University of Mentouri Brothers - Constantine 1
Institute of Veterinary Sciences El Khroub (ISVK)
Dr. Abdeltif Besma
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2.Oogenesis

Oogenesis is the set of processes involving **cell multiplication and differentiation** of the **female germ line cells**. It allows the production of **specialized reproductive cells, haploid female gametes (ova)** from **diploid stem cells called oogonia**, which are cells capable of being fertilized. Oogenesis takes place in the **female reproductive system**, specifically within the **ovarian follicles**.

An **ovarian follicle** is a structure that contains the **oocyte**, a spherical cluster of cells in the ovaries that is **released during ovulation**. Unlike the **male reproductive system**, the **female reproductive system** is not limited to the production of **gametes and sex hormones**. It is also the site of **fertilization, gestation (pregnancy), parturition (childbirth), and lactation**.

The **female reproductive system** includes

- ✓ **Two ovaries**, which perform: **Germinal functions** (production of oocytes) and **endocrine functions** (secretion of **estrogens and progesterone** by follicular cells and the **corpus luteum**, respectively)
- ✓ **Genital ducts:**

- **The oviduct (fallopian tube)**, where **fertilization occurs**
- **The uterus**, where **gestation takes place**
- **The vagina and the vulva**, which are **copulatory organs**

2.1. Site of oogenesis and its development over time

The **formation of female gametes** takes place in the **ovaries**. The ovaries are **ovoid-shaped organs**, small in size, and their size varies depending on **age and the stage of the estrous cycle**.They are covered by a **simple cuboidal epithelium**, under which **two regions can be distinguished (Figure 3):**

- ✓ **A central region**, formed of **connective tissue** in which **blood vessels, lymphatic vessels, and nerves circulate**.
- ✓ **A peripheral cortical region**, composed of **connective tissue**, where the **ovarian structures are located**, namely **follicles and corpora lutea**.

Oogenesis begins during **intrauterine life**, continues **after birth with acceleration at puberty**, and reaches its **highest level at ovulation**.

Three phases are distinguished, **the first two occurring in the fetal ovary**

- ✓ **Multiplication phase**

Primordial germ cells, or **oogonia**, undergo a series of **mitotic divisions**, giving rise to **numerous oogonia**. This **period of oogonia multiplication is limited in time**; in the **cow**, it stops **around the end of the third month of intrauterine life**.

✓ Growth phase

Oogonia become **primary oocytes (oocyte I)** through the **accumulation of cytoplasmic reserves**, resulting in an **increase in the size of the gametes**. Primary oocytes **enter meiosis I (reductional division)** but stop at the **prophase I stage**. Thus, the **primary oocyte remains a cell with 2n chromosomes**. At the same time, each oocyte becomes surrounded by a **layer of follicular cells**, forming a **primordial follicle**.

These processes are **completed before the end of intrauterine life**. No further development occurs **until puberty**. Many follicles **degenerate**, but a **significant number remain dormant until puberty**.

✓ Maturation phase

This phase **begins during fetal life**: primary oocytes start the **first meiotic division (reductional division)** but remain **arrested in prophase I**. This stage **continues after birth**. It **resumes at puberty** and occurs **cyclically**. A few hours **before ovulation**, the **primary oocyte** (located at this stage in a **mature follicle**) **completes the first meiotic division**, producing **two haploid (n) cells of unequal size**:

- a **small cell (first polar body)**
- a **large cell (secondary oocyte or oocyte II)**

The **secondary oocyte** begins the **second meiotic division**, but it **stops at metaphase II**. If **fertilization occurs**, the **secondary oocyte completes the second meiotic division**, producing **two haploid cells**:

- a **small cell (second polar body)**
- a **large cell called the ootid or ovum**

If **fertilization does not occur**, the **secondary oocyte degenerates**.

2.2. Chronology of ovarian follicle development during oogenesis *(primordial follicle, primary follicle, cavitary follicle, mature follicle, corpus luteum, corpus albicans)*

Folliculogenesis is the process of **follicular development**, during which a follicle evolves from a **primordial follicle to a mature (Graafian) follicle**. During **fetal life**, the **somatic cells of the ovarian stroma** associate with **primary oocytes (oocyte I)** and form a **layer of flattened follicular cells around them**.

These first cellular associations constitute the **primordial follicles** *(Table 1)*. From **birth**, follicles enter **successive stages of folliculogenesis in groups**. **Primary follicles** are formed through the **multiplication of follicular cells**, which organize into a **single layer of cuboidal cells** *(Table 1)*.

The **primary oocyte**, still **arrested in prophase I**, becomes surrounded by a **hyaline layer called the zona pellucida**. Its origin is still debated: it may be **secreted either by the oocyte or by the follicular cells**. The structure is surrounded by a **membrane called the Slavjanski membrane**. The **follicular cells** form an increasingly large cluster around the oocyte called the **granulosa**. Around the **granulosa**, two layers of stromal cells develop:

- the **theca interna**
- the **theca externa**

This stage corresponds to the **secondary follicle**

Follicular cells of the secondary follicle begin to secrete a fluid known as **follicular fluid** (fluid-filled gaps between the follicular cells) to form the **follicular cavity** (antrum): this is the **tertiary follicle** (Table 2). Before puberty, all follicles reaching the tertiary stage degenerate.

At puberty, several follicles begin their growth under the influence of pituitary **FSH** (Follicle-Stimulating Hormone). However, a large number of them degenerate; only one follicle will undergo maturation to become the **Graafian follicle** (pre-ovulatory follicle). Its cavity is filled with fluid, and at one of its poles, the follicular cells remain more numerous, forming a protrusion into the cavity called the **cumulus oophorus**, within which the oocyte is located (Table 2). The oocyte is surrounded by the **zona pellucida**, which is itself surrounded by a layer of cells: the **corona radiata**, located at the center of the cumulus oophorus.

After ovulation (ovulation is the release of the female gamete at the **oocyte II stage blocked in metaphase II**), the remains of the mature follicle within the ovary constitute the **dehiscent follicle**. The dehiscent follicle heals, thus forming a temporary endocrine gland called the **corpus luteum**. The granulosa cells of the corpus luteum become **luteal cells**, capable of synthesizing **progesterone**. The internal theca cells continue to synthesize **estrogens**. Within the ovary, the corpus luteum eventually degenerates and forms the **corpus albicans** (white body), which is then phagocytized by phagocytic cells.

2.2. Phases of the Ovarian Cycle: Follicular Phase, Ovulation, and Luteal Phase

Ovarian Cycle The ovarian cycle corresponds to all the cyclic modifications and reorganizations of the cellular elements of the ovarian cortex. Its essential event is the production of female gametes during ovulation. It includes a **follicle maturation phase** leading to ovulation and a **luteal phase**, the period of formation and functioning of the corpus luteum.

- ✓ **The Follicular Phase** This is the first phase of the ovarian cycle characterized by the growth and maturation of follicles. At the beginning of the cycle, the levels of circulating hormones (estrogens-progesterone) are low; the production of **FSH** and **LH** is then stimulated. FSH acts on the follicles, causing them to secrete **estrogens**. The increase of estrogens in the blood triggers a massive release of LH (**LH surge**), which leads to the rupture of the follicle and ovulation.

- ✓ **Ovulation** An essential step of the ovarian cycle, as it allows the release of one or more female gametes at the oocyte II stage, ready to be fertilized. Under the influence of a surge of the pituitary hormone (**L.H.: Luteinizing hormone**) and the forces exerted by the follicular fluid, the oocyte II, the zona pellucida, the corona radiata, and a few cells of the cumulus oophorus are expelled from the ovary into the outer third of the **oviduct** (fallopian tube).

- ✓ **The Luteal Phase** This is the phase of formation, functioning, and lysis of the **corpus luteum (CL)**. The evolution of the corpus luteum depends on the fate of the oocyte; it is destined to regress more or less quickly depending on whether fertilization and gestation occur. In the case of fertilization, the CL is called the **gestational corpus luteum** and persists throughout pregnancy. In the absence of fertilization, the CL is called the **cyclic corpus luteum** and degenerates. LH stimulates the transformation of the dehiscent follicle into the corpus luteum. The CL then exhibits the characteristics of an endocrine gland by producing high levels of **progesterone** (Figure 5).

➢ Cycle Types

Ovarian cycle regulation is ensured by the interaction between pituitary hormones (FSH and LH) and ovarian hormones (estrogen and progesterone), all under the control of the hypothalamus (**GnRH**) (Figure 5).

Two other types of cycles are distinguished: the **estrous cycle** and the **menstrual cycle**.

- ✓ **Estrous Cycle:** Characterized by the periodic appearance of "estrus" behavior or acceptance of the male during the period preceding ovulation (in all mammals except primates). The cycle represents the interval between two estruses, and thus two ovulations.
- ✓ **Menstrual Cycle:** In primates and humans, females may accept mating outside of the time of ovulation; there is no characterized estrus. During this cycle, cyclic activity is manifested by the periodic appearance of uterine bleeding or **menstruation**. Menstruation marks the beginning of the menstrual cycle.

➢ Regulation Cycle

The regulation of the ovarian cycle relies on a complex communication system between the **hypothalamic-pituitary axis** and the **ovaries**, operating through a series of hormonal feedback loops.

1. The Central Control: The Hypothalamic-Pituitary Axis

The Hypothalamus: It secretes **GnRH** (Gonadotropin-Releasing Hormone) in a pulsatile manner. This hormone stimulates the anterior pituitary gland.

The Pituitary Gland: In response to GnRH, it releases two gonadotropins:

FSH (Follicle-Stimulating Hormone): Responsible for the recruitment and growth of follicles during the follicular phase.

LH (Luteinizing Hormone): Responsible for triggering ovulation (the **LH surge**) and the transformation of the ruptured follicle into the corpus luteum.

2. Ovarian Feedback Mechanisms

The ovaries "respond" to the central nervous system through the secretion of steroid hormones (estrogens and progesterone):

Negative Feedback (Early and Late Cycle):

Low to moderate levels of **estrogens** inhibit the release of FSH and LH to prevent the maturation of too many follicles at once.

During the luteal phase, **progesterone** (combined with estrogens) exerts a powerful negative feedback, blocking any new ovulation.

Positive Feedback (Just Before Ovulation):

When the Graafian follicle reaches maturity, it secretes a massive amount of estrogens. Once a specific threshold is crossed, the effect reverses.

This triggers a sudden and massive release of LH: this is the **LH surge**, which is essential for ovulation.