

Cyclical changes in the female body

The female body goes through many cyclical changes due to the change in hormone levels, these changes are mainly connected with the menstrual cycle. This applies not only to the endometrium, but also to the mammary glands and the vaginal mucosa.

Oocyte development

At the end of the 1st month of intrauterine development, **oogonia** appear in the cortex of the developing ovary and multiply by mitotic division until the end of the 5th month of intrauterine life. From the 3rd month of intrauterine development, some oogonia begin to enlarge and turn into **primary oocytes**. A single layer of follicular cells attaches to the oocytes, forming **primordial follicles**. Primary oocytes then enter the prophase of the 1st meiotic division (up to the dictyotene stage lasting at least until puberty). The first meiotic division of the primary oocyte is completed just before ovulation, when **the first polar body** is released - **the secondary oocyte** is formed. During ovulation, the II meiotic division is started, stopping at metaphase. It is completed only in the case of fertilization, when the **2nd polar body** is separated. If the egg is not fertilized, it dies.

Development of the ovarian follicle

A growing **primary unilaminar follicle** - primary oocyte surrounded by a single layer of follicular cells.

A growing **primary multilaminar follicle** - primary oocyte surrounded by multiple layers of follicular cells that divide mitotically during development. The follicular cells form here a cover, which we call **membrana granulosa**. Just around the oocyte we find a radially arranged layer of follicular cells - **corona radiata**. A zona pellucida (glycosaminoglycans and glycoproteins) is gradually formed between the oocyte and the corona. The outermost layer of follicular cells sits on a strongly developed basement membrane - **Slavjanski membrane**. In the vicinity of the membrana granulosa, the sparse collagenous tissue is transformed into **the theca folliculi externa et interna**, where we find thecal cells, which have the character of steroid producing cells. Gradually, the entire follicle increases in size, its shape also changes from originally spherical to slightly ovoid, and sinks deeper into the cortex of the ovary. The growing primary multilaminar follicle represents an active, **hormone-producing** structure (androgens as estrogen precursors).

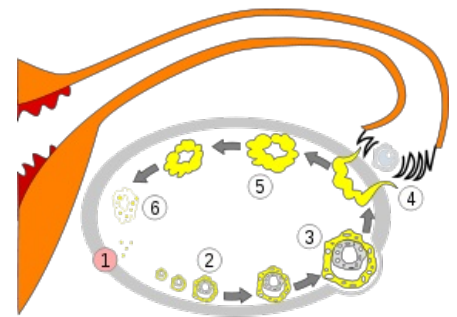


Diagram of oocyte development. 1. immature oocyte, 2. maturing oocyte, 3. mature oocyte, 4. ovulation, 5. corpus luteum, 6. degeneration of corpus luteum

Growing **secondary follicles** - at this stage, fluid begins to accumulate between the follicular cells - **liquor folliculi**, and a cavity - **antrum folliculi** - is gradually formed.

A mature **Graafian follicle** - arches onto the surface of the ovary. The enlargement of the follicle is caused by the accumulation of fluid, the cells no longer divide.

Ovulation

During ovulation, **the wall of the mature follicle ruptures** and **the oocyte is released**, which is subsequently captured by the funnel-shaped opening of the fallopian tube. It occurs **around the 14th day** of the cycle. A woman usually releases one oocyte, but rarely two or even more oocytes are released at the same time. Ovulation occurs due to **an increase in the level of luteinizing hormone from adenohypophysis**. The actual mechanism of ovulation is still being studied, the greatest importance is now given to proteases, which cause local vasoconstriction of the tissue leading to small ischemia above the bulging follicle. After the follicular fluid is emptied, the **follicle collapses**. The cells of the membrana granulosa and the cells forming the theca folliculi interna form a yellow body - **corpus luteum**, which plays the role of a temporary exocrine gland. It occurs in two forms - corpus luteum **menstruationis** and corpus luteum **graviditatis**.

Membrana granulosa cells produce progesterone after ovulation, they make up most of the parenchyma of the corpus luteum. Cells of the theca folliculi interna also contribute to the formation of the corpus luteum, producing estrogens to a small extent. A certain level of luteinizing hormone is necessary for the existence of corpus luteum. Progesterone from the corpus luteum has an inhibitory effect on LH synthesis. Therefore, if **fertilization of the oocyte does not occur**, the corpus luteum menstruationis persists for ten to fourteen days, then its **degeneration** (atresia) occurs. If **fertilization occurs**, the choriogonadotropic hormone produced by the chorion and later by the placenta prevents the disappearance of the corpus luteum, which enlarges (sometimes as much as 5 cm) and turns into the **corpus luteum graviditatis**. We can find the corpus luteum of pregnancy like this for about 6 months, then it shrinks, but it produces progesterone until the end of the pregnancy. It also produces **relaxin** - a hormone that softens the connective tissue (especially the symphysis ossis pubis) and facilitates childbirth. Both types of corpus luteum undergo autolysis after the end of their function and a **corpus albicans** (white corpuscle) is formed, which remains in the cortex of the ovary for a longer time.

Menstrual cycle

The menstrual cycle is a set of **cyclical morphological changes in endometrium and uterine fundus**. It occurs due to the action of ovarian hormones (estrogens and progesterone) and gonadotropic hormones of the adenohypophysis (FSH and LH). The length of the menstrual cycle is not always the same for all women, on average it is **around 28 days**. **Menarche** – i.e. the first menstruation occurs between the 12th and 15th year of a girl's life, **menopause**, i.e. the period when a woman's last menstruation appears, is usually around 45-50. years of age.

Phases of the menstrual cycle

Proliferative phase (cycle days 5-15)

A follicle develops in the ovary and estrogen is produced. The cells lining the base of the endometrial glands proliferate actively, by the end of the 5th day they cover the entire inner surface of the endometrium. Proliferation trvá po celé toto období. Proliferation continues throughout this period. Furthermore, there is a proliferation of fibrous cells of the lamina propria mucosae and deposition of intercellular matter around the glands.

→ The result is a **thickening of the entire endometrium** (2-3 mm thick at the end of the proliferative phase), the glands are straight and narrow.

Spiral arterioles penetrate the regenerating tissue of the lamina propria mucosae.

Secretory phase (cycle days 16-28)

This phase begins at the time of ovulation, it is influenced by progesterone produced by the cells of the corpus luteum. In the epithelial cells lining the glands, glycogen accumulates, later the amount of glycogen decreases and the cells actively secrete glycoproteins. There is an accumulation of secretions in the lumen of the glands, which then twist slightly. However, the expansion of the glands is not uniform, so they acquire a typical irregular saw-like appearance. The glands usually dilate in the area of the body, dividing the zona functionalis into two parts – **pars spongiosa** and **pars compacta**. Pars spongiosa – fibroblasts increase here, glycogen and lipid droplets are stored in the cytoplasm. Cells are starting to look like decidual cells. In the lamina propria mucosae, the spiral arteries continue to lengthen and twist. There is seepage and edema of the entire mucosa (endometrium at the end of the secretory phase about 6-7 mm wide). We call these changes in the endometrium **pseudodecidual transformation**.

Ischemic phase (cycle day 28)

The ischemic phase is caused by a drop in progesterone and estrogen levels (the corpus luteum has disappeared). **Contraction of smooth muscle cells in the wall** of spiral arterioles occurs, **resulting in** ischemia of the zona functionalis. **The zona basalis continues to be supplied with blood from aa. rectae. Here we find necrosis of elements of the stroma, glands and vessel walls.**

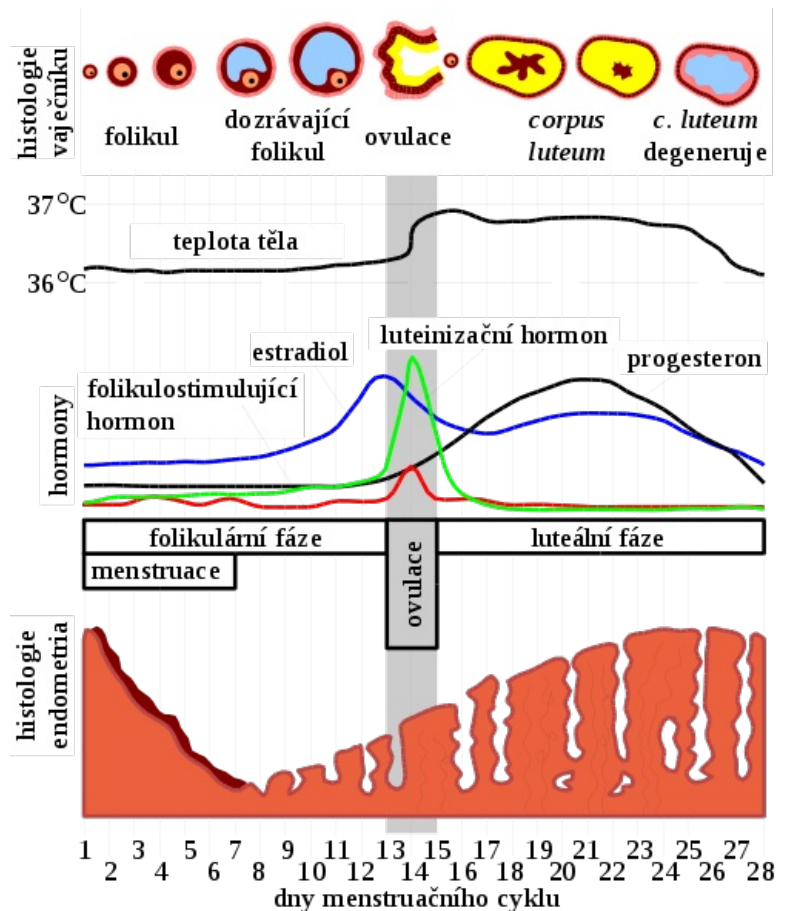
Menstrual phase (cycle day 1-4)

After a few hours of ischemic phase, muscle contraction in blood vessels is released. Sudden congestion of blood vessels damaged by autolytic processes (necrotic changes) leads to **vessel rupture** and **bleeding** into the stroma and endometrial glands. The entire zona functionalis is washed away by menstrual blood from the uterine cavity into the vagina.

Menstrual bleeding

The duration of menstrual bleeding, like the entire menstrual cycle, is an individual matter, but on average it is **3-5 days**. It is terminated by vasoconstriction of the supply arterioles in the myometrium. The amount of menstrual blood is about **40-50 ml**. It is a mixture of arterial and venous blood, mucus, tissue fluid with parts of autolyzed mucosa. Enzymes released during the breakdown of mucous cells (**plasmin**) prevent menstrual blood from clotting.

Menstrual cycle in other areas of the body



Menstrual cycle

(Průměrné hodnoty. Průběh a hodnoty se mohou lišit u různých žen nebo u různých cyklů.)

Isthmus uteri

There are no significant cyclical changes in the endometrium of the isthmus uteri area, only the most superficial layer of the lamina epithelialis and the lamina propria mucosae separates during the menstrual phase.

Cervix uteri

The tunica mucosa of the cervix uteri is not cyclically removed. However, there are **changes in the secretion** of the cervical glands. In the period of **ovulation** the cervical secretion has a **thin** consistency (to allow the penetration of spermatozoa into the uterus). In the **secretory** phase or during pregnancy, the secretion becomes more **viscous** and prevents the penetration of microorganisms and also spermatozoa into the cavum uteri.

Vagina

Changes in the vaginal mucosa are divided into the same phases as the endometrial cycle of the uterus, but there is no menstrual phase. During the cycle, layers of cells increase, which gradually die in the second half of the cycle and are subsequently separated with menstrual blood from the uterus.

Mammary gland

Even the mammary gland is under the influence of sex hormones and goes through a repeating cycle. The glandular ducts change, preparing for the post-fertilization state, for later lactation. A woman's breasts can therefore be variously sensitive, even painful, during the cycle.

Cycle notes

Even if we divide the menstrual cycle into the aforementioned phases, the structural changes taking place in the endometrium and other areas smoothly transition into each other. In practice, we count the beginning of the menstrual cycle as the day when menstrual bleeding begins, i.e. after the separation of the entire zona functionalis, when only the zona basalis with the bases of the uterine glands remains from the endometrium.

Links

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- Menstrual cycle
- Cyclic bleeding disorders

Resources

- KONRÁDOVÁ, Václava – UHLÍK, Jiří – VAJNER, Luděk. *Funkční histologie*. 2. edition. Jinončany : H&H, 2000. pp. 214-227. ISBN 978-80-86022-80-2.
- ČIHÁK, Radoslav. *Anatomie 2*. 2. edition. Praha : Grada, 2000. pp. 302-350. ISBN 802470143X.
- Lectures on histology for the 1st year of general medicine, 2nd Faculty of Medicine, Charles University in Prague (prof. MUDr. Václava Konrádová DrSc., MUDr. Jiří Uhlík PhD., doc. MVDr. Luděk Vajner CSc.)
- Lectures on anatomy for the 1st year of general medicine, 2nd Faculty of Medicine, Charles University in Prague (prof. MUDr. Rastislav Druga CSc.)