Reproductive Physiology

How to Study!

- Slides (check the notes).
- Lecture.
- Reference book: Guyton and Hall Textbook of Medical Physiology (John E. Hall; Michael E. Hall). (14^{th} edition)

Female Physiology Before Pregnancy and Female Hormones Female reproductive functions

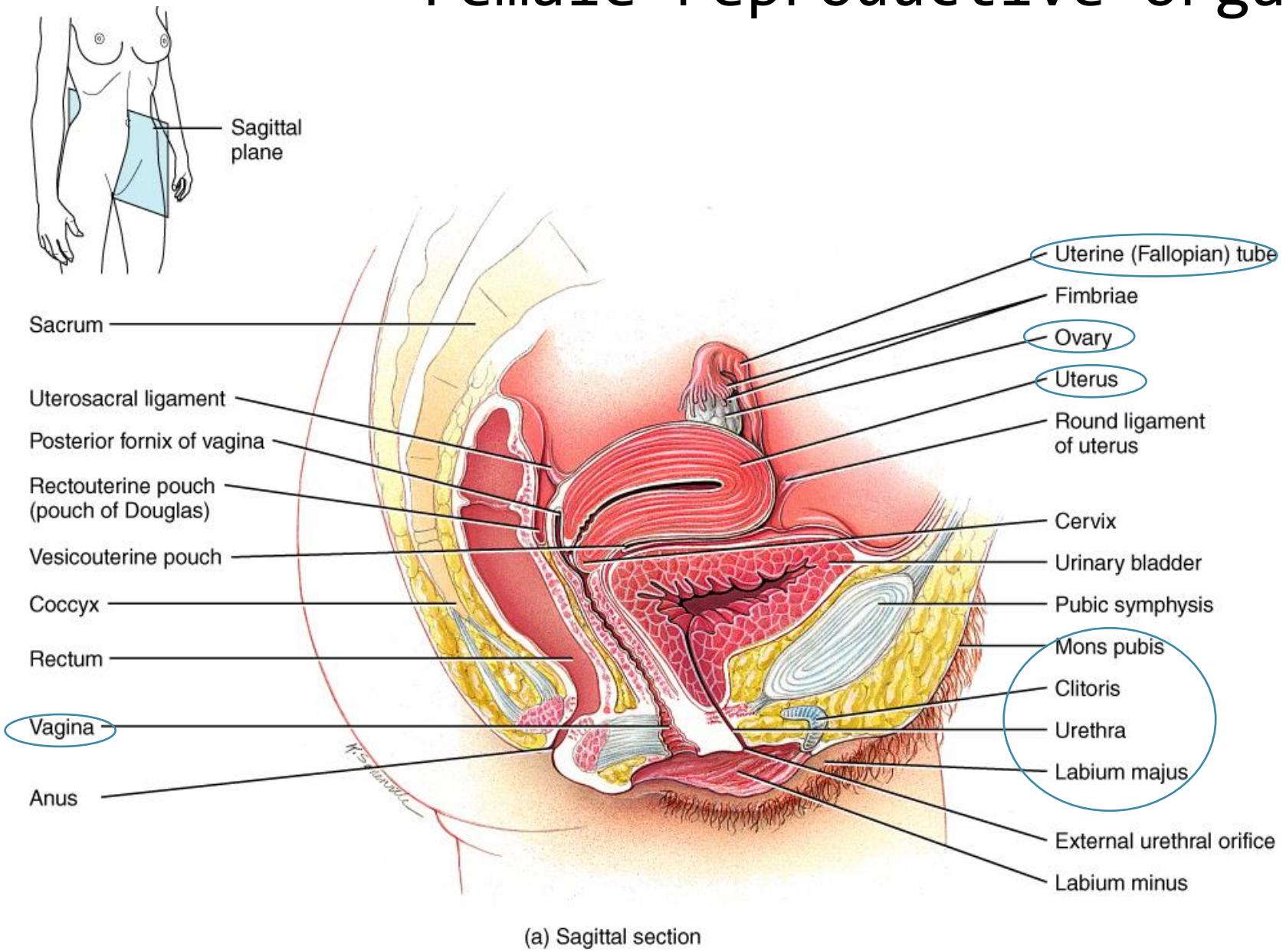
Chapter 82

Female Reproductive Functions:

1) preparation of the female body for conception and pregnancy

(2) the period of pregnancy itself.

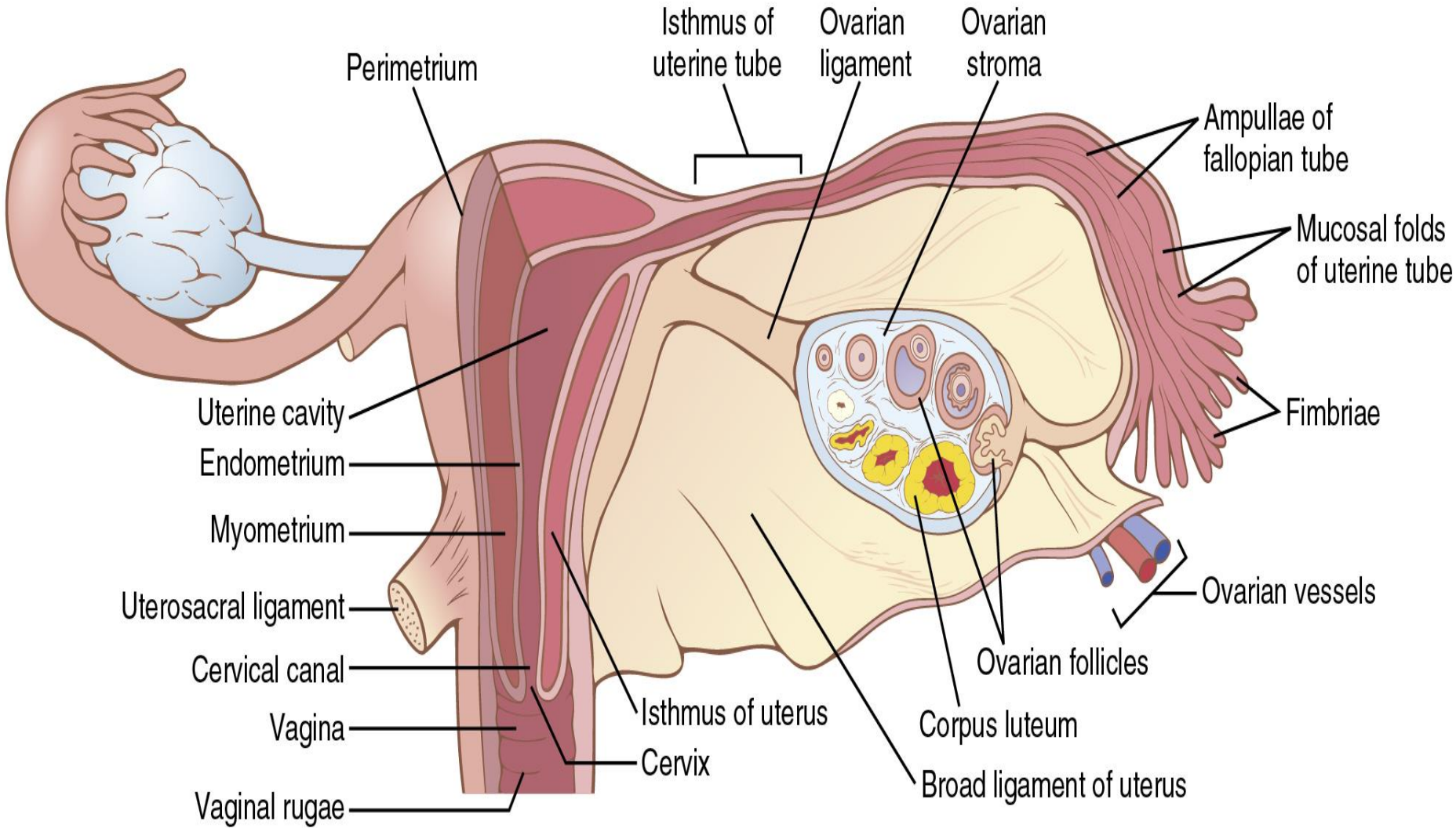
Female reproductive organs



(a) Sagittal section

+Mammary glands

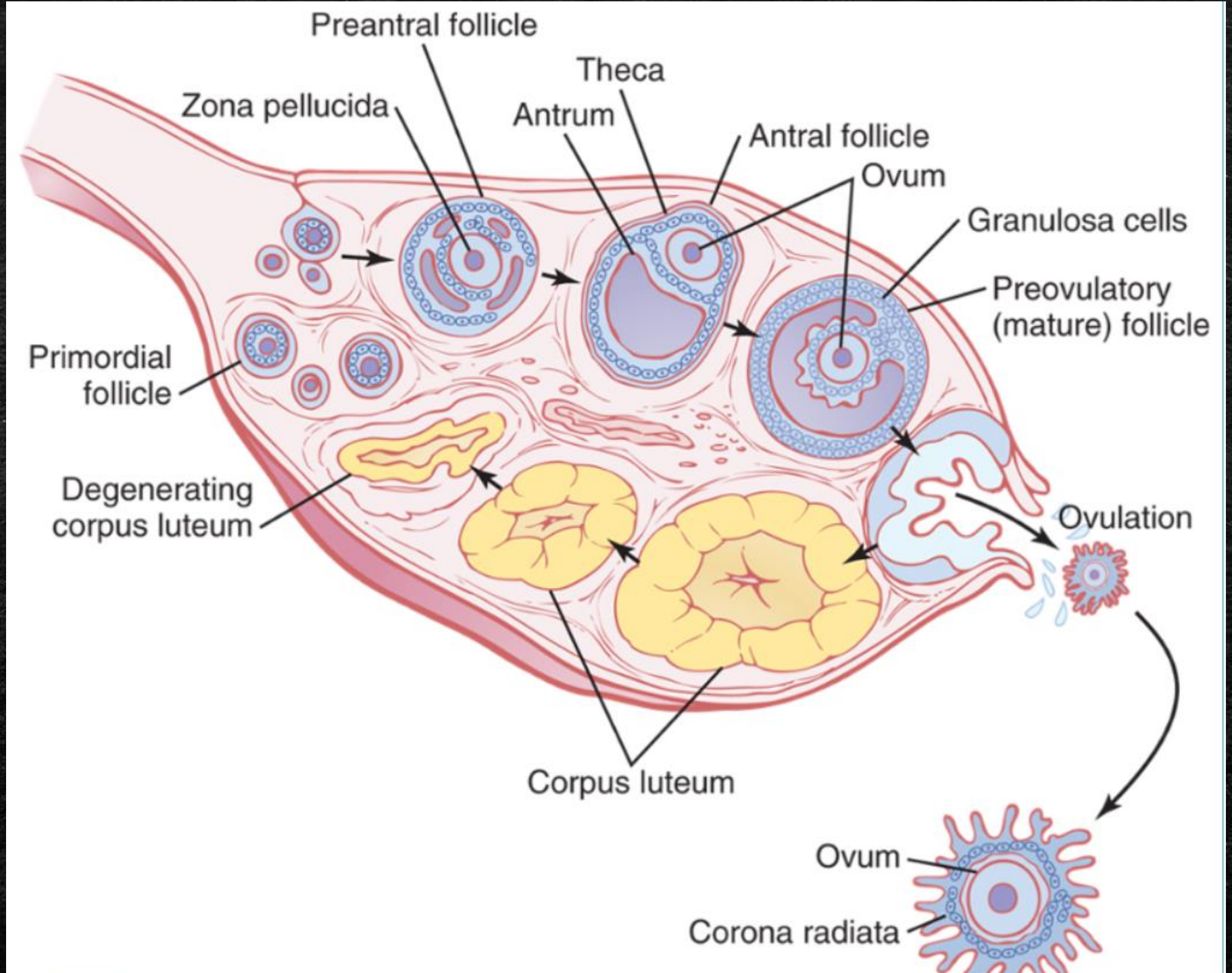
Relationship of the uterine tubes to the ovaries, uterus, and associated structures

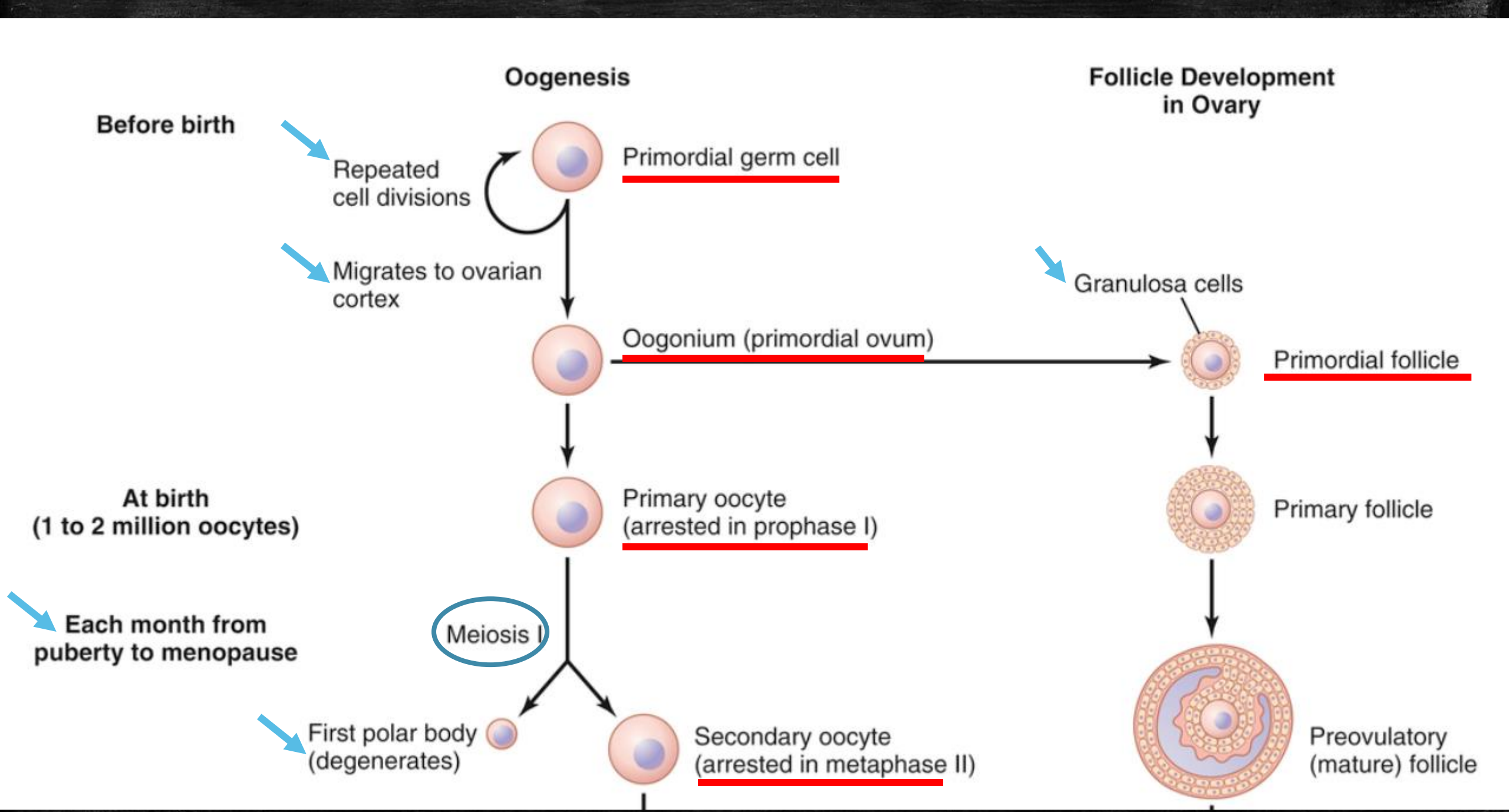


Note:

- ** Reproduction begins with the development of ova in the ovaries. In the middle of each monthly sexual cycle, a single ovum is expelled from an ovarian follicle into the abdominal cavity near the open fimbriated ends of the two fallopian tubes. This ovum then passes through one of the fallopian tubes into the uterus; if it has been fertilized by a sperm, it implants in the uterus, where it develops into a fetus, a placenta, and fetal membranes—and eventually into a baby.

Oogenesis


Preantral follicle
Theca
Zona pellucida
Antrum
Antral follicle
Ovum
Granulosa cells
Preovulatory
(mature) follicle
Primordial
follicle
Degenerating
corpus luteum
Ovulation
Corpus luteum
Ovum
Corona radiata


Oogenesis
Follicle Development in Ovary
Before birth
Repeated cell divisions
Primordial germ cell
Migrates to ovarian cortex
Granulosa cells
Oogonium (primordial ovum)
Primordial follicle
At birth (1 to 2 million oocytes)
Primary oocyte (arrested in prophase I)
Primary follicle
Each month from puberty to menopause
Meiosis I
First polar body (degenerates)
Secondary oocyte (arrested in metaphase II)
Preovulatory (mature) follicle

Note :

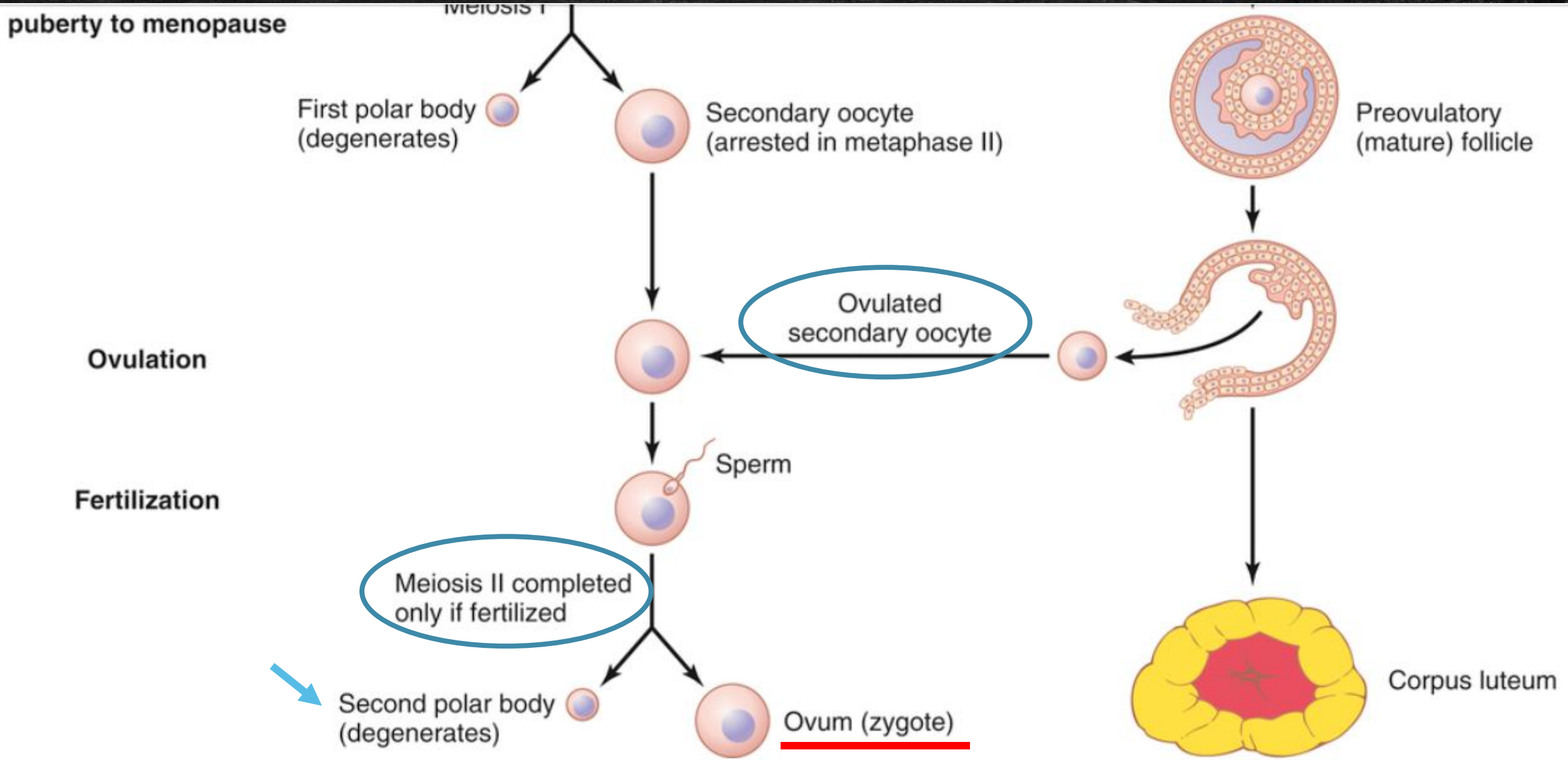
During early embryonic development, **primordial germ cells migrate to the outer surface of the ovary, which is covered by a germinal epithelium.

During this migration, the germ **cells divide repeatedly.

Once these primordial germ cells reach the germinal epithelium, they migrate into the substance of the ovarian cortex and become **oogonia or primordial ova.

Each primordial ovum then collects around it a layer of spindle cells from the **ovarian stroma (the supporting tissue of the ovary) and causes them to take on epithelioid characteristics; these epithelioid-like cells are then called **granulosa cells**. The ovum surrounded by a single layer of granulosa cells is called a **primordial follicle**. At this stage, the ovum is still immature and is called a **primary oocyte.**

The first meiotic division of the oocyte is completed **after puberty. Each oocyte divides into two cells, a large ovum (secondary oocyte) and a small first polar body. Each of these cells contains 23 duplicated chromosomes.


puberty to menopause
Meiosis I
First polar body
(degenerates)
Secondary oocyte
(arrested in metaphase II)
Preovulatory
(mature) follicle
Ovulated
secondary oocyte
Ovulation
Sperm
Fertilization
Meiosis II completed
only if fertilized
Second polar body
(degenerates)
Ovum (zygote)
Corpus luteum

Note :

**The ovum undergoes a second meiotic division, and after the sister chromatids separate, there is a pause in meiosis. If the ovum is fertilized, the final step in meiosis occurs and the sister chromatids in the ovum go to separate cells.
**

NOTE!!

- The oogonia in the embryonic ovary complete mitotic replication, and the first stage of meiosis starts by the **fifth month of fetal development**.
- The germ cell mitosis then ceases and **no additional oocytes are formed**.
- At birth the ovary contains about 1 to 2 million primary oocytes.

NOTE ! !

- At puberty, only about 300,000 oocytes remain in the ovaries, and only a small percentage of these oocytes become mature.

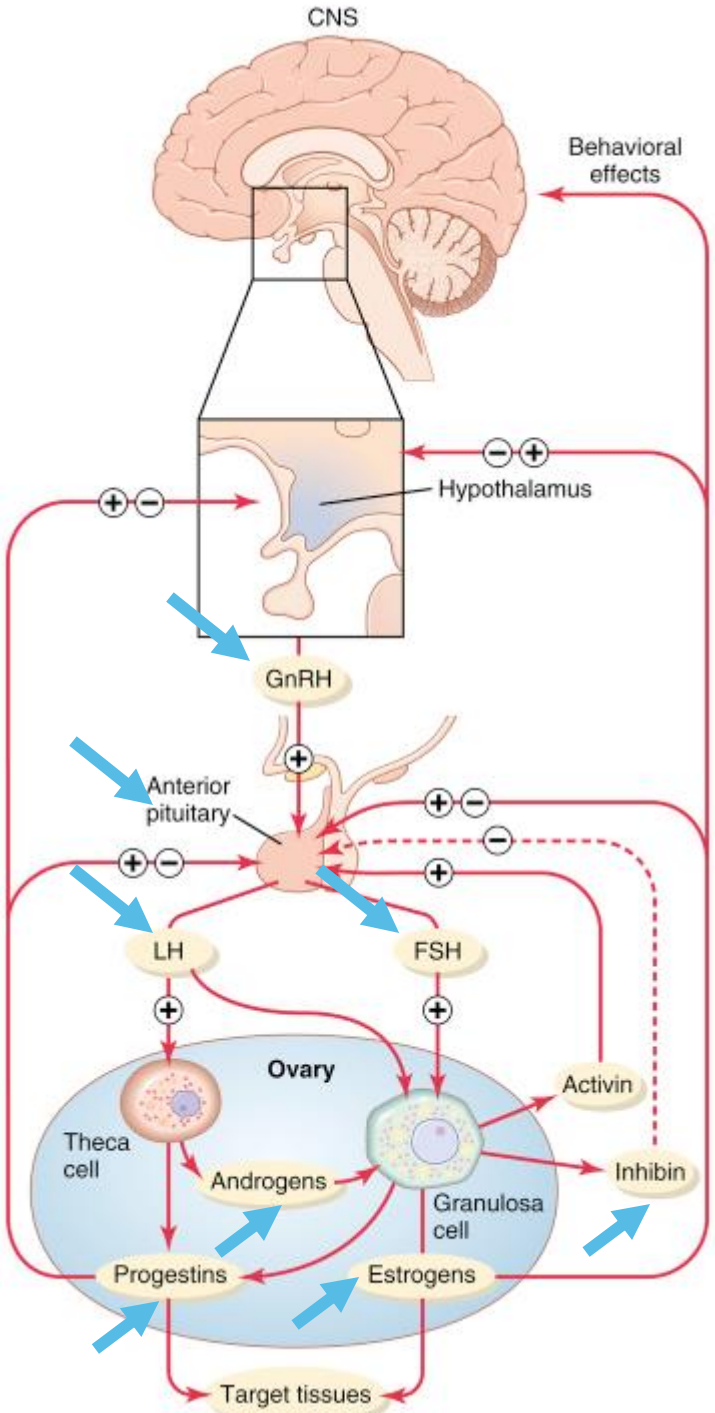
- During all the reproductive years of adult life, between about 13 and 46 years of age on average, only 400 to 500 of the primordial follicles develop enough to expel their ova, one each month; the remainder degenerate (i.e., become atretic).

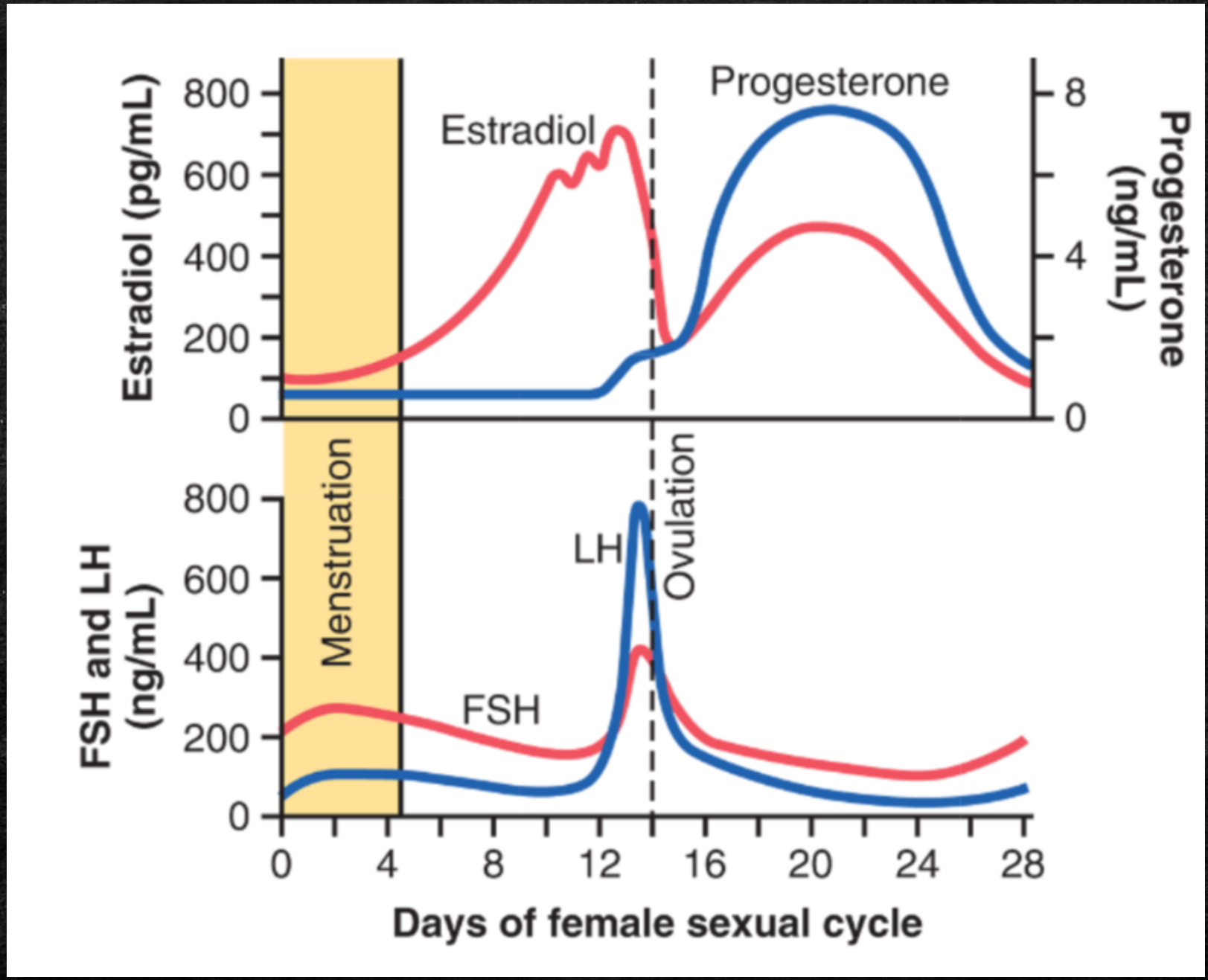
- At the end of reproductive capability (at menopause), only a few primordial follicles remain in the ovaries, and even these follicles degenerate soon thereafter.

Female Hormonal System

Gonadotropic Hormones and Their Effects on the Ovaries

- The ovarian changes that occur during the sexual cycle depend completely on the gonadotropic hormones FSH and LH.
- In the absence of these hormones, the ovaries remain inactive, which is the case throughout childhood, when almost no pituitary gonadotropic hormones are secreted.
- At age 9 to 12 years, the pituitary begins to secrete progressively more FSH and LH, which leads to onset of normal monthly sexual cycles beginning between the ages of 11 and 15 years.
- This period of change is called *puberty*, and the time of the first menstrual cycle is called *menarche*.

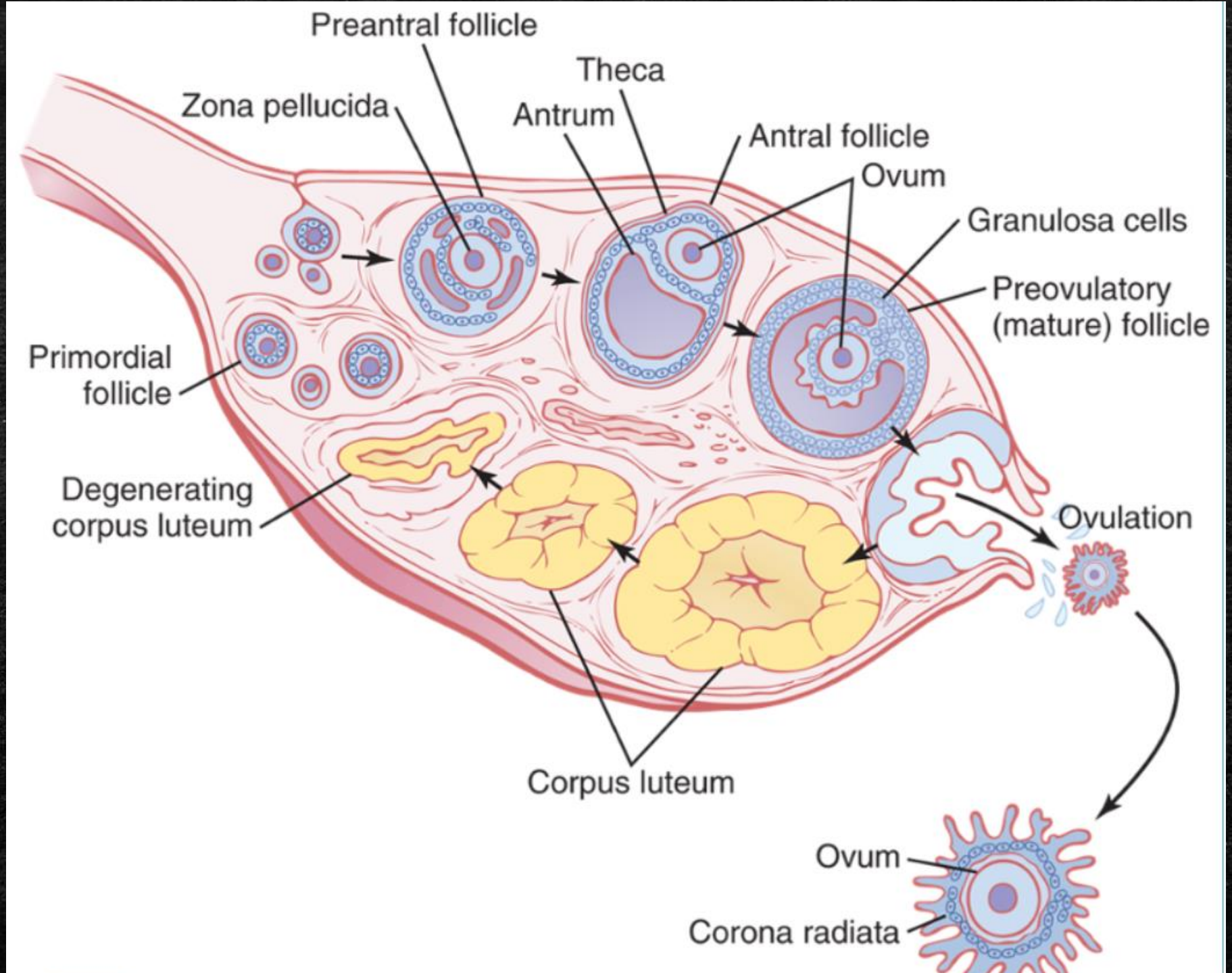

CNS
Behavioral effects
Hypothalamus
GnRH
Anterior pituitary
LH
FSH
Ovary
Theca cell
Androgens
Activin
Inhibin
Granulosa cell
Progestins
Estrogens
Target tissues


Estradiol (pg/mL)
800
600
400
200
0
Estradiol
Progesterone
8
4
0
Progesterone (ng/mL)
Menstruation
Ovulation
FSH and LH (ng/mL)
800
600
400
200
0
LH
FSH
0
4
8
12
16
20
24
28
Days of female sexual cycle

Note :

**These various hormones are secreted at drastically differing rates during different parts of the female monthly sexual cycle.
** The amount of GnRH released from the hypothalamus increases and decreases much less drastically during the monthly sexual cycle. It is secreted in short pulses averaging once every 90 minutes.
** During the first few days of each monthly female sexual cycle, the concentrations of FSH and LH secreted by the anterior pituitary gland increase slightly to moderately, with the increase in FSH slightly greater than that of LH and preceding it by a few days.
** FSH, cause accelerated growth of 6 to 12 primary follicles each month.

Follicular Developments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Primordial
follicle
Degenerating
corpus luteum
Ovulation
Corpus luteum
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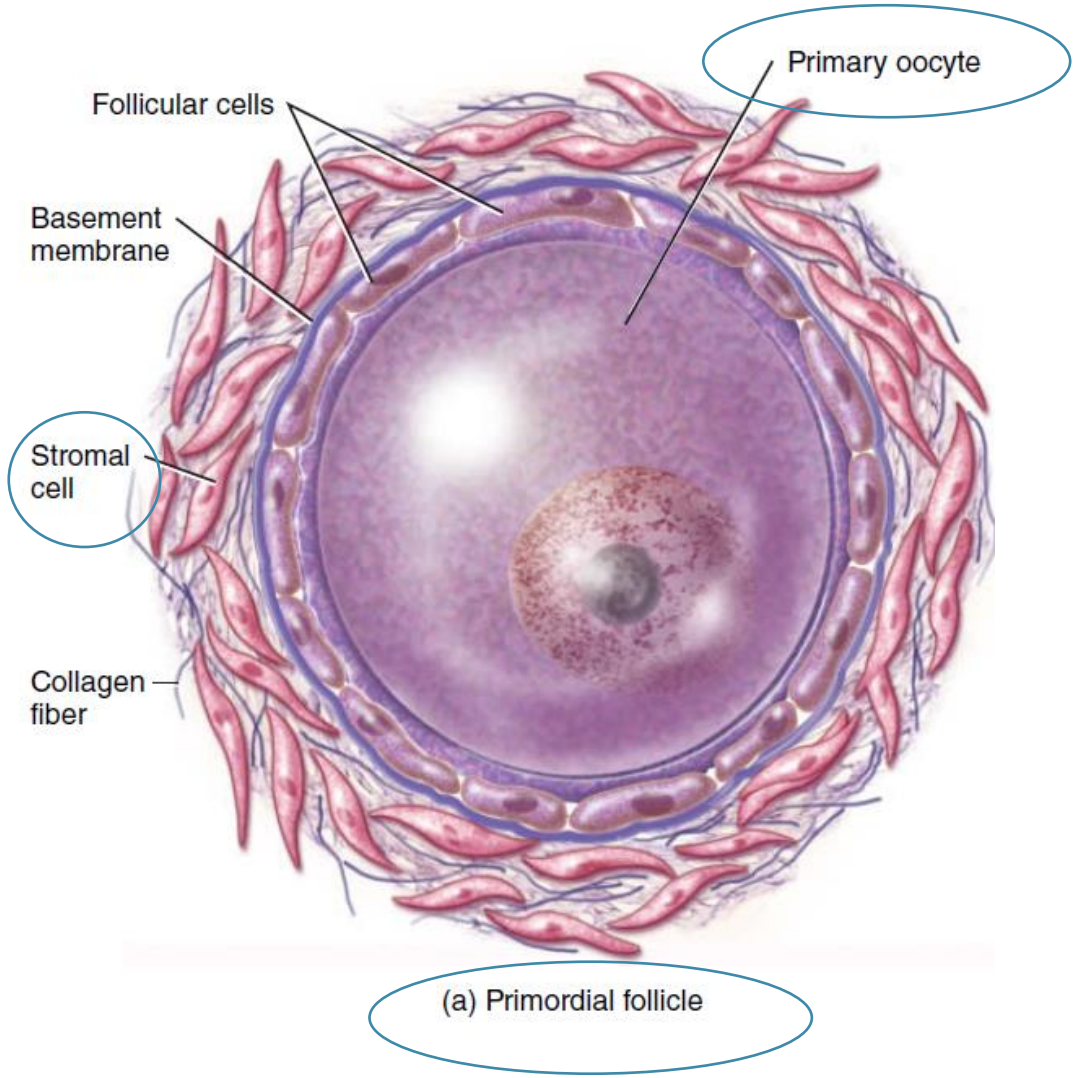
Corona radiata

Primordial follicle

- When a **female child is born**, each ovum is surrounded by a single layer of granulosa cells; the ovum, with this granulosa cell sheath, is called a **primordial follicle**.

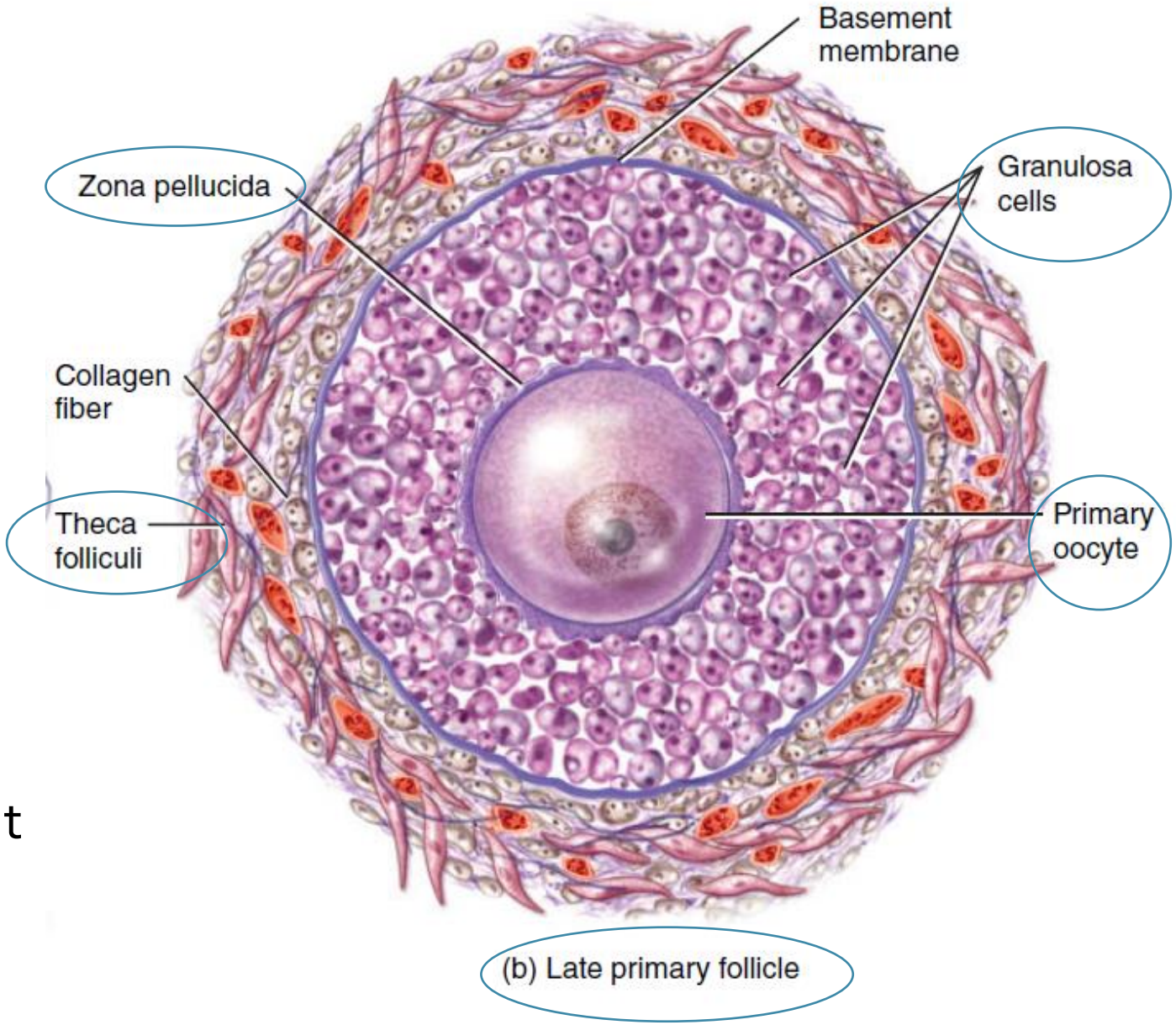
- **Throughout childhood,** the granulosa cells are believed to provide **nourishmen**t for the ovum and to secrete an ***oocyte maturation-inhibiting factor*** that keeps the ovum suspended in its primordial state in the prophase stage of meiotic division.



Primary follicle

- Then, after puberty, when FSH and LH are secreted in significant quantities, the ovaries (together with some of the follicles within them) begin to grow.

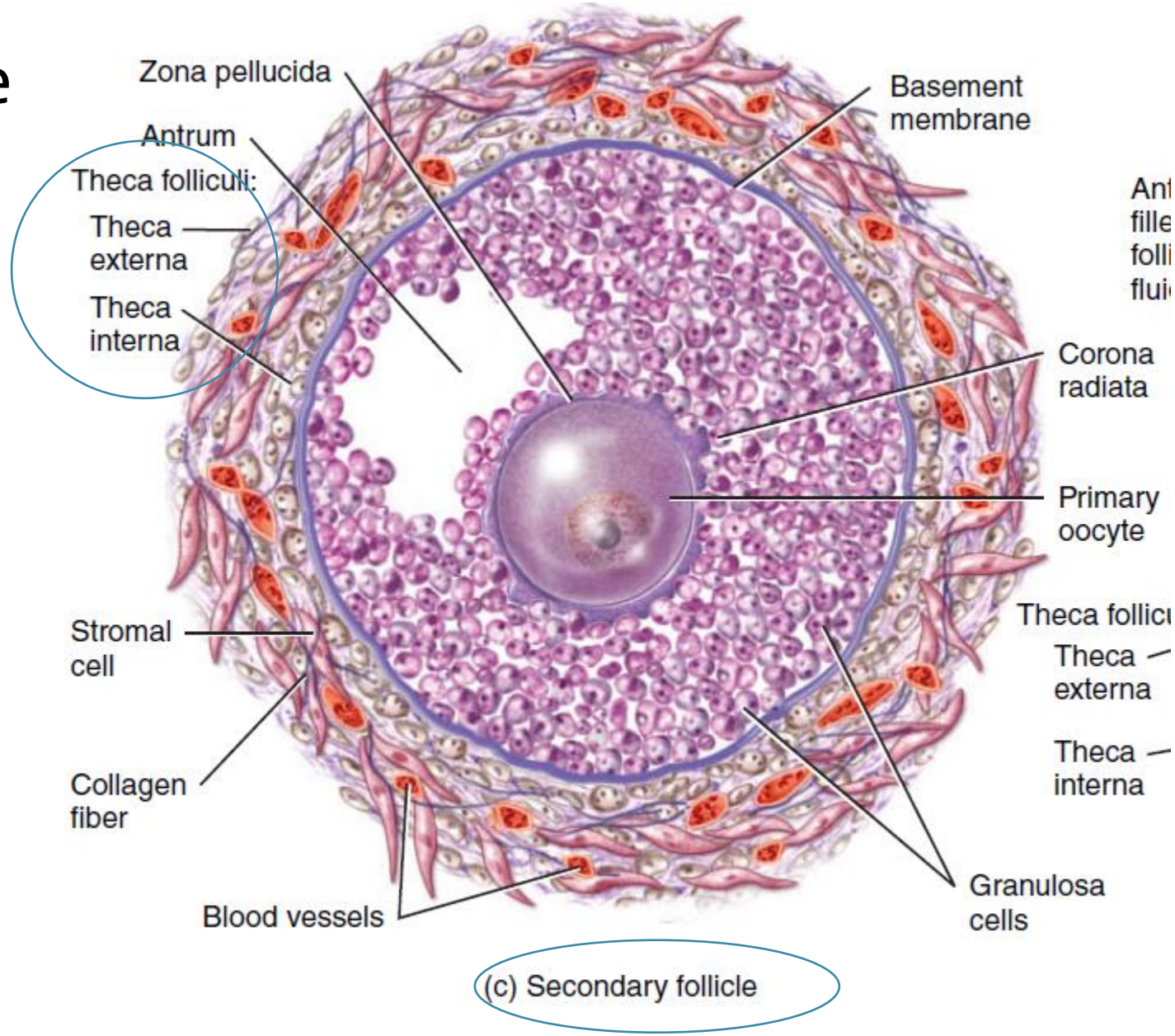
- Consists of a primary oocyte that is surrounded by **several layers** of cuboidal and low columnar **granulosa cells.**
- **zona pellucida,** a clear glycoprotein layer
- Stromal cells surrounding the basement membrane begin to form.



Secondary follicle

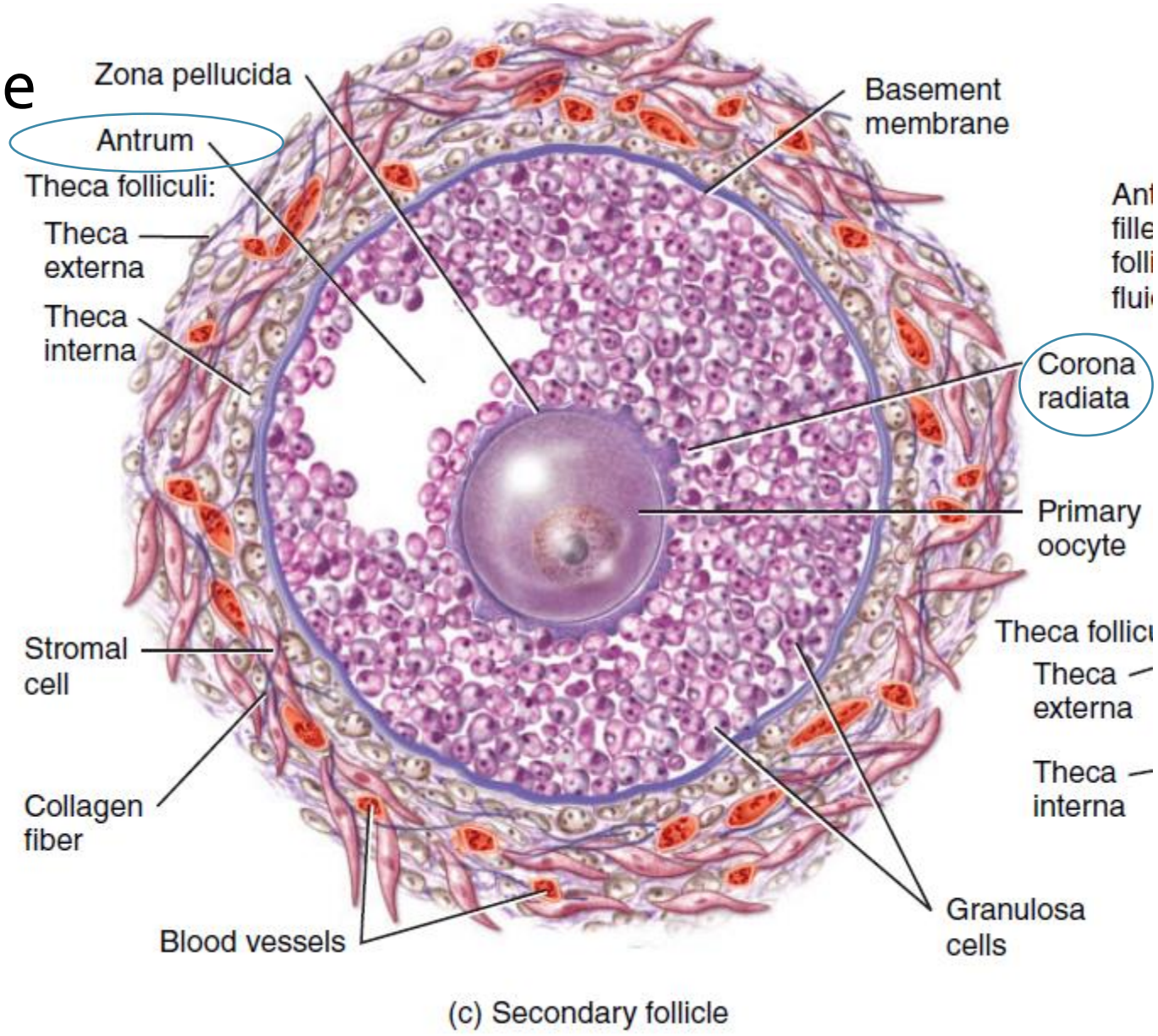
The theca differentiates into two layers:

1) Theca interna, epithelioid characteristics, secrete additional steroid sex hormones.
2) The theca externa, develops into a highly vascular connective tissue capsule.



Secondary follicle/Antral stage

- The granulosa cells begin to secrete follicular fluid, which builds up in a cavity called the **antrum. (high concentration of estrogen)**
- The innermost layer of granulosa cells becomes firmly attached to the zona pellucida and is now called the **corona radiata.**



(c) Secondary follicle

Vesicular follicle

- The early growth of the primary follicle up to the antral stage is stimulated mainly **by FSH alone**.
- Greatly **accelerated growth** then occurs, leading to still larger follicles called vesicular follicles and this due to :

- 1. **Estrogen** is secreted into the follicle and causes the **granulosa cells** to form increasing numbers of **FSH receptors**, which causes a **positive feedback effect** because it makes the granulosa cells even more sensitive to FSH.

Vesicular follicles

- 2. The pituitary **FSH and the estrogens** combine to promote **LH receptors** on the original granulosa cells, thus allowing LH stimulation to occur in addition to FSH stimulation and creating an **even more rapid increase in follicular secretion.**

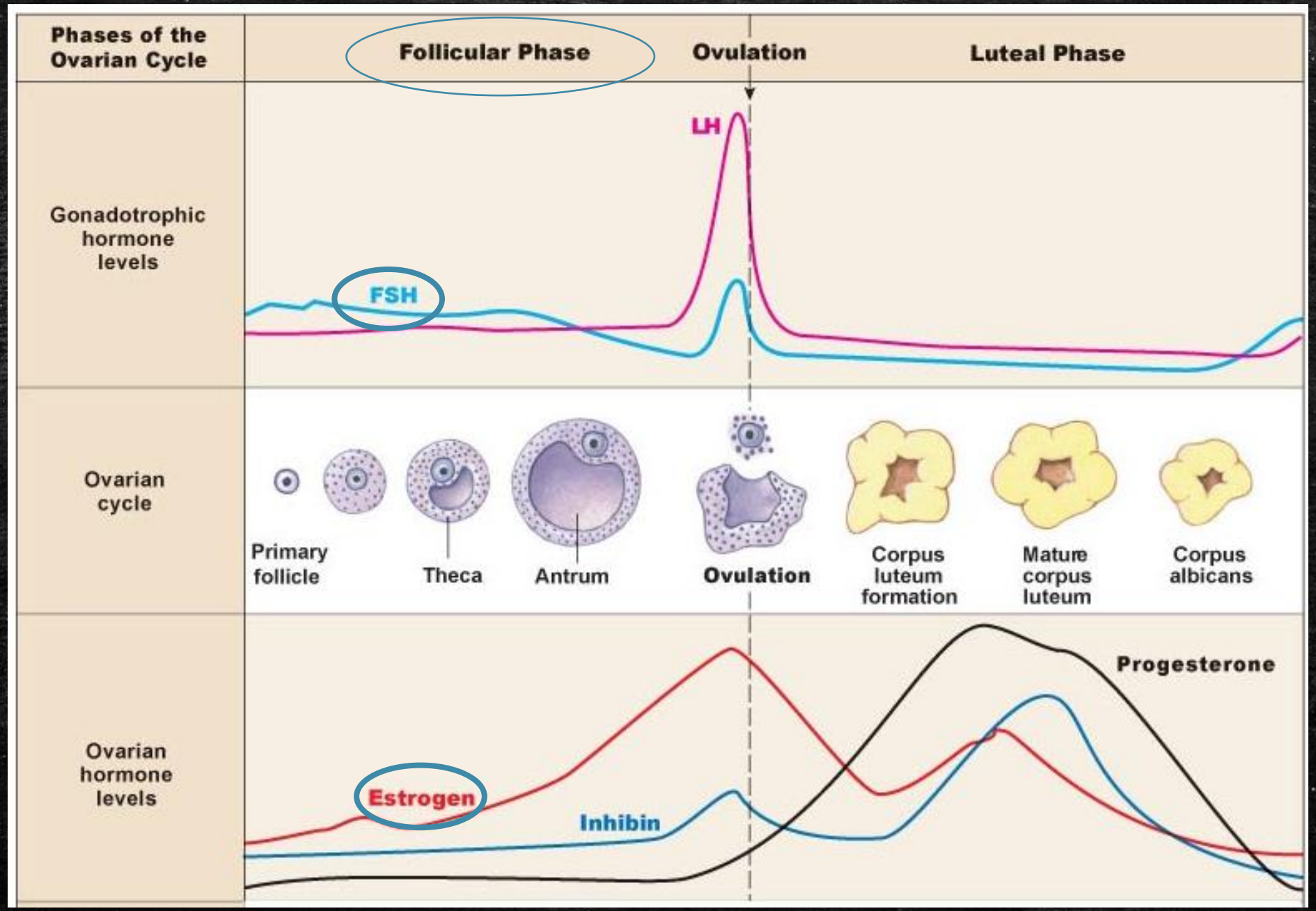
- 3. The increasing **estrogens** from the follicle plus the **increasing LH** from the anterior pituitary gland act together to cause proliferation of the follicular **thecal cells** and increase their secretion.

Only One Follicle Fully Matures Each Month, and the Remainder Undergo Atresia.

- Before ovulation occurs, one of the follicles begins to outgrow all the others; the remaining 5 to 11 developing follicles involute (a process called *atresia)*
- The large amounts of estrogen from the most rapidly growing follicle → the hypothalamus to depress further enhancement of FSH secretion →in this way blocking further growth of the less well developed follicles.
- → The largest follicle continues to grow because of its intrinsic positive feedback effects, while all the other follicles stop growing and actually involute.
- This process of atresia is important because it normally allows only one of the follicles to grow large enough each month to ovulate.

Note:

- ** About every 28 days, gonadotropic hormones from the anterior pituitary gland cause 8 to 12 new follicles to begin to grow in the ovaries.
- ** One of these follicles finally becomes “mature” and ovulates on the 14th day of the cycle.


Phases of the Ovarian Cycle
Follicular Phase
Ovulation
Luteal Phase
Gonadotrophic hormone levels
LH
FSH
Ovarian cycle
Primary follicle
Theca
Antrum
Ovulation
Corpus luteum formation
Mature corpus luteum
Corpus albicans
Ovarian hormone levels
Progesterone
Estrogen
Inhibin

Note:

**The early growth of the primary follicle up to the antral stage is stimulated mainly by FSH alone.

Ovulation

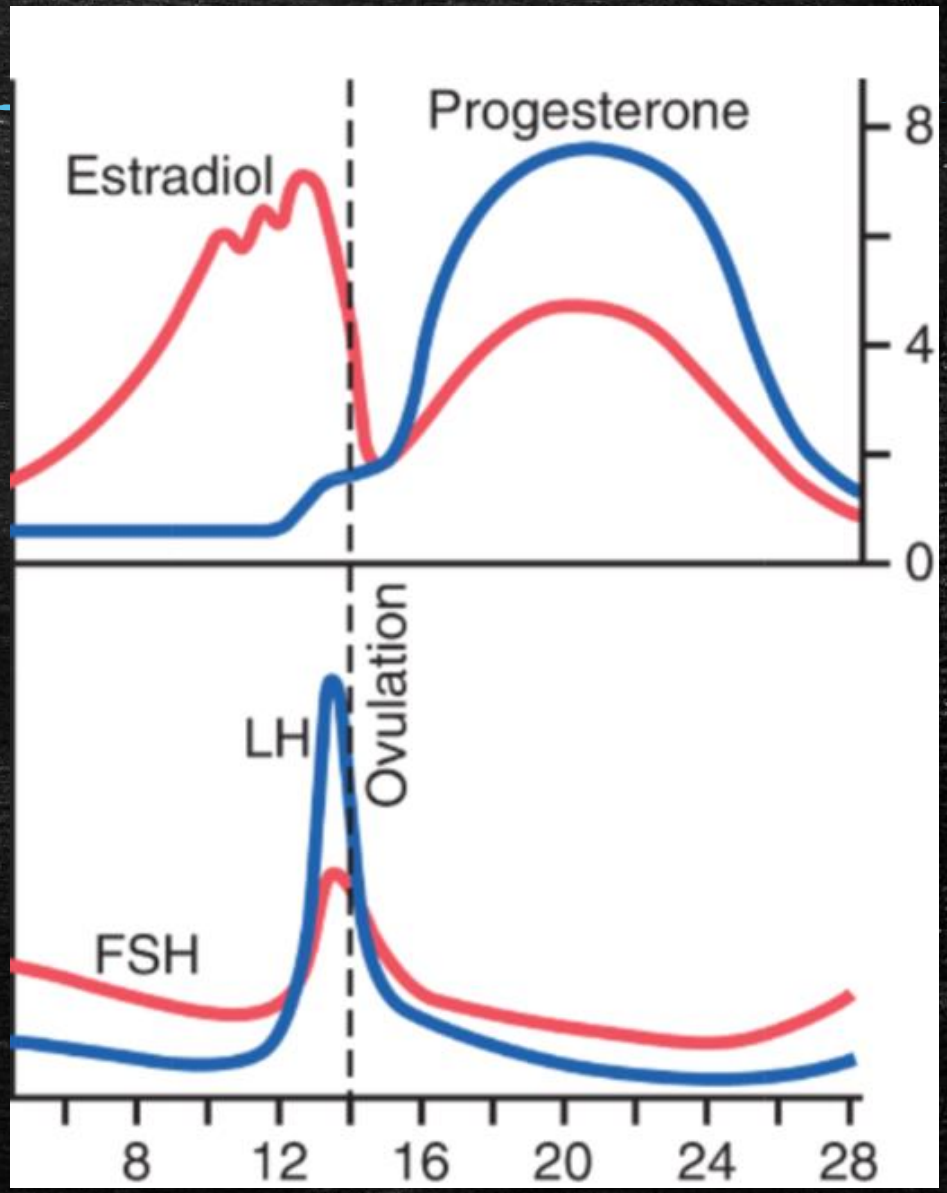
A Surge of Luteinizing Hormone Is Necessary for Ovulation

- LH is **necessary** for **final follicular growth** and **ovulation**.
- **Without** this hormone, even when large quantities of FSH are available, the **follicle will not progress to the ovulation** stage.
- FSH and LH act **synergistically** to cause **rapid swelling** of the follicle during the last few days before ovulation.
- The LH also has a specific effect on **the granulosa and theca cells**, converting them **mainly** to **progesterone-secreting cells**.
- Therefore, the rate of **estrogen** secretion begins to **fall** about 1 day before ovulation, while increasing amounts of **progesterone begin** to be secreted.

A Surge of Luteinizing Hormone Is Necessary for Ovulation

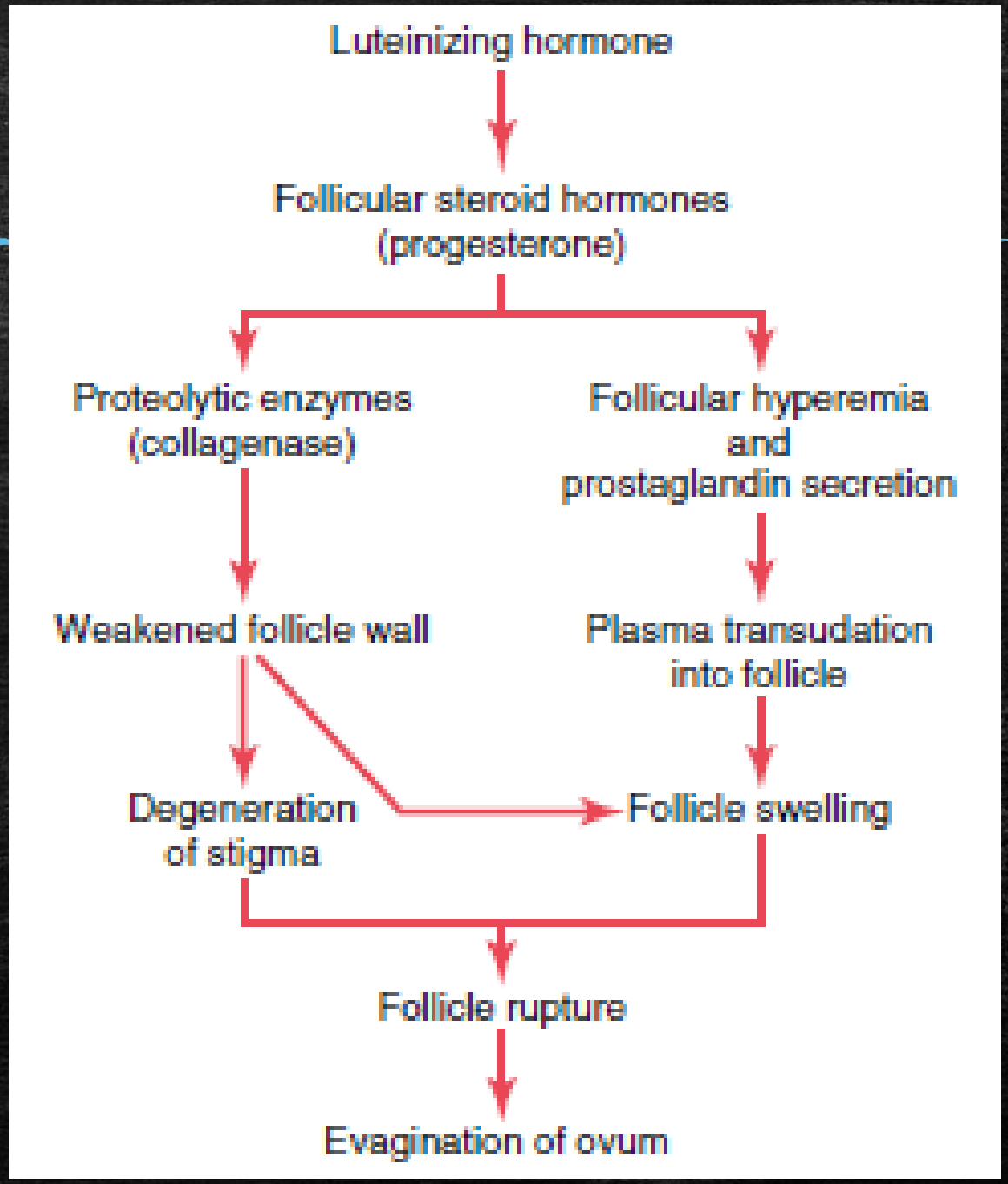
- (1) rapid growth of the follicle
- (2) preovulatory surge of LH
- (3) initiation of secretion of progesterone.
- (4) diminishing estrogen secretion after a prolonged phase of excessive estrogen secretion.

- → ovulation occurs.



Mechanism of Ovulation!

- LH surge
- Theca Externa release enzymes
- Rapid growth of new blood vessels into follicular wall
- Follicle swelling and degeneration of the stigma
- Follicle rupture
- Ovum discharge



Note :

- LH causes rapid secretion of follicular steroidhormones that contain progesterone. Within a few hours,two events occur, both of which are necessary for ovulation:

(1)The *theca externa* (the capsule of the follicle) begins to release proteolytic enzymes from lysosomes, and these cause dissolution of the follicular capsular wall and consequent weakening of the wall, resulting in further swelling of the entire follicle and degeneration of the stigma.

(2) Simultaneously there is rapid growth of new blood vessels into the follicle wall, and at the same time, prostaglandins (local hormones that cause vasodilation) are secreted into the follicular tissues. These two effects cause plasma transudation into the follicle, which contributes to follicle swelling. Finally, the combination of follicle swelling and simultaneous degeneration of the stigma causes follicle rupture, with discharge of the ovum.

Positive Feedback Effect of Estrogen Before Ovulation—The Preovulatory Luteinizing Hormone Surge

- Experiments have shown that estrogen infusion into a female **above** a **critical rate** for 2 to 3 days during **the latter part of the first half** of the ovarian cycle will cause rapidly accelerating growth of the ovarian follicles, as well as rapidly accelerating secretion of ovarian estrogens. During this period, secretions of FSH and LH by the anterior pituitary gland are at first **slightly suppressed**. Secretion of **LH** then **increases** abruptly 6-fold to 8-fold, and secretion of **FSH** increases about 2-fold.

Causes of LH surge

- The cause of this abrupt surge in LH secretion is not known. However, the following explanations are possible:

- 1. It has been suggested that at this point in the cycle, **estrogen (high level)** has a **peculiar positive feedback** effect of stimulating pituitary secretion of LH and, to a lesser extent, FSH. which is in sharp contrast to the normal negative feedback effect of estrogen that occurs during the remainder of the female monthly cycle.

Causes of LH surge

- 2. The granulosa cells of the follicles begin to secrete small but **increasing quantities of progesterone** a day or so before the preovulatory LH surge, and it has been suggested that this secretion might be the factor that stimulates the excess LH secretion.

Physiology

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Go to settings > privacy> location> services> make sure that location services is ON