

YU - Medicine

Passion Academic Team

The Urogenital System

Sheet# 8 - Physiology

Lec. Title : Female Reproductive
System

Written By : Rahma Marie
Sawsan Radi


If you come by any mistake , please kindly report it to
shaghafbatch@gmail.com





Female reproductive system

المحاضرة من الكتاب تبدأ صفحة 470
دعواتكم، كل الحُبِّ

- 
- The female reproductive tract consists of:
 1. The female gonads (the **ovaries**)
 2. the uterus
 3. the fallopian tubes.

 - The ovaries have two functions:
 1. oogenesis
 2. secretion of the female sex steroid hormones
 - Progesterone
 - estrogen.

The ovary

- The ovary has three zones:
 1. The **cortex** is the outer and largest zone. It is lined by germinal epithelium and **contains all of the oocytes**, each of which is enclosed in a follicle. The ovarian follicles are also responsible for **steroid hormone synthesis**.
 2. The **medulla** is the middle zone and is a **mixture** of cell types.
 3. The **hilum** is the inner zone, through which **blood vessels and lymphatics pass**.
- The ovarian steroid hormones have both **paracrine** and **endocrine** functions.
- Paracrine: Locally (within the ovaries) the ovarian steroid hormones support the development of the ova.
- Endocrine: Systemically, the ovarian steroid hormones act on a variety of target tissues including **uterus, breast, and bone**.
- The functional unit of the ovaries is the **single ovarian follicle** (= **one germ cell surrounded by endocrine cells**).

Functions of the ovarian follicle

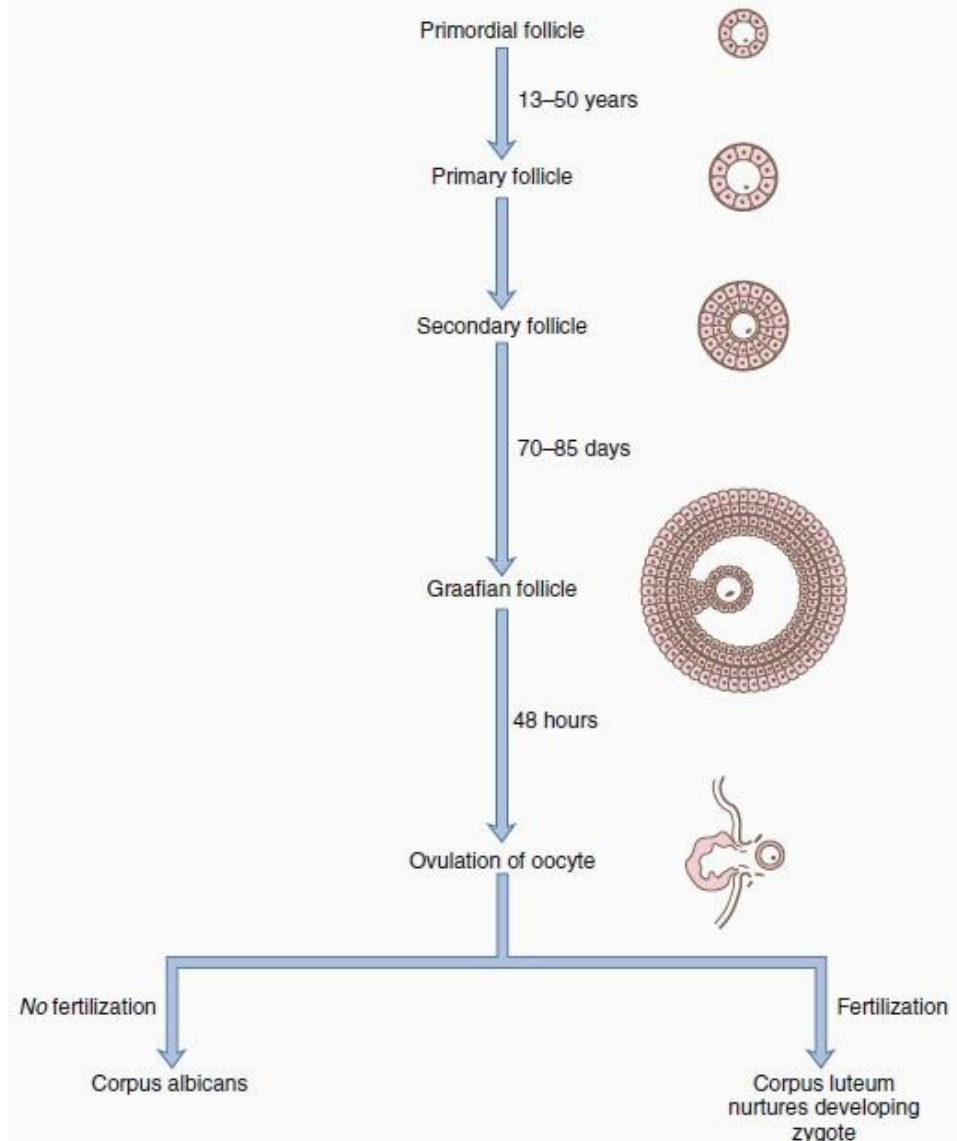
- Provides **nutrients** for the developing oocyte
- **Releases the oocyte** at the proper time (**ovulation**)
- **Prepares the vagina and fallopian tubes** to aid in fertilization of the egg by a sperm
- **Prepares** the lining of the **uterus for implantation** of the fertilized egg
- **Maintains steroid hormone production for the fetus** until the placenta can assume this role.

Oogenesis

- In the developing ovaries → primordial germ cells produce **oogonia** by **mitotic divisions** until gestational weeks 20-24.
- At gestational weeks 8-9 → some of the oogonia enter the **prophase of meiosis** and become **primary oocytes**.
 - **6 months** after birth → **all oogonia have become oocytes**.
- The oocytes remain in a state of suspended prophase.(that's related to the High level of cyclic AMP and MAPK pathway)
- We start off oogenesis with 7 million oogonia. but, there is an attrition of some oocytes. (apoptosis of oocytes)
- Just to know : MAPK pathways relay, amplify and integrate signals from a diverse range of stimuli and elicit an appropriate physiological response including cellular proliferation, differentiation, development, inflammatory responses and apoptosis in mammalian cells

Development of ovarian follicles

- **First stage:**
 - It parallels the prophase of the oocyte.
 - It lasts many years (13-50 years).
 - As the **primary oocyte grows**, the granulosa cells proliferate and nurture the oocyte with **nutrients and steroid hormones**.
 - The **primordial follicle develops into a primary follicle**, theca interna cells develop, and granulosa cells begin to secrete fluid.
 - **No follicle progresses beyond this first stage in prepubertal ovaries.**



Development of ovarian follicles – Second stage

- It takes place over a period of **70–85 days** and is present **only during the reproductive period**.
- During each menstrual cycle, a few follicles enter this sequence.
- A fluid containing steroid hormones, mucopolysaccharides, proteins, and **FSH** accumulates in a central area of the follicle called the **antrum**.
- The steroid hormones reach the antrum by **direct secretion from granulosa cells**. The granulosa and theca cells continue to grow.
- At the **end of the second stage**, the follicle is called a **graafian follicle** and has an average diameter of 2–5 mm.

Development of ovarian follicles – Third stage

- It occurs **5–7 days after menses** (menses marks the end of the previous cycle and means the flow of blood).
- A **single graafian follicle** achieves dominance over its cohorts, and the cohorts regress.
- Within 48 hours (after 5-7 days), the **dominant follicle** grows to 20 mm in diameter.
- On day 14 of a 28-day menstrual cycle, **ovulation** occurs and the dominant follicle ruptures and **releases its oocyte into the peritoneal cavity**.
- At this time, the **first meiotic division is completed** and the resulting secondary oocyte enters the nearby **fallopian tube**, where it **begins the second meiotic division**.
- In the fallopian tube, if fertilization by a sperm occurs, the second meiotic division is completed, producing the **haploid ovum (1n) with 23 chromosomes**.

Development of ovarian follicles –in other way

• هون التقسيمة مختلفة عن ال stages

- **Preantral phase/follicle:** primordial follicle + primary follicle + secondary follicle.

- Parallels to stage 1 & 2

- Those follicles :

1) **do not contain fluid filled antrum.**

2) Their development is **gonadotropin independent.** Are not influenced by Hypothalamic-pituitary axis hormones.

- **Eantral phase/follicle:** the same of **graafian follicle**, also called **third follicle**

- Parallels to stage 3

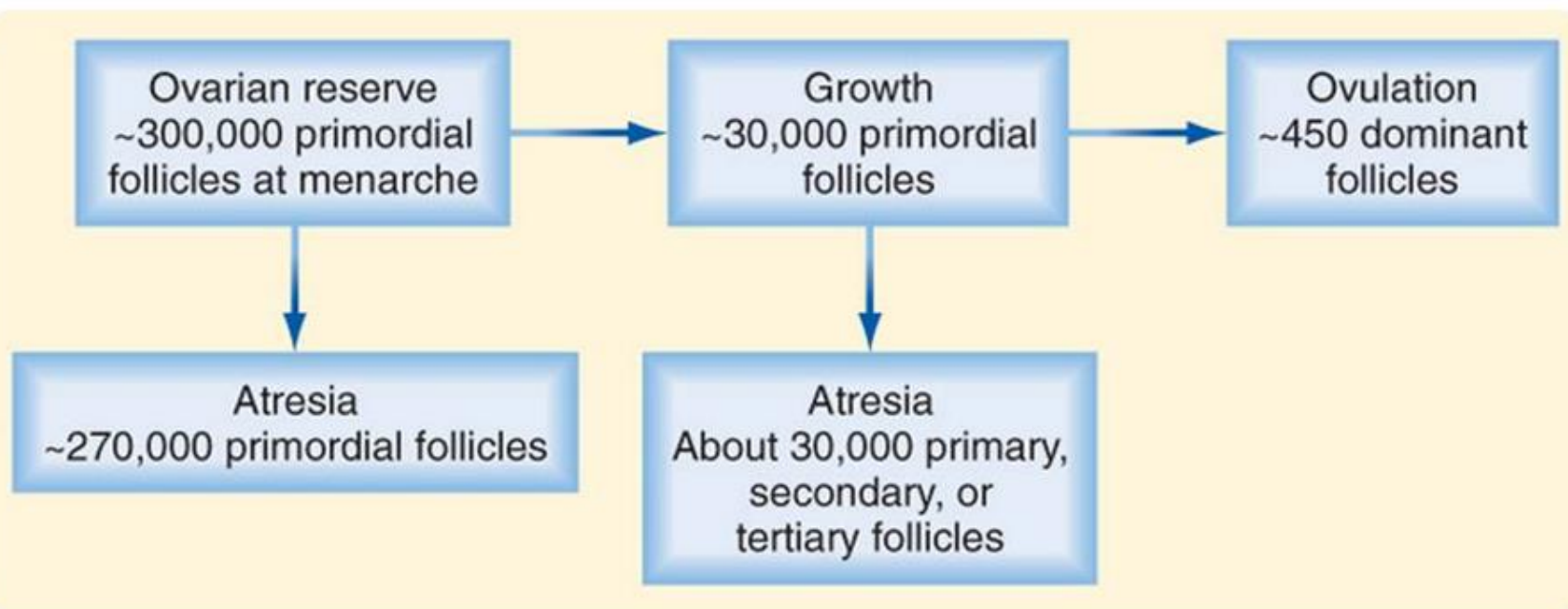
- Each menstruation, one of these follicle will be ovulated

- If there is fertilization, this follicle will complete the second mitosis

- The residual elements of the ruptured primary follicle form the **corpus luteum**.
 - Composed primarily of **granulosa** cells, but also of **theca** cells, **capillaries**, and **fibroblasts**.
 - It **synthesizes and secretes steroid hormones**, which are necessary for **implantation** and **maintenance** of the zygote. So it **must still for 14 (+/- 2) days** , and the **life span may be elongated to 9 month** if fertilization occure..... If the corpus luteum life span is less than 14 days, that can lead to **infertility**.
- **If fertilization *does* occur** → the corpus luteum will secrete steroid hormones until the placenta assumes this role, later in pregnancy.
- **If fertilization *does not* occur**, the corpus luteum **regresses** during the next 14 days (the second half of the menstrual cycle) and is replaced by a scar called the **corpus albicans**.
- corpus luteum regression occurs due to **prostaglandins ($PGF_{2\alpha}$)** ***“limiting factor”***

From Berny & Levy page 800:

- The **primordial follicles** represent the **ovarian reserve** of follicles
- This reserve is **reduced** from a starting number of about **7 million** to **less than 300,000 follicles** at reproductive maturity.
- Of these, a woman will **ovulate about 450** between **menarche** (first menstrual cycle) and **menopause** (cessation of menstrual cycles).
- At menopause, less than **1000 primordial follicles** are left in the **ovary**. (Primordial follicles are lost primarily from death as a result of follicular atresia.)



Notes:

- the ovarian follicular reserve represents a fixed finite number, the rate at which resting primordial follicles die or begin to develop (or both) will **determine the reproductive life span** of a woman.
- Age at the onset of menopause has a **strong genetic component** but is also **influenced by environmental factors**.
- For example, cigarette smoking significantly **depletes the ovarian reserve**. How?

An overly **rapid rate of atresia or development** will deplete the reserve and **give rise to premature ovarian insufficiency**.

- During the early weeks of gestation, we do not want antimüllerian hormone. However, we do need it later on as that **level (1-3ng/ml)** is needed to **maintain the ovarian reserve**. How?

This is because it counteracts the effects of FSH hormone (which **tries to push oocytes into the growth phase for ovulation**).

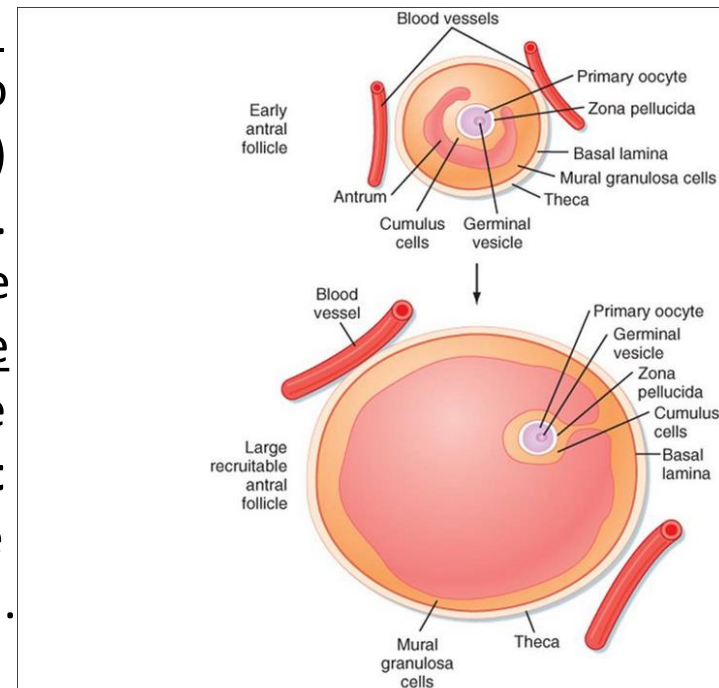
- To stop the recruitments of follicles in large amounts by FSH, we need **antimüllerian hormone**. Otherwise, "ovarian failure" happens due to FSH.

Notes:

- **Sperms bind to species specific receptor** (each mammalian has its own receptors) which **triggers the oocyte to start the second meiotic division.**
- **Zona pellucida** around the oocyte is **responsible** for forming the species specific receptor.
- There is no duct for ovaries allows the follicle to leave from during ovulation.
- The ova/dominant follicle **grows in size.** as a result, the wall of the ovaries **pinches** to form a **hole** from which the dominant follicle can leave from , by triggering an **inflammatory cascade** (This hole means there is an injury in this site.)
- the hole will be repaired later by **rapid epithelial cell proliferation** and **scar formation.**
- **This is repeated each cycle.**

From Berny & Levy page 801:

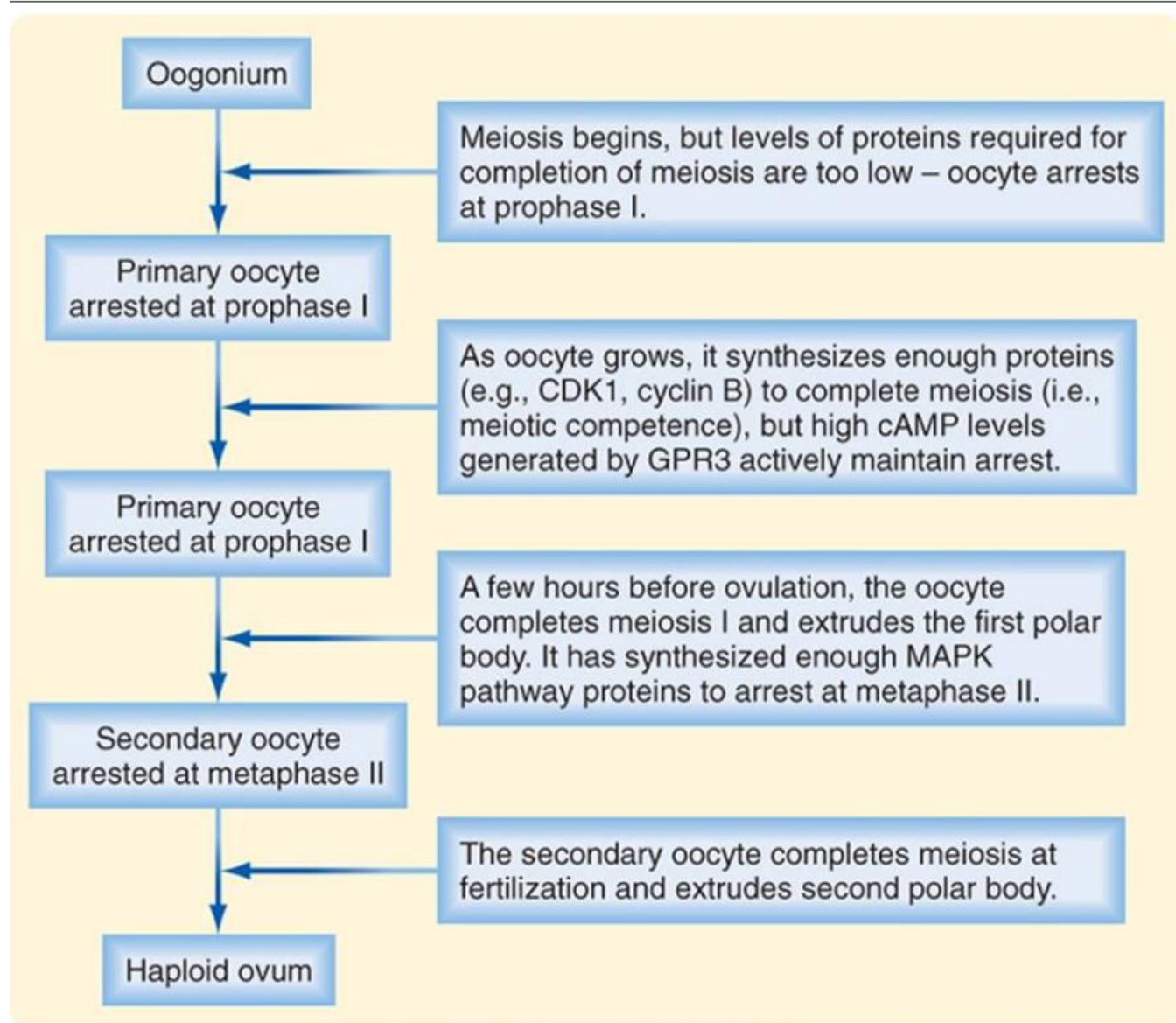
- **Mural granulosa** cells (also called the stratum granulosum) form the **outer wall of the follicle**. The basal layer is adherent to the basal lamina and in close proximity to the outer-lying thecal layers.
- In antral phase, become highly **steroidogenic** and remain in the ovary after ovulation to **differentiate** into the **corpus luteum**.
- **Cumulus cells** are the **inner cells** that surround the oocyte (also referred to as the cumulus oophorus and corona radiata).
- The **innermost layer** of cumulus cells **maintains gap and adhesion** junctions with the oocyte.
- Cumulus cells are released with the oocyte (collectively referred to as the **cumulus-oocyte complex**) during the process of ovulation.
- Cumulus cells are crucial for the ability of the fimbriated end of the oviduct to “capture” and **move** the oocyte by a **ciliary transport** mechanism along the length of the oviduct to the site of fertilization.



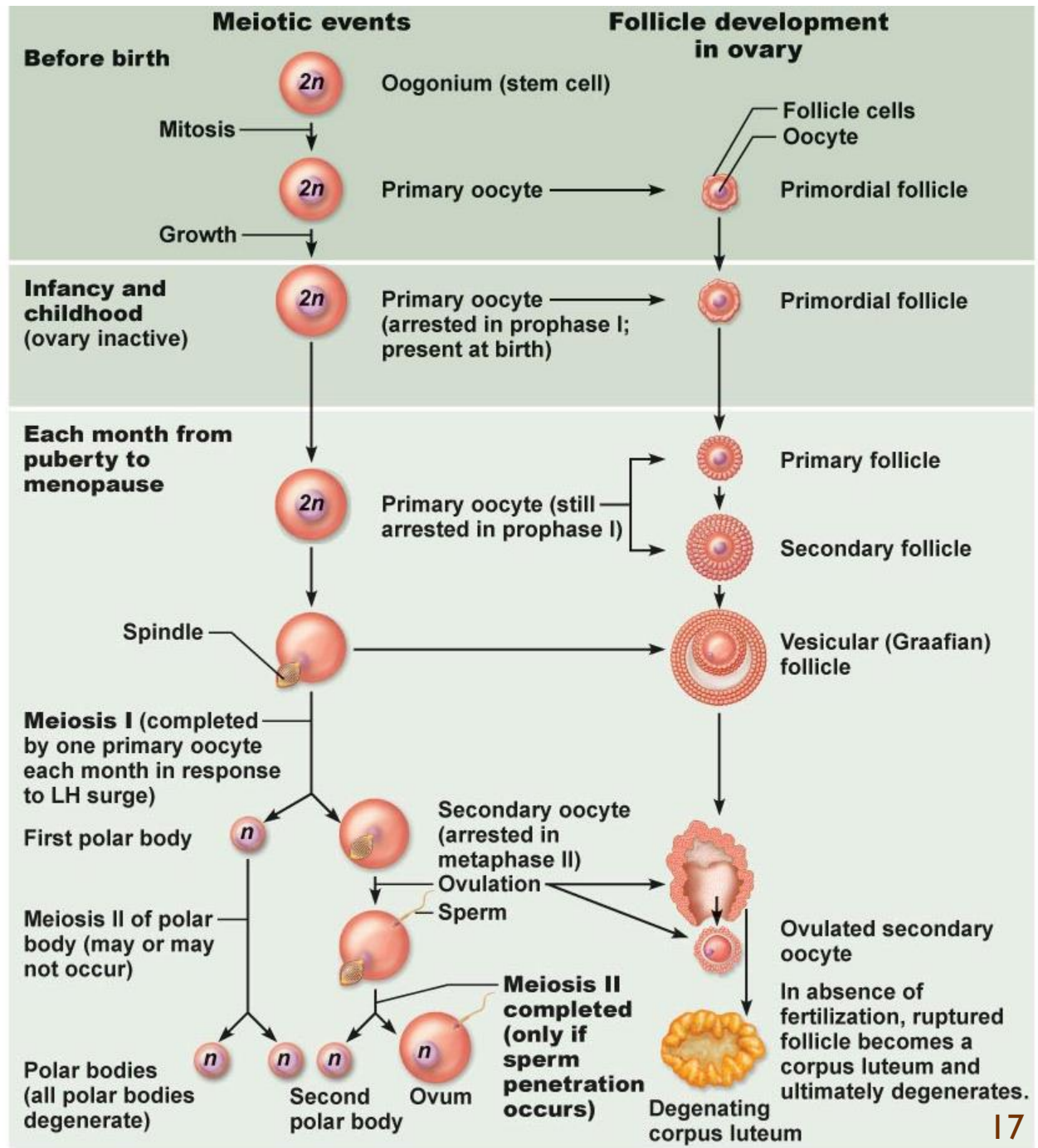
Summary of ovarian follicle trajectory

- The ovarian follicle is the functional unit of the ovary, and it performs both gametogenic and endocrine functions. A histological section of the ovary from a premenopausal cycling woman contains follicular structures at many different stages of development. The life history of a follicle can be divided into the following stages:
 - 1. **Resting primordial follicle**
 - 2. **Growing preantral (primary and secondary) follicle**
 - 3. **Growing antral (tertiary) follicle**
 - 4. **Dominant (preovulatory, graafian) follicle**
 - 5. **Dominant follicle within the periovulatory period**
 - 6. **Corpus luteum (of menstruation or of pregnancy)**
 - 7. **Atretic follicles**

Summary:

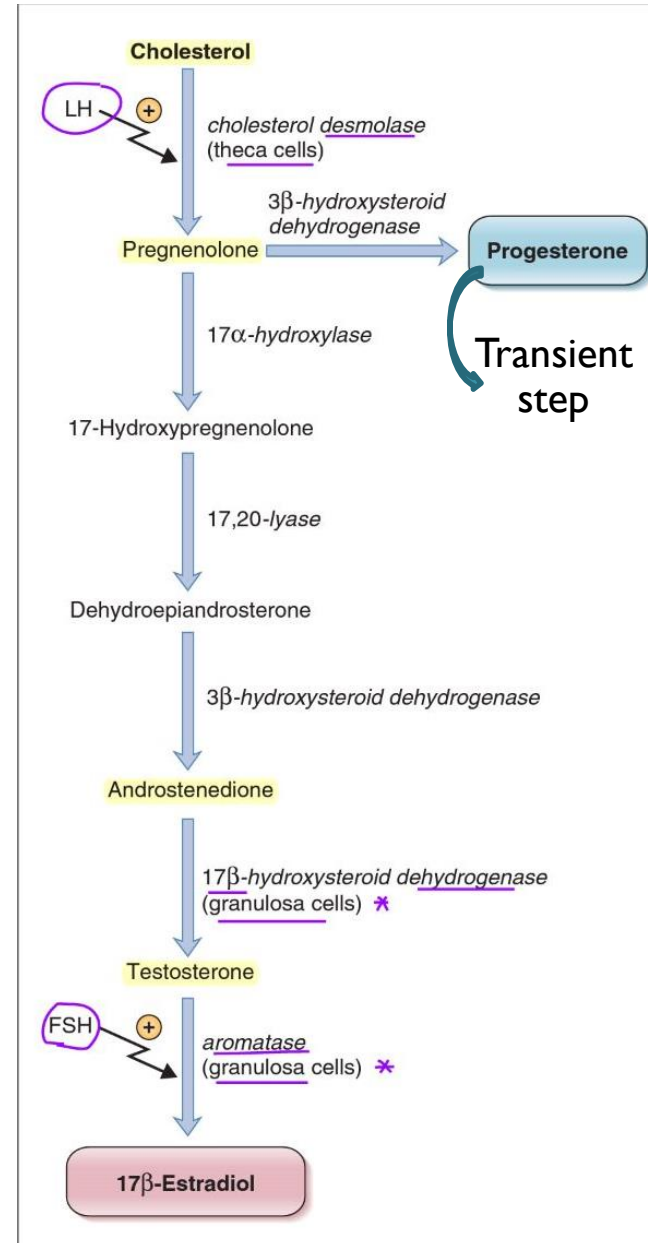


Summary:

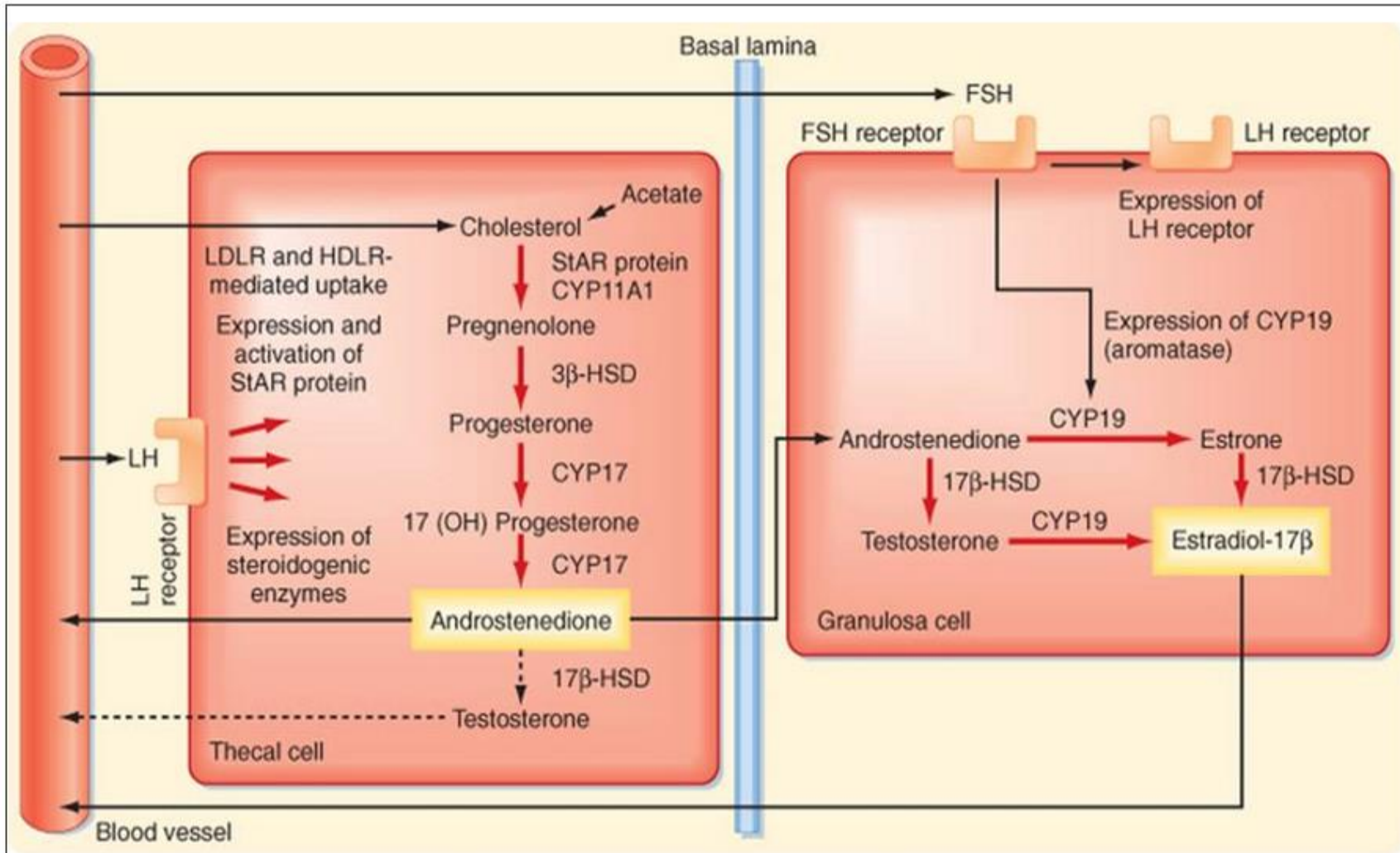


Synthesis and secretion of estrogen and progesterone

- **Theca cells produce progesterone (stimulated at the first step by LH).**
- Theca cells also synthesize androstenedione → androstenedione diffuses to the nearby **granulosa cells**, which contain
 - **17 β -hydroxysteroid dehydrogenase**, which converts androstenedione **to testosterone**
 - **Aromatase or CYP19**, which converts testosterone **to 17 β -estradiol** (stimulated by FSH).
 - Later on, **granulosa cells** produce other hormone called **Inhibin...**
 - **Low levels of estrogen and inhibin negatively feed back on FSH secretion..** thereby contributing to selection of the follicle with the most FSH-responsive cells.



From Berny & Levy page 803 :



Koepfen & Stanton: Berne and Levy Physiology, 6th Edition.
 Copyright © 2008 by Mosby, an imprint of Elsevier, Inc. All rights reserved