
بسم الله الرحمن الرحيم
صدر حبا
madaniwallpaper

Normal menstrual cycle

Lec1
Dr. Sawsan Talib
assistant professor in department of obstetrics and gynecology
College of medicine/ Diyala University

- Menstruation is the visible manifestation of cyclical physiologic uterine bleeding due to shedding of the endometrium as a result of invisible interplay of hormones mainly through hypothalamo pituitary ovarian axis.

- Characters of normal menstruation:

- Menarche : 11-15 ys average 13 ys.
- n Duration the period: 4-5 days.
- Continue at interval : 21-35 days with mean 28 days
- n Amount : 30-80 ml average 35 ml.

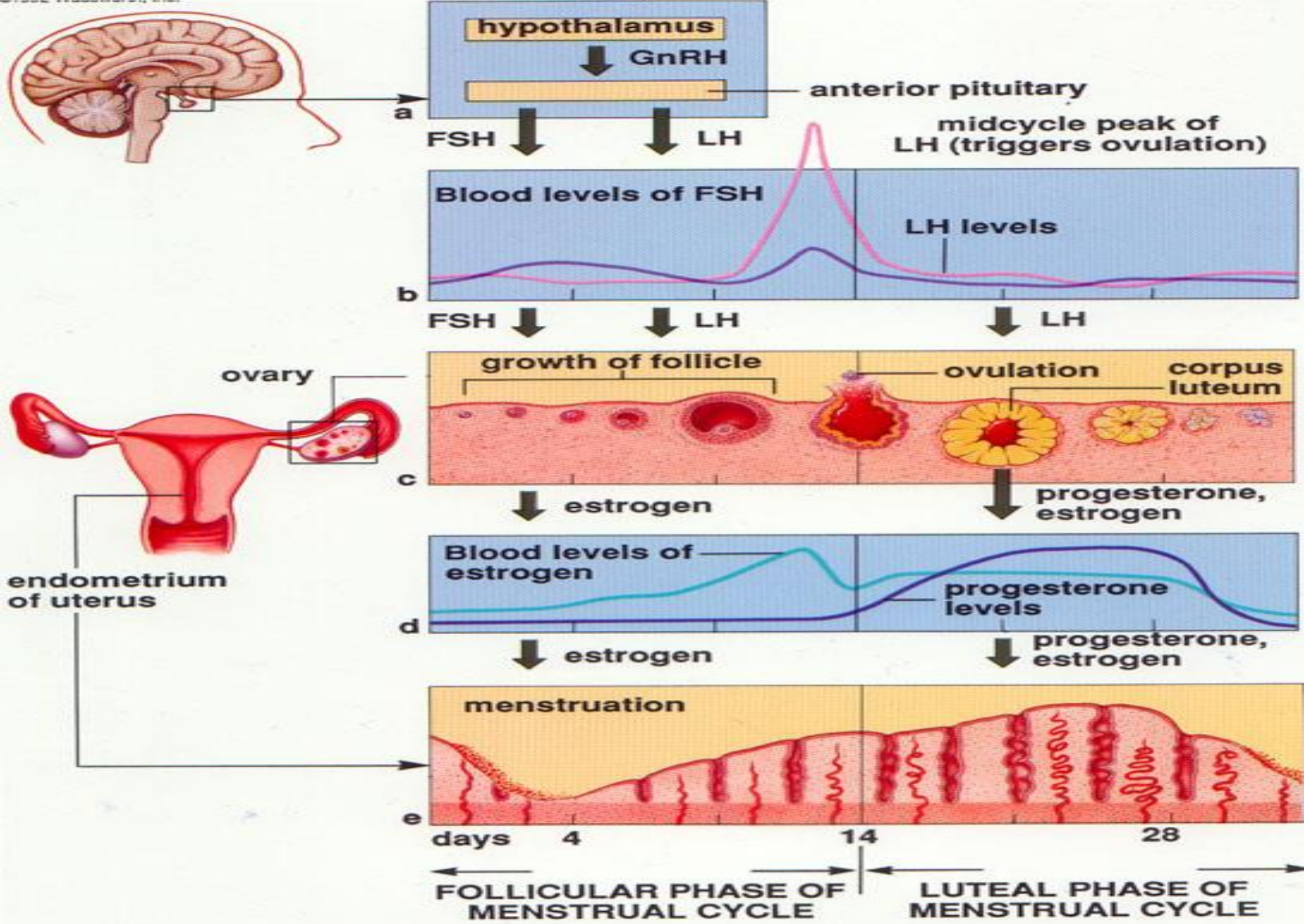
- The menstrual discharge consists mainly of dark altered blood, mucus, vaginal epithelial cells, fragments of endometrium, prostaglandins, enzymes and bacteria

- Total number of oocytes at 20 weeks of intrauterine life is about 6–7 million. At birth, the total number of primordial follicles is estimated to be about 2 million.

- At puberty, some 400,000 primary oocytes are left behind, the rest become atretic. During the entire reproductive period, some 400 are likely to ovulate

Components of normal menstruation:

- hypothalamo-hypophyseal axis.
- Ovarian Cycle.
- Endometrial cycle
- Cervical cycle
- Vaginal cycle



Changing hormone levels during the menstrual cycle.

The hypothalamo-hypophyseal axis: The hypothalamus secrets:

- GnRH in pulsatile manner (every 60-90 min).
- GnRH stimulates the production of FSH and LH from the anterior pituitary

OVARIAN CYCLE CONSIST OF:

1- Recruitment of groups of follicles

(Preantral phase) The cohort of the growing follicles undergoes a process of development and differentiation which takes about 85 days and spreads over 3 ovarian cycles. The initial recruitment and growth of primordial follicles are not under the control of any hormone. After a certain stage (2-5 mm in size) the growth and differentiation of primordial follicles are under the control of FSH. Unless the follicles are rescued by FSH at this stage, they undergo atresia.

2- Selection of a dominant follicle and its maturation

♥ FSH ⇨ primordial follicle
(oocyte arrested in the diplotene stage of the 1st meiotic division surrounded by a single layer of granulosa cells)

⇨ ⇨ 1ry follicle
(oocyte surrounded by a single layer of granulosa cells basement membrane & thica cells)

⇨ ⇨ 2ry follicle or preantral follicle
(oocyte surrounded by zona pellucida , several layers of granulosa cells & thica cells)

⇨⇨ tertiary or antral follicle
2ry follicle accumulate fluid in a cavity “antrum”
oocyte is in eccentric position
surrounded by granulosa cells “cumulous oophorus”

Ovarian follicles

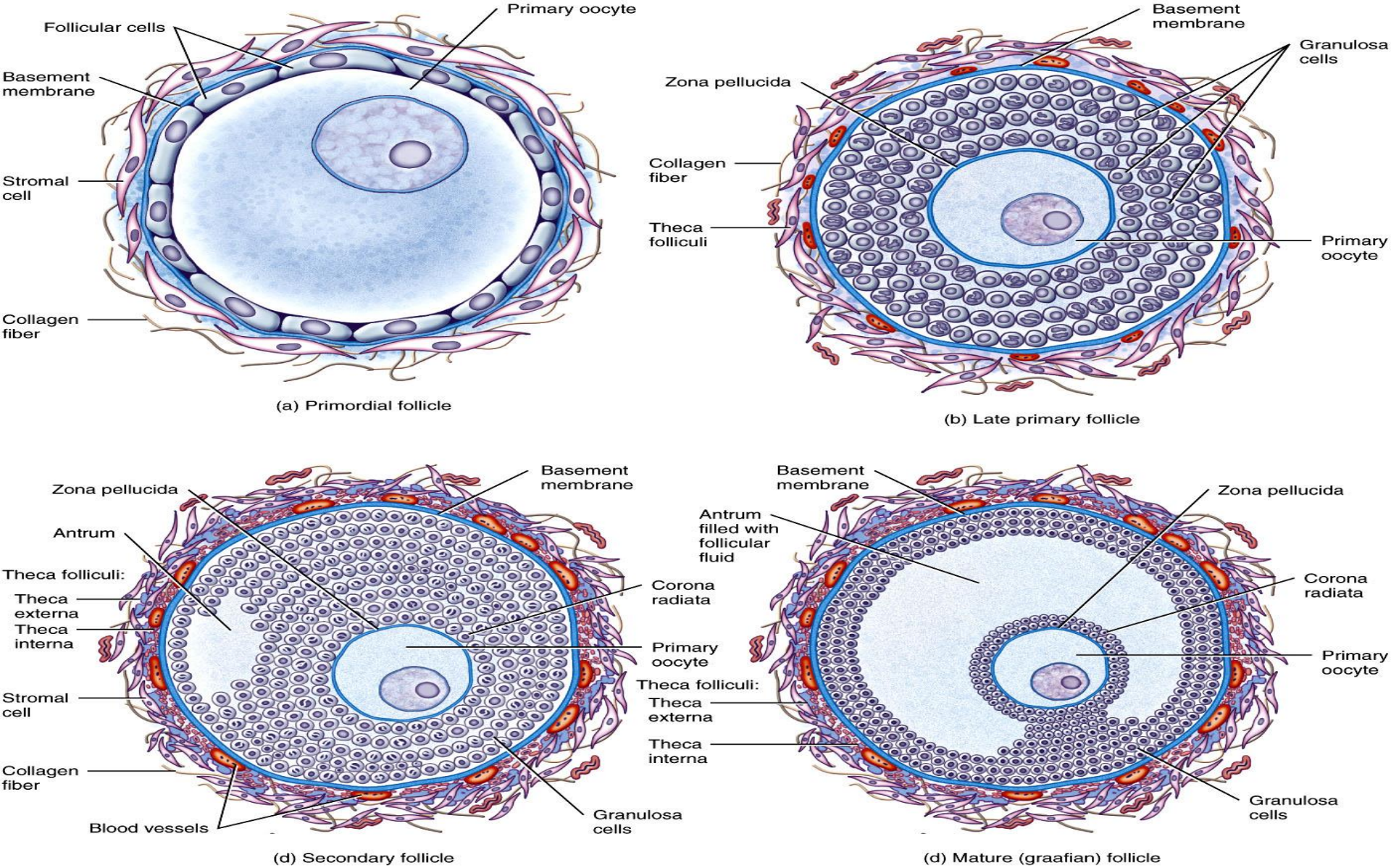


Figure 28.14abcd Tortora - PAP 12/e

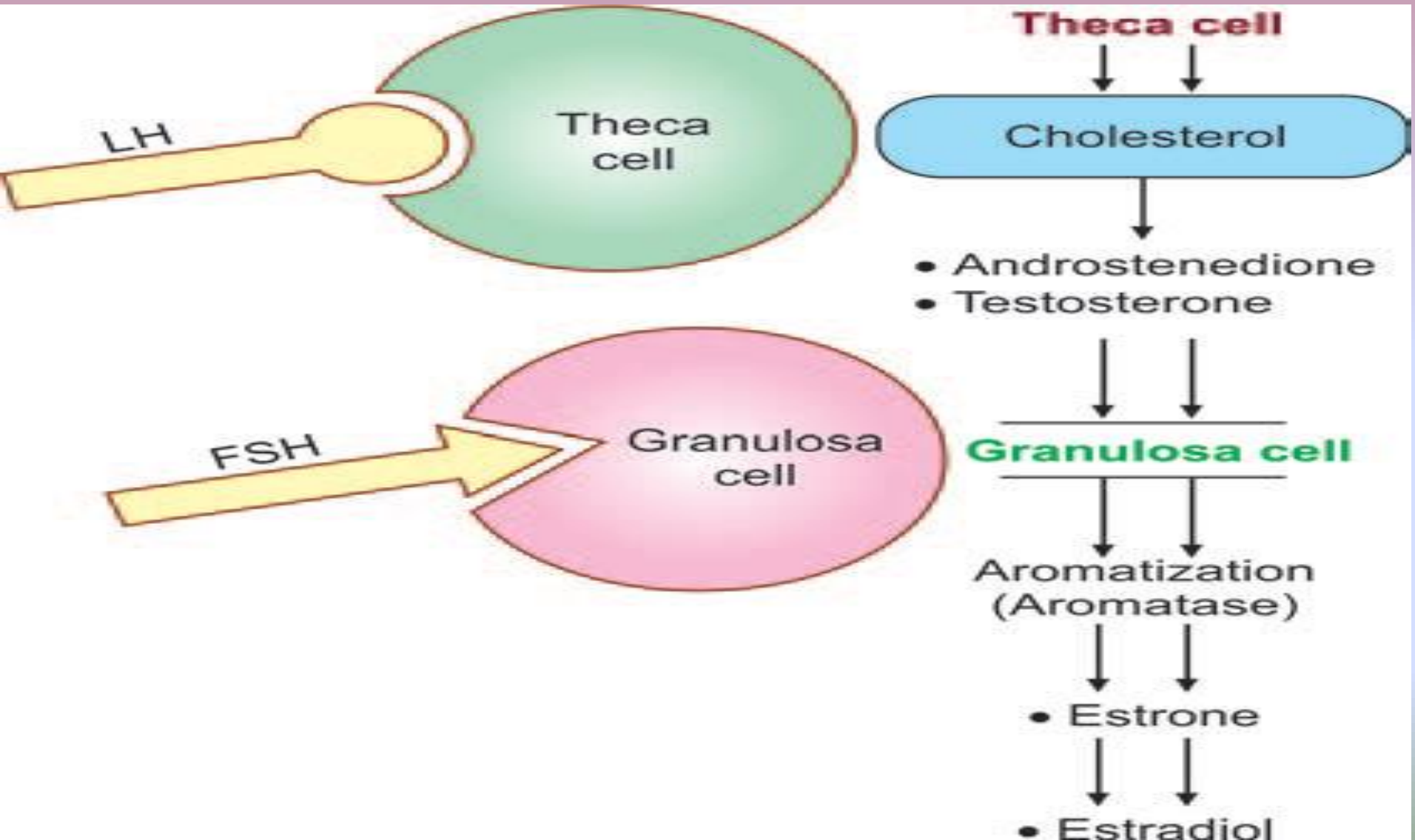
3-Dominant Follicle

- As early as day 5-7, one of the follicles out of so many becomes dominant and undergoes further maturation.

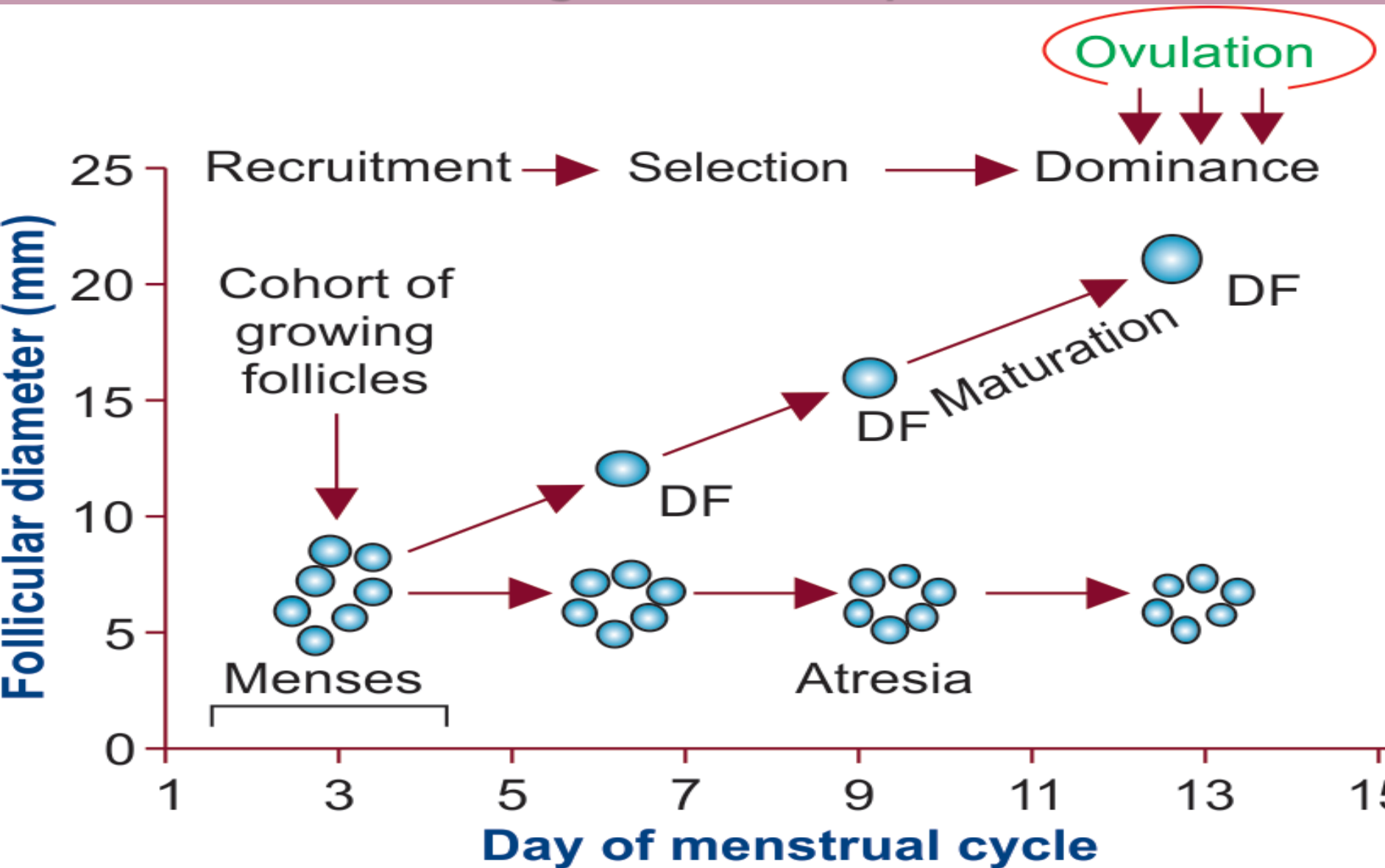
- one with highest antral concentration of estrogen and lowest androgen: estrogen ratio (estrogenic microenvironment) and whose granulosa cells contain the maximum receptors for FSH, becomes the dominant follicle. The rest of the follicles become atretic by day 8

- At this stage, FSH induces LH receptors on the granulosa cells of the dominant follicle. LH receptor induction is essential for the midcycle LH surge to induce ovulation, luteinization of the granulosa cells to form corpus luteum and secretion of progesterone (two cell, two gonadotropin therapy

Two cell two gonadotropin theory of ovarian steroidogenesis



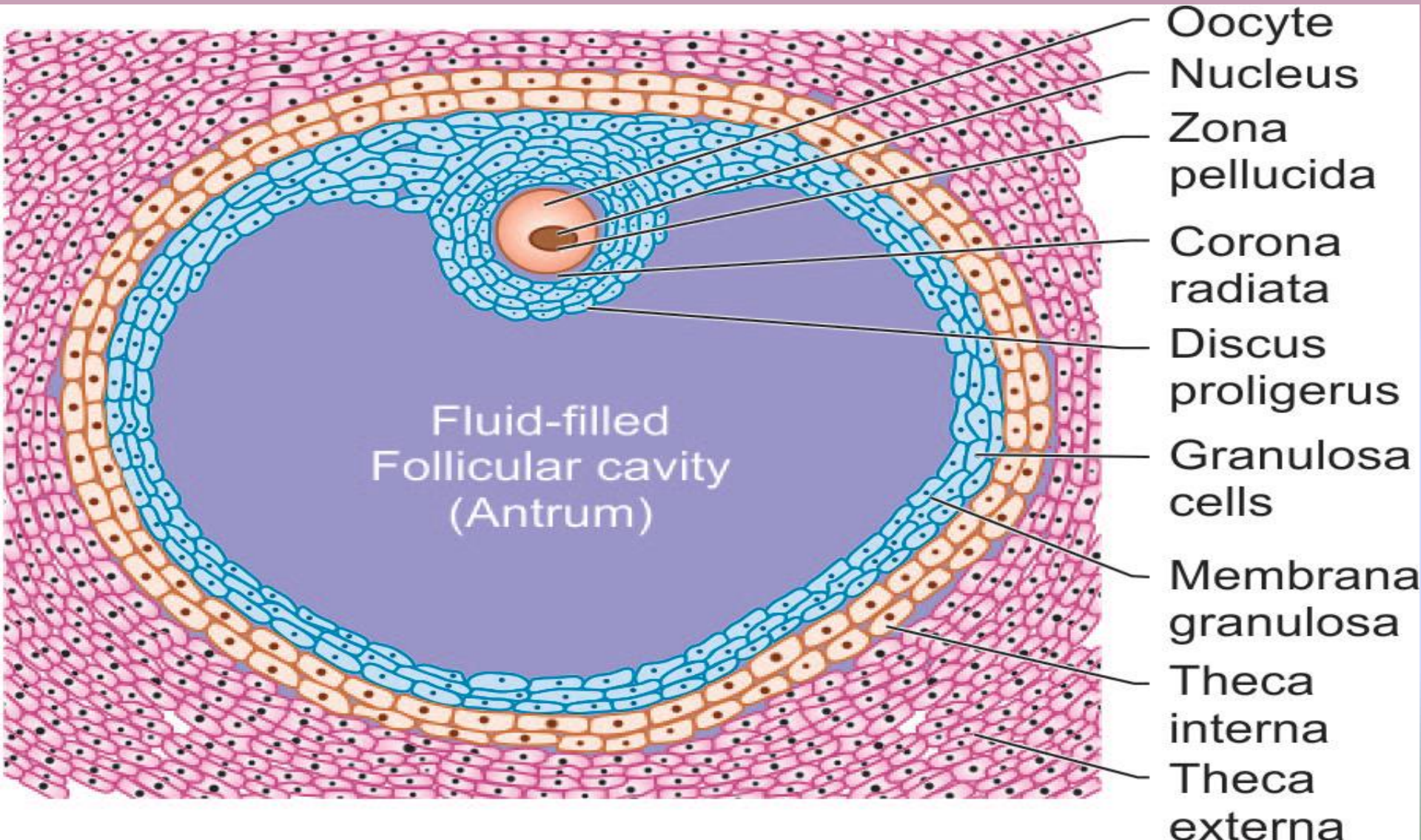
Selection and maturation of the dominant follicle (DF) during a natural cycle



- The fully mature Graafian follicle just prior to ovulation measures about 20 mm, and is composed of the following structures from outside inward:
- a. Theca externa.
- b. Theca interna.
- c. Membrana granulosa (limitans).
- d. Granulosa cell layer.
- e. Discus proligerus in which the ovum is incorporated with cells arranged radially (corona radiata).
- f. Antrum containing vesicular fluid.

- The follicular fluid is increased in amount.
- The fluid contains estrogens, FSH, trace amount of androgen, prolactin, OMI (oocyte maturation inhibitor), LI (luteinization inhibitor), inhibin—which acts centrally to inhibit FSH, proteolytic enzymes, plasmin, etc.

A mature Graafi an follicle



♥FSH ACTIONS

-recruitement

-mitogenic effect ⇨ ↑ No. of granulosa cells

↑ FSH receptor

-stimulates aromatase activity ⇨ conversion of androgens ⇨ estrogens "estrone & estradiol"

- ↑ LH receptors

♥ ESTROGEN

Acts synergistically with FSH to

- induce LH receptors
- induce FSH receptors in granulosa & thica cells

♥LH ⇨ thica cells ⇨ uptake of cholesterol & LDL ⇨ androstenedione & testosterone

-INHIBIN

- Local peptide in the follicular fluid
- -ve feed back on pituitary FSH secreation
- Locally enhances LH-induced androstenedione production

-ACTIVIN

- Found in follicular fluid
- Stimulates FSH induced estrogen production
- ↑ gonadotropin receptors
- ↓androgen
- No real stimulation of FSH secretion in vivo (bound to protein in serum)

PREOVULATORY PERIOD

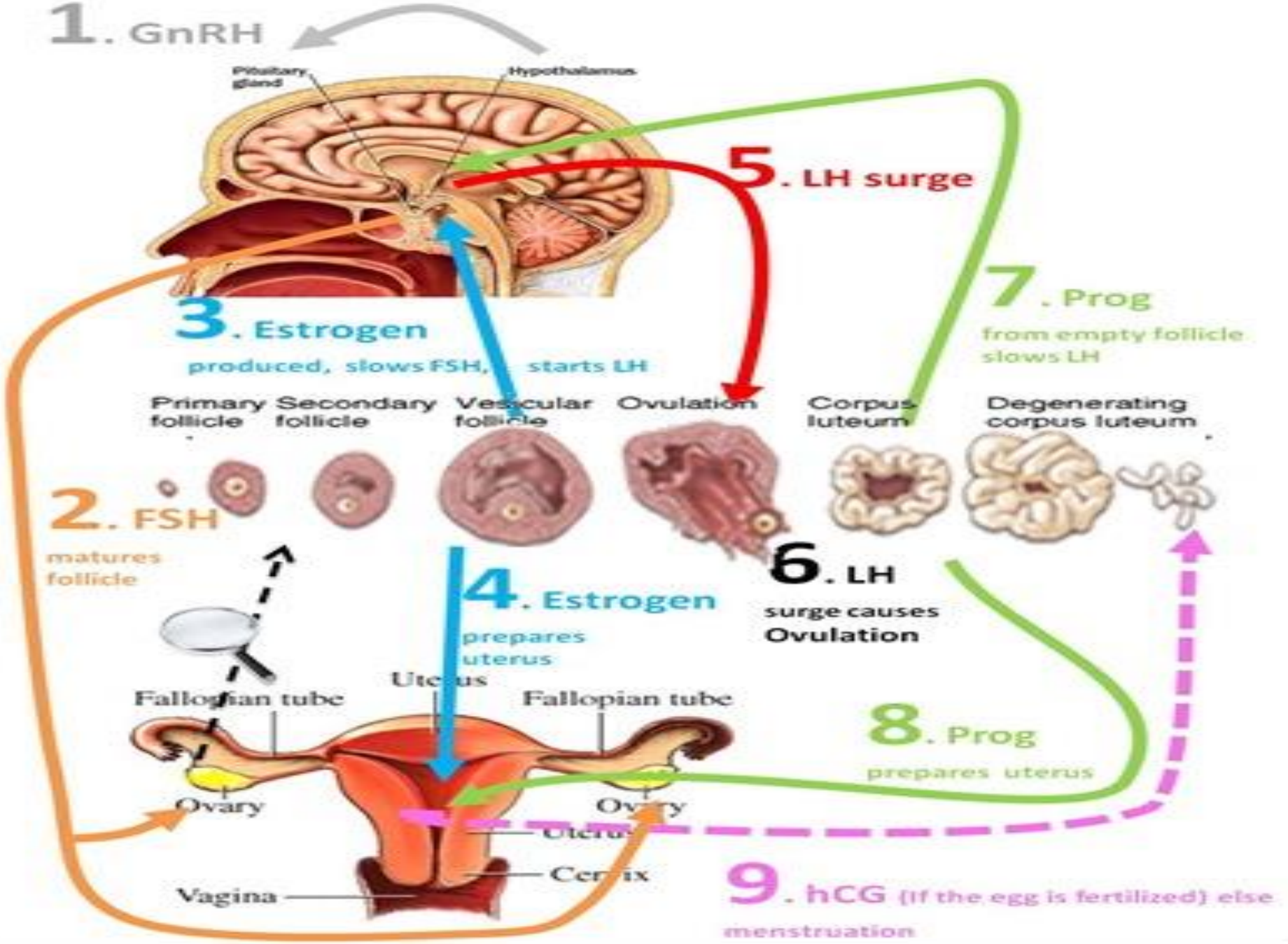
♥ NEGATIVE FEEDBACK ON THE PIUITARY

-↑ estradiol & inhibin ⇨-ve feed back on pituitary ⇨ ↓ FSH

-This mechanism operating since childhood

♥ POSITIVE FEEDBACK ON THE PITUITARY

- ↑ ↑ estradiol (reaching a threshold concentration) ⇨ ⇨ +ve feed back on the pituitary (facilitated by low levels of progestrone) ⇨ ⇨ LH surge ⇨ secretion of progestrone
- Operates after puberty
- +ve feed back on pituitary ⇨ ↑ FSH


1. GnRH
Pituitary gland
Hypothalamus
5. LH surge
7. Prog
from empty follicle
slows LH
3. Estrogen
produced, slows FSH, starts LH
Primary follicle
Secondary follicle
Vesicular follicle
Ovulation
Corpus luteum
Degenerating corpus luteum
2. FSH
matures follicle
4. Estrogen
prepares uterus
6. LH
surge causes Ovulation
Fallopian tube
Uterus
Fallopian tube
8. Prog
prepares uterus
Ovary
Ovary
Uterus
Cervix
Vagina
9. hCG (If the egg is fertilized) else menstruation

PREOVULATORY PERIOD

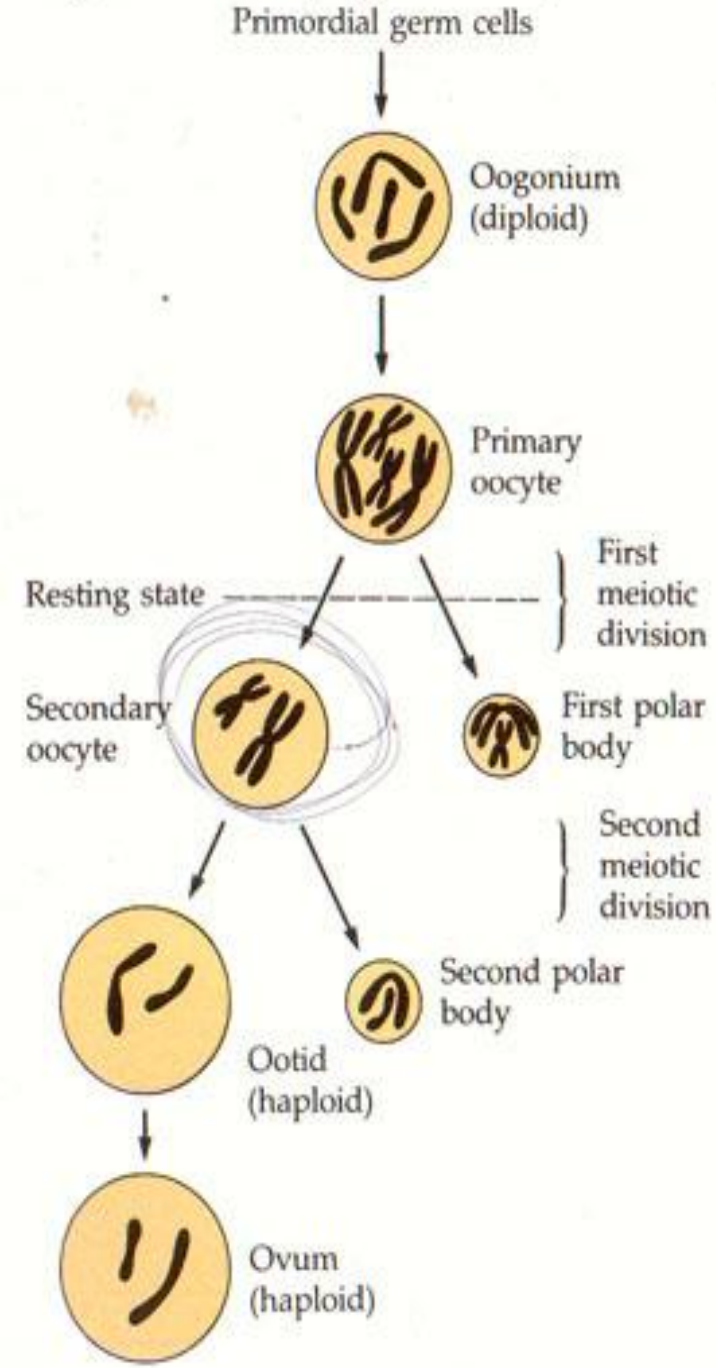
LH SURGE

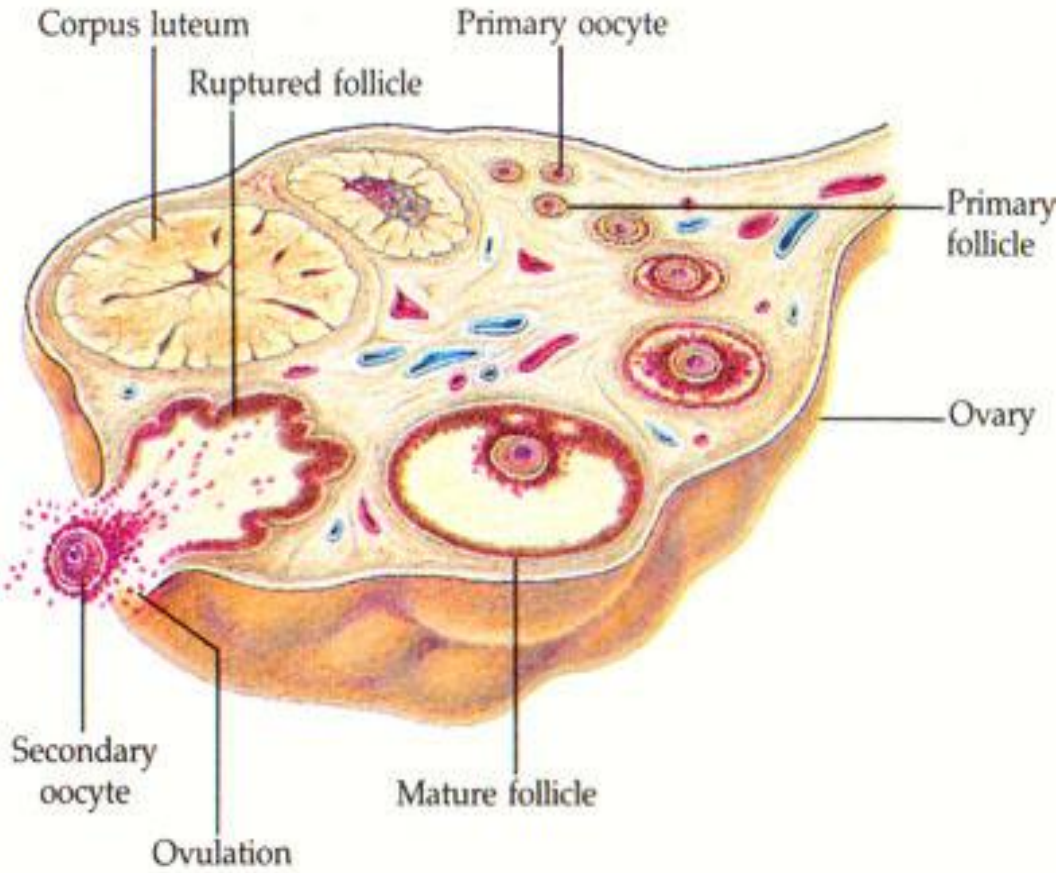
- Lasts for 48 hrs
- Ovulation occurs after 36 hrs
- Accompanied by rapid fall in estradiol level
- Triggers the resumption of meiosis
- Affects follicular wall ⇨ follicular rupture
- Granulosa cells ⇨ lutenization ⇨ progestrone synthesis

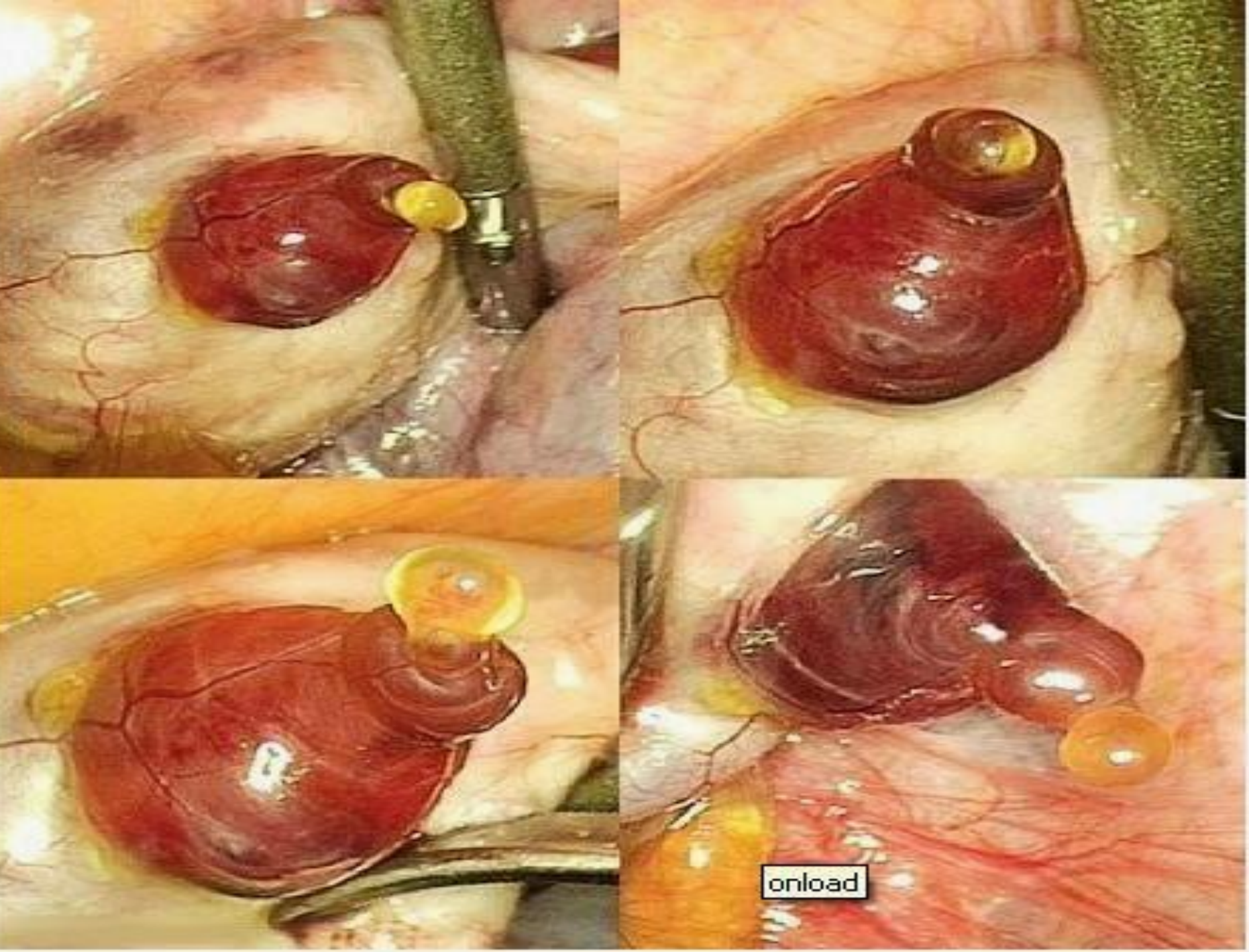
4-Ovulation

- The dominant follicle, shortly before ovulation reaches the surface of the ovary.
- The cumulus becomes detached from the wall, so that the ovum
- with the surrounding cells (corona radiata) floats freely in the liquor folliculi.
- The oocyte completes the first meiotic division with extrusion of the first polar body which is pushed to the perivitelline space.
- The follicular wall near the ovarian surface becomes thinner.
- The stigma develops as a conical projection which penetrates the outer surface layer of the ovary and persists for a while (30–120 seconds) as a thin membrane.
- The cumulus escapes out of the follicle by a slow oozing process, taking about 60–120 seconds along with varying amount of follicular fluid.
- The stigma is soon closed by a plug of plasma.

Oogenesis (Figure 42.14)






onload

possible explanations which may operate singly or in combination leading to thinning of the ovarian wall include the followings:

- 1. Endocrinal

LH surge: stimulates completion of reduction division of the oocyte and initiates luteinization of the granulosa cells, synthesis of progesterone and prostaglandins.

FSH rise Preovulatory rise of 17-α-hydroxy progesterone facilitates the positive feedback action of estrogen to induce FSH surge → increase in plasminogen activator → plasminogen → plasmin → helps lysis of the wall of the follicle.

Thus, the combined LH/FSH midcycle surge is responsible for the final stage of maturation, rupture of the follicle and expulsion of the oocyte.

- 2. Stretching factor
- passive stretching causing necrobiosis of the overlying tissue rather than rise in intrafollicular pressure which remains static at about 10–15 mm Hg.
- 3. Contraction of the micromuscles
- in the theca externa and ovular stroma due to increased local prostaglandin secretion.

- Following ovulation, the follicle is changed to corpus luteum.

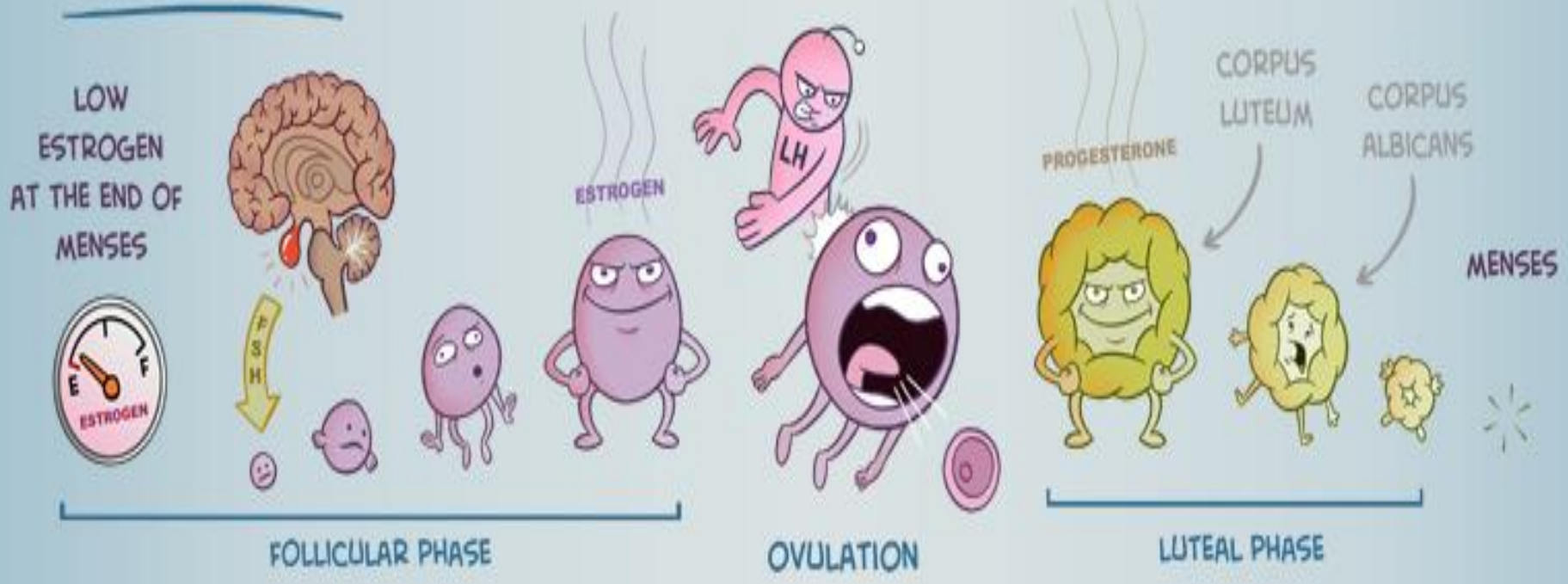
Corpus Luteum

- The life cycle is divided into four stages:
- Proliferation The opening through which the
- ovum escapes soon becomes plugged with fibrin.
- The granulosa cells undergo hypertrophy without
- multiplication. The color of the corpus luteum at this stage is greyish yellow due to presence of lipids
- Vascularization Within 24 hours of rupture of the follicle, small capillaries grow into granulosa layer towards the lumen accompanied by lymphatics and fibroblasts.
- Maturation By 4th day, the luteal cells have attained the maximum size. Approximately about 7–8 days following ovulation, the corpus luteum attains a size of about 1–2 cm and reaches its secretory peak. The lutein cells become greatly enlarged and develop lipid inclusion, giving the cells a distinctive yellowish color. The color is due to the pigment carotene.

- ・Regression
- On the day 22–23 of cycle, retrogression starts.
- There is deposition of fat in the lutein cells and appearance of hyaline tissue between them. The lutein cells atrophy and the corpus luteum becomes corpus albicans.
- Progesterone levels are at their highest in the cycle during the luteal phase. This also has the effect of suppressing FSH and LH secretion to a level that will not produce further follicular growth in the ovary during that cycle.
- The luteal phase lasts 14 days in most women, without great variation.
- In the absence of beta human chorionic gonadotrophin (bHCG) being produced from an implanting embryo, the corpus luteum will regress in a process known as luteolysis.
- The mature corpus luteum is less sensitive to LH, produces less
- progesterone, and will gradually disappear from the ovary.

THE MENSTRUAL CYCLE

OVARIAN CYCLE



UTERINE CYCLE

PROLIFERATIVE PHASE: INFLUENCED BY ESTROGEN, THE THICKNESS OF THE ENDOMETRIUM RAPIDLY INCREASES

SECRETORY PHASE: INFLUENCED BY PROGESTERONE, THE LINING BECOMES HIGHLY VASCULAR AND EDEMATOUS

ENDOMETRIAL CHANGES DURING THE MENSTRUAL CYCLE

1-Basal layer of the enometrium

-Adjasent to the mometrium

-Unresponsive to hormonal stimulation

-Remains intact throughout the menstrual cycle

2-Functional layer of the endometrium

Composed of two layers:

-zona compacta ⇨ superficial

-Spongiosum layer

1-Follicular /proliferative phase

Estrogen ⇨ mitotic activity in the glands & stroma ⇨
↑ enometrial thickness from 2 to 8 mm
(from basalis to opposed basalis layer)

2-Luteal /secretory phase

Progestrone ⇨- Mitotic activity is severely restricted
-Endometrial glands produce then secrete glycogen rich vacules
-Stromal edema
-Stromal cells enlargement
-Spiral arterioles develop, lengthen & coil

MENSTRUATION

- Periodic desquamation of the endometrium
- The external hallmark of the menstrual cycle
- Just before menses the endometrium is infiltrated with leucocytes
- Prostaglandins are maximal in the endometrium just before menses
- Prostaglandins ⇨ constriction of the spiral arterioles ⇨ischemia & desquamation

  Followed by arteriolar relaxation, bleeding & tissue breakdown

HYPOTHALAMIC ROLE IN THE MENSTRUAL CYCLE

- The hypothalamus secretes GnRH in a pulsatile fashion
- GnRH activity is first evident at puberty
- Follicular phase GnRH pulses occur hourly
- Luteal phase GnRH pulses occur every 90 minutes
- Loss of pulsatility ⇨down regulation of pituitary receptors ⇨ ↓ secretion of gonadotropins
- Release of GnRH is modulated by –ve feedback by:
  - steroids
  - gonadotropins
- Release of GnRH is modulated by external neural signals

Cervical Cycle:




Day 3	Day 6	Day 14	Day 22
She's still menstruating .	firm, os is closed, and she has no cervical fluid	soft, os is open, and her CF is stretchy, like eggwhite, probably about to ovulate	firmer, os is closed, and mucus is viscid than it was on Day .14

Vaginal cycle

	1st half	2nd half
epithelium	cornified	proliferated
Smears	Cornified cells	leukocytes infiltration
Discharges	watery	thick mucus

Breast cycle

	Estrogen	Progesterone
Histologically	proliferation of mammary ducts	growth of lobules and alveoli
Clinically	Nearly free	breast swelling, tenderness and pain 10 days preceding menstruation

Luteal Phase - Where Premenstrual Syndrome(PMS) starts to occur

- Progesterone increases.
- Oestrogen level is high.

- Depression
- Skin troubles
- Breast tenderness
- Increased appetite causes binge
- Fatigue
- Body temperature increases

Uterus :
If the implantation doesn't occur, the endometrium begins to break down.

Ovary :
The corpus luteum grows in the ovary where a mature egg was released at ovulation.

Bleeding Phase

- Progesterone and oestrogen levels decrease.

- Weak defence system
- Skin gets dry
- Low body temperature

Uterus :
The broken down endometrium layers shed as menstruation.

Ovary :
A mature egg is released from the ovary.

Ovulatory Phase

- Progesterone slowly decreases.
- Oestrogen level reaches optimal level.

- Skin is in its best condition
- High body temperature
- Appetite increases
- Less energetic
- Social withdrawal

Uterus :
Endometrium secretes proteins in preparation for a fertilised egg to implant.

Ovary :
Ovulation is the 14th day of the menstruation cycle. The egg is released.

Follicular Phase

- Progesterone stays low.
- Follicle-stimulating hormone increases.
- Oestrogen is released.
- Testosterone level rises.

- High in metabolism
- Skin is at optimal level of absorption
- Energetic
- Positive mood
- Outgoing and enjoy social meetings

Uterus :
The endometrium grows and thickens to prepare for the implantation of an embryo.


THANK
YOU