

Female Reproductive Systems I and II

Of course, for Histology the pictures are important. The lecture notes for Female Reproductive Systems are pretty thorough so I have added to a few places and tried to organize in a way that is easy to internalize. Be sure to look at the slides that accompanied the lecture and the lab.

I. Notes on Ovarian Cycle*

- a. Recall that in the female fetus, the reproductive organs are arrested until Gonadotropic hormones (by pituitary) initiate puberty
- b. Follicular Phase → Ovulatory Phase → Luteal Phase
 - i. Follicular Phase
 1. Development of primordial follicle into mature follicle
 - ii. Ovulatory Phase
 1. LH surge → mature follicle ruptures → release of gamete
 - iii. Luteal Phase
 1. Residual follicular cells (granulosa cells and theca interna) → corpus luteum
- c. 14th day of menstrual cycle → high levels of blood estrogen → shut off FSH release and LH surge → oocyte completes meiosis I → secondary oocyte and first polar body → secondary oocyte arrested in metaphase of meiosis II until fertilization → complete second meiotic division → ovum and second polar body

II. Notes on Menstrual Cycle*

- a. Menstrual phase → proliferative phase → secretory phase
 - i. Menstrual phase
 1. corpus luteum become nonfunctional about 14 days after ovulation → lowers levels of progesterone and estrogen → functional layer of uterus becomes deprived of blood due to constricted arteries → necrosis and hemorrhagic discharge (menses)
 - ii. proliferative (follicular) phase
 1. endometrium proliferates in first half of cycle in response to estrogen
 - iii. secretory (luteal) phase
 1. endometrium prepares for implantation of the blastocyst in response to progesterone
- b. Estrogen is the major steroid synthesized during the first half of the menstrual cycle
- c. Estrogen: prepares female genital tract for receipt of male gametes

III. Notes on Fertilization

- a. Fusion of sperm and oocyte
 - i. Usually occurs in the ampulla of oviduct

- ii. Binding of spermatozoa to ZP3 molecules → acrosomal enzyme release → spermatozoon penetrate zona pellucida → enter perivitelline space → oocyte → cortical reaction which prevents polyspermy
- iii. Cortical Reaction
 - 1. Fast component: A change in resting membrane potential of oocyte plasma membrane
 - 2. Slow component: Release of contents of cortical granules into cytoplasm → hydrolyze ZP3 molecules
- b. Fusion of female pronucleus and male pronucleus → fertilization complete

IV. Things to Identify: Internal Reproductive Organs

- a. **Hypothalamus** produces gonadotropin-releasing hormone (GnRH)
 - i. Hypothalamic neuron axons travel to median eminence and GnRH is released into circulation → reaches the anterior pituitary via the hypothalamo-hypophyseal portal circulation
- b. → **Hypophysis** (Pituitary) synthesizes and releases LH and FSH
 - i. Anterior Pituitary houses **basophils** that produce LH and FSH
 - ii. Anterior Pituitary also has separate **acidophils** that release growth hormone, prolactin
 - iii. Elevated Prolactin can inhibit GnRH
- c. Paired Ovaries
 - i. **Ovary**
 - 1. Layers
 - a. Covered by germinal epithelium
 - i. referred to as germinal because early authors thought oocytes were derived in this. (We know now that primordial germ cells travel from the yolk sac)
 - ii. Low cuboidal
 - iii. Derived from mesothelial epithelium
 - b. Tunica albuginea**
 - i. Dense irregular collagenous capsule
 - c. Cortex**
 - i. Connective tissue stroma
 - ii. Houses Ovarian Follicles at various stages
 - d. Medulla**
 - i. richly vascularized loose connective tissue
 - 2. Functions
 - a. Produce gametes (in this case oocytes)
 - b. Produce steroids
 - i. Estrogen: promotes growth and maturation of internal and external sex organs
 - ii. Progesterone: prepares the internal sex organs for pregnancy
 - 1. mainly uterus by promoting changes in the endometrium

2. mammary gland for lactation by promoting lobular proliferation

ii. Ovarian Follicles

1. Surrounded by stromal tissue
2. Consist of primary oocyte (arrested in prophase of meiosis I) and follicular cells
3. Development is dependent on FSH
4. 50 follicles begin to mature for each menstrual cycle, 5 may reach graafian follicle stage, usually one ovulates and the rest undergo atresia
5. 4 stages

a. primordial follicle

- i. single layer of flattened follicular cells
- ii. most oocytes within the ovary are in primordial follicles

b. unilaminar primary follicle

- i. single layer of cuboidal follicular (also called granulosa) cells
- ii. oocyte is becoming bigger
- iii. has an enlarged nuclei (called the germinal vesicle) with a characteristic nucleolus

c. multilaminar primary follicle

- i. multiple layers of (stratified cuboidal) follicular cells
- ii. **zona pellucida**
 1. between oocyte and follicular cells, definitely secreted by the oocyte and probably by both
 2. points of attachments between oocyte and granulosa cell processes remain
- iii. stroma cells are organized into **theca interna** (vascularized cellular layer) and **theca externa** (outer layer of fibrous connective tissue)
- iv. oocyte and granulosa layer are becoming bigger

d. secondary follicle

- i. **liquor folliculi** in antrum (single fluid-filled chamber)
- ii. follicle under control of FSH and producing estrogen
- iii. In the theca interna → cholesterol is converted to androgens (in response to LH) → diffuses across basal lamina to granulosa cells → converted to estrogens (in response to FSH)

e. Graafian (preovulatory, mature) follicle

- i. Continued proliferation and formation of liquor folliculi

- ii. follicle still under control of FSH and producing estrogen
 - iii. **cumulus oophorus** is formed (primary oocyte surrounded by small group of granulosa cells)
 - iv. oocyte is covered by a single layer of follicular cells called the **corona radiata** that are attached firmly to the zona pellucida
 - v. oocyte and corona radiata detach from cumulus oophorus and float in liquor folliculi
6. **Interstitial gland**: thought to develop from theca interna of some atretic follicles
- a. Function unknown
 - b. Lipid droplets → maybe involved in steroid metabolism

iii. Corpus Luteum

1. After ovulation, the remaining follicular cells collapse → basal lamina between theca interna and granulosa cells breaks down → blood vessels grow into granulosa cells from the theca interna → form a central clot → clot removed by phagocytes → both luteinize (**granulosa lutein cells**: large, pale-staining and **theca lutein cells**: small, dark-staining) → increase in cell size, decrease in RER, increase in SER, increase in **lipid droplets** (containing cholesterol) → more specialized towards synthesis and secretion of progesterone and estrogen (converted from androgens produced by theca interna cells) inhibit the secretion of LH and FSH (which prevents development of new follicles)
2. Major hormone-secreting gland: **Progesterone** is major hormone produced
3. If pregnancy occurs, human chorionic gonadotropin secreted by the placenta maintain the corpus luteum for 3 months

d. Oviducts

- i. Oviduct (Uterine tube, Fallopian tube)
 1. A conduit for spermatozoa to reach the primary oocyte and to convey the fertilized egg to the uterus
 - a. Curled, with unusual shape due to infoldings of mucosa
 - b. Lined with columnar epithelium
 - c. Fertilization usually takes place in expanded **ampulla**
 2. Abundance of blood vessels
 - a. Arteries have an unusual arrangement of smooth muscle with elastic lamina appearing in the middle of the muscle layer
 3. **Isthmus** is the narrowed portion
 4. Presence of Mast cells
 5. **Infundibulum** ends in **Fimbriae** (fingerlike processes)

e. Fimbriae

- i. **Ciliated Cells.** The cilia are thought to beat towards the uterus and aid in transport of the oocyte and/or fertilized ovum. Also helps prevent bacteria from outside the body from entering the peritoneal cavity
- ii. **Secretory Cells** produce nutrients and protective environment for the oocyte, spermatozoa, and fertilized ovum and elaborate substances leading to capacitation of the spermatozoan
- iii. **Basal Cells** are stem cells from which the other epithelium cells are derived
- iv. Endocrine Cells

f. Uterus

- i. Lined with low columnar epithelium that continues into the glands
- ii. Uterine stroma is loose connective tissue with blood vessels
- iii. There are cyclic changes in the uterus during the menstrual cycle that prepare the uterus for implantation
- iv. 3 layers
 - 1. **Perimetrium** (peritoneum): we did not look at slides of this layer
 - 2. **Myometrium**
 - a. Some Phasal changes, but not as distinct as for the Endometrium
 - i. Largest and most numerous during pregnancy
 - ii. Prostoglandins and oxytocin stimulate uterine contractions during parturition
 - b. Composed of three layers
 - i. Inner and outer layer longitudinal muscle
 - ii. Vascularized middle layer contains smooth muscle bundles
 - 3. **Endometrium**
 - a. Layers
 - i. Simple columnar epithelium and lamina propria housing tubular glands
 - 1. Glycogen
 - a. secretion from the coiled glands
 - b. nourishes conceptus before formation of placenta
 - c. displaces nuclei of epithelium apically
 - 2. channel system in nuclear envelope may facilitate transfer of ribosomal components
 - ii. **Functionalis**
 - 1. thick superficial layer
 - 2. supplied by coiled helical arteries
 - 3. sloughed at menstruation
 - iii. **Basalis**
 - 1. deep narrow layer

2. cells proliferate to regenerate the functionalis layer during each menstrual cycle
3. supplied by straight arteries (constrict to Estrogen)

b. Proliferative Phase

- i. Straight glands with narrow lumina
- ii. Much thinner layer than in Secretory Phase
- iii. Characterized by reepithelialization of lining, reconstruction of glands, connective tissue and coiled arteries of lamina propria and renewal of functionalis

c. Secretory Phase

- i. Uterine glands are coiled with wider lumina
- ii. Much thicker layer than in Proliferative Phase
- iii. Characterized by thickening of endometrium as a result of edema and accumulated glycogen

d. Implantation

- i. Blastocysts invades endometrium → embeds and proliferates into inner Cytotrophoblast and outer syncytiotrophoblast
 1. cytotrophoblast differentiates into villi with fetal blood vessels
 - a. nuclei of cells are larger and lighter staining
 2. vacuoles form in syncytiotrophoblast → maternal blood leaks into vacuoles forming lacuna
 - a. smaller darker staining nuclei
- ii. Negative feedback → LH and FSH from pituitary decreased → levels drop unless implantation occurs

v. Uterine Cervix

1. lumen is lined by mucus-secreting simple columnar epithelium
2. external surface is covered by stratified nonkeratinized epithelium
3. During proliferative phase (high estrogen levels) mucus becomes alkaline, copious, and thin
4. During secretory phase (high progesterone level) a smaller amount of less alkaline, and more viscid mucus is produced (presenting a barrier to migrating spermatozoa)

g. Vagina

- i. Fibroelastic tube composed of mucosa, muscular layer, adventitia
- ii. Thick stratified Nonkeratinized epithelium
 1. the thickness of which is estrogen-dependent
 2. store large deposits of glycogen

- a. metabolized by bacterial flora → lactic acid → low pH
→ restrict pathogenic invasion
 - iii. Underlying connective tissue (lamina propria)
 - 1. has blood vessels present (veins) resemble those of the erectile tissue of the penis
 - 2. rich in elastic fibers
 - iv. Devoid of glands (lubrication is from these blood vessels and cervix)
- h. Umbilical cord**
 - i. Connects fetus to placenta
 - ii. 2 umbilical arteries
 - 1. carries deoxygenated blood from fetus to placenta
 - 2. lumen is closed, preventing exsanguinations of fetus after the cord is cut
 - 3. walls are composed of smooth muscle and very few elastic laminae
 - iii. 1 umbilical vein
 - 1. carries oxygenated blood from placenta to fetus
 - 2. open and filled with blood
 - 3. thick wall composed of several layers of smooth muscle and elastic laminae
 - iv. Vessels are surrounded by **Wharton's jelly** (fetal connective tissue)
 - 1. protects the vessels from collapsing due to movement of the fetus
 - 2. fetal fibroblasts
- i. Placenta**
 - i. Decidua**
 - 1. Decidua Basalis**
 - a. endometrium of uterus
 - b. chorionic villi facing it form chorion frondosum
 - i. those attached to deciduas basalis are called anchoring villi
 - 2. Decidua parietalis**
 - a. Part of deciduas lining the cavity of uterus not occupied by embryo
 - ii. Maternal-fetal barrier/placental villi**
 - 1. Syncytiotrophoblast
 - a. Outermost portion of the villus
 - b. clumped nuclei
 - c. synthesize hormones
 - 2. basal lamina
 - 3. fetal capillary endothelium (fetal RBC inside)
 - 4. Hofbauer cells: macrophages in the villi
 - iii. Functions
 - 1. Nutrients and oxygen diffuse across barrier

2. endocrine organ secreting hCG (human chorionic gonadotropin), progesterone, estrogen, chorionic thyrotropin, chorionic somatomammotropin
 3. Assumes role of corpus luteum around week 8 of gestation
 4. Placenta produces progesterone → fetal adrenal cortex converts to androgens and cortisol → placenta converts to estrogen: estrogen levels are indicative of fetal health
- iv. Outside of villi
1. **Fibrinoid layer:** Thought to be part of system preventing mother from rejecting fetus
 2. maternal RBC outside villi

j. Mammary Glands

- i. Compound tubuloalveolar glands with 15-20 lobes
 1. each lobed drained by lactiferous duct
- ii. Stages
 1. Resting/Inactive
 - a. Non-pregnant woman of fertile age
 - b. Composed of adipose tissue (lipid storages as droplets) with a few duct systems that develop due to estrogen during puberty
 2. Developing/Active
 - a. During pregnancy → estrogen → growth of duct system
 - b. During pregnancy → progesterone → growth of lobulo-alveolar system (replaces adipose tissue)
 3. Lactating
 - a. Lactating woman → prolactin → milk production begins in alveolar cells (large lumina with milk)
 - b. Plasma cells in stroma of alveolar tissue secrete dimeric IgA
 - c. Oxytocin → contraction of myoepithelial cells → milk pushed out of ducts

k. External Genitalia

- i. Clitoris
- ii. Labia Majora
- iii. Labia Minora

V. Clinical Correlations

- a. Cytologic Pap Smears
 - i. Superficial epithelial cells used for screening for cervical cancer
 - ii. Negative cervical smear: squamous cells with small pyknotic nuclear and abundant cytoplasm
- b. Endometriosis
 - i. Endometrial tissue in the pelvis or peritoneal cavity
 - ii. This tissues also undergo cyclic changes in response to the ovarian cycle
 - iii. Hemorrhaging may cause adhesion and extreme pain

- iv. Pelvic viscera may become a fibrotic mass → infertility
- c. Polycystic Ovarian Disease
 - i. Enlarged ovaries with follicular cysts
 - ii. Unusually thick tunica albuginea → prevents ovulation of mature follicles

**Additionally, the ovarian cycle and the menstrual cycle were covered in the Endocrine section of Physiology (Unit 54: April 21 and 25) and in Embryology (Unit 1: Sept 15). Check these out for additional information.*