Chapter 01: Gametogenesis

Part II: Oogenesis and Folliculogenesis

Introduction

The female reproductive system plays a far more complex role than the male reproductive system. Not only must it produce gametes, but it must also prepare itself to support a developing embryo for nine months. Oogenesis and folliculogenesis are crucial processes ensuring the formation and maturation of female gametes. These processes begin before birth, remain dormant during childhood, and resume at puberty, continuing cyclically until menopause.

Understanding these processes is essential for grasping reproductive biology, fertility, and hormonal regulation. Any dysfunctions in oogenesis or folliculogenesis can lead to infertility, hormonal imbalances, or reproductive disorders such as polycystic ovary syndrome (PCOS) or premature ovarian failure.

I. Female Reproductive System

The female reproductive system consists of several organs that work together to ensure reproductive function. These include:

- **Two ovaries**: Responsible for gamete production and hormone secretion.
- **Two fallopian tubes**: Muscular ducts that transport gametes and embryos, serving as the site of fertilization.
- **Uterus**: A hollow muscular organ where embryo implantation and fetal development occur.
- **Cervix**: The lower part of the uterus that secretes cervical mucus, acting as a barrier and a selective channel for sperm passage.
- **Vagina**: A muscular-membranous conduit that serves as the passage for sperm entry and childbirth, also playing a role in maintaining vaginal microbiota for protection against infections.

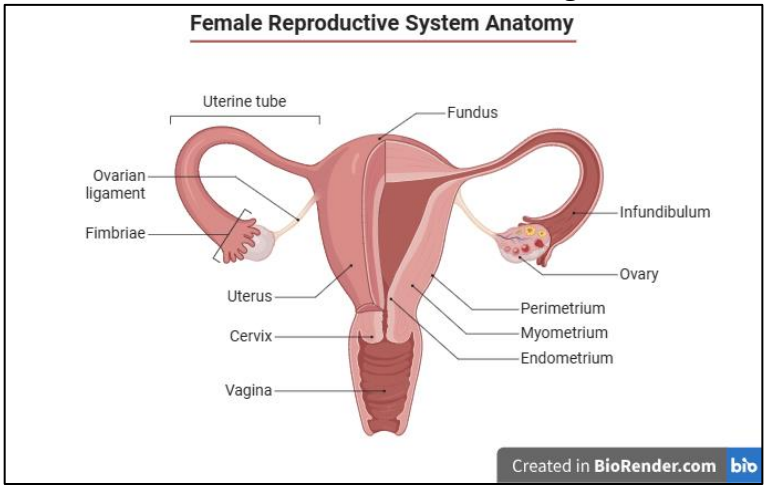


Figure 12. Female reproductive anatomy

1. The Ovaries

The **ovaries** are almond-shaped organs located in the pelvic cavity, measuring approximately **3 to 4 cm in length** and **2 cm in width**. They consist of:

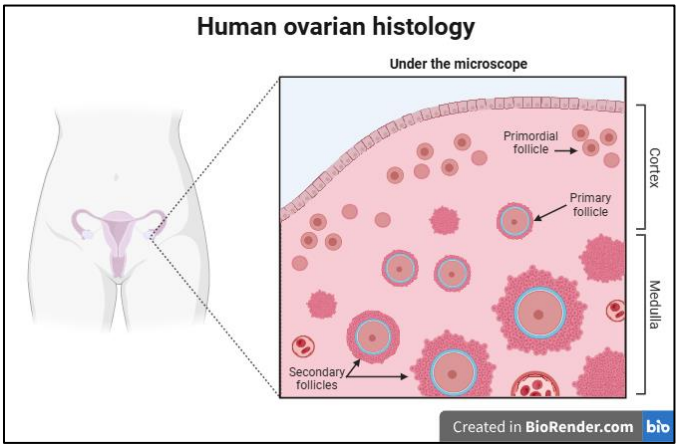


Figure 13. Ovarian histology

- **The ovarian cortex**: The outer region containing follicles at different developmental stages.
- **The ovarian medulla**: The central region, which houses blood vessels, lymphatic vessels, and nerves.

The ovaries perform two essential functions:

- **Oogenesis**: The production of female gametes (oocytes).
- **Hormonal secretion**: The synthesis of estrogen and progesterone, regulating the menstrual cycle and preparing the uterus for implantation.

These functions are cyclical and controlled by a delicate interplay of hormones, ensuring the release of one mature oocyte per cycle.

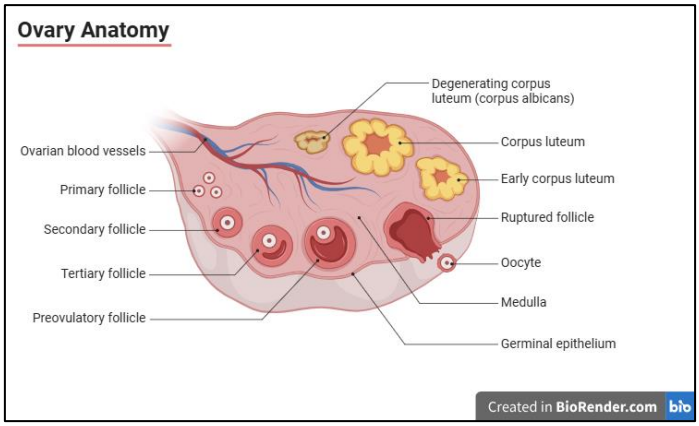


Figure 14. Anatomy of the ovary

II. Oogenesis and Folliculogenesis

1. Definition

Oogenesis is the **process of female germ cell development**, starting during fetal life. It involves **mitotic proliferation, meiotic division, and differentiation**, resulting in the formation of **mature oocytes**. This process pauses at birth, resumes at puberty, and ceases at menopause.

Folliculogenesis, on the other hand, is the **growth and maturation of ovarian follicles**, which support and nourish the oocyte. Without proper folliculogenesis, ovulation cannot occur, leading to reproductive challenges.

2. Follicle and Oocyte

Each oocyte develops within a **follicle**, a spherical structure that nourishes and protects the oocyte until ovulation. The follicle plays a crucial role in endocrine regulation by secreting hormones such as **estrogen**, which modulates the menstrual cycle and prepares the endometrium for potential implantation.

III. The Menstrual Cycle

The **menstrual cycle** is a series of hormonal and physiological changes that occur in the female reproductive system, typically lasting **28 days**. It prepares the body for potential pregnancy and consists of three main phases:

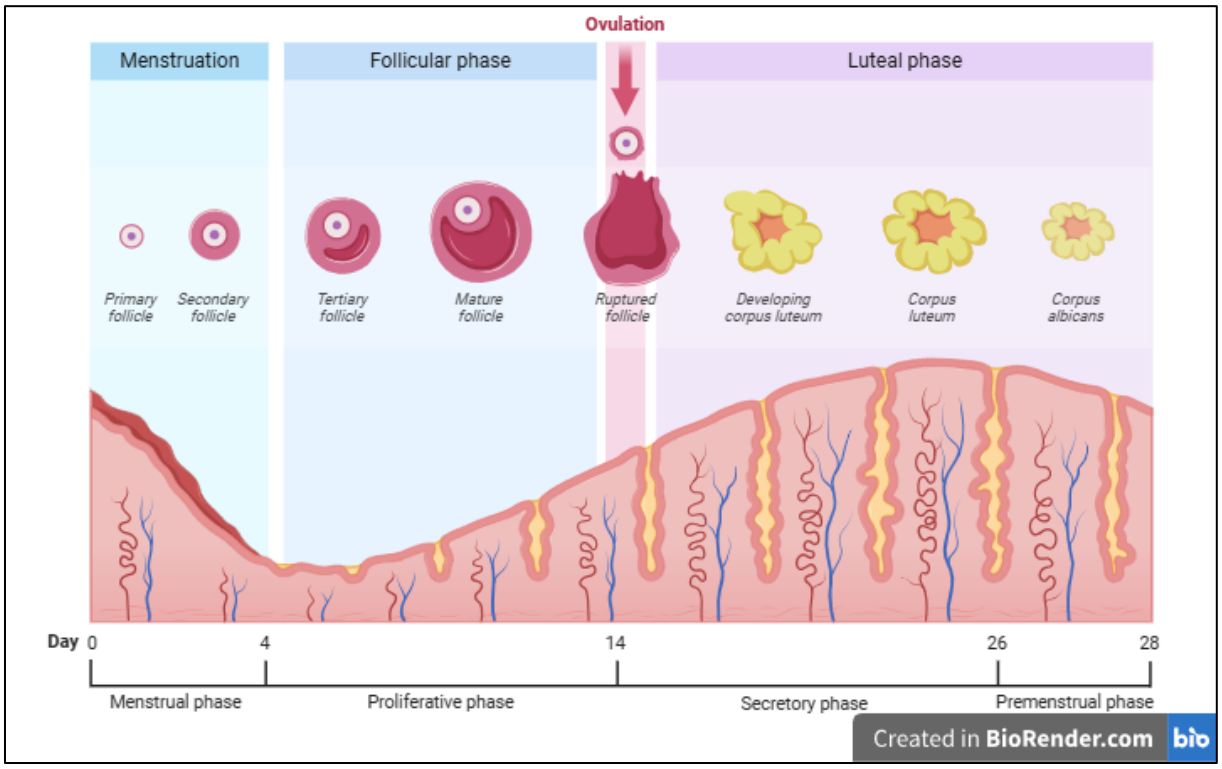


Figure 15. The human uterine cycle

1. Menstrual Phase (Days 1-5)

- The **endometrial lining** of the uterus sheds due to a drop in **progesterone and estrogen levels**.
- This phase is marked by **menstrual bleeding**, which removes the unfertilized oocyte along with the uterine lining.

2. Follicular Phase (Days 6-14)

- **Follicle-stimulating hormone (FSH)** stimulates the growth of ovarian follicles.
- The developing follicles **secrete estrogen**, which thickens the uterine lining (endometrium).
- Around **day 14**, a surge in **luteinizing hormone (LH)** triggers **ovulation**, where a mature oocyte is released from the dominant follicle.

3. Luteal Phase (Days 15-28)

- The ruptured follicle transforms into the **corpus luteum**, which secretes **progesterone and estrogen**.
- These hormones maintain the endometrial lining, preparing for implantation.
- If fertilization does not occur, hormone levels drop, leading to the next menstrual phase.

4. Corpus Luteum Formation

After ovulation, the ruptured follicle transforms into the **corpus luteum**, a temporary endocrine structure that secretes **progesterone and estrogen**:

- **Without fertilization**, the corpus luteum degenerates after **14 days**, leading to menstrual shedding.
- **With fertilization**, it persists for the first three months of pregnancy to support early embryonic development by maintaining progesterone levels.

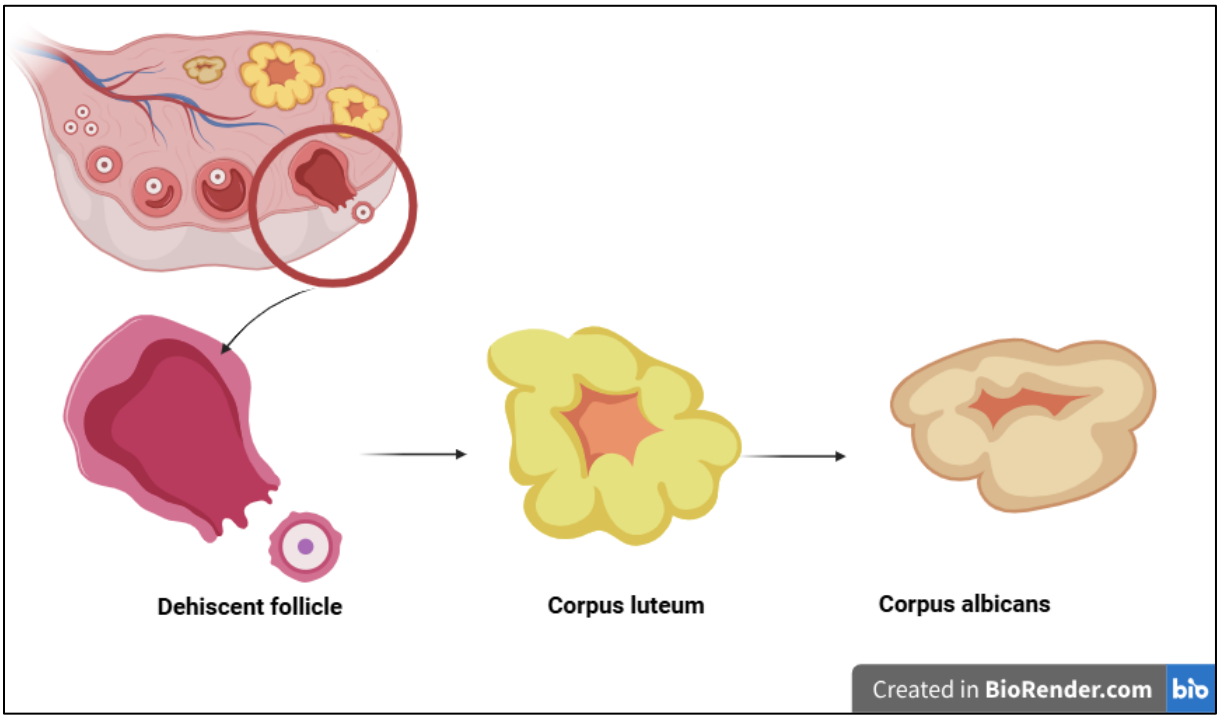


Figure 16. Formation of the corpus luteum (luteinisation)

This stage is crucial for establishing pregnancy; failure in corpus luteum function can lead to implantation failure or early miscarriage.

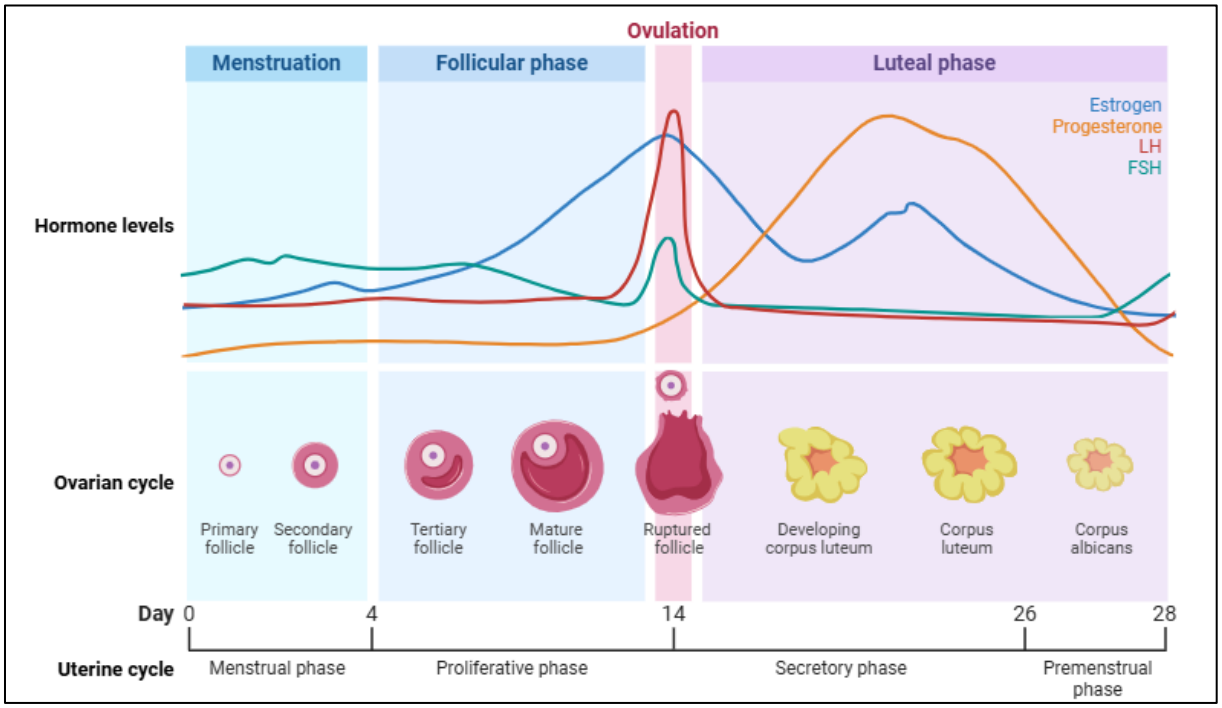


Figure 17. Hormonal fluctuations during the uterine cycle

Stages of Oogenesis

1. Prenatal Period

During this stage, oogonia multiply through mitosis from the 15th week of development until the 7th month of fetal life, forming primary oocytes. These oocytes begin meiosis but arrest at the first stage of division until puberty. During childhood, the ovaries remain completely inactive.

At the end of multiplication, oogonia are surrounded by a layer of follicular cells, forming primordial follicles. Within these follicles, the oogonium transforms into a primary oocyte (oocyte I).

A primordial follicle consists of an oocyte arrested in the prophase of the first meiotic division (oocyte I) surrounded by flattened follicular cells. The number of oocytes declines from approximately 7 million at the end of the 7th month in utero to 1 million at birth and 400,000 at puberty, with complete depletion at menopause.

2. From Puberty to Menopause

Oogenesis ensures the production of a fertilizable gamete once every 28 days. It takes place in the cortical region of the ovary. At puberty, with the establishment of the menstrual cycle, folliculogenesis begins, allowing the development of primordial follicles into mature follicles.

a. Primordial Follicle

At puberty, the number of oocytes decreases to approximately 400,000 per ovary. From puberty until menopause, once a month (on the 5th day of the cycle, right after menstruation), around twenty primordial follicles continue folliculogenesis. Typically, only one follicle reaches maturity, while the others degenerate. The primordial follicle consists of an oocyte I, arrested in prophase I, surrounded by a few flattened follicular cells.

b. Primary Follicle

The follicle increases in size, and cell division resumes (prophase I). This follicle consists of:

- A single layer of cuboidal follicular cells
- A zona pellucida between the oocyte I and the follicular cells
- An undifferentiated theca
- A Slavjansky membrane between the undifferentiated theca and the follicular cells

c. Secondary Follicle

Follicular cells multiply, forming multiple layers around oocyte I, which constitutes the granulosa. At this stage, the theca differentiates into an internal and an external theca.

d. Tertiary Follicle

The follicle nearly reaches its mature size. The large oocyte I migrates to a thickened region of the granulosa, becoming eccentric, known as the cumulus oophorus. Lacunae filled with follicular fluid appear in the granulosa, and the internal theca cells begin secreting estrogen.

e. Mature Follicle - Graafian Follicle

The lacunae merge into a large, singular cavity known as the antrum, filled with follicular fluid. A few hours before ovulation, oocyte I completes its reductional division, producing a secondary oocyte (oocyte II, n) arrested in metaphase II.

In mammals, the Graafian follicle is a tertiary ovarian follicle preceding the ovulation of the secondary oocyte. It consists of:

- An external fibrous theca
- A vascularized internal theca that secretes estrogen
- The granulosa, which surrounds a central cavity, the antrum

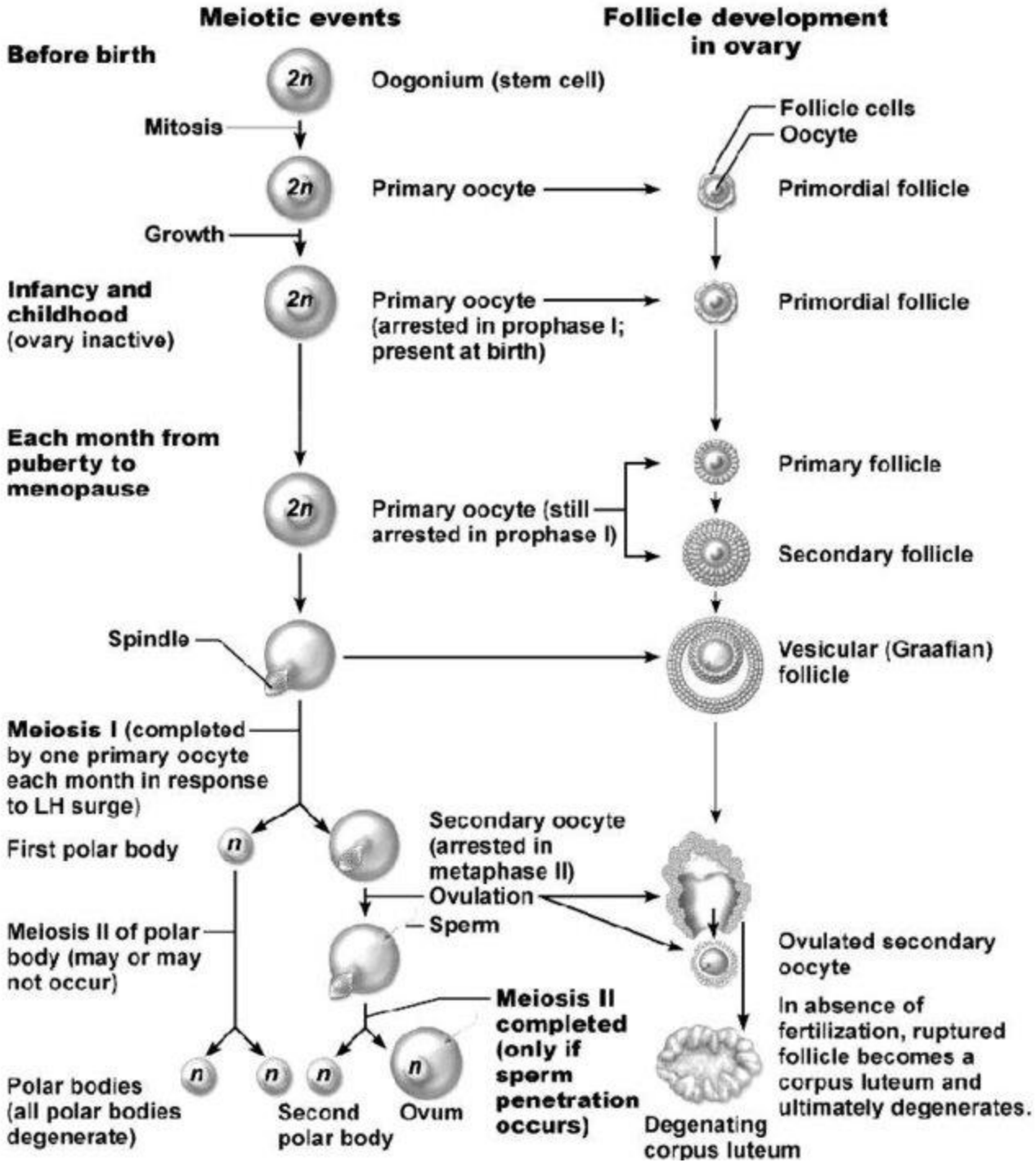


Figure 18. Schematic Representation of Oogenesis and Follicle Development in Ovary

Hormonal Regulation in Women

The regulation of oogenesis and folliculogenesis is controlled by a complex interplay of hormones:

- **Gonadotropin-releasing hormone (GnRH)**: Secreted by the hypothalamus, it stimulates the pituitary gland to release gonadotropins.

- **Follicle-stimulating hormone (FSH)**: Secreted by the anterior pituitary, FSH promotes follicular growth and estrogen production.
- **Luteinizing hormone (LH)**: Also secreted by the anterior pituitary, LH triggers ovulation and the formation of the corpus luteum.
- **Estrogen**: Produced by the granulosa cells of developing follicles, estrogen plays a role in the proliferation of the endometrial lining and feedback regulation of FSH and LH.
- **Progesterone**: Secreted by the corpus luteum after ovulation, progesterone supports endometrial maintenance for potential implantation.

The menstrual cycle consists of follicular, ovulatory, and luteal phases, each regulated by hormonal fluctuations that ensure the maturation and release of the oocyte while preparing the uterus for possible pregnancy.

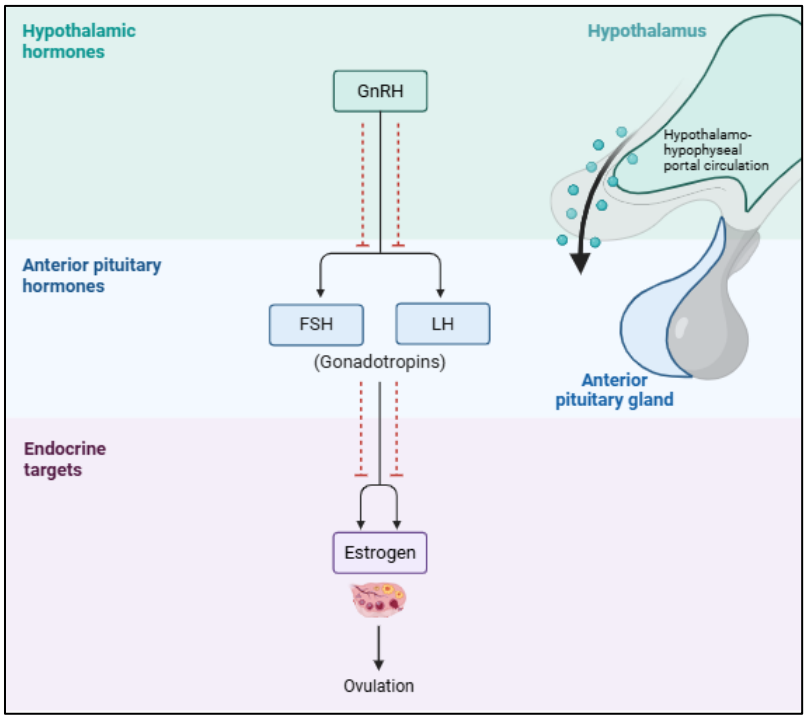


Figure 19. Hormonal regulation in women