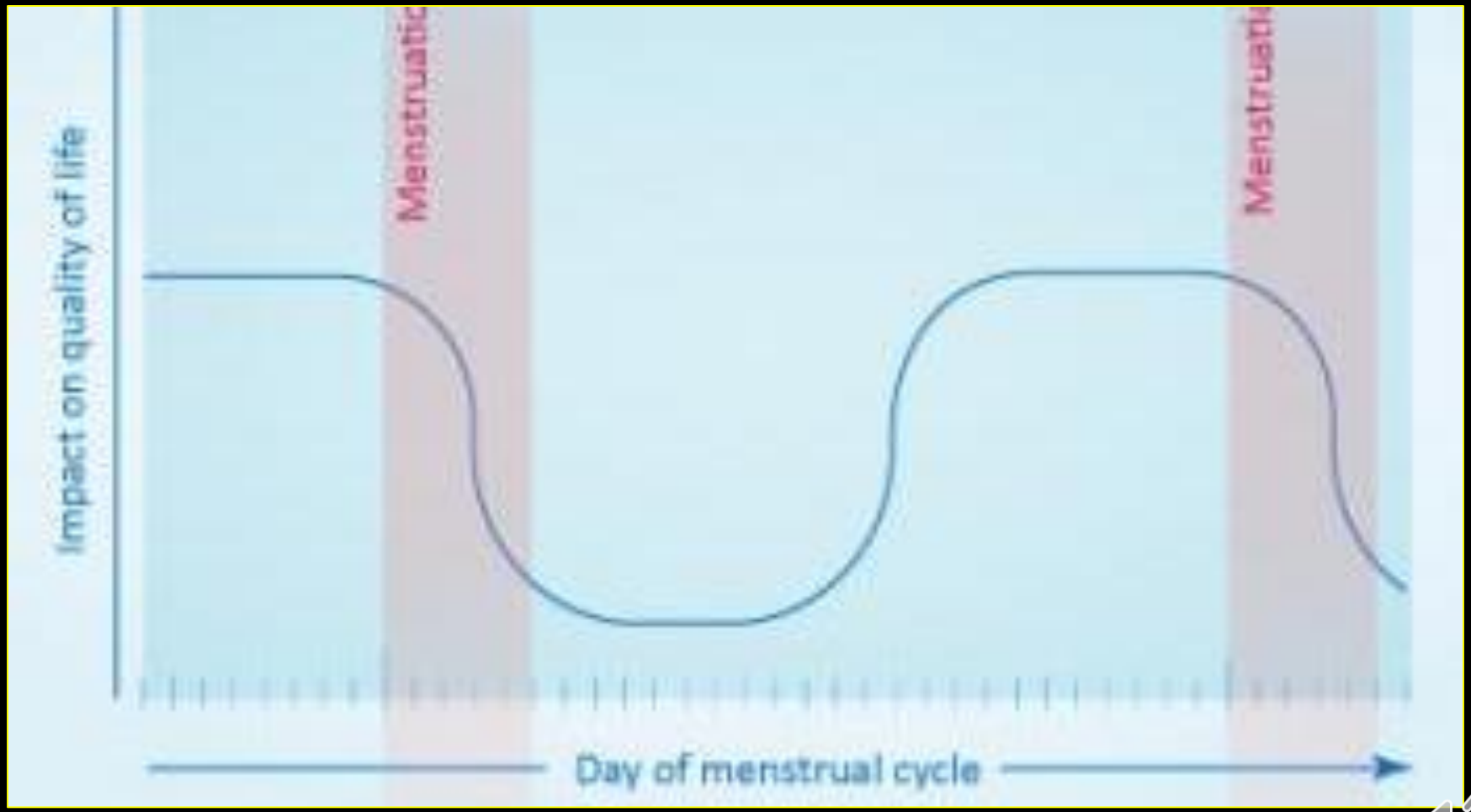
- Premenstrual tension (PMT)!
- Premenstrual syndrome (PMS)!

Most women experience a certain degree of premenstrual symptoms before menstruation.

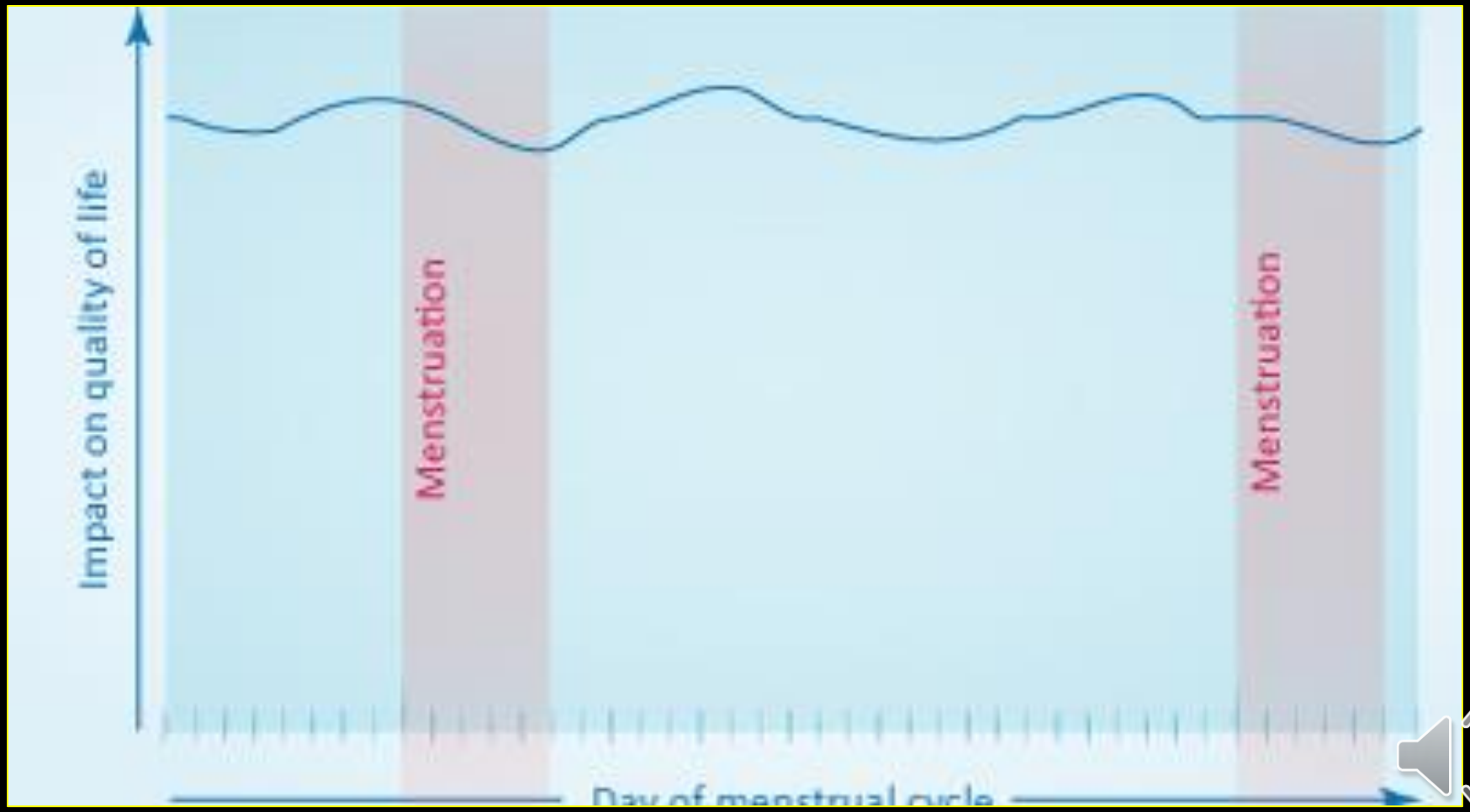
Physiological when the severity of symptoms is not enough to have a serious impact on the quality of life, but is noticeable to the woman.

Symptoms occur in a cyclical nature with a symptom free week in the follicular phase.

Physiological premenstrual symptoms (mild premenstrual disorder)



Symptoms are not cyclical require appropriate non-gynaecological treatment



Premenstrual disorders (PMD)

Impairment of daily activities and interpersonal relationships

Impact on many aspects of a woman's everyday life for most of their reproductive years

The International Society for Premenstrual Disorders (ISPMD)

Core and Variant

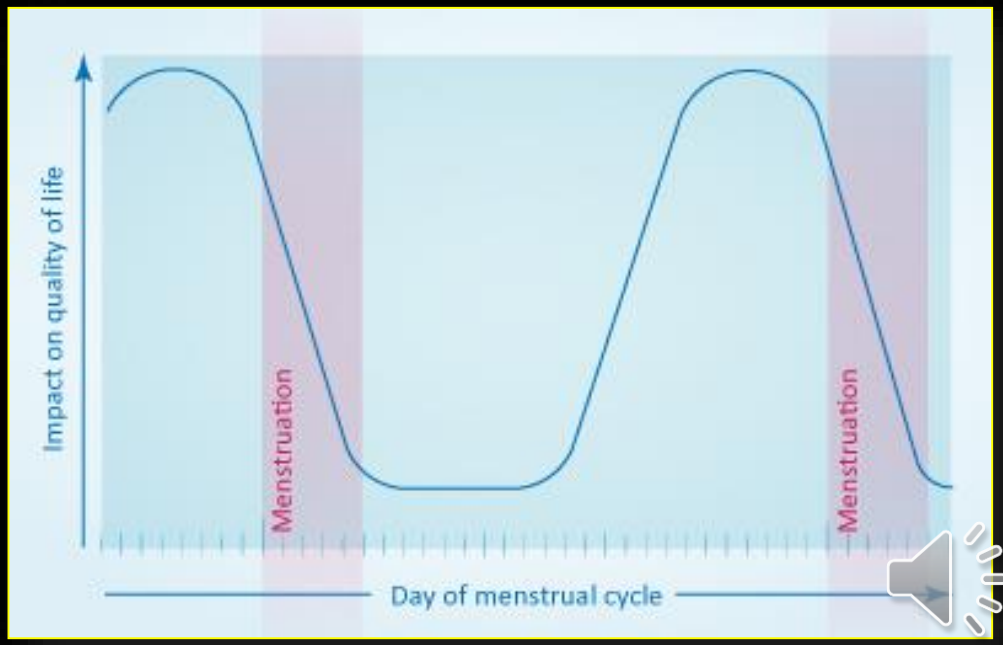
On the basis of the ISPMD, the criteria for diagnosing Core PMD include:

- Cyclical
- Symptoms resolved during or shortly after menstruation (1 week free from menstruation to ovulation)
- Symptoms must be prospectively rated
- Symptoms are not an exacerbation of an underlying psychological or physical disorder.
- Impairment of daily activities including work, social interactions and family activities.

Core premenstrual disorder

Based on symptoms, core premenstrual disorders are further subdivided into:

- Predominantly physical symptoms
- Predominantly psychological symptoms
- Mixed - both psychological and physical symptoms



Variant premenstrual disorder

- Premenstrual exacerbation (PME)

Worsening underlying medical, psychological or physical condition (e.g. depression, diabetes, migraine, asthma, epilepsy, etc) during the premenstrual phase

Symptoms throughout the cycle, with worsening before and reduction after menstruation

- Premenstrual disorder with absent menstruation

Hysterectomy, endometrial ablation or IUS

- Progestogen-induced premenstrual disorder

Exogenous progestogens, e.g. HRT / hormonal contraception

- Premenstrual disorder due to non-ovulatory ovarian activity (rare)

Symptoms and diagnosis

- 200 reported symptoms
- Timing of these symptoms is more important than their character and severity
- Prospective symptom rating over two consecutive menstrual cycles

Clinical features

Physical symptoms:

breast tenderness or pain

abdominal swelling / bloating

headaches

skin disorders

weight gain

swelling of extremities (hands or feet or both)

joint pain, muscle pain, back pain.

Psychological and behavioural symptoms:

mood swings

Irritability/ anger, aggression

Anxiety/ depressed mood

Confusion/ tension

sleep disturbances

changes in appetite

fatigue, lethargy, or lack of energy

restlessness

poor concentration

social withdrawal/ not in control

lack of interest in usual activities

Loneliness/ hopelessness

Aetiology

- **Unknown**

- Following menstruation, women often report a positive mood leading up to and culminating around the same time as the estradiol peak prior to ovulation (Backström et al 1983). Therefore, it is thought that the **corpus luteum produces a symptom-provoking factor** (Backstrom 2011).

- Concept of **hormonal imbalance** has been popular, but there is no supportive evidence/ hormonal profile same as asymptomatic

- Women with PMS are **more susceptible to their normal ovarian** hormone cycle (especially progesterone). The increased sensitivity may be due to **neurotransmitter dysfunction (possibly serotonin**)

Treatment

Symptom-based treatment strategy

Mild- support, reassurance and good nutrition, exercise and stress reduction

Core- 2 approaches:

- **Suppression of ovulation**
  - GnRha/ COCP/ Danazol/ Estrogen
  - Surgery
- **Treatment w/o suppression of ovulation**
  - SSRI/ Diuretics
  - Non-pharmaceutical treatment
    - Herbal supplements
    - Cognitive behavioural therapy
    - Vitamin B6/ Calcium
    - Exercise

Heavy menstrual bleeding (HMB)

Clinically defined as menstrual blood loss (MBL) that is subjectively considered to be excessive by the woman and interferes with her quality of life.

Subjective assessment: combines information of sanitary protection usage, flooding, clots, duration of menstruation and the woman's personal opinion of her menstrual loss.

inaccurate

Objective assessment: does not improve clinical care and is not undertaken in modern clinical practice.

Causes of HMB

40–60% idiopathic

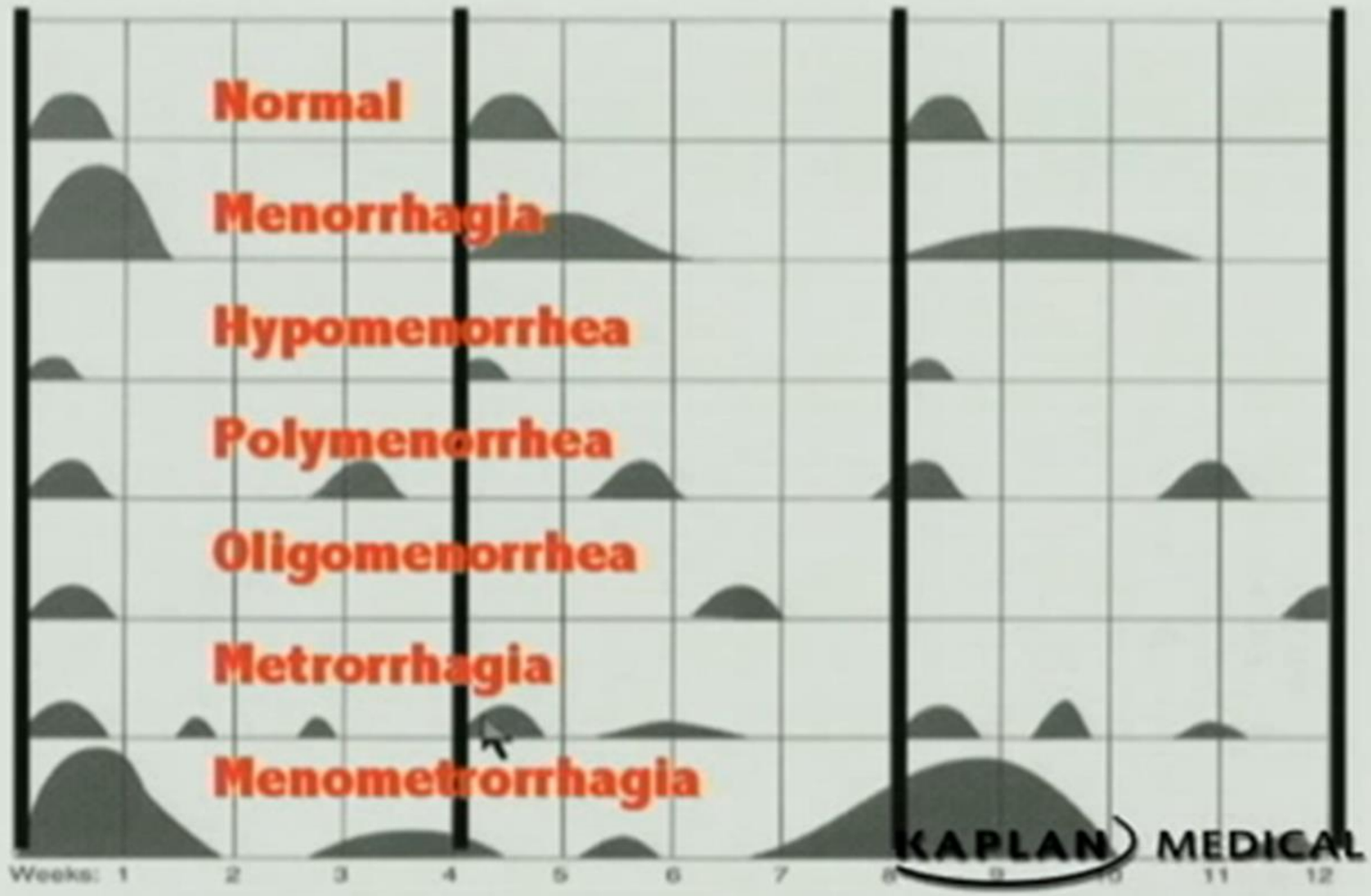
formerly termed DUB of ovulatory /anovulatory

Most HMB is due to a combination of coagulopathy, ovulatory or endometrial dysfunction

Pathological causes of HMB include:

- uterine fibroids (20–30%)
- uterine polyps (5–10%)
- adenomyosis (5%)
- endometriosis rarely presents as AUB, but is identified in <5% of cases of AUB
- Gynaecological malignancy rarely presents as HMB, but can present as prolonged IMB, PCB, PMB and as a pelvic mass

Old Terminology



Terminology to describe AUB

Terms to be kept in new terminology	
Abnormal uterine bleeding (AUB)	Any menstrual bleeding from the uterus that is either abnormal in **volume** , **regularity**, **timing** or is **non-menstrual** (IMB, PCB or PMB)
Heavy menstrual bleeding (HMB)	subjective diagnosis as it is defined by the woman based on how it interferes with her quality of life.
Intermenstrual bleeding (IMB*)*	Uterine bleeding that occurs between clearly defined cyclic and predictable menses.

Postmenopausal bleeding (PMB)	**Genital tract bleeding that recurs in a menopausal woman at least one year after cessation of cycles**
Postcoital bleeding (PCB)	**Non-menstrual genital tract bleeding immediately (or shortly after) intercourse**
Chronic AUB	**AUB has been present for the majority of the past 6 months.**
Acute AUB	**Excessive AUB bleeding that requires immediate intervention to prevent further blood loss. Acute AUB may present in the context of existing chronic AUB or might occur without such a history**

FIGO classification of the causes of AUB

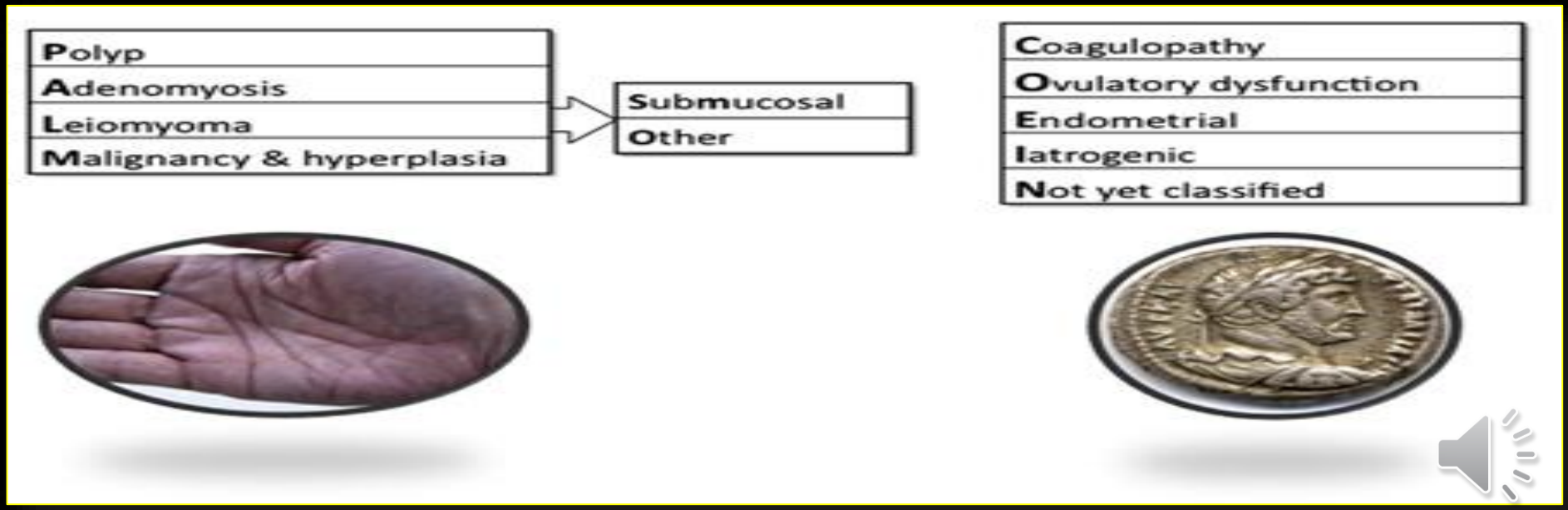
R/O Pregnancy

New classification system **PALM-COEIN**:

- **Structural causes** for AUB:

polyp; **a**denomyosis; **l**eiomyoma; **m**alignancy &hyperplasia

- **Non-structural causes** for AUB: **c**oagulopathy; **o**vulatory dysfunction; **e**ndometrial; **i**atrogenic; and **n**ot yet classified.



Examples

Non-structural	
C	**Systemic coagulopathy**, e.g. thrombocytopenia, von Willebrand's disease, leukaemia, warfarin
O	**Disorders of ovulatory function**, e.g. PCOS, CAH, hypothyroidism, Cushing's disease, hyperprolactinaemia
E	Primary **endometrial disorders**, e.g. disturbances of local endometrial haemostasis, vasculogenesis or inflammatory response (chronic endometritis)
I	**Iatrogenic causes**, e.g. combined oral contraceptives, progestins, tamoxifen, IUCD, traumatic uterine perforation
N	Generally **rare causes**, e.g. arteriovenous malformations, myometrial hypertrophy, sex steroid secreting ovarian neoplasm, chronic renal or hepatic disease, endometriosis

PMB

Causes of vaginal bleeding in postmenopausal women	
Endometrial atrophy	30%
Endometrial carcinoma	8–10%
Polyps	30%
Submucosal fibroids	20%
Hyperplasia	8–15%
Ovarian, tubal, cervical malignancy	2%

IMB-causes

Infection

Endometritis/ Cervicitis/ Vulvovaginitis

Iatrogenic

Breakthrough bleeding/ Secondary to examination/smear test

Structural (benign)

Uterine/cervical polyps/fibroids

Ectropion

Vaginal adenosis

Structural (premalignant/malignant)

Uterine/cervical/vaginal/vulval cancer

CIN/VaiN/VIN

Ovarian estrogen secreting tumours

Natural

1–2% of women will have midcycle spotting, associated with ovulation

Endometrial polyps

Localised hyperplastic overgrowths of endometrial glands & stroma.

HMB, PMB, IMB & abnormal vaginal discharge

Large or multiple are implicated in subfertility

Diagnosis is achieved with USS, SIS & hysteroscopy.

Mx removed hysteroscopically in postmenopausal patient or >1cm in size in an asymptomatic premenopausal patient

Assessment

History

P/E

Investigations

Management

Symptoms

Heavy menstrual loss

Detailed history of the menstrual cycles

IMB, PCB

Tiredness, weakness, or easy fatigability

Associated symptoms

- Dysmenorrhea primary vs secondary
- Dyspareunia endometriosis or PID
- Pressure symptoms
- Offensive vaginal discharge may be present in pelvic infections.
- The influence patients lifestyle

Other relevant history

- Detailed past gynaecological history contraception(&fertility plan), pap smear ..
- Obstetric history
- Past medical history

  pre-existing bleeding tendencies/FH
- Anticoagulant medications/ Tamoxifen
- Weight gain, constipation, and hair loss suggest thyroid disorder.
- Past surgical history may influence the treatment.
- Risk of STI
- Family history of gynaecological history

Signs

General examination

BMI

look for tachycardia, hypotension, and pallor

signs of hypothyroidism

bruises or gum bleeding

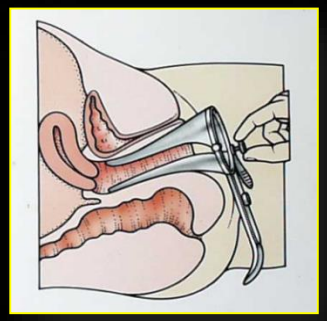
Abdominal examination

look for any tenderness or masses

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

Speculum examination

- look for any local cervical or vaginal lesions
- Assess the severity of the blood loss
- Bimanual examination

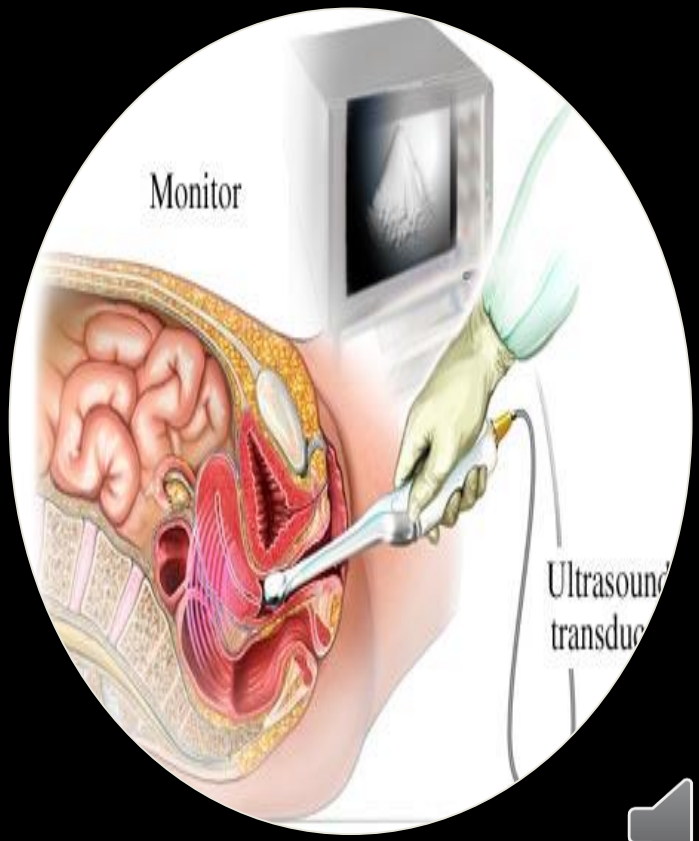


uterine size, shape, tenderness & mobility

- Enlarged uterus -fibroids / adenomyosis
- Restricted mobility - endometriosis and pelvic infections
- Tenderness – adenomyosis/ endometriosis/ PID

Investigations

TVS USS— good to identify fibroids , polyps, and measuring endometrial thickness.



Endometrial thickness ET

96% of postmenopausal women with endometrial cancer will have an endometrial thickness (ET) >4 mm

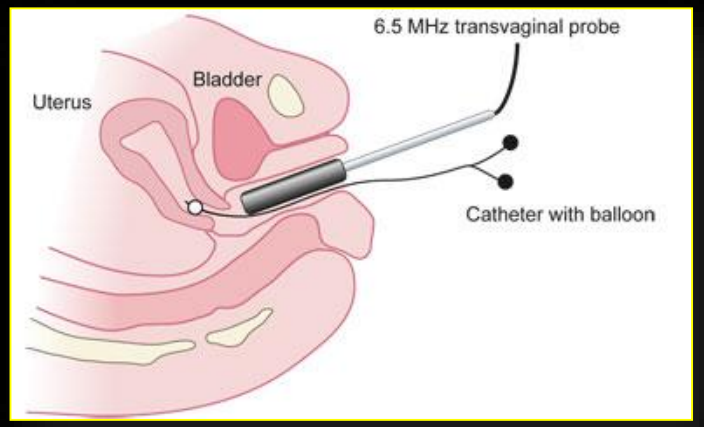
Women with PMB whose ET is <4 mm still have a 1–2% risk of having endometrial cancer.

endometrial biopsy is required if ET is:

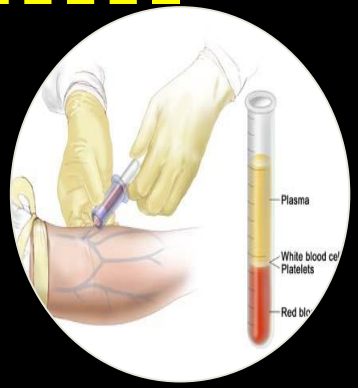
- >4 mm in postmenopausal women
- May be selectively performed in postmenopausal women with ET <4 mm if other historical, clinical or sonographic risk factors are present.

Saline infusion sonography(SIS)

Visualisation of uterine and endometrial pathology.



Investigations.....



R/O Pregnancy

- FBC (Hb + MCV).
- TFTs

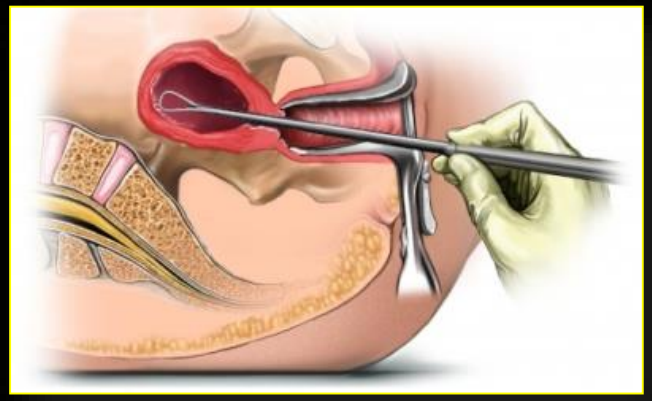
  clotting screens are *not* routine
- Cervical smears
- STI screen including *Chlamydia*.
- **E**ndometrial biopsy to exclude hyperplasia or cancer

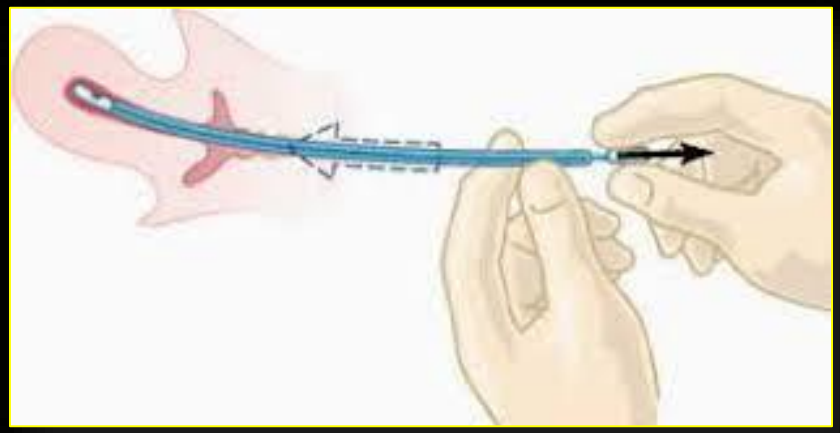
Endometrial sampling

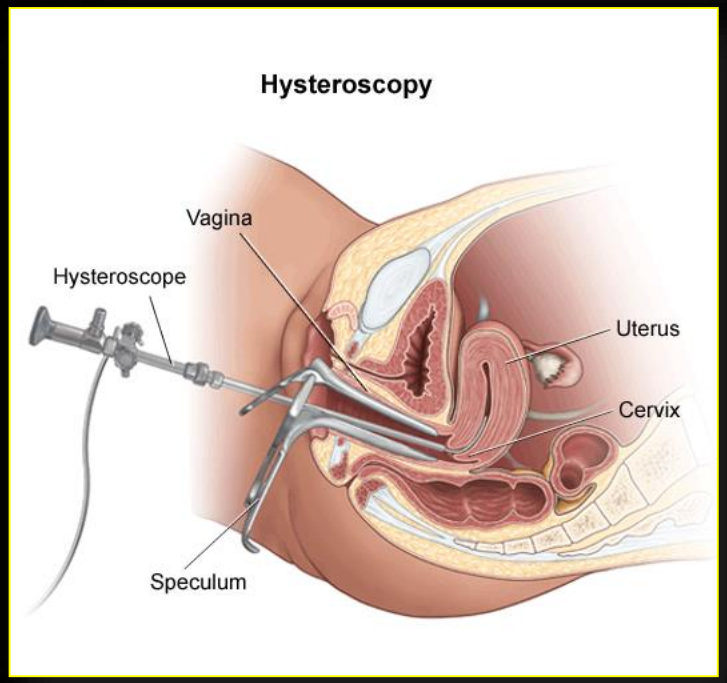
D&C

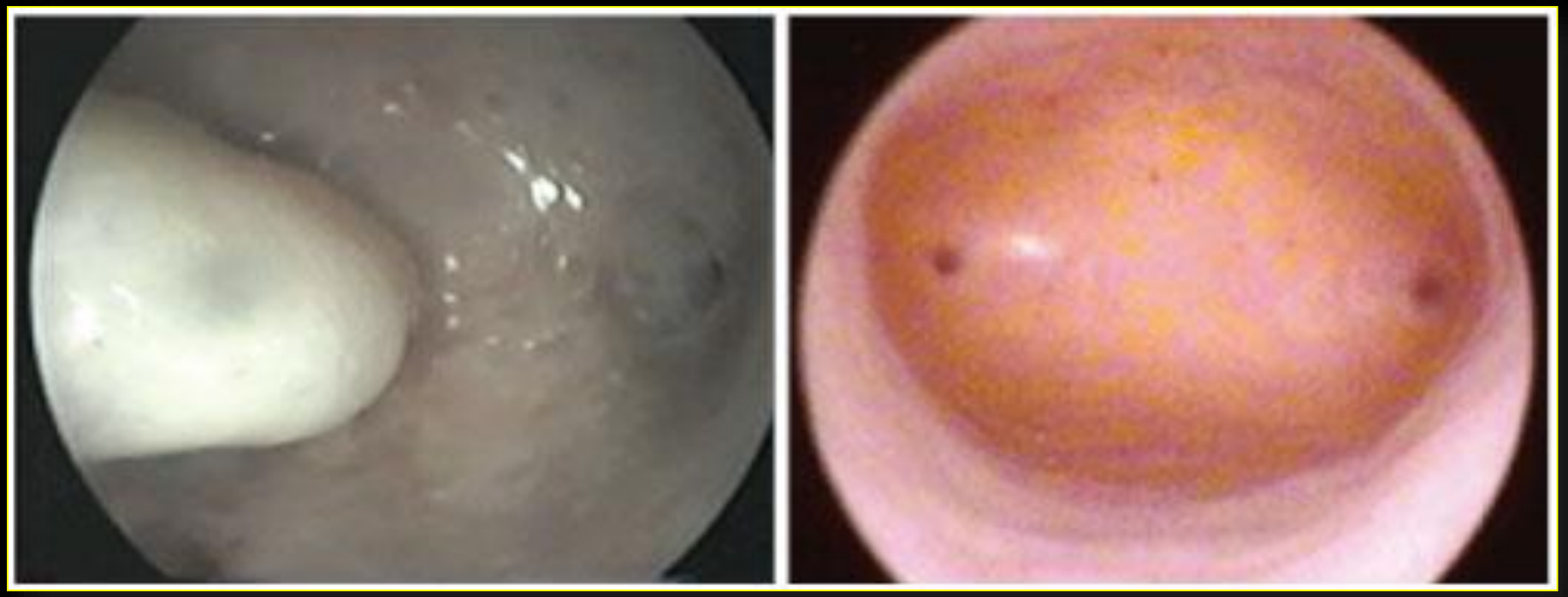
Hysteroscopy

Pipelle









Treatment-Medical

Hormonal

❖ Mirena IUS

levonorgestrel ⟶ atrophic endometrium

Blood loss ↓ by up to 90% and ~ 30% will be amenorrhoeic at 12mths.

Provides contraception

▸ This IUS has resulted in a major ↓ in number of hysterectomies.

❖ Progesterone from day 5 to 26 in a cyclical manner.

from day 15 or 19 to day 26 of the cycle

Cyclical progesterone for 21 days of the cycle results in a significant reduction in menstrual blood loss.

❖ Combined oral contraceptive

Non-hormonal

- ***Antifibrinolytics:*** tranexamic acid 1g tds days 1–4 (50%↓ in loss)

- ***NSAIDS:*** mefenamic acid 500mg tds days 1–5 (30-40 ↓ in loss and significant ↓ in dysmenorrhoea)

Surgical treatment

Endometrial Ablation

Hystrectomy

Age specific issues in evaluation: Children

6 year old girl presents with bleeding

If there is AUB before menarche then a **pelvic examination (usually under anaesthesia)** should be performed.

D.Dx:

trauma, sexual abuse, assault or congenital malformations, malignancy.

Age specific issues in evaluation: Adolescents

15 yr noted menarche at the age of 14 but has only had 3 or 4 periods since. She has missed school because of “massive bleeding”

Age specific issues in evaluation: Reproductive Age

24 yr woman who can't predict when her period will come and when it does it is very heavy. Some months it's ok though.

Age specific issues in evaluation: Perimenopausal

49 yr woman now with heavy irregular menses but they used to be “like clockwork”

Age specific issues in evaluation: Post-Menopausal

69 yr woman, no vaginal bleeding for last 10 years noted two days of spotting like light period

Thank you