Female Reproductive System

I. Introduction

II. Keywords

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   A. Ovary
      1. General structure
      2. Follicles
         a. Pre-ovulation
         b. Post-ovulation
   B. Genital Tract
      1. Uterine tube
      2. Uterus
         a. General structure
         b. Phases
            i. Proliferative
            ii. Secretory
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         c. Placenta
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      3. Cervix/Vagina
   B. Breast (Mammary Gland)
      1. General structure
      2. Phases
         a. Resting
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Keywords

Antrum
Atretic follicle
Basal layer
Cervix
Corona radiata
Corpus albicans
Corpus luteum
Cumulus oophorus
Ectocervix
Endometrial glands
Endometrium
Fibrous support tissue
Follicle
Follicular antrum
Follicular cells
Functional layer
Granulosa cells
Granulosa lutein cells
Lactiferous duct
Mammary gland
Mature (Graafian) follicle

Myoepithelial cells
Myometrium
Ovary
Perimetrium
Placenta
Primary follicle
Primary oocyte
Primordial (resting) follicle
Secondary (antral) follicle
Secondary oocyte
Spiral arteries
Surface (germinal) epithelium
Theca externa
Theca folliculi
Theca interna
Theca lutein cells
Uterine (fallopian) tube
Uterus
Cervix/Vagina
Zona granulosa
Zona pellucida
the ovaries consist of an outer cortex containing ovarian follicles in various stages of development; the medulla is devoid of follicles and is composed of loose CT with large blood vessels that enter the ovary at the hilum; despite what is seen on the slide above, the distinction between cortex and medulla is not always apparent
the cortex of the ovary is surrounded by a layer of dense CT called the **tunica albuginea** (Lt. “white coat”); covering the tunica is a layer of simple cuboidal epithelium simply referred to as **surface epithelium** (historically known as **germin al epitlium** – a misnomer); the surface epithelium is continuous with the peritoneal mesothelial cells (simple squamous) of the mesovarium at the ovarian hilum; the **stroma** of the cortex is a cell-rich connective tissue found between the follicles.
ovarian follicles are the basic functional units of the ovary; each follicle contains an oocyte surrounded by epithelial cells (follicular or granulosa cells, depending upon developmental stage); the appearance of the follicles differ greatly – as seen above – depending upon their stage of folliculogenesis (follicle maturation)
primordial follicles are generally localized in the outer cortex – directly below the tunica albuginea; as the follicles develop they “migrate” deeper into the ovary, toward the medulla, and undergo profound changes to the size of the oocyte as well as changes to the surrounding granulosa (follicular) epithelial cells, making it possible to identify the different follicular stages.
**Primordial (resting) follicles** consist of a primary oocyte (arrested in prophase I) surrounded by a layer of simple squamous follicular cells upon a basement membrane separating the follicle from the surrounding stroma; the oocyte contains minimal cytoplasm surrounding a large nucleus with a prominent nucleolus; starting at puberty, about 30 primordial follicles will begin folliculogenesis each month (menstrual cycle); however, it will take at least 3 months for any of the follicles to fully develop into a mature follicle for ovulation, and the majority will all undergo atresia.
as **primordial follicles** mature into **primary follicles** three significant changes are visually apparent: (1) there is a substantial increase in the size of the oocyte – due to cytoplasmic expansion; (2) the squamous follicular cells become cuboidal/columnar cells, with eosinophilic, slightly granular cytoplasm (so called **granulosa cells**), which will begin to stratify; (3) the **zona pellucida** forms around the oocyte
each month about 30 primary follicles develop; the oocyte produces a thick glycoprotein coat known as the 
 zona pellucida (Lt. “transparent zone”); the cuboidal/columnar epithelial granulosa cells surround the oocyte 
as either a single layer or multilayered (collectively referred to as the zona granulosa); connective tissue 
stromal cells surrounding the follicle form the theca folliculi (Lt. “coat of the follicle”)
the granulosa cells of the multilaminar primary follicle begin producing a fluid rich in hyaluronic acid; the fluid eventually coalesces into a single cavity within the zona granulosa known as the follicular antrum; the antrum serves as the defining characteristic of a secondary (or antral) follicle
secondary (antral) follicles (now FSH dependent) are characterized by a fluid-filled follicular antrum within the zona granulosa; the granulosa cells that remain adjacent to the zona pellucida are known as the corona radiata (Lt. “crown with rays”) – which will be ovulated with the oocyte; the theca folliculi divides into two specific layers: the theca externa, with normal fibrous CT, and the theca interna, containing steroid-producing cells that are larger and paler-staining; the theca interna cells lack aromatase so produce androgens that diffuse to the aromatase-containing epithelial granulosa cells to be converted into estrogens (estradiol).
each month, from the pool of secondary follicles a single follicle will continue to develop into the mature (Graafian) follicle which will be ovulated – on routine slides it is generally arbitrary to define a follicle as a Graafian follicle; the follicular antrum greatly expands, causing the follicle to fill the cortex and creating an outward bulge of the ovarian surface; in response to a surge of LH, the follicle ruptures and releases the oocyte and surrounding corona radiata; it takes at least 90 days for a primordial follicle to develop to the Graafian stage.

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primary or secondary follicle? examine this follicle closely; notice that the “space” is between the zona pellucida and oocyte – this is not an antrum; this is a multilaminar primary follicle

cumulus oophorus (Lt. “egg-bearing mound”) is the pedestal of granulosa cells between the oocyte and follicular wall

corona radiata

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overall, more than 99% of all follicles will undergo a form of programmed cell death called **atresia**; this can occur at any stage of folliculogenesis, so the appearance of an atretic follicle depends upon the stage of follicular development reached before undergoing degeneration; additionally, it is important to distinguish between true atresia from simple artifacts of slide preparation.

**general features of atretic follicles:**

- **oocyte** appears to be degenerating
- **zona pellucida** collapses but persists longer than oocyte
- **debris** begins to fill the antrum
- **glassy membrane**: thickening of basement membrane between granulosa cells and theca folliculi
- **disaggregation** of tightly-packed granulosa cells
after ovulation, the follicle forms a large corpus luteum (Lt. “yellow body”); the granulosa cells greatly increase in size and become granulosa lutein cells, while the theca interna cells also increase in size and become theca lutein cells; the basement membrane between the granulosa cells and theca interna breaks down, vasculature invades, and the structure takes on the general appearance of an endocrine organ; the corpus luteum will last 12-14 days unless pregnancy has occurred and HCG from the placenta prevents it from degenerating.
as the granulosa and theca cells undergo hypertrophy (increase in cell size), large folds of the tissue occur along the periphery of the corpus luteum; the granulosa cells form the bulk of the gland with the theca interna cells becoming located within the crevices between the folds and around the periphery.
the corpus luteum is responsible for progesterone production and the luteal phase of the menstrual cycle – driving development of the endometrium of the uterus; the luteal cells have the characteristic appearance of steroid-producing cells: the granulosa lutein cells, the majority of the luteal cells, secrete progesterone and estrogens; the theca lutein cells secrete progesterone and androgens, as they lack aromatase to form estrogens.
notice how large the **corpora lutea** are within the ovaries – they grow to occupy the majority of the area seen on the slides and are much larger than any of the follicles seen
if a pregnancy does not occur, about 10 days after ovulation the corpus luteum begins to degenerate and is invaded by fibrous connective tissue to form an inactive corpus albicans (Lt. “whitening body”); if a pregnancy does occur, the corpus luteum will become much larger and persist longer before becoming a corpus albicans, which can then persists for years within the ovary.
in the post-menopausal ovary seen on the slide above, notice the absence of nearly all follicles in the cortex, demonstrating that virtually all follicles eventually undergo atresia; several small corpora albicantia can be seen on the slide in addition to the large corpus albicans identified above; considering the several decades of ovulations, the fact that only a few corpora albicantia are present (instead of several hundred) demonstrates that most completely regress into the stroma
**Slide 145: Fallopian Tube, H&E**

**uterine tubes (Fallopian tubes)** extend from the uterus out toward the ovaries; they are the normal site of fertilization, as they are responsible for “capturing” the ovulated ovum from the ovary and conducting it to the uterus; sperm which pass through the cervix and enter the uterus can swim into either uterine tube, but since only one ovary ovulated, only one uterine tube will have an ovum, so half the sperm will go “up the wrong tube.”
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IV. Summary
the highly-folded mucosa of the uterine tube consists of two epithelial cell types: secretory non-ciliated peg cells that produce the nutritive fluid for support of the ovum and fertilization, and ciliated columnar cells which rhythmically beat to move fluid and the ovum toward the uterus (a 3 day journey), aided by the peristaltic contraction of the muscularis.
the **uterus** is composed of: an inner mucosal lining called the **endometrium**; a thick, muscular middle layer called the **myometrium**; and an outer serosa, or visceral peritoneum, called the **perimetrium**; the endometrium changes dramatically throughout the menstrual cycle, varying in thickness from 1-5mm, while the myometrium – the thickest layer (despite what is seen in the slide above) – is relatively static throughout the cycle but increases greatly in size during pregnancy.
the mucosal **endometrium** is composed of two layers: the apical **functional layer** and the deeper **basal layer** which borders the myometrium; the **basal layer** undergoes little change throughout the menstrual cycle and is not shed during menstruation; the **functional layer**, on the other hand, varies greatly throughout the cycle, both in thickness and in appearance, and it is shed during menstruation if pregnancy has not occurred.
Slide 176 (NW): Repair Endometrium, H&E

Spiral arteries are found extending from the basal layer into the functional layer of the endometrium; these highly-coiled arteries given off numerous branches supplying blood to the functional layer; the arteries are responsive to hormonal changes and, in the absence of progesterone, will undergo constriction leading to ischemia of the functional layer, which then is shed during menstruation.
*days 5-14 of cycle*
*corresponds with follicular phase of ovary*
*influenced by estrogen from ovarian follicles*
*few glands in endometrium*
*glands generally appear long and straight*
*lots of space between glands*
Slide 178 (NW): Secretory Endometrium, H&E

- days 15-28 of cycle
- corresponds with luteal phase of ovary
- influenced by progesterone from corpus luteum
- more numerous glands in endometrium
- glands often appear jagged and coiled and begin to fill with mucus
- presence of thin-walled, blood-filled lacunae in stroma
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**Slide 178 (NW): Secretory Endometrium, H&E**

- small, thin-walled **lacuna** which will continue to enlarge and fill with blood
- **endometrial gland**
- **spiral artery** (arteriole)
Slide 82: Late Secretory Endometrium, H&E

Blood-filled lacunae are larger and more conspicuous.

Mucous secretory product within lumen of endometrial gland.
Slide 83: Endometrium, H&E

- days 1-4 of cycle
- corresponds with start of follicular phase of ovary
- influenced by rapid drop in hormone levels by degeneration of corpus luteum
- constriction of spiral arteries leads to ischemia of functional layer with a characteristic pooling of blood from the lacunae into the stroma
- functional layer will slough off as menses
by the end of the menstrual phase, the functional layer of the endometrial has been shed and all that remains is a thin layer of the endometrium consisting largely of stroma with only a few small, inconspicuous endometrial glands present.
development of the placenta involves both fetal and maternal tissue contributions; the principal structures of the placenta are the vast number of branched chorionic villi containing fetal vessels continuous with the vessels of the umbilical cord; maternal blood in the intervillous spaces allows for nutrient, waste, and gas exchange between the fetal and maternal circulations across the thin layers of tissue of the chorionic villi walls
the umbilical cord consists primarily of two umbilical arteries and one umbilical vein; like in the pulmonary circulation, the oxygenation levels in the vessels are opposite those found elsewhere in the systemic circulation (i.e., umbilical vein carries oxygenated blood and umbilical arteries carry deoxygenated blood); the vessels are embedded within a mesenchymal ground substance known as Wharton's jelly (also contains potent stem cells)
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IV. Summary
the cervix (Lt. “neck”) is the most inferior part of the uterus and projects into the vagina; the cervical canal is lined by the endocervical mucosa with underlying mucous endocervical glands (changes in mucus during the menstrual cycle are an indication of ovulation and fertile days); the ectocervix bulges into the vagina and is lined by the ectocervical mucosa; the transition area (squamocolumnar junction) between the two types of epithelium is more inferior in younger females, increasing the susceptibility to infections of the genital tract.
the vagina (Lt. “sheath”) is the inferior aspect of the genital tract, joining it to the external body surface; the wall of the vagina consists of stratified squamous epithelium overlying thick bundles of smooth muscle that form the bulk of the vaginal wall; the vaginal wall lacks glands, so vaginal mucus is produced by the endocervical glands.
each of the paired, compound tubuloacinar **mammary glands** consists of 15-20 lobes drained by **lactiferous ducts** which drain into lactiferous sinuses at the nipple; the lobes are separated by dense CT into **lobules** containing intralobular ducts that empty into larger **interlobular ducts** (which coalesce into lactiferous ducts)
Slide 190 (NW): Breast - Lactating, H&E

within each lobule are **secretory acini** and **ducts**, however distinguishing between them can be difficult depending upon the level of mammary gland activity; surrounding both the acini and ducts are **myoepithelial cells** – within the basement membrane, unlike the myofibroblasts seen in the testis; the myoepithelial cells are contractile and assist in moving the secretory product (milk) out of the glands and toward the nipple.
The resting mammary gland consists of small lobules generally surrounded by large amounts of connective tissue stroma and adipose tissue; most of the glandular tissue is ducts with few developed secretory acini.
during pregnancy, the **active mammary gland** begins proliferating, greatly increasing the size of the lobules by growth of the secretory acini at the ends of the intralobular ducts; the amount of surrounding connective tissue stroma is reduced, and there is an increasing numbers of cells – especially plasma cells – found within the tissue
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the **lactating mammary gland** has greatly enlarged lobules with only thin septa of stromal CT between them; the lumens of both the secretory portions and duct portions of the gland are filled with eosinophilic milk.
Common Confusion:
Seminal vesicle vs. Uterine tube

**Seminal vesicle**: secretory gland of male reproductive tract, producing majority of seminal fluid volume; consists of single tube coiled upon itself; joins with ductus deferens to form ejaculatory duct

Look for: (1) general appearance of multiple lumens as result of coiling of tube; (2) highly-folded mucosa, often having fine "honeycomb" appearance; (3) non-ciliated pseudostratified columnar epithelium with lipid droplets in cytoplasm giving "foamy" appearance; (4) lipofuscin pigment is often seen in mucosa

**Uterine** or **Fallopian tube (ampulla)**: tube leading from uterus toward ovary; tube transmits ovum to uterus and is the usual site of fertilization, usually in the ampulla

Look for: (1) single-lumen tube surrounded by generally well-defined muscularis; (2) mucosal folds often appear “thicker” than in seminal vesicle due to more lamina propria; (3) ciliated simple columnar and non-ciliated peg cells present in epithelium; (4) size of muscularis changes with region of tube, generally thin in ampulla and thick in isthmus
### Characteristics of the Uterine Wall throughout the Menstrual Cycle

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**B. Breast (Mammary Gland)**
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- Phases
  - Resting
  - Active
  - Lactating
Compare and Contrast Structures of the Female Reproductive System

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