The Female Reproductive System

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Functions

- Its functions are to produce female gametes (oocytes).

- Hold a fertilized oocyte during its complete development through embryonic and fetal stages until birth.

- Produces sexual hormones that control organs of the reproductive system and influence other organs of the body.
Ovaries

Arteries and veins
Germinal epithelium
Tunica albuginea
Primordial follicles

Medullary region

Cortical region

Corpus luteum
Corpus albicans
Growing follicles
Preovulatory follicle

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Ovarian Follicles

• An ovarian follicle consists of an oocyte surrounded by one or more layers of **follicular** cells, or **granulosa cells**.

• A basal lamina underlies the follicular cells and marks the boundary between the follicle and the surrounding stroma.
Primordial Follicles

- Formed during fetal life.

- Consist of a primary oocyte enveloped by a single layer of flattened follicular cells.

- These follicles are found in the superficial layer of the cortical region.

- Around puberty the ovaries contain about 300,000 oocytes.
Primordial Follicles

- The oocyte in the primordial follicle is a spherical cell about 25 µm in diameter.
- Its nucleus is large and has a large nucleolus.
- These cells are in the first prophase of meiosis.
- The chromosomes are mostly uncoiled and do not stain intensely.

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Follicular Growth

• Beginning in puberty, each day a small group of primordial follicles begins a process called follicular growth.

• This consists of modifications of:
  – The oocyte
  – The granulosa cells
  – The stromal fibroblasts that surround these follicles.

• The whole process of growth from primordial to mature follicle lasts about 90 days.
Unilaminar Primary Follicle

- Follicular cells divide by mitosis and form a single layer of cuboidal cells.
Multilaminar Primary or Preantral Follicle

- The follicular cells continue to proliferate and form a stratified follicular epithelium, or **granulosa layer**, whose cells communicate through gap junctions.

- A thick amorphous layer, the **zona pellucida**, composed of several glycoproteins, is secreted and surrounds the oocyte.
Secondary or Antral Follicles

- Liquid (liquor folliculi) begins to accumulate between the follicular cells.

- The small spaces that contain this fluid coalesce, and the granulosa cells reorganize themselves to form a larger cavity, the antrum.
Secondary or Antral Follicles

- Follicular fluid contains components of the plasma and products secreted by follicular cells:
  - Glycosaminoglycans.
  - Several proteins (steroid-binding proteins).
  - High concentrations of steroids (progesterone, androgens, and estrogens).
Secondary or Antral Follicles

- During the reorganization of the granulosa cells to form the antrum, some cells of this layer concentrate at a certain point on the follicular wall.

- This group forms a small hillock of cells, the **cumulus oophorus**, that protrudes toward the interior of the antrum and contains the oocyte.

- A group of granulosa cells concentrates around the oocyte and forms the **corona radiata**.
Secondary or Antral Follicles

- The fibroblasts of the stroma immediately around the follicle differentiate to form the **theca folliculi**.

- This layer subsequently differentiates into:
  - Theca interna
  - Theca externa
Theca Cells

- The cells of the **theca interna** acquire the ultrastructural characteristics of cells that produce steroids.
- These cells are known to synthesize a steroid hormone **androstenedione** that is transported to the granulosa layer.

- The **theca externa** consists mainly of organized layers of fibroblasts that surround the theca interna.
Mature, Preovulatory, or Graafian Follicle

- During each menstrual cycle, usually one follicle grows much more than the others and becomes the dominant follicle.

- At the peak of its development, this follicle is so large (about 2.5 cm in diameter) that it protrudes from the surface of the ovary.
### Stages of Ovarian Follicular Development

<table>
<thead>
<tr>
<th>Stage</th>
<th>FSH-Dependent</th>
<th>Oocyte</th>
<th>Zona Pellucida</th>
<th>Follicular Cells or Granulosa</th>
<th>Liquor Folliculi</th>
<th>Theca Interna</th>
<th>Theca Externa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primordial follicle</td>
<td>No</td>
<td>Primary</td>
<td>None</td>
<td>Single layer of flat cells</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Unilaminar primary follicle</td>
<td>No</td>
<td>Primary</td>
<td>Present</td>
<td>Single layer of cuboidal cells</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Multilaminar primary follicle</td>
<td>No</td>
<td>Primary</td>
<td>Present; plasmalemma of primary oocyte forms gap junctions with filopodia of corona radiata cells</td>
<td>Several layers of follicular cells (now called granulosa cells)</td>
<td>None</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Secondary follicle</td>
<td>Yes</td>
<td>Primary</td>
<td>Present with gap junctions</td>
<td>Spaces develop between granulosa cells</td>
<td>Accumulates in spaces between granulosa cells</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Graafian follicle</td>
<td>Yes, until it becomes the dominant follicle</td>
<td>Primary, surrounded by corona radiata in cumulus oophorus</td>
<td>Present with gap junctions</td>
<td>Forms membrana granulosa and cumulus oophorus</td>
<td>Fills the antrum</td>
<td>Present</td>
<td>Present</td>
</tr>
</tbody>
</table>
Stages of Ovarian Follicular Development

- Primordial follicle
  - Oocyte
  - Stromal cells
  - Follicular cell

- Unilaminar primary follicle
  - Basal lamina
  - Zona pellucida forming
  - Follicular cell

- Multilaminar primary follicle
  - Zona pellucida
  - Granulosa cells
  - Theca interna

- Antral follicle
  - Antrum
  - Theca interna
  - Theca externa
  - Granulosa cells

- Mature (graafian) follicle
  - Theca externa
  - Theca interna
  - Antrum
  - Granulosa cells
  - Corona radiata
  - Cumulus oophorus

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Follicular Atresia

- Cessation of mitosis in the granulosa cells.
- Detachment of granulosa cells from the basal lamina.
- Death of the oocyte and granulosa cells.
- Macrophages invade the follicle to phagocytose the debris.
- Fibroblasts occupy the follicle and produce a scar of collagen that may persist for a long time.
Ovulation

- Ovulation consists of the rupture of part of the wall of the mature follicle and liberation of the oocyte.

- It takes place in approximately the middle of the menstrual cycle, i.e., around the fourteenth day of a 28-day cycle.

- In the human, usually only one oocyte is liberated by the ovary during each cycle.

- The stimulus for ovulation is a surge of (LH) secreted by the anterior pituitary gland in response to high levels of circulating estrogen produced by the growing follicles.
Ovulation

- An indication of impending ovulation is the appearance on the surface of the follicle of the **stigma**, in which the flow of blood ceases, resulting in a local change in color and translucence of the follicular wall.
Ovulation

• The first meiotic division is completed just before ovulation.

• The chromosomes are equally divided between the daughter cells:
  – One of the secondary oocytes retains almost all of the cytoplasm.
  – The other becomes the first polar body, a very small cell containing a small nucleus and a minimal amount of cytoplasm.

• Immediately after expulsion of the first polar body, the nucleus of the oocyte starts the second meiotic division, which stops in metaphase.
Corpus Luteum

• After ovulation, the granulosa cells and the cells of the theca interna of the ovulated follicle reorganize to form a temporary endocrine gland called the **corpus luteum**.

• Release of the follicular fluid during ovulation results in collapse of the follicle's wall so that it becomes folded.

• Some blood flows into the follicular cavity, where it coagulates and is later invaded by connective tissue.
Corpus Luteum

- Although the granulosa cells do not divide after ovulation, they increase greatly in size.

- They make up about 80% of the parenchyma of the corpus luteum and are then called granulosa lutein cells with the characteristics of steroid-secreting cells.
Corpus Luteum

- Cells of the theca interna also contribute to the formation of the corpus luteum by giving rise to theca lutein cells.

- These cells are similar in structure to granulosa lutein cells but are smaller and stain more intensely.

- They are located in the folds of the wall of the corpus luteum.

- The blood capillaries and lymphatics now grow into the interior of the corpus luteum and form the rich vascular network of this structure.
Corpus Albicans

- The corpus luteum that lasts for only part of a menstrual cycle is called the **corpus luteum of menstruation**.

- Its cellular remnants are phagocytosed by macrophages.

- Neighboring fibroblasts invade the area and produce a scar of dense connective tissue called the **corpus albicans**.

- If pregnancy occurs the corpus luteum is called **corpus luteum of pregnancy**.
Interstitial Cells

- The theca interna cells frequently persist in isolation or in small groups throughout the cortical stroma and are called **interstitial cells**.

- Present from childhood through menopause, interstitial cells are active steroid secretors, stimulated by LH.
Oviducts
Oviducts

• The wall of the oviduct is composed of three layers:
  • (1) Mucosa
  • (2) Thick muscularis:
    – An inner circular or spiral layer of smooth muscle
    – An outer longitudinal layer of smooth muscle
  • (3) Serosa: Composed of visceral peritoneum.
Oviducts

- The mucosa has longitudinal folds that are most numerous in the ampulla.
- In cross sections, the lumen of the ampulla resembles a labyrinth.
- These folds become smaller in the segments of the tube that are closer to the uterus.
- In the intramural portion, the folds are reduced to small bulges in the lumen, so its internal surface is almost smooth.
Oviducts

- The mucosa is composed of a simple columnar epithelium and a lamina propria composed of loose connective tissue.

- The epithelium contains two types of cells:
  - Ciliated cells
  - Secretory cells

- The cilia beat toward the uterus, causing movement of the viscous liquid film that covers its surface.

- This liquid consists mainly of products of the secretory cells interspersed between ciliated cells.

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Oviducts

- Fertilization usually occurs in the **ampulla** and reconstitutes the diploid number of chromosomes typical of the species.

- It also serves as a stimulus for the oocyte to **complete the second meiotic division**.

- The **corona radiata** is usually still present when the spermatozoon fertilizes the oocyte.
Ectopic Pregnancy

Diagram showing an ectopic pregnancy located in the Fallopian tube, not in the Uterus.
Uterus

Diagram of the uterus with labeled parts:
- infundibulum
- ampulla
- isthmus
- fundus
- uterine tube
- cavity of uterus
- body
- internal os
- supravaginal cervix
- cervical canal
- vaginal cervix
- external os
- vagina
- ureter
- lateral fornix
- ovarian artery
- fimbriae
- uterine artery

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Myometrium

- The thickest tunic of the uterus
- Composed of bundles of smooth muscle fibers separated by connective tissue.
- The bundles of smooth muscle form four poorly defined layers:
  - The first and fourth layers are composed mainly of fibers disposed longitudinally
  - The middle layers contain the larger blood vessels.

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Endometrium

• The endometrium consists of:
  ➢ Epithelium
  ➢ Lamina propria containing simple tubular glands.

• Its covering epithelial cells are a mixture of ciliated and secretory simple columnar cells.

• The epithelium of the uterine glands is similar to the superficial epithelium, but ciliated cells are rare within the glands.
Endometrium

- The endometrial layer can be subdivided into two zones:
- (1) **The basalis:**
  - The deepest one.
  - Contains lamina propria and the closed tips of the uterine glands.

- (2) **The functionalis:**
  - Contains the remainder of the lamina propria and the glands, as well as the surface epithelium.
• **Arcuate arteries** are circumferentially oriented in the middle layers of the myometrium.

• From these vessels, two sets of arteries arise to supply blood to the endometrium:
  - **Straight arteries**, which supply the basalis
  - **Spiral arteries**, which bring blood to the functionalis.
The Menstrual Cycle

- Estrogens and progesterone control the organs of the female reproductive system.

- The proliferation and the differentiation of epithelial cells and the associated connective tissues depend on these hormones.

- After menopause, the diminished synthesis of these hormones causes a general involution of the reproductive organs.
The Menstrual Cycle
The Proliferative, Follicular, or Estrogenic Phase

- The endometrium is covered by a simple columnar epithelium.
- The glands, formed by simple columnar epithelial cells, are straight tubules with narrow lumens.
- These cells gradually accumulate more cisternae of rough endoplasmic reticulum, and the Golgi complex increases in size in preparation for secretory activity.
- At the end of the proliferative phase, the endometrium is 2–3 mm thick.
The Secretory, or Luteal, Phase

- The epithelial cells begin to accumulate glycogen below their nuclei.

- Later, the amount of glycogen diminishes, and glycoprotein secretory products dilate the lumens of the glands.

- One important feature of this phase is that the glands become highly coiled.

- In this phase, the endometrium reaches its maximum thickness (5 mm) as a result of the accumulation of secretions and of edema in the stroma.
The Secretory, or Luteal, Phase

- If fertilization has taken place, the embryo has been transported to the uterus and attaches to the uterine epithelium during the secretory stage, around 7 or 8 days after ovulation.

- The secretion of the glands is the major source of embryonic nutrition before embryo implantation.

- Progesterone inhibits the contractions of smooth muscle cells of the myometrium.
The Menstrual Phase

• When fertilization of the oocyte and embryo implantation do not occur and the corpus luteum ceases functioning, the consequent rapid decrease of blood levels of progesterone and estrogens causes menstruation.

• Several factors are involved in the shedding of the endometrium:
  ➢ Cycles of contraction and relaxation of the spiral arteries
  ➢ Activation (by lack of progesterone) of locally produced matrix metalloproteinases
  ➢ Local release of prostaglandins, cytokines, and nitric oxide
Pregnant Endometrium

- If implantation occurs, embryonic trophoblast cells produce HCG, which stimulates the corpus luteum to continue secreting progesterone.

- Progesterone makes the uterine glands wider, more tortuous, and able to contain more secretions than during the secretory stage.

- The endometrium as a whole becomes thicker during the beginning of pregnancy.
Decidua
The placenta is a temporary organ and is the site of physiological exchanges between the mother and the fetus.

- It consists of a fetal part (chorion) and a maternal part (decidua basalis).

- The decidua basalis supplies maternal arterial blood to, and receives venous blood from, spaces that exist inside the placenta.

- The placenta is also an endocrine organ, producing hormones such as HCG, a placental prolactin, estrogens, and progesterone.

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Uterine Cervix

• The cervix is the lower, cylindrical part of the uterus.

• The lining consists of a mucus-secreting simple columnar epithelium.

• The cervix has few smooth muscle fibers and consists mainly (85%) of dense connective tissue.

• The external aspect of the cervix that bulges into the lumen of the vagina is covered with stratified squamous epithelium.

• The mucosa of the cervix contains the mucous cervical glands.
Vagina

- The wall of the vagina is devoid of glands and consists of three layers:
  - Mucosa
  - Muscular layer
  - Adventitia
Vagina

- The epithelium of the vaginal mucosa of an adult woman is stratified squamous.

- The mucus found in the lumen of the vagina comes from the glands of the uterine cervix.

- Under the stimulus of estrogen, the vaginal epithelium synthesizes and accumulates a large quantity of glycogen, which is deposited in the lumen of the vagina when the vaginal cells desquamate.

- Bacteria in the vagina metabolize glycogen and form lactic acid.
Vagina

- The lamina propria of the vaginal mucosa is composed of loose connective tissue that is very rich in elastic fibers.

- The muscular layer of the vagina is composed mainly of longitudinal bundles of smooth muscle fibers.
- There are some circular bundles, especially in the innermost part (next to the mucosa).

- Outside the muscular layer, a coat of dense connective tissue, the adventitia, rich in thick elastic fibers, unites the vagina with the surrounding tissues.
External Genitalia

- **Clitoris**
- **Labia minora**
- **Labia majora**
- **Glands** that open into the vestibulum
Mammary Glands

- Each mammary gland consists of 15–25 lobes of the compound tubuloalveolar type.

- Each lobe, separated from the others by dense connective tissue and much adipose tissue, is really a gland in itself with its own excretory lactiferous duct.

- These ducts, 2–4.5 cm long, emerge independently in the nipple, which has 15–25 openings, each about 0.5 mm in diameter.
Breast Development

- Female before puberty
- Female at puberty
- Female, first half of menstrual cycle
- Female, second half of menstrual cycle
- Pregnant female
- Lactating female
- Female after cessation of lactation
- Female after menopause

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Milk secretion

- During lactation, milk is produced by the epithelial cells of the alveoli and accumulates in their lumens and inside the lactiferous ducts.

- These lipid droplets pass out of the cells into the lumen and in the process are enveloped with a portion of the apical cell membrane.

- Lipids constitute about 4% of human milk.
Milk secretion

- Proteins constitute approximately 1.5% of human milk:
  - Several caseins
  - α-Lactalbumin
  - Plasmocyte-produced IgA

- Lactose, the sugar of milk, is synthesized from glucose and galactose and constitutes about 7% of human milk.
Cancer of the Breast

- About 9% of all women born in the US will develop breast cancer at some time during their lives.

- Most of these cancers (carcinomas) arise from epithelial cells of the lactiferous ducts.
The End of Histology Course

Basic Histology
Text & Atlas

JUNQUEIRA'S Basic Histology
Text & Atlas

Anthony L. Mescher

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