FEMALE REPRODUCTIVE SYSTEM

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Learning Objectives

1. Understand the organization of the ovary.
2. Understand the arrangement of cells that make up an ovarian follicle.
3. Understand the functions of different cell types that make up an ovarian follicle.
4. Know the differences between primordial, primary, secondary and mature follicles.
5. Know the physiological events in developing follicles and what happens at ovulation.
6. The growth and maturation of the oocyte.
7. Follicular atresia and apoptosis.
8. The histology and functions of the corpus luteum.
9. Histology and functions of the oviduct.
10. The structure of the uterus.
11. A general understanding of the estrus cycle.
12. A brief knowledge of the menstrual cycle.
13. The histology of the vaginal epithelium.
14. The histology of the mammary gland and how this changes during pregnancy and lactation.

INTRODUCTION

The major components are:
1. Ovaries
2. Oviducts (Fallopian tubes)
3. Uterus
4. Vagina
5. External genitalia

Also included in the discussion
6. The mammary glands

The major functions are:
1. Production of the female gametes (ovaries), an exocrine function
2. Production of sex hormones (ovaries), an endocrine function.
3. Transportation of the egg, site of fertilization, transportation of the zygote (oviduct)
4. Serve as the site of fetal development (uterus)
5. Copulatory organ and birth canal (vagina)
6. Nourishment for the offspring (mammary glands)
All these structures are, in one way or another, under the influences of sex hormones and gonadotropins.

**THE OVARIES**

In the female animal, the embryonic indifferent gonad develops into the ovary without being subjected to the influence of the testicular-determining factor (TDF) or that of the müllerian-inhibiting factor.

The ovaries have two major functions: To produce the **female gametes** (oöcytes, eggs) and to produce the **sex hormones** (estrogens).

**General Architecture**

1. The ovary is an ovoid structure that can be divided into the outer **cortex** and the inner **medulla**. In the mature mare, these areas are reversed. The cortical tissue in this case remains on the surface only in the ovulation fossa that is the location of all ovulations.
2. The surface of the ovary is covered by a low cuboidal epithelium, the **germinal epithelium**. In spite of its name, this epithelium is not involved in the production of germ cells and the term surface epithelium appears to be more appropriate.
3. Immediately beneath the surface epithelium is a layer of connective tissue called the **tunica albuginea**.
4. **Cortex** --- In this zone are ovarian follicles in various stages of development and corpora lutea. These structures are embedded in a loose connective tissue **stroma**.
5. Canine ovary has narrow channels lined by cuboidal epithelium that may be continuous with the surface epithelium. These structures are called **cortical tubules**.
6. **Medulla** --- This zone contains connective tissue and blood vessels. It is continuous with the mesovarium.

**Follicular Development**

**Folliculogenesis** --- the continuous process occurring throughout reproductive life whereby cohorts of primordial follicles undergo maturation during each reproductive cycle.
A follicle is a structure containing an oöcyte surrounded by specialized epithelial cells. The size, content and the wrapping of the follicle vary depending on the stage of development.
A histological section of a mature ovary shows follicles in various stages of growth and degeneration.
Follicular growth and maturation is dependent on FSH from the adenohypophysis. LH is important for estrogen synthesis and ovulation.
**Primordial Follicles**

A primary oöcyte enclosed by flattened simple squamous follicular cells. The primary oöcyte arose from an oögonium that in turn was derived from the yolk sac endoderm*. The oögonia enter the first meiotic division and become primary oöcytes. The first meiotic division is arrested and remains that way for a long time to come. Stromal cells form a single layer of flat follicular cells that wrap around the primary oöcyte. This layer of follicular cells rests on a distinct basal lamina. Primordial follicles are found in the outer portion of the cortex, usually just beneath the tunica albuginea. They may occur in clusters in carnivores and are evenly distributed in ruminants and the sow. Primordial follicles are retained in a resting stage from the time they formed in the fetal ovary. Primordial follicles that “come out” of the resting stage become primary follicles*.

**Primary Follicles**

**Unilaminar Primary Follicle:** A primary oöcyte enclosed by a simple cuboidal layer of follicular cells. The oöcyte is larger than that found in a primordial follicle. The follicular cells rest on a distinct basal lamina.

**Multilaminar Primary Follicle:** A primary oöcyte enclosed by several layers of follicular cells. The follicular cells proliferate through mitosis and are now called granulosa cells. They rest on a basal lamina. These cells acquire receptors for FSH, follicle stimulating hormone, important in the development of the follicle.

Polyovular follicles, containing several oöcytes, may develop in carnivores, sows and ewes.

At the interphase between the oöcyte and the granulosa cells a glycoprotein layer called the zona pellucida develops. The zona pellucida is a gel-like, homogeneous, acellular material, mainly composed of neutral proteins manufactured by the granulosa cells with some possible contributions by the oöcyte. It stains positive with the PAS reaction. Microvilli from the oöcyte penetrate the zona and are in contact with microvilli on the surfaces of the granulosa cells that also extend into the zona. Gap junctions are present at the points of contact. Three major proteins have been identified in the zona pellucida and they play important roles in fertilization. Sperms have receptors to at least one of these proteins.

With the growth of the follicle under the influence of FSH, the stromal cells surrounding it differentiate into several layers of spindle-shaped theca cells (Gk. theke, box). The theca cells are large, pale staining and have the morphology of steroid producing/metabolizing cells. The layers are highly vascularized but the capillaries do not penetrate the basal lamina of the granulosa cells.
Secondary Follicles (Antral)

As the follicle becomes larger, small liquid-filled areas appear between the granulosa cells. Eventually a liquid-filled cavity, the antrum, develops among the granulosa cells. The material inside the antrum is called liquor folliculi.

As the antrum becomes larger and larger, the oöcyte is pushed off to one side of the follicle. The oöcyte is surrounded by a layer of follicular cells (corona radiata** and sits on a little hillock of granulosa cells (cumulus oöphorus).

The granulosa cells are involved in protein and steroid synthesis. They convert androgens produced by the theca interna cells into estrogens.

The theca differentiates into an inner theca interna and an outer theca externa.

The cells in the theca interna are large and well endowed with blood vessels. These cells have abundant SER and lipid droplets and are active in steroid synthesis and metabolism. In response to LH, they synthesize androgens (androstenedione), which diffuse to and are converted by the enzyme aromatase in the granulosa cells into estrogens (in response to FSH) via the process of aromatization. The cells in the theca interna are well vascularized.

The theca externa resembles connective tissue and blends into the rest of the stroma.

Mature (Graëfian) Follicle

The mature, large follicle, close to ovulation, is also called the Graëfian follicle (also called the preovulatory follicle). The oöcyte, with its attached corona radiata cells, detaches from the cumulus oöphorus, and floats free in the follicular fluid.

The follicular cells acquire luteinizing hormone receptors (LH), a step critical for the development of the corpus luteum later.

Ovulation

An ovulatory follicle is about 20mm in diameter in cows, 50-70mm in mares, 10mm in goats, ewes, and sow; and 2mm in bitches and queens.

As the Graëfian follicle reaches its full size, there is a rapid accumulation of liquid in the follicle without significant increase in pressure. The follicle bulges out at the surface of the ovary. A small oval area, the macula pellucida or stigma appears. This area sticks outward as a clear cone. This area undergoes localized changes in color, translucency and integrity. Estrogen secretion reaches the maximum level just before ovulation.
After a LH surge, ovulation takes place at the site of the stigma. This surge is essential for ovulation. Ovulation involves the rupture of the follicle and the sudden release of follicular fluid along with the ovum, which is surrounded by the corona radiata. The cells of the corona radiata will later disperse in the presence of spermatozoa (due to the enzymatic actions of the acrosome). In ruminants, the oocytes have already lost their corona at the time of ovulation. The very active fimbriae end of the oviduct picks up the ovum.

If fertilized ---- the zygote (fertilized ovum) undergoes cleavage; it then makes its way to the uterus for implantation. If not fertilized ---- degenerates in 24 hours. In some species, one ovary ovulates more frequently than the other (left ovary in the mare and the right ovary in the cow). Most domestic animals ovulate spontaneously. Induced ovulators include the rabbit, ferret, cat and mink. These animals require coitus or some comparable stimulation for ovulation to take place.

Maturation of the Oöcyte

Primary Oöcyte

Oögonia --- primordial germ cells. From yolk sac endoderm, migrate into the germinal ridge. Divide extensively. Form primary oocytes*.

The primary oöcyte began the first meiotic division during fetal development. This is arrested at prophase after the completion of crossing over. There is an exchange of genetic material between non-sister chromatids of homologous chromosomes. The primary oöcyte is incorporated into a primordial follicle.

Mitotic prophase arrest continues until the animal reaches reproductive age. The first meiotic division resumes shortly before ovulation. The chromosomes are equally divided between the two daughter cells. However, the secondary oöcyte gets most of the cytoplasm. The other daughter cell gets only a tiny bit of cytoplasm and is cast off as the first polar body that degenerates.

Secondary Oöcyte

This enters the second meiotic division. This division is also arrested.

If the ovum is fertilized, the meiotic division proceeds to completion. Once again one daughter cell gets most of the cytoplasm and becomes the mature ovum. The other daughter cell is the small secondary polar body that is cast off and degenerates.
The ovum is haploid and has N number of chromosomes.

If the secondary oöcyte is not fertilized, the second meiotic division never goes to completion and the oöcyte will degenerate.
In most domestic animals the first meiotic division is completed shortly before ovulation producing a secondary oöcyte.
In the bitch and mare, the first meiotic division is completed after ovulation; thus a primary oocyte is ovulated.

Fusion of the ovum and sperm restores the diploid number of chromosomes and a zygote is formed.

**Follicular Atresia**

Although millions of primordial follicles are formed during fetal development*, only a small number of them ever reach maturity and are released through ovulation. The majority of the follicles degenerate through a process called atresia.

Atresia is a form of programmed cell death and involves apoptosis. Atresia can affect follicles in any stage of development. In the bovine ovary, a cohort of 40 follicles may develop at the beginning of a cycle and only one follicle ovulates.

The oöcyte, the zona pellucida, and the follicular cells degenerate and are resorbed. The basal lamina of the granulosa cells may become hyalinized and is then called glassy membrane. This too, will eventually disappear.

The theca interna cells blend back with the stroma. In the queen, bitch and rodents, the theca interna cells may persist as interstitial endocrine cells.

**Corpus Luteum**

After the ejection of the ovum the collapsed follicle becomes the corpus hemorrhagicum as blood flows into the antrum. Small ruminants and carnivores bleed less than mares, cows and sows. The basal lamina of the follicular cells breaks down and the capillaries from the stroma invade the collapsed follicle and convert it into a highly folded, greatly vascularized temporary endocrine organ called the corpus luteum. The corpus luteum can be very large and occupies a significant portion of the ovary. However, it is still considered to be in the cortex.

The corpus luteum is dependent on LH from the adenohypophysis for its initial growth.

The granulosa cells of the follicle become very large and contain many small lipid droplets. These are called the granulosa lutein cells. In response to FSH and LH, these cells produce progesterone and estrogens.
The theca interna cells are incorporated into the folds and become thecal lutein cells. In response to LH, these cells produce androstenedione and progesterone.

Yellow pigment, lutein, appears in the luteal cells of carnivores, mares and cows, thus the term “yellow body” (“corpus”, body; “luteum”, yellow). This pigment is not present in the corpus luteum of sows, ewes and goats.

The corpus luteum has a finite lifespan.

Without pregnancy, the corpus luteum lasts for several days (14-15 in cows) and then degenerates (luteolysis). The high levels of progesterone secreted lead to a prostaglandin-induced corpus luteum regression in species such as the ewe. Over a period of time, there is deposition of fibrous connective tissue in this area. The resultant fibrous scar is called corpus albicans.

If there is pregnancy, the corpus luteum is maintained for a longer period of time. Then the corpus luteum slowly declines but still secretes some progesterone and estrogen until the end of the pregnancy. After delivery, its involution is accelerated. The scar left behind is larger and is also called a corpus albicans.

Most of the corpora albicans are eventually reabsorbed and replaced by ovarian stroma.

The corpus luteum of pregnancy also secretes relaxin. This polypeptide hormone may be involved in cervical dilation and softening, increases in oxytocin-receptor synthesis of the myometrium, relaxation of the pubic synthesis and other pelvis joints. In horses the placenta is the main source of relaxin.

* Recent studies indication that the bone marrow and blood may contain stem cells that can enter the ovary and develop into oocytes in animals after birth. This is an area of very active research.

** Some histologists use the term corona radiata only for the granulosa cells surrounding the oocyte when it is free floating and not when it is still attached to the cumulus oophorus.

THE OVIDUCT (UTERINE TUBE)

The oviduct derived from the parts of the müllerian ducts.

**Gross**

The oviduct is a muscular tube situated in the edge of the mesosalpinx. At one end it opens into the uterine cavity and at the other end it opens to the peritoneal cavity. It can be divided into four parts: The part that transverses the wall of the uterus is the pars interstitialis. The narrow portion next of the uterine wall is the isthmus. The expanded
intermediate segment is the **ampulla**. The funnel-shaped abdominal opening is the **infundibulum**. The free margins are drawn into many tapered, finger-like processes, and the **fimbriae**.

**Histology**

**Mucosa**

The mucosal membrane contains a linear system of complex **folds** with elaborate branches. In the ampulla the folds and branching become quite elaborate. In the isthmus the folds are simple, longitudinal ridges. In the interstitial region, they are low ridges.

**Epithelium**

The surface epithelium is simple columnar or pseudocolumnar. The epithelium is highest in the ampulla and diminishes in height toward the uterus.

There are two types of cells in the epithelium.

i) **Ciliated cells** are most numerous on the fimbriae surface, somewhat less so in the ampulla, and fewer still in the isthmus and interstitial segments.

ii) **Peg cells** are wedge-shaped cells that do not have cilia. They have secretory granules in the cytoplasm. The secretion provides nutrients to the ovum during its passage through the oviduct.

The height and activities of these cells change with changes in the hormonal environment.

**The Muscularis Externa and the Serosa**

The muscularis externa contains an inner circular layer of smooth muscles and a less developed outer longitudinal layer.

The serosa has a layer of simple squamous epithelium on some connective tissue.

**Functions**

**Receives** the ovum. The oviduct is very active at the time of ovulation. The opening of the infundibulum comes into contact with the surface of the ovary. An ovum that is released through a ruptured follicle is usually picked up by the fimbriae and directed into the duct.

The rhythmic peristaltic contractions of the oviduct are important in picking up the ovum and transport it toward the uterus. The actions of the cilia also help the transport.

Secretions from the epithelium promote **capacitation** of sperms.

**Provides** a favorable microenvironment for **fertilization**, which usually takes place in the ampulla of the oviduct.

**Transports** the zygote (fertilized ovum) to the uterus for implantation.
THE UTERUS

This organ derived from part of the müllerian duct.

It receives the sperms through the cervix and serves as the site for the development of the fetus.

Components

**Cornua** --- bilateral horns (in most species).

**Corpus uteri** --- the bulk of the organ, the body of the uterus.

**Isthmus** --- the slightly constricted portion below the corpus.

**Cervix** --- the cylindrical lower part of the uterus.

**Cervical canal** --- slender passage from the internal os in the uterine cavity to the external os that opens into the vagina.

**Fornix vaginae** --- fornix uteri, the recess at the vault of the vagina.

**Peritoneum** covers part of the uterus.

**Myometrium** --- most of the thickness of the uterine wall is made up of smooth muscles.

**Endometrium** --- a glandular mucosa lines cavity of the uterus.

The Myometrium

This is made up of several layers of smooth muscles, which are not sharply demarcated.

**Stratum submucosum** --- immediately beneath the mucosa, fibers run mostly longitudinally. **Stratum vasculare** --- thickest middle layer, contains many large blood vessels; circular and oblique muscle bundles. **Stratum subserosum** --- outermost layer, thin longitudinal.

The maintenance of the smooth muscles depends on estrogens.

There are numerous gap junctions between the smooth muscle cells. These facilitate coordinated contractions of the myometrium.

The smooth muscle cells may enlarge in size ten folds during pregnancy, while the mass of the uterus itself may increase by 20 times. Physiological hyperplasia, increase in cell number and hypertrophy, increase in cell size).

During pregnancy, myometrial contraction is inhibited by relaxin.

During parturition, uterine contractility is increased by oxytocin from the neurohypophysis.

The Endometrium

Functions

Preparation for the implantation of the embryo.
Participate in the formation of the maternal portion of the placenta.

**Histology**

The endometrium can be divided into two zones or strata based on their functions and structures. The *stratum functionalis* is the superficial layer that degenerates partially or completely after pregnancy or estrus. The *stratum basalis* is the layer that remains after these events. It is from this deeper layer that regenerates the stratum functionalis.

The surface epithelium of the stratum functionalis varies from simple columnar (mare, bitch, queen) to simple or pseudostratified columnar (sows and ruminants). The lamina propria is very cellular.

Simple coiled, branched tubular *uterine glands* are found in the endometrium of most species. The epithelium of these glands is simple columnar and contain both secretory and nonsecretory cells. The height and functions of these cells, as well as the overall morphology of the glands, are hormone dependent.

In ruminants, thickened regions of the endometrium are present. These regions, called *caruncles*, are highly vascularized and lack uterine glands. Caruncles represent sites of attachment between the maternal and fetal placenta.

**Cyclic Changes in the Uterine Horns and Body**

**Estrus** --- Greek, oistros, mad desire. Heat. That portion of phase of the sexual cycle of female animals characterized by willingness to permit coitus; readily detectable behavioral and other physical signs are exhibited by animals during this period. (Stedman's Medical Dictionary).

The endometrium is dependent on the female hormones. It changes during the estrus cycle as the hormones fluctuate. Generally speaking, estrogen is associated with proliferation of the tissues while progesterone is associated with secretory activities.

Proestrus ---- estrogens
Estrus ---- estrogens
Metestrus ---- estrogens and progesterone
Diestrus ---- progesterone

**Cows**

Proestrus ---- Under the influence of estrogen from the growing follicle, the endometrium becomes thickened through the proliferation of surface epithelium and the stroma. The tissue becomes congested (containing an abnormal amount of blood) and edematosus (containing an abnormal amount of fluid). The uterine
glands elongate through cell proliferation. The epithelial cells of the uterus and glands increase in height.

**Estrus** --- Maximum level of estrogen is secreted by the follicle. A LH surge precedes ovulation. The uterine mucosa increases further in thickness through cell proliferation. The uterine glands elongate further and begin to branch, also through cell proliferation. The epithelial cells continue to increase in height as well.

Metrorrhagia, small bleeding, occurs in the zona functionalis shortly before ovulation. The myometrium is highly contractile.

**Metestrus** --- With the formation of the corpus luteum, circulating progesterone increases and estrogen levels decline. The uterine mucosa reaches its maximal thickness with edema and hyperemia (congestion). The uterine glands continue to branch. Bleeding stops around mid-metestrus.

**Diestrus** --- Progesterone levels reach a maximum with the maturity of the corpus luteum at mid-diestrus. The endometrium and glands enter a secretory phase. This activity is greatest during the first portion of diestrus. If pregnancy does not take place, the endometrial line begins to decline as the regressing corpus luteum secretes less and less progesterone. There is involution of the endometrium, regression of the glands and cessation of secretory activities.

**Mares**

**Anestrus** (period of quiescence between estrus cycles) --- The epithelial lining of the endometrium is made up of simple cuboidal cells. The uterine glands are straight and have cuboidal cells.

**Proestrus** --- The height of the epithelial cells in the endometrium increases under the influence of estrogen. The uterine glands begin to coil.

**Estrus** --- The cells of the epithelium are tallest during early estrus and then become shorter in late estrus. The endometrium becomes edematous and thickened. The uterine glands proliferate through cell division and become secretory. The myometrium is contractile.

**Metestrus** --- This phase is not easily defined histologically in the mare.

**Diestrus** --- The endometrial lining is made up of simple columnar cells. Tissue edema tissue decreases. The uterine glands become less secretory.

**Carnivores**
Carnivores have only one or two estrus cycles per year. Anestrus is the period between the cycles.

**Proestrus** --- The endometrium becomes edematous and congested. Bleeding, metrorrhagia occurs in bitches.

**Estrus** --- Ovulation occurs shortly after the onset of estrus. Progesterone levels increases after the formation of the corpus luteum. Uterine glands and the stroma begin to proliferate.

**Diestrus** --- This may last for 70 days in bitches and is called physiological pseudopregnancy. The corpus luteum continues to produce progesterone and the endometrium resembles that found during pregnancy.

**Anestrus** --- The endometrium is thin and regressed, the surface and glandular epithelium are nonsecretory. The uterine glands are straight.

**Menstrual Cycle in Old World Primates**

The stratum functionalis undergoes periodic degeneration (destruction) during the menstrual cycle. This is due to the presence of hormone-sensitive spiral arteries in this tissue.

**Proliferative Phase** --- The endometrium proliferates under the influence of estrogens from the developing follicle.

**Secretory Phase** --- The uterine glands become secretory under the influence of progesterone from the corpus luteum.

**Ischemia and Menstruation** --- Without pregnancy, the corpus luteum declines and the stratum functionalis degenerates, resulting in menstrual bleeding. Menstrual blood includes arterial blood, venous blood and tissue debris from the degenerated stratum functionalis.

At the end of menstrual bleeding the endometrium regenerates with cells from the stratum basalis and the cycle starts anew under the influence of estrogen from the developing follicle.

The stratum basalis does not contain spiral arteries and does not undergo cyclic changes and destruction. This forms the basis for regeneration of the stratum functionalis.

**Cervix**
The cervix is the channel through which sperms travel from the vagina into the uterine cavity. Through this channel also travels the newborn. On the other hand, pathogens can also enter the uterus via this route.

The cervix is the neck of the uterus and is thick-walled, muscular structure. The mucosa may be thrown into prominent primary, secondary and tertiary folds.

The epithelium of the cervical mucosa is usually simple columnar with mucigenous cells being the dominant cell type. In small ruminants and the sow there may be simple tubular cervical glands.

Muscularis mucosae is not present in the cervix. The propria-submucosa contains connective tissues (much elastic fibers) and blood vessels. This tissue becomes edematous (accumulation of excessive fluid) during estrus and at the time of birth.

The muscularis externa consists of inner circular and outer longitudinal smooth muscle layers. These muscles are continuous with those of the uterus and the vagina. The serosa is made up of loose connective tissue.

The amount of cervical mucus produced and its chemical composition are hormone dependent. During estrus there is an increase in mucus production. The mucus is thick and forms a seal during pregnancy.

**VAGINA**

This is a fibromuscular tube with three layers: the mucosa, the muscularis and the adventitia.

The **mucosa** is thrown into numerous folds (rugae), separated by furrows of variable depth.

The epithelium is mostly stratified squamous epithelium. Patches of simple columnar epithelium with mucigenous and goblet cells also occur, especially between the folds.

A muscularis mucosae is not present. The propria-submucosa contains connective tissue, and, in the caudal portion of the organ, lymphoid nodules.

Smooth muscles in the **muscularis externa** are arranged circularly and longitudinally. An additional layer of longitudinal muscles, found inside the circular layer, is present in the vagina of sows and bitches.

The **adventitia** is a thin layer of dense connective tissue with extensive venous plexus.

**Cyclical Changes in the Vaginal Epithelium**
The vaginal epithelium, like other reproductive tissues, is hormone dependent. The height of the epithelium and the degree of keratinization vary with hormonal fluctuations during the estrus cycle. These changes can be monitored by examining stained vaginal smears from the animal. An example of these changes is given here:

**Bitch**

**Anestrus** --- Stratified squamous epithelium is thin with only two to three cell layers. Vaginal smears: Numerous unstained nonkeratinized squamous cells. A few stained large cells with pyknotic (condensation and reduction in size) nuclei. A few neutrophiles and lymphocytes.

**Proestrus** --- Stratified squamous epithelium with keratinization. Thick, up to 20 cell layers. Vaginal smears: Numerous squamous keratinized cells. Many RBCs of uterine origin.

**Estrus** --- Keratinization of the epithelium reaches maximum during early estrus and then declines. Intraepithelial mucus glands are present. Vaginal smears: Squamous keratinized cells, which begins to disintegrate and become invaded by bacteria during later estrus. Less RBCs of uterine origin.

**Metestrus-Diestrus** --- Epithelium becomes thinner along with a decrease in keratinization. Vaginal smears: Nonkeratinized squamous epithelial cells. Neutrophiles are numerous early in metestrus and then decline in number.

**VESTIBULE**

**Mucosa**
Stratified squamous epithelium lines the mucosa that contains low folds. Mucigenous cells decrease in number from cranial to caudal.

**Propria-submucosa**

- **Bulbus vestibule**, an erectile plexus, is found in mares and bitches.
- **Major vestibular glands** --- secrete mucus for lubrication, found in queens and ruminants.
- **Minor vestibular glands** --- mucus glands found in most domestic animals.
- **Subepithelial lymph nodules** --- present in all species, part of the mucosa-associated lymphoid tissue.

**Muscularis externa**
This is similar to that of the vagina and is made up mainly of smooth muscles. Circular skeletal muscle bundles (constrictor vestibuli) are also present.
EXTERNAL GENITALIA

Vulva

Two labia, covered by skin with sebaceous glands and fine hair. The dermis and hypodermis have a vascular plexus that becomes congested during estrus, especially in sows and bitches. In the hypodermis are skeletal muscle fibers of the constrictor vulvae.

Clitoris

Consists of a paired, joined erectile corpora cavernosa clitoridis, a rudimentary glans clitoris, and a preputium clitoridis. The clitoris is richly supplied with sensory and autonomic nerve endings.
MAMMARY GLAND

The mammary glands are specialized, compound tubuloalveolar skin glands. They are under the influence of pituitary (esp. prolactin), gonadal, and a host of other hormones.

The gland is divided into lobes and then lobules by connective tissue. Neurovascular bundles, lymphatics and fat are also present in the interstitial tissue.

Alveoli

The secretory unit of the mammary gland is the alveolus. Several alveoli open into a common, larger collecting space, or collecting alveolus.

An alveolus has an inner layer of cuboidal secretory epithelial cells and an outer layer of myoepithelial cells.

The secretory epithelial cell is polarized with rER at the base, the nucleus near the center, lipid droplets and protein micelles in the apical cytoplasm. The lipid droplets are released with a small amount of cytoplasm and a portion of the cell membrane (apocrine secretion). The protein micelles are released by exocytosis (merocrine secretion).

Myoepithelial cells, with numerous microfilaments in their cytoplasm, are found between the secretory cells and the surrounding basal lamina. These cells form a ‘net’ around the alveolus. Contraction of these cells help to force the milk from the secretory alveoli into the ducts. This process is called milk letdown and is dependent on oxytocin released from the neurohypophysis.

Plasma cells in the stroma secrete dimeric IgA that is released into the milk and provides passive immunity to the suckling young.

Ducts

Secretory alveoli drain into collecting alveoli. These drain into intralobular ducts then into interlobular ducts that continue into lobar lactiferous ducts and finally opening into lactiferous sinus. The lactiferous sinus is continuous with the teat sinus that in turn opens into the teat surface via the papillary duct. There are species differences in how the ducts open to the surface.

Small ducts are lined by simple cuboidal epithelium. Larger ducts and sinuses are lined by stratified cuboidal (2 cell layers) to columnar epithelium. The papillary duct has a stratified squamous keratinized epithelium. Myoepithelial cells also line the ducts. Longitudinal smooth muscle fibers are found associated with the lactiferous ducts and larger ducts.
**Teat**

The teat or nipple contains the terminal openings of the ducts from the secretory units. The mucosa is lined by stratified cuboidal epithelium. This is surrounded by smooth muscle bundles, numerous blood vessels and dense irregular connective tissue. The mucosa blends with the skin. Small clusters of secretory alveoli may be present in the lamina propria.

The papillary duct is lined with stratified squamous epithelium. Circular smooth muscle bundles in the mucosa form a sphincter and hold the milk until suckling or milking forces it out.

**Involution of Mammary Gland**

After the lactation period or sudden arrest of suckling or milking, the mammary glands undergo involution. The accumulated milk is phagocytized and some of the epithelial cells degenerate. After involution, there are a few alveoli left and low cuboidal nonsecreting epithelial cells line them. The myoepithelial cells are quite prominent. There is an increase in the amount of interstitial connective and adipose tissues. *Corpora amylacea* are small, dark-staining casein concretions found in the alveoli, ducts and interstitium.