MENSTRUAL CYCLE AND ITS DISORDERS

CONTENTS

MENSTRUAL CYCLE

- Cyclical changes in women that occurs regularly over a period of about one month, which is the periodic preparation of the reproductive system for fertilization and implantation of the fertilized ovum .
- Average duration is 28 days

MENSTRUAL CYCLE

- The cyclical changes are brought about by the cyclic production of oestrogen and progesterone by the ovaries
- It comprises:

1. OVARIAN CHANGES(OVARIAN CYCLE)
2. UTERINE CHANGES(UTERINE CYCLE)
3. CERVICAL CHANGES(CERVICAL CYCLE)
4. VAGINAL CHANGES(VAGINAL CYCLE)
5. BREAST CHANGES
6. HORMONAL CHANGES

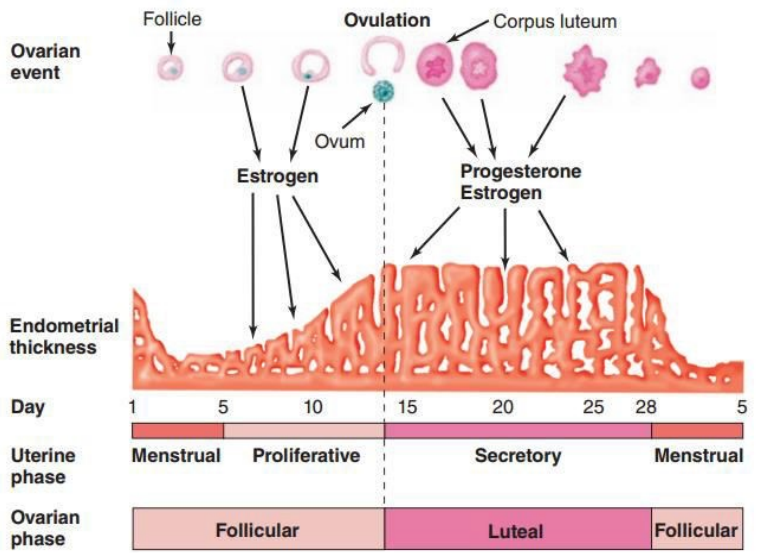
- The most conspicuous feature is the periodic vaginal bleeding called menstruation

Duration of menstrual cycle

- The length of the cycle usually averages 28 days from the start of one menstrual period to the start of the next
- Duration of cycles is not same in all women
- Normally it ranges from 25 - 35 days

Ovarian cycle

1. Follicular phase
2. Ovulation
3. Luteal phase



Relationship between ovarian and uterine changes during the menstrual cycle. (Reproduced

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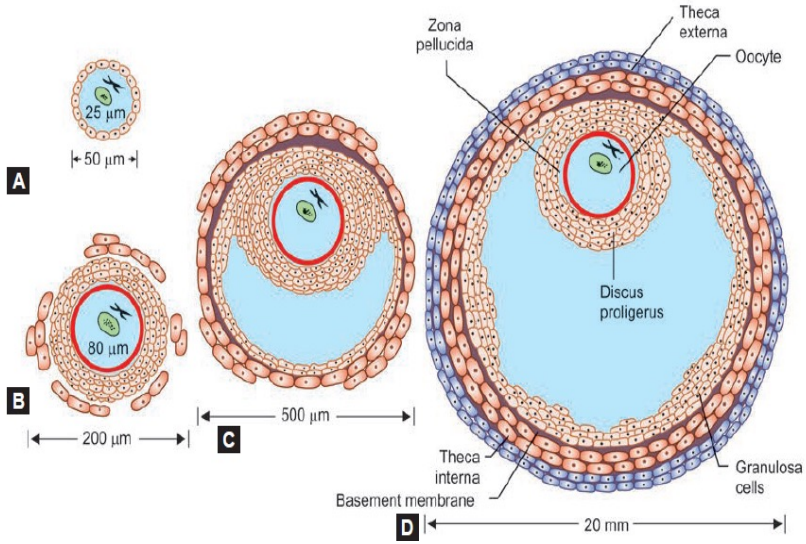
Follicular phase



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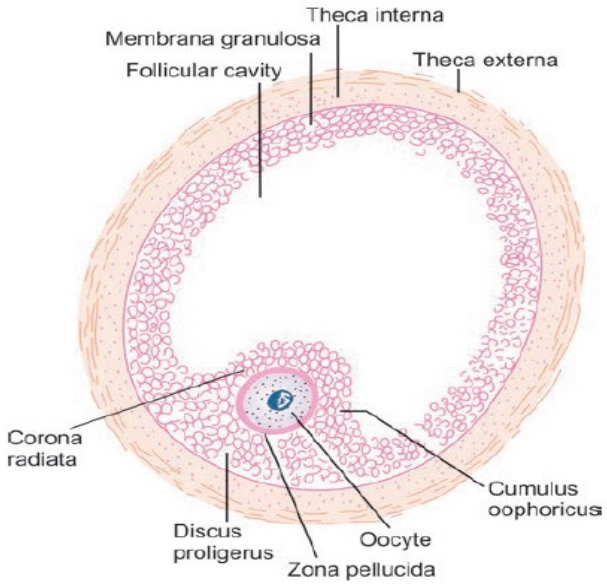

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- Dominant follicle
- Zona pellucida
- Membrana granulosa
- Cumulus oophoricus
- Discus proligerus
- Theca interna
- Theca externa
- Graffian follicle

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- Period from onset of bleeding to the day of ovulation
- i.e. day 1 to day 14 of a 28 day cycle
- Alteration of the length of the menstrual cycle occurs due to alteration in the duration of follicular phase
- It is called follicular phase as the dominant follicle in the ovary matures in this phase to terminate in ovulation at the end of this phase
- As this phase occurs before ovulation, its also called **preovulatory phase**
- Follicular phase is divided into 2 :

1. MENSTRUAL PHASE – menstrual bleeding
2. PROLIFERATIVE PHASE – proliferation of uterine endometrium

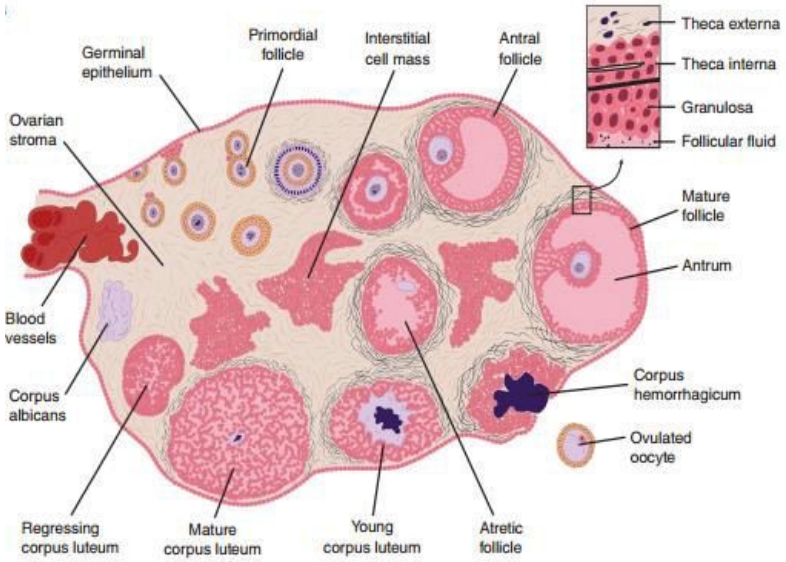
Ovulation

- 14^{th} day of the cycle
- LH surge

Luteal phase

- Corpus hemorrhagicus
- Mittelschmer sign
- Corpus luteum
- Secrete estrogen & progestrone
- Corpus luteum persist if pregnancy occurs
- No pregnancy → corpus albicans

Sequential development of a follicle , formation of corpus luteum and follicular regression



- Series of changes which begins with formation of a follicle & degeneration of corpus luteum constitute ovarian cycle.

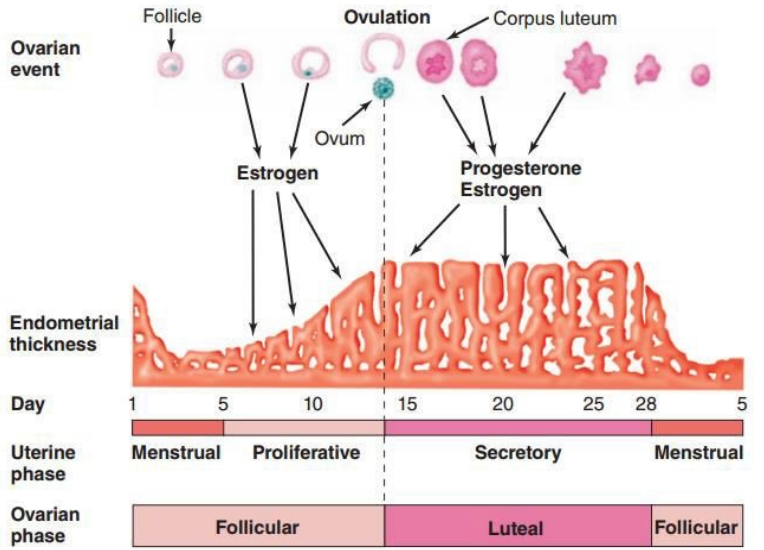
UTERINE CYCLE

- Cyclical production of estrogen & progestrone from ovary influence hypothalamo-pituitary axis to bring cyclical changes in uterine endometrium and produce bleeding per vaginum
- Phases

✓Proliferative/preovulatory/follicular phase

✓Secretory phase/luteal phase

✓Menstruation



Relationship between ovarian and uterine changes during the menstrual cycle. (Reproduced

Proliferative/preovulatory/follicular phase

❖ **UTERINE CHANGES IN PROLIFERATIVE PHASE(DAY 5- DAY14)**

- Under the influence of oestrogen secreted from the developing follicle, a new endometrium regrows → thickness of endometrium rapidly increases from 5th day to 14th day of the cycle
- CHANGES ARE:

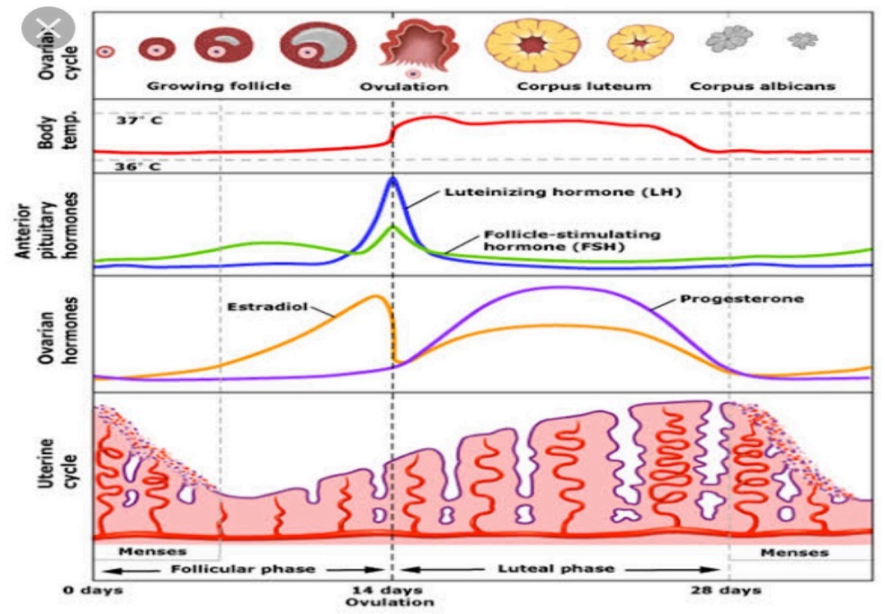
1. The uterine endometrium undergoes **hyperplasia and hypertrophy and increases in size and thickness(upto 3- 4mm)**

2. The endometrial glands(lined with columnar epithelium) also increase in length but donot become convoluted; they contain glycogen but they are nonsecretory
3. The endometrium is vascularized with formation of more number of spiral arteries that increase blood supply to the deeper layers
4. Endometrial veins also grow in size

Secretory phase/luteal phase

- 15^{th} -28^{th} day
- Preparation of uterus for implantation
- Period between ovulation and next menstruation. It corresponds to luteal phase of ovarian cycle
- hormone responsible is progesterone and estrogen.
- Endometrial thickness increase from 6 to 8 mm.
- Endometrial gland become crenated &cork screw shaped

- Proliferation of cytoplasm, deposition of lipids and glycogen
- Increased vascularity of endometrium
- Spiral arteries become more tortuous.

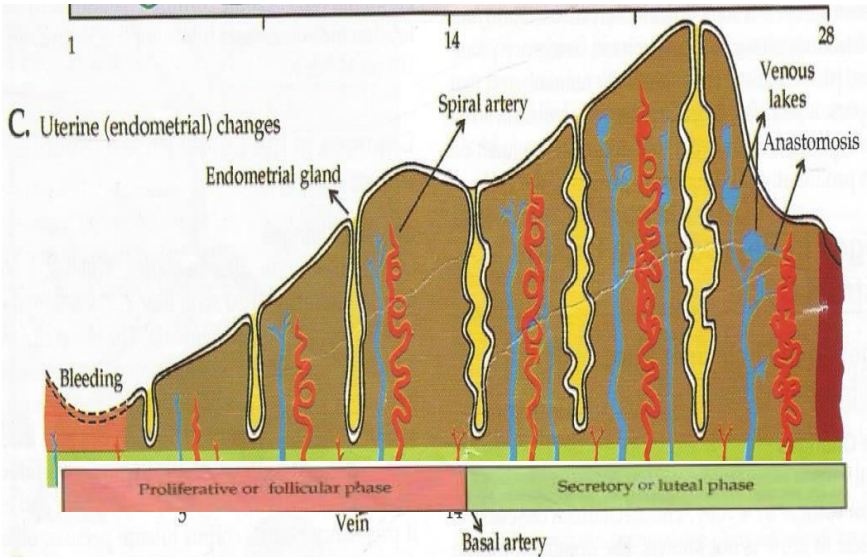


Mensturation

- When pregnancy fails to occur,Corpus luteum regresses, so that the hormone support is withdrawn and thus endometrium becomes thin.
- The spiral arteries become more tortuous and undergo vasospasm by PGF2α.
- Leads to ischemia and necrosis of tissue and the walls rupture.
- Sequential shedding occurs layer by layer in 3–5 days.

- Menstrual blood is predominantly arterial with only 25% of blood being venous in origin
- Contains tissue debris, PGs, fibrinolysins
- Fibrinolysins lyse clot from endometrial tissue **(physiological basis)**
- Flow is excessive- clot forms
- Average blood loss-30-50ml
- >80ml- menorrhagia

UTERINE CHANGES IN MENSTRUAL CYCLE



- <u>The sequents of events are:</u>

1. Intense spasm of spiral arteries hypoxia(reduces blood supply to the endometrium) and ischaemia (mediated by local production of prostaglandins)
2. This leads to endometrial necrosis and also the walls of spiral arteries
3. Necrosis of the walls of spiral arteries → opening up of blood vessel → seepage of blood into the surrounding necrotic endometrial tissue
4. The bleeding along with the sloughing of the necrosed endometrium results in menstrual bleeding

- **IMMEDIATE FATE OF MENSTRUAL BLOOD INSIDE UTERINE CAVITY**

✓ Gets clotted

✓ But soon gets liquefied by fibrinolysins present in endometrial debris

✓ Reason why menstrual blood does not normally contain blood clots unless the blood flow is excessive

- **SIGNIFICANCE OF PROSTAGLANDINS**

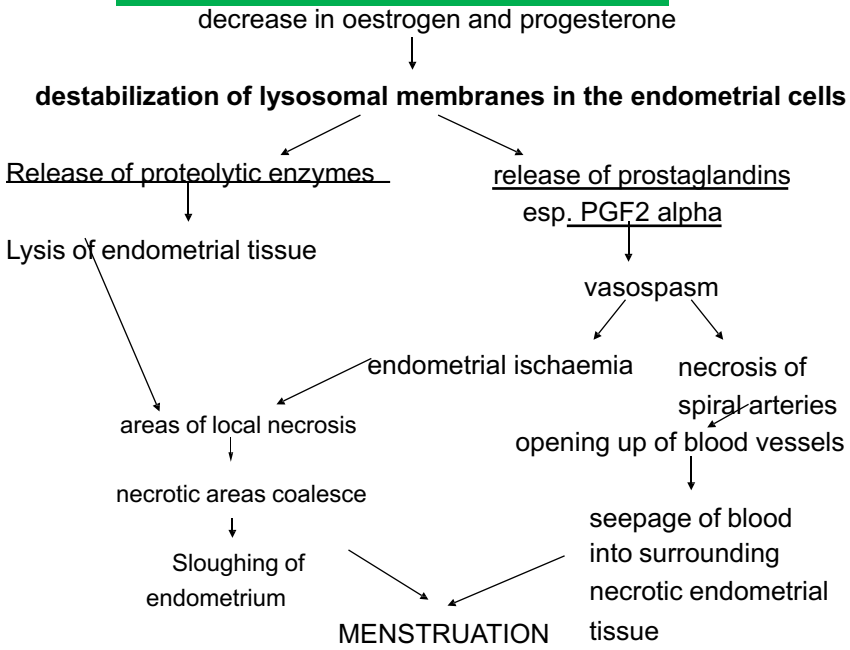
✓ Prostaglandins → uterine contractions → dysmenorrhea(menstrual cramps)

✓ Prostaglandins → smooth muscle contraction in other parts of the body → nausea, vomiting, headache associated with dysmenorrhea

- **IMPORTANT NOTE:**

✓ **During menstrual phase, about 2/3rd of the superficial endometrium is sloughed off and only a thin basal layer(<2mm) is left behind**

MECHANISM OF MENSTRUATION



Cervical cycle

- No shedding of mucosa occurs, but mucous show changes due to action of hormone

During proliferative phase*:*

- *Cervical secretion is thin alkaline* due to estrogen
- enable sperm survival and transportation.

- ***During ovulatary phase****:*

✓ *Cervical secretion is thinnest,* increase elasticity or spinnbarkeit, therefore can be stretched to 8–12 cm.

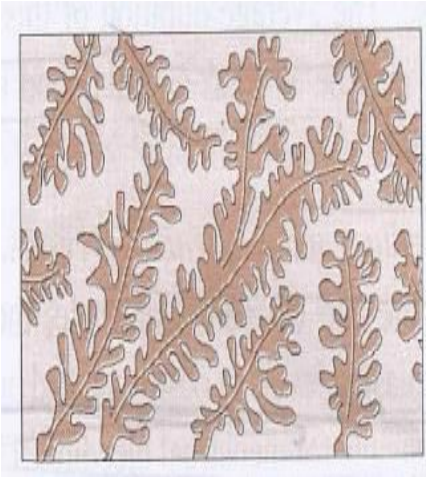
✓ dries in an arborizing fern-like pattern when a thin layer is spread on a slide(fern test)

- ***Secretory phase****:*

✓ *Cervical secretion is thick, tenacious and* cellular

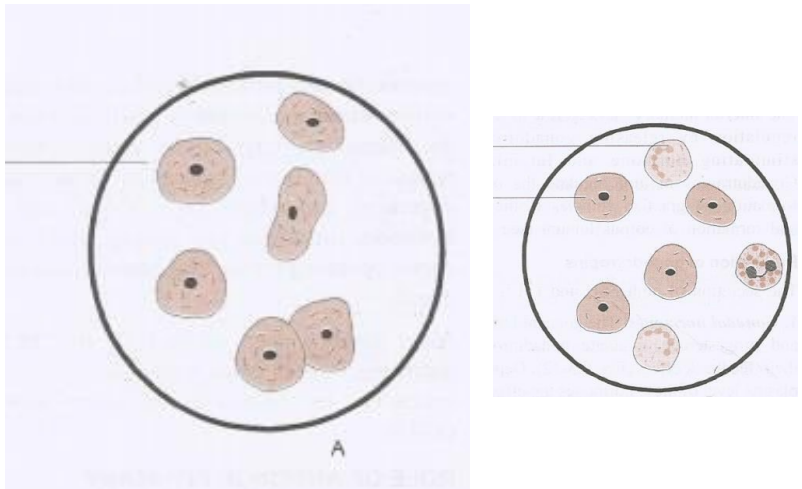
At the time of ovulation, (14th day), the cervical mucus is thinnest and its elasticity is maximum

- It can be stretched like long thin elastic thread upto 8-12cm (**spinnbarkeit effect)**



Vaginal cycle

- ❖During proliferative phase under the influence of estrogen, vaginal epithelium becomes cornified and can be identified as vaginal smear.
- ❖During secretory phase under influence of progesterone, the epithelium proliferates and become infiltrated with leukocytes.

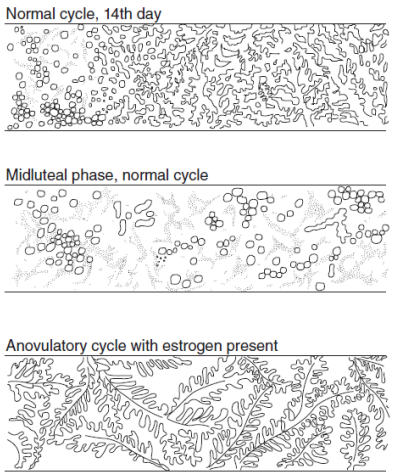


Changes in breast

- **Estrogen** causes proliferation of mammary ducts
- **Progestrone** causes growth of lobules & alveoli
- The breast swelling, tenderness and pain experienced by many women during the 10 days preceding menstruation are probably due to distension of the ducts, hyperemia, and edema of the interstitial tissue of the breast

Indicators of Ovulation

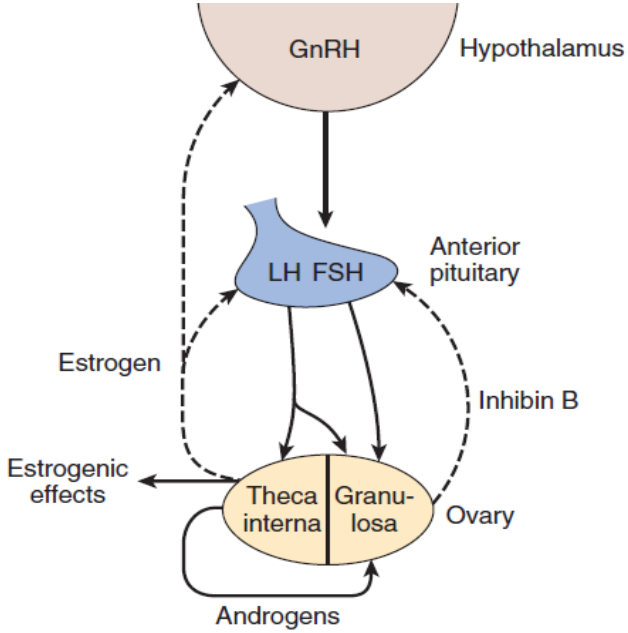
1. Basal body temperature
2. Changes in cervical mucus
3. Vaginal cytology
4. Endometrial biopsy
5. Serial USG of ovaries
6. Hormone estimation



HORMONAL CHANGES IN MENSTRUAL CYCLE/HORMONAL REGULATION OF MENSTRUAL CYCLE

- The menstrual cycle is influenced by the hormones oestrogen and progesterone secreted by the ovary
- Secretion of these hormones are under the control of anterior pituitary gonadotropins FSH and LH
- Secretion of these hormones are regulated by gonadotropin releasing hormone (GnRH) secreted from the hypothalamus

- GnRH has a pecuiliar pulsatile nature of secretion being released in episodic bursts.
- At the same time, there is a negative feedback effect of oestrogen and progesterone both at the hypothalamic and pituitary level, inhibiting the secretion of GnRH from hypothalamus and FSH or LH from the anterior pituitary



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HORMONAL CHANGES IN MENSTRUAL CYCLE

1. **ESTROGEN** – has 2 peaks

1^{st} peak — occurs about 48 hrs before ovulation

2^{nd} peak — post mid-luteal phase

With the growth of ovarian follicle, estrogen concentration slowly ↑

↓

Conc. ↑ rapidly from day 8

↓

Reaches 1^{st} peak 48 hours before ovulation

↓

Conc. thereafter ↓ and further ↓ after ovulation

↓

2 days after ovulation, again oestrogen conc ↑

to reach the 2^{nd} peak(due to its secretion from corpus luteum) in the post midluteal phase

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2. GnRH

•Hypothalamus secretes GnRH which is in episodic bursts

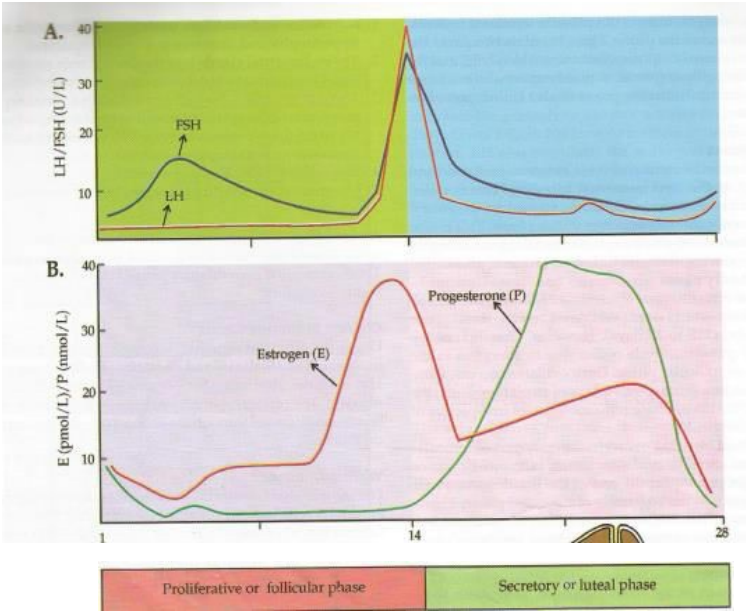
•Frequency is increased by estrogens and decreased by progesterone and testosterone.

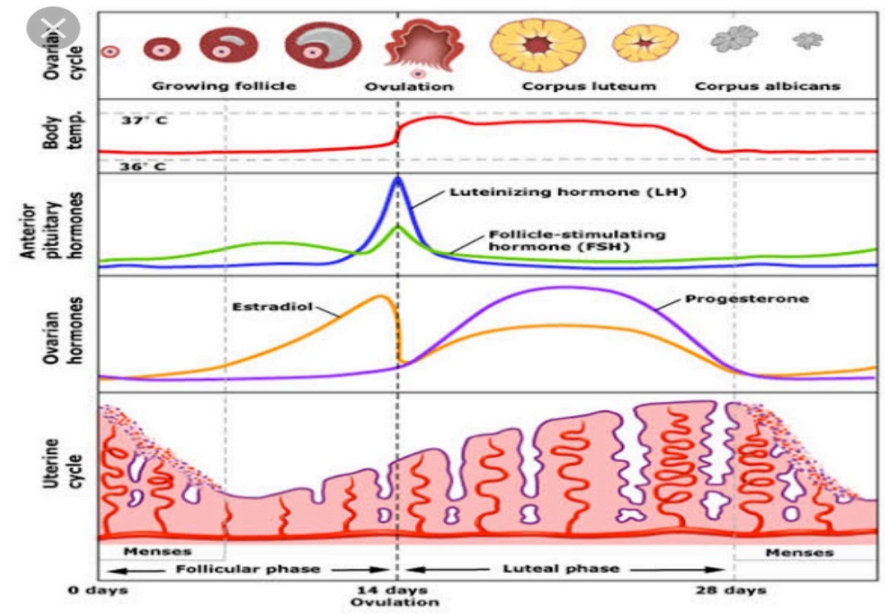
•The frequency increases late in the follicular phase of the cycle, culminating in the LH surge.

•At the time of the midcycle LH surge, the sensitivity of the gonadotropes to GnRH is greatly increased because of their exposure to GnRH pulses at a specific frequency.

•During the secretory phase, the frequency of GnRH decreases as a result of the action of progesterone

•but when estrogen and progesterone secretion decrease at the end of the cycle, the frequency once again increases.





3. PROGESTERONE

-Minimal in proliferative phase

-It starts rising following ovulation in the secretory phase and reaches peak 4-5 days after ovulation

-Peak is maintained till corpus luteum is active

-It decreases towards the end of luteal phase with regression of corpus luteum

4. LH

-Remains low almost throughout the proliferative phase

-However, a day before ovulation, LH secretion increases to reach the peak about 9 hrs before ovulation → LH surge

-Then it declines fast in 24-48 hours and remains low in the rest of the secretory phase

5. FSH

-FSH secretion increases in the early part of follicular phase(menstrual phase) and then declines slowly

-Synchronous with the rise in LH , secretion of FSH rises towards ovulation

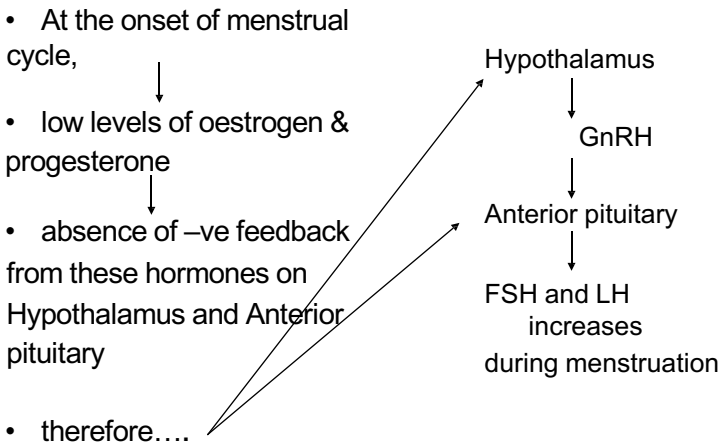
-Therefore, at the same time when LH peak occurs, FSH concentration also suddenly rises to a peak i.e. FSH surge(rise is < LH peak) and thereafter the pattern of change in FSH is similar with LH pattern

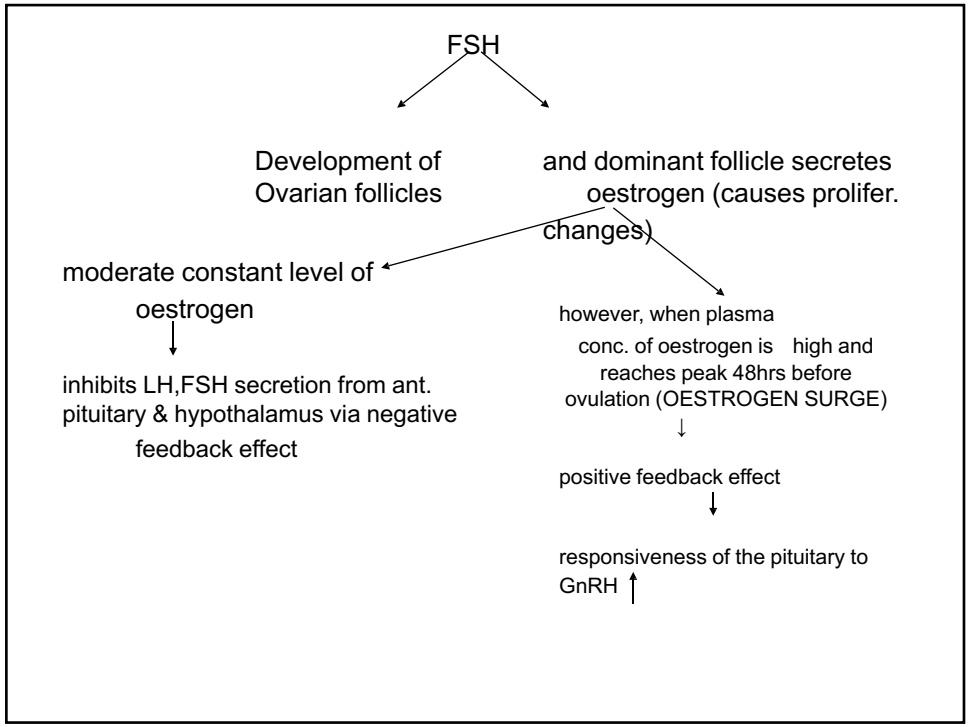
6. INHIBIN

-Pattern of change of Inhibin B coincides with change in conc.of FSH

-Pattern of change of Inhibin A coincides with change in conc.of Progesterone

SUMMARY OF HORMONAL CHANGES IN MENSTRUAL CYCLE




FSH
Development of Ovarian follicles
and dominant follicle secretes oestrogen (causes prolifer. changes)
moderate constant level of oestrogen
inhibits LH,FSH secretion from ant. pituitary & hypothalamus via negative feedback effect
however, when plasma conc. of oestrogen is high and reaches peak 48hrs before ovulation (OESTROGEN SURGE)
positive feedback effect
responsiveness of the pituitary to GnRH

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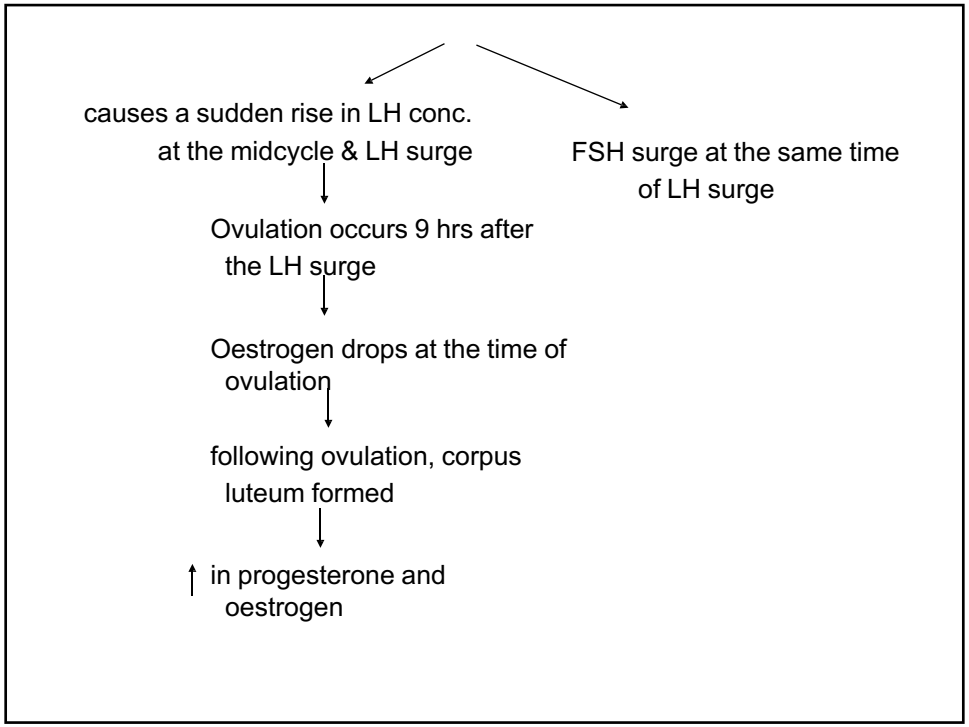
causes a sudden rise in LH conc. at the midcycle & LH surge
FSH surge at the same time of LH surge
Ovulation occurs 9 hrs after the LH surge
Oestrogen drops at the time of ovulation
following ovulation, corpus luteum formed
in progesterone and oestrogen

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thus, progesterone, oestrogen increases along with inhibin during the 2nd half of the cycle

Progesterone

↓

Acts on the endometrium primed by oestrogen

↓

Produces the secretory phase

`

Inhibit FSH and LH secretion via negative feedback effect on hypothalamus & ant.pituitary

↓

GnRH ↓

↓

FSH & LH fall to very low values for the rest of the cycle

- Thus, the thickened endometrium with large amounts of nutrients is ready to provide appropriate conditions for fertilization &implantation of the fertilized ovum during this phase

If pregnancy occurs

↓

corpus luteum persists

↓

continues to secrete oestrogen & progesterone

If fertilization doesn't takes place

↓

corpus luteum regresses

↓

Oest and Proges secretion fall rapidly

↓

absence of negative feedback inhibition

↓

GnRH increases, FSH and LH ↑

↓

subsequently leads to a new cycle with onset of menstruation

DISORDERS OF MENSTRUAL CYCLE

- AMENORRHEA
- HYPOMENORRHEA
- ANOVULATORY CYCLES
- OLIGOMENORRHEA
- DYSMENORRHEA
- MENORRHAGIA
- METRORRHAGIA
- POLYMENORRHEA
- PREMENSTRUAL SYNDROME

DISORDERS OF MENSTRUAL CYCLE

1. ANOVULATORY CYCLES

•Menstrual cycles occur at normal intervals but ovulation does not occur

•They are normal entity in the following situations:

1.Upto 1-2 yrs after menarche

2.In lactating women

3.Before the onset of menopause

•It also occurs in severe job related stress or severe strenuous exercise

- Anovulatory cycles are due to insufficient preovulatory LH surge

•Lack of ovulation → failure of development of corpus luteum→ almost no secretion of progesterone during latter portion of the cycle→ so, the effect of progesterone on endometrium is absent

- Oestrogen continues to cause proliferative endometrium
- The time it takes for bleeding to occur is variable, but it usually occurs in < 28 days from the last menstrual period.
- The flow is also variable and ranges from scanty to relatively profuse

2. AMENORRHEA

- Absence of menstrual bleeding
- 2 types: primary and secondary amenorrhea

	PRIMARY AMENORRHEA	SECONDARY AMENORRHEA
EXPLANATION	Menstrual bleeding has never occurred	Cessation of menstrual cycle in a women who previously had normal and regular cycles
CAUSES 1.PHYSIOLOGICAL	May not occur even at the age of 18yrs without any abnormality (i.e. constitutional)	1.Peripubertal amenorrhea (in the first 1-2 years of onset of menarche) 2.Pregnancy 3.Lactation 4.Emotional disturbance 5.Environmental changes 6.menoapuse
2. PATHOLOGICAL	When menstrual cycle does not start till the age of 18 years due to some prevailing disease: 1. Turner's syndrome 2. Kallman's syndrome 3. Congenital malformations of reproductive tract	1.Hypothalamic disorders →↓GnRH →amenorrhea 2.Pituitary disorders(Sheehan's syndrome)→↓LH and FSH 3.Ovarian diseases→ ↓ O & P (Polycystic ovarian disease) 4.Uterine pathology(congenital absence of uterus, underdeveloped uterus) 5.Systemic illness - c/c hypothyroidism, chronic renal failure, liver cirrhosis 6.Drugs - phenothiazine derivatives, contraceptive pills → Inhibit hypothalamic release of GnRH 7.After ovariectomy or hypophysectomy 8.In Anorexia nervosa – emaciation and stress → inhibit LH secretion

3. HYPOMENORRHEA

•Decreased menstrual bleeding in amount, duration or both is called hypomenorrhea

•Can be constitutional, due to uterine pathology, or hormonal disorders

4. OLIGOMENORRHEA

•Decreased frequency of menstrual cycle(cycle > 35 days)

•Due to ovarian pathology

5. DYSMENORRHEA

•Painful menstrual bleeding

•Due to prostaglandins

•Can be primary or secondary

•Primary – no visible pelvic pathology

•Secondary – due to uterine or pelvic pathology

6. MENORRHAGIA

•Increased menstrual bleeding in amount, duration or both is called menorrhagia

•Usually due to uterine pathology rather than any ovarian dysfunction

7. METRORRHAGIA

•Uterine bleeding in between the periods

•Usually caused by benign or malignant lesion of genital tract

8. POLYMENORRHEA

•Increased frequency of menstrual cycle(<21 days) is called polymenorrhea

9. PREMENSTRUAL SYNDROME

•About 7-10 days before the onset of menstrual bleeding, some women experiences symptoms like edema, painful or swollen breasts, irritability, lack of concentration, feeling of depression, behavioural changes and emotional disturbances

Etiology

•Due to salt & water retention in the body caused by the effect of oestrogen

•Recent view-complex interplay between the sex steroids& brain neurotransmitters

Treatment

•Tranquilizers(alprazolam)

•Serotonin uptake inhibitor

•GnRH agonists

MENOPAUSE

- It is the period of life when menstruation naturally caeses as the ovary becomes unresponsive to the gonadotropins
- Onset of menopause occurs between the age of 45-55 yrs
- The average age at onset of the menopause is 52 years.

Cause

- Senile changes in the ovary which no longer reacts to the stimulatory effect of gonadotropins
- Thus, ovaries stop secreting oestrogen and progesterone in appreciable amount

Clinical features

•Vasomotor changes like:

-**HOT FLUSHES** → flushing of skin of face, neck called hot flushes i.e. sensation of warmth

-cause unknown but it coincides with LH surge

-Feeling of suffocation and night sweats

•psychological symptoms

Treatment

•Proper care, counselling and assurance

•Hormonal supplementation of oestrogen is helpful in problematic cases of hot flushes and psychological symptoms

IMPORTANT QUESTIONS

- Menstrual cycle and hormonal basis
- Disorders of menstrual cycle