Histology of the Female reproductive system (part 2)

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Corpus luteum

After ovulation, and under the effect of LH the remaining granulosa cells and theca interna of the ovulated follicle reorganize and modified to form a larger temporary endocrine gland, the corpus luteum (L., yellowish body) within the ovarian cortex. Ovulation is followed immediately by the collapse and folding of the granulosa & thecal cell layers, and blood from disrupted capillaries accumulate as a clot in the former antrum (which is known as **corpus hemorrhagicum**). The corpus luteum is composed of granulosa lutein cells (modified granulosa cells) and theca lutein cells (modified theca interna cells).

- **Granulosa lutein cells** are derived from granulosa cells as they increase greatly in size without dividing and constitute about 80% of the corpus luteum. They are becoming more of steroid-secreting cells than protein-secreting. They are large, pale cells that possess an abundance of smooth endoplasmic reticulum (SER), RER, many mitochondria, a well-developed Golgi complex, and lipid droplet. Their function is to produce progesterone and convert androgen into estrogen.
- **Theca lutein cells** derived form theca interna cells forming the rest of the corpus luteum. They are smaller than granulosa lutein cells and are typically aggregated in the folds of the wall of the corpus luteum, LH causes these cells to produce large amount of progesterone as well as androstenedione.

The fate of the corpus luteum depends on whether pregnancy occurs or not. The ovulatory LH surge causes the corpus luteum to secrete progesterone for 12 days (luteal phase). Without further LH stimulation and in the absence of pregnancy both cell types of corpus luteum undergo apoptosis and degeneration resulting in decreased level of progesterone as well as estrogen inducing menstruation. Reducing estrogen stimulates FSH release to begin a new cycle of follicular growth. The corpus luteum that persists for one menstrual cycle called **corpus luteum of menstruation** that degenerates and remnants of its regression are phagocytosed by macrophages and becoming a fibrosed scar dense connective tissue called **corpus albicans** (L. white body).

If pregnancy occurs, the level of progesterone should be maintained to prevent menstruation to keep the embryo from loss, therefore, trophoblast cells of the implanted embryo produce a glycoprotein hormone called **human chorionic gonadotropin** (**hCG**) with targets and activity similar to that of LH. hCG maintains corpus luteum and promotes its growth to produce progesterone for 3-4 months after pregnancy until placenta is developed and starts to synthesize progesterone and other hormones itself. The corpus luteum that persists during pregnancy called **corpus luteum of pregnancy**.

Uterine tubes (Oviducts or Fallopian tubes)

A paired tubes each measures 10-12 cm in length supported by ligaments and mesenteries to allow movement. Each opens into the peritoneal cavity near the ovary, with regions:

- **Infundibulum** which has finger-like fimbriated open end next to the ovary.
- **Ampulla** is the longest and expanded region where fertilization normally occurs.
- **Isthmus**, a narrower portion nearer the uterus.
- **Uterine** (intramural) part which traverses the wall of the uterus.

The wall of each oviduct consists of folded mucosa with extensive branching longitudinal folds of the mucosa are most prominent in the ampulla resembling a labyrinth in cross section, these folds become smaller towards the uterine part where it is absent.

The mucosa is lined by simple columnar epithelium on a lamina propria of loose connective. The epithelium contains two functionally important cells:

- **Ciliated cells** that respond to estrogen to elongate the cilia and undergo hypertrophy to help sweep fluid and the ovum by ciliary movement towards the uterine cavity.
- **Secretory peg cells**, non-ciliated and darker staining with apical bulge into the lumen. Its main function is to secrete glycoproteins of a protective and nutritive function for both the oocyte and the sperm including *capacitation factors* that activate sperm to facilitate oocyte fertilization.

A thick muscularis layer of inner circular (or spiral) and longitudinal layers of smooth muscle and a thin serosa covered by visceral peritoneum and mesothelium.

Uterus

the uterus is a pear-shaped organ with thick, muscular walls. It has three regions, body (corpus) which receives left and right oviducts, the fundus is the area between the tubes, the isthmus and the lower cylindrical structure, the cervix, the cervical canal, has constricted openings at each end: the internal os (L. os, mouth) that opens to the uterine cavity and the external os opens to the vagina.

The wall of the uterus is composed of three major layers:

The **perimetrium** is the outer layer of the uterus. It is adventitial in some areas, but largely a serosa in others.

A thick **myometrium**, which is a highly vascular smooth muscle layer composed of three poorly defined layers of smooth muscle fibers separated by connective tissue containing venous plexus and lymphatics. During pregnancy, the myometrium goes through a period of great growth as a result of both hyperplasia (increase in number) and hypertrophy (increase in size) of preexisting smooth muscle fibers and increased collagen production. The amount of connective tissue also increased. After pregnancy there is destruction of some smooth muscle cells, reduction in the size of others. The collagen produced during pregnancy enzymatically degraded by the cells which secrete it, then, the uterus is reduced in size almost to its pre-pregnancy dimensions.

The **endometrium** is the inner layer of the uterine wall, its lining epithelium is simple columnar epithelium which has both ciliated and secretory cells, the secretory glandular cells line the simple tubular uterine glands that lie deep in the lamina propria (these glands sometimes branch in their deeper potions). The endometrium has two distinct zones that both undergo cyclical alterations under the influence of ovarian hormones throughout the menstrual cycle:

- **Stratum basalis**: it is deep layer adjacent to the myometrium has a more highly cellular lamina propria and contains the deep basal ends of the uterine glands. It is preserved during menstruation.
- **Stratum functionalis**: it is superficial layer that is less cellular with rich ground substance and includes most of the length of the uterine glands. It undergoes most profound changes and is sloughed off during menstruation.

The blood vessels supplying the endometrium arise from arcuate arteries of the uterine artery. Arcuate artery in the middle layer of the myometrium gives off two sets of smaller arteries into the endometrium; straight

arteries that supply only the basal layer, and long **spiral arteries** (progesterone-sensitive) that extend into functional layer. Spiral arteries give arterioles that supply rich capillary bed and then dilated vascular lacunae drained into venules.

Menstrual cycle

From puberty until menopause at about age 45-55, pituitary gonadotropins produce cyclic changes in ovarian hormone levels, which cause the endometrium to undergo cyclic modifications during the menstrual cycle. The duration of the menstrual cycle may be variable but averages 28 days.

Day 1 of the menstrual cycle is usually taken as the first day of menstrual bleeding. The menstrual discharge consists of degenerating (sloughed off) endometrium mixed with blood from ruptured microvasculature. The **menstrual phase** (period) lasts for 3-5 days on average.

Proliferative phase

This phase is of variable length (8-10 days on average). It occurs after menstrual phase at which the mucosa is thin (0.5 mm). The proliferative phase coincides with the rapid growth of the recruited group of ovarian follicles until one of these reaches the mature Graafian stage. Estrogen is the predominant hormone during this phase, it acts on endometrium to induce regeneration of the stratum functionalis lost during menstruation.

- Stem cells in the basal ends of the uterine glands proliferate, migrate upwards to form the new surface epithelium.
- Formation of the uterine glands as straight narrow empty glands reaching to the surface of functionalis.
- Formation of stromal tissue with mitotic figures can be seen among fibroblasts.
- Lengthening of spinal arteries as the functionalis layer is reformed.

At the end of the proliferative phase, the endometrium is 2-3 mm thick.

Secretory phase

This phase occurs after ovulation as it coincides with the ovarian luteal phase at which progesterone secreted by corpus luteum. Progesterone stimulates:

- Epithelial cells of the uterine glands that formed during the proliferative phase to secrete and accumulate glycogen, dilating the glands lumen and causing gland to become coiled and tortuous.
- The superficial microvasculature includes thin-walled blood-filled lacunae.
- The stroma to accumulate secretions and become edematous (swollen).

Endometrium thickness reaches to 5 mm during secretory phase.

If fertilization occurs after one day of ovulation, the developing embryo is being transported to the uterus by about 5 days to be attached to the uterine epithelium when the endometrium is suitable for implantation and nutrition of the implanting embryo. Progesterone also inhibits strong contractions of the myometrium that may affect embryo implantation.

Menstrual phase

When fertilization does not occur, the corpus luteum begins to regress and circulating levels of progesterone and estrogen start to decrease causing the onset of menstruation. Reduced level of progesterone produces:

- Vasospasm of the spiral arteries supplying the stratum functionalis causing loss of blood supply.

- Increased prostaglandins synthesis by arterial cells which produce further vasoconstriction and local hypoxia.

Both of these events cause degeneration and sloughing off of the stratum functionalis with some blood from the open ends of venules (menses).

The basal layer of the endometrium, not dependent on the progesterone-sensitive spiral arteries, is relatively unaffected by these activities.

At the end of the menstrual phase, the endometrium is usually reduced to a thin layer (0.5 mm) and is ready to begin a new cycle.

Endometriosis is a condition in which the pelvic peritoneal cavity contains uterine endometrial tissue. It is associated with hormone-induced changes in the ectopic endometrium during the menstrual cycle. As the endometrium is shed, bleeding occurs in the peritoneal cavity, causing severe pain and the formation of cysts and adhesions. It may lead to sterility because the ovaries and oviducts become deformed and embedded in scar tissue. The factors that contribute to the occurrence of endometriosis are not known.