

Reproductive tract pathology

Development of gonadal sex

- ⌘ Each embryo will have either XX or XY chromosomes
- ⌘ In normal XX embryo, the outer cortical layer of the indifferent gonads becomes the ovary, while the medullary region of the indifferent gonads develop as the testis in normal XY
- ⌘ Gonadal hormones (limited to products from testicular tissue) control subsequent differentiation & modeling of tubules & external genitalia
- ⌘ A male fetus castrated in utero early in development, although₂ genetically male, will develop female internal & external

- ⌘ The two critical fetal testis products are **Müllerian inhibitory substance (SIM)** & **testosterone**
- ⌘ MIS & testosterone functions to force tissues of the indifferent, early embryo towards differentiation into male structure

Developmental defects of female reproductive tract

⌘ Freemartinism

- ‖ Occurs when a genetic female co-twin with a male
- ‖ Anastomosing placental circulation allows the ***male sex hormones*** to be carried to the female fetus and sterilizing the female
- ‖ **If anastomosing fails to develop, the female is not damaged**
- ‖ The male gonads develop earlier than the females
- ‖ female gonads are stunted & there is hypoplastic seminiferous tubules, hypoplastic vestibule and

- ⌘ The uterine horns are hypoplastic, or absent or lack communication with vagina
- ⌘ A consistent feature & key diagnostic is the presence of poorly developed vesicular glands that are found attached to the lower fused segment of the paramesonephric duct
- ⌘ The vagina is short & non patent
- ⌘ The external genitalia commonly have enlargement of the clitoris, a small vulva & a prominent tuft of hair



Fig. 18-5 Bovine freemartinism. A, Phenotypically female, reproductive tract, cow. The freemartin is the female of a set of male and female twins. Freemartins are chimeras. There is a vulva and vagina with a prominent clitoris. The internal genitalia consist of bulbourethral and vesicular glands, ductus deferentes, and short incomplete segments of uterus. The gonads are testis with epididymides attached. This major anomaly renders the cow infertile. B, Placenta, twin fetuses. Placental vascular anastomoses, which allow exchange of blood between fetuses, are a requirement for the occurrence of a freemartin. These anastomoses occur most often in the bovine species. (A and B, Courtesy Dr. R.A. Foster, Ontario Veterinary College, University of Guelph)

Hermaphrodites

- ⌘ Hermaphrodites have ambiguous genitalia, with part or all of the genital organs of both sexes present
- ⌘ The intersex is classified as true & pseudo
- ⌘ True hermaphrodite :-presence of both type of gonads
- ⌘ Pseudohermaphrodite:-has single type of gonadal tissue

Ovary

Developmental anomalies

Agenesis:-one or both

In bilateral agenesis, the tubular genitalia may be absent as part of the defect or underdeveloped

Hypoplasia:-usually bilateral

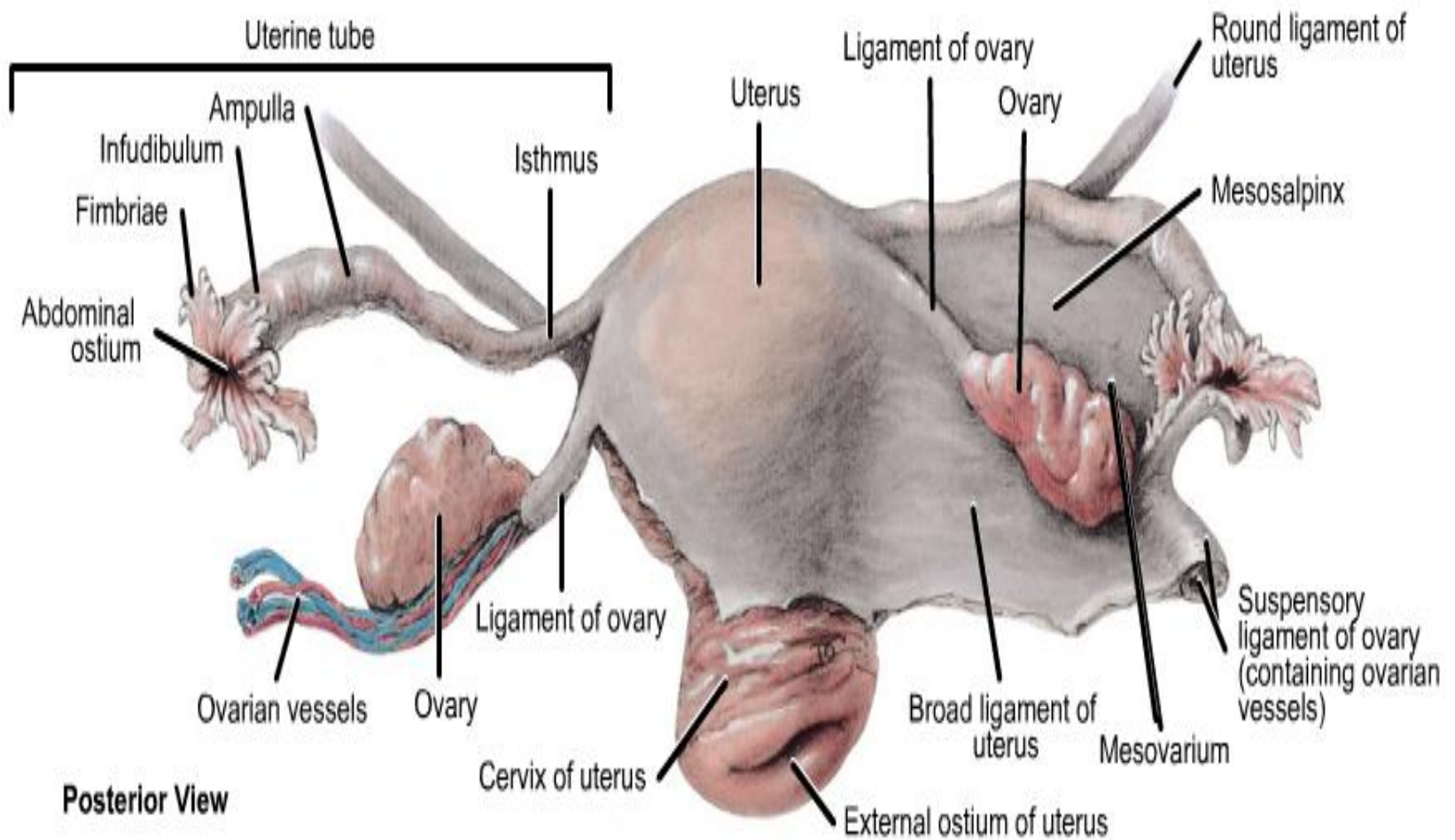
Severe hypoplasia- the defective gonads varies in size from cord-like thickening in the anterior boarder of the mesovarium to flat smooth, bean shaped

There are neither follicles nor luteal scars

Microscopically the ovary is largely composed medullary connective tissue

⌘ **Ovarian bursal adhesion**

- | Adhesion of the ovary with the walls of the ovarian bursa (peritoneal pouch formed around the ovary by the broad ligament and mesosalpinx)
- | It is caused by physical trauma from manipulations of the ovary and in RFM (retained fetal membrane)



Mesonephric Cystic Disease

- There are 3 types of **cysts that develop from mesonephric tubules**: cystic rete, cystic epoopphoron, and cystic paroophoron.
- **Cystic epoopphoron** develops from the cranial mesonephric tubules, whereas **cystic paroophoron** is found on the caudal surface of the ovary.
- Because these cysts are found near the ovary, they are casually referred to as being *parovarian cysts*.

- Cystic epoophorn are quite large, especially in the mare.
- Cystic rete are common in cat and dog, and arise from the rete ovary
- More precise identification can be achieved either through closer examination (the location relative to the ovary is very helpful), or by histopathology.

- Cysts of the epoophoron and paroophoron are movable cysts and have a thin wall of connective tissue and muscle fibers, are lined by epithelium with clear cytoplasm, and have a basement membrane.
- The epithelial lining is cuboidal in small cysts, tends to become squamous in slightly larger cyst and is usually absent due to pressure atrophy in larger cysts.
- Only the cystic rete commonly progress to compress ovarian tissues to such a degree as to compromise ovarian function.
- Adenomatous hyperplasia of the rete epithelium is common

- **Cystic rete tubules** have been observed in the bitch, cat and cow. Those in the cow seldom attain significant size, but those of the bitch and cat become large enough to be confused with cystic follicles.
- **Cysts of paramesonephric duct** origin are very common in the mare. They are located on the fimbria of the oviduct and are called *fimbrial cysts*, *hydatids of Morgagni*, or *accessory oviducts*

- **Cystic subsurface epithelial structures (cystic SES) of the bitch.**
- The modified peritoneal cells covering the surface of the ovary of the bitch normally extend into the ovary a short distance where they are arranged as small single epithelial-lined cavities called “subsurface epithelial structures” or “S.E.S.”.
- They frequently they give rise to single, or more commonly multiple, cysts extending along the ovarian surface
- S.E.S. occasionally undergo neoplastic transformation. Neoplasms of the SES are usually adenomas, but carcinomas do occur. These tumors tend to form cysts and have a folded, papillary pattern.

- The incidence of cysts of the S.E.S. increases with age.
- They are small, seldom larger than 5 mm in diameter.
- These cysts are lined by cuboidal epithelium.
- They do not appear to have any effect on fertility but, since the subsurface epithelial structures are hormonally sensitive, cyst formation may be associated with hormonal dysfunction.
- The lining of the cysts, like the surface epithelium and the subsurface epithelial structures, expresses ***cytokeratin and this allows differentiation from atretic follicular cysts***

Cystic follicular diseases

Dx depends on

- Differentiating anovulatory cystic follicles from normal antral tertiary follicles
- An important criterion for this differentiation is size
- Follicles larger than they should normally be at ovulation, persistence, & possible associated signs of **hyperestrogenism** are features of cystic follicular disease

- Normal follicular diameters near ovulation are ~ **2cm** in cow/1cm in sheep & pig/0.75cm in dog.

⌘ Follicular Cysts

- | **Luteinized cyst-** develops when ovulation fails to occur, there is no ovulation papilla and the luteal mass is smooth and rounded. It occurs due to failure of the hypophysis to release LH
- | **Cystic corpora lutea-** have ovulation papilla which distorts the outline of the cyst at the point of ovulation

General comparison

- ⌘ Follicular cysts, cyst that has a thin wall (less than 3 mm by), with low progesterone level in peripheral blood and the affected cows will be either anestrus or nymphomaniacal.
- ⌘ Luteinized cysts, however, the thickness of the cystic wall is over 3 mm, peripheral blood shows high progesterone levels, and the cystic wall reveals either luteinized granulosa or theca or both, and the affected cows will be anestrus.

Cystic follicular disease in cows

- ⌘ Follicular cysts in cattle are usually greater than 2.5cm in diameter than fail to ovulate & may persist
- ⌘ Aberration of the preovulatory surge of luteining hormone, either the absence of the surge or the mistiming of the surge is incriminated as cause
- ⌘ The cyst may be single or multiple on one or both ovaries
- ⌘ Patches of luteal tissue can be seen grossly in the wall of some of the cysts

- ⌘ Degeneration of granulosa cells takes place first, the cells undergo pyknosis & karyorrhexis & sloughing into the lumen
- ⌘ The changes of the theca interna are variable
- ⌘ The theca is partially luteinized in some cases, whereas degenerated in others & infiltrated by fibrous tissue
- ⌘ The luteal tissue may occur in patches or form a crescent of variable thickness

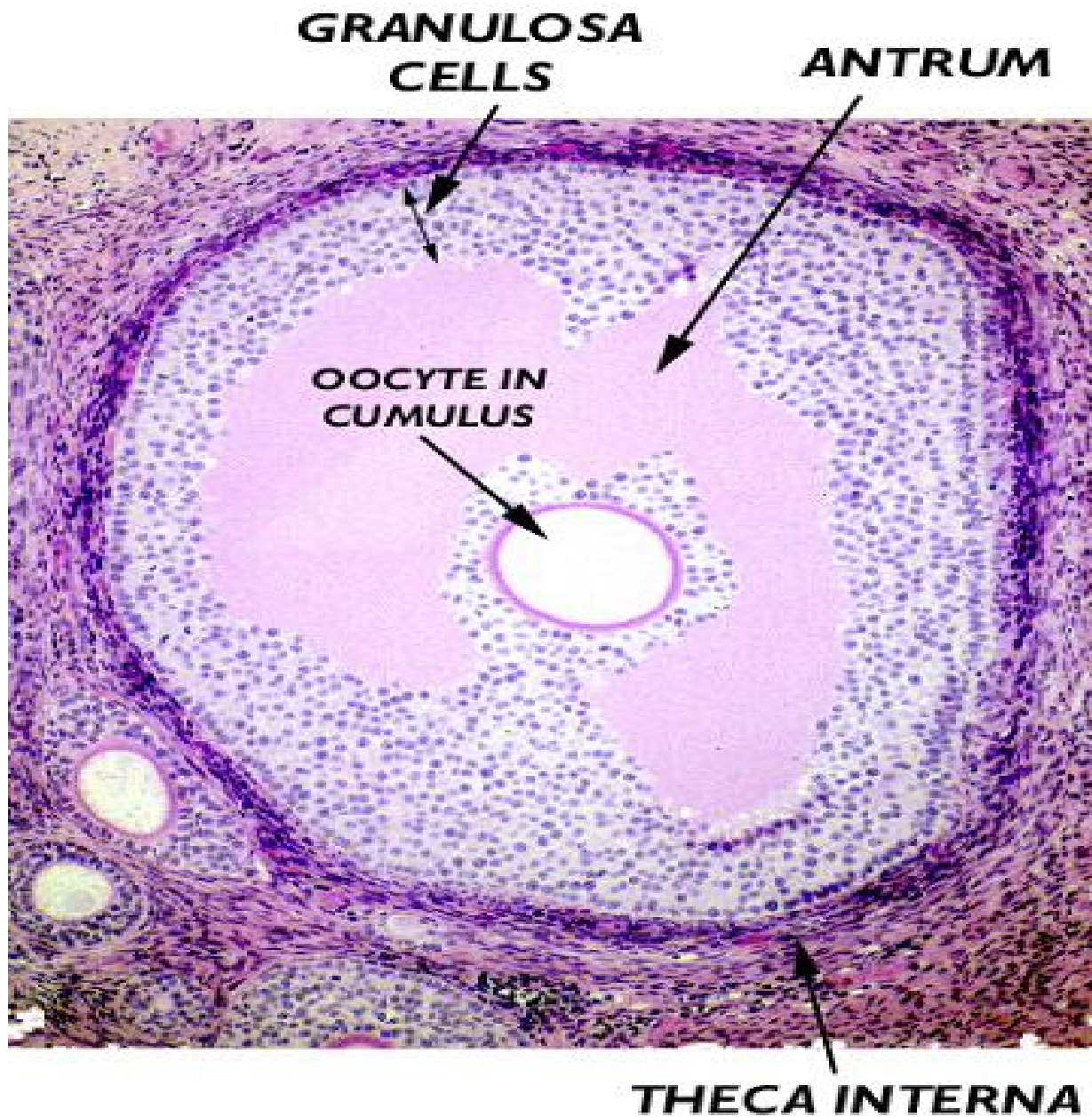




Fig. 18-11 Cystic Graafian follicle, ovary, cow (also called follicular cysts). Follicular cysts are larger than normal follicles and usually greater than 2.5 cm in diameter. They are the macroscopic lesions of cystic ovarian disease in the cow. They arise when ovulation of a normal follicle does not occur.

(Courtesy Dr. R.B. Miller, Ontario Veterinary College, University of Guelph.)

Luteinized cysts

- ⌘ Develop when ovulation fails to occur & the theca undergoes luteinization
- ⌘ There is no ovulation papilla & the luteal mass is smooth & rounded
- ⌘ The cavity of the cyst is spherical & lined by a layer of fibrous tissue adjacent to the zone of luteinized cells

Cystic corpus luteum

- Should not be confused with anovulatory luteinized cysts
- It is formed after ovulation & in which the central cavity has persisted in a mass of luteal tissue
- Can be distinguished by ovulation papilla that distorts the outline of the cyst at the point of ovulation



Fig. 18-12 Cystic corpus luteum, ovary, cow. A cystic corpus luteum is a normal corpus luteum complete with an ovulation papilla and a prominent cystic center. There is also a normal Graafian follicle (left) present. (Courtesy Dr. R.B. Miller, Ontario Veterinary College, University of Guelph)

Extraovarian lesions associated with cystic ovarian degeneration

Changes in other organ develop only if the cyst persist & functional

- The uterus is enlarged & the wall is edematous
- The cervix is enlarged, the external os patent, the plicae edematous
- There may be some degree of cystic endometrial hyperplasia (tiny gray white elevated blister in surface/ to naked eye)
- Mucus (mucometra) & cystic endometrial hyperplasia progress with time » anestrus & by then endometrium is very cystic & mucus accumulated to 100-1000ml or more 27

(COW)

- The vagina is edematous when the cyst is active but the striking change is formation of cyst in the Gartner's duct (mesonephric duct vestige)
- The vulva may be edematous when the cysts are active

Polycystic ovarian disease:-rare but very dangerous in **bitch** (species sensitive to estrogen)

- ⌘ Can induce lethal bone marrow suppression(hyperestrogenism)
- ⌘ It can affect either one or both ovaries, the affected ovary being greatly enlarged by multiple , thin walled cysts that vary 1 to 12mm in diameter
- ⌘ Leads to hyperestrogenism & include persistent estrus with cornification of vagina & Swelling of the mammary glands
- ⌘ Toxic effect of hyperestrogenism on the bone marrow with resultant pancytopenia

⌘ The pancytopenia results in:

- Thrombocytopenia with bleeding (epistaxis)
- Granulocytopenia with increased susceptibility to infection
- Estrogen appears to inhibit the differentiation of pluripotent stem cells

⌘ Degenerating oocytes can be identified in some of the cysts but the disease not just one of anovulation (100 of follicles recruited)

⌘ The granulosa & theca linings of the cysts is **attenuated** in the larger cysts

- ⌘ Patchy areas of luteinization form in the walls of some of the cysts
- ⌘ This luteinization may involve individual cells or sheet of cells & either the theca or the granulosa

Neoplastic diseases of the ovary

Tumors arising from tissues that are specifically ovarian can be divided into 3

- surface celomic epithelium tumors

- gonadal stromal tumors

- germ cell tumors

Tumors from non gonadal supportive tissues can be of the usual variety of fibroblastic, smooth muscle & vascular tumors

Tumors of the surface epithelium & its tubular invagination give rise to papillary & cystic adenomas (rarely papillary adenocarcinoma)

Gonadal stromal tumors are tumors of granulosa & theca cells

- Sex-cord stromal tumors can produce varying amounts of progesterone, estrogen, testosterone, and inhibin, and these hormones can profoundly influence the reproductive behavior of the affected animal
- and induce changes in extraovarian

Granulosa-theca cell tumor

Gross Morphology

- These frequently are large tumors that are either multinodular or symmetrical, uni- or bilateral
- they include both solid and cystic areas, with or without scattered areas of hemorrhagic necrosis.
- The cysts frequently contain yellow to red thin fluid. Some tumors contain a single large central cystic cavity.
- ♣ The surface of the granulosa-theca cell tumor is smooth & the cut surface may be solid or cystic
- ♣ The solid portions of the tumor are white or yellow, depending on the lipid contents

Histological Types

- Classification of sex-cord stromal tumors is based on the appearance of the predominant cell population and its resemblance to the normal constituents of the ovarian endocrine apparatus.
- It must be stressed, however, that more than one cell type often is present in a single neoplasm and that the histological appearance of an individual tumor may vary markedly in different areas

- Granulosa Cell Tumor
- Granulosa cell tumor is the most common sex-cord stromal tumor.
- It consists of irregular accumulations of granulosa cells ***separated by a supporting stroma of spindle cells***, imparting a distinct resemblance to disorganized attempts at follicle formation
- In some, the stroma resembles thecal tissue, giving rise to the designation *granulosa-theca cell tumor*.

- in some tumors, the neoplastic granulosa cells arranged in solid sheets, cords, trabeculae, or nests.
- The appearance of some granulosa cell tumors, particularly in the bitch but also in the mare, closely resembles that of testicular Sertoli cell tumors, designation of *Sertoli cell tumor of the ovary*
- Tumor cells in this variant are spindle shaped and are **arranged in tubules** that frequently are separated by a **fibrous stroma**.

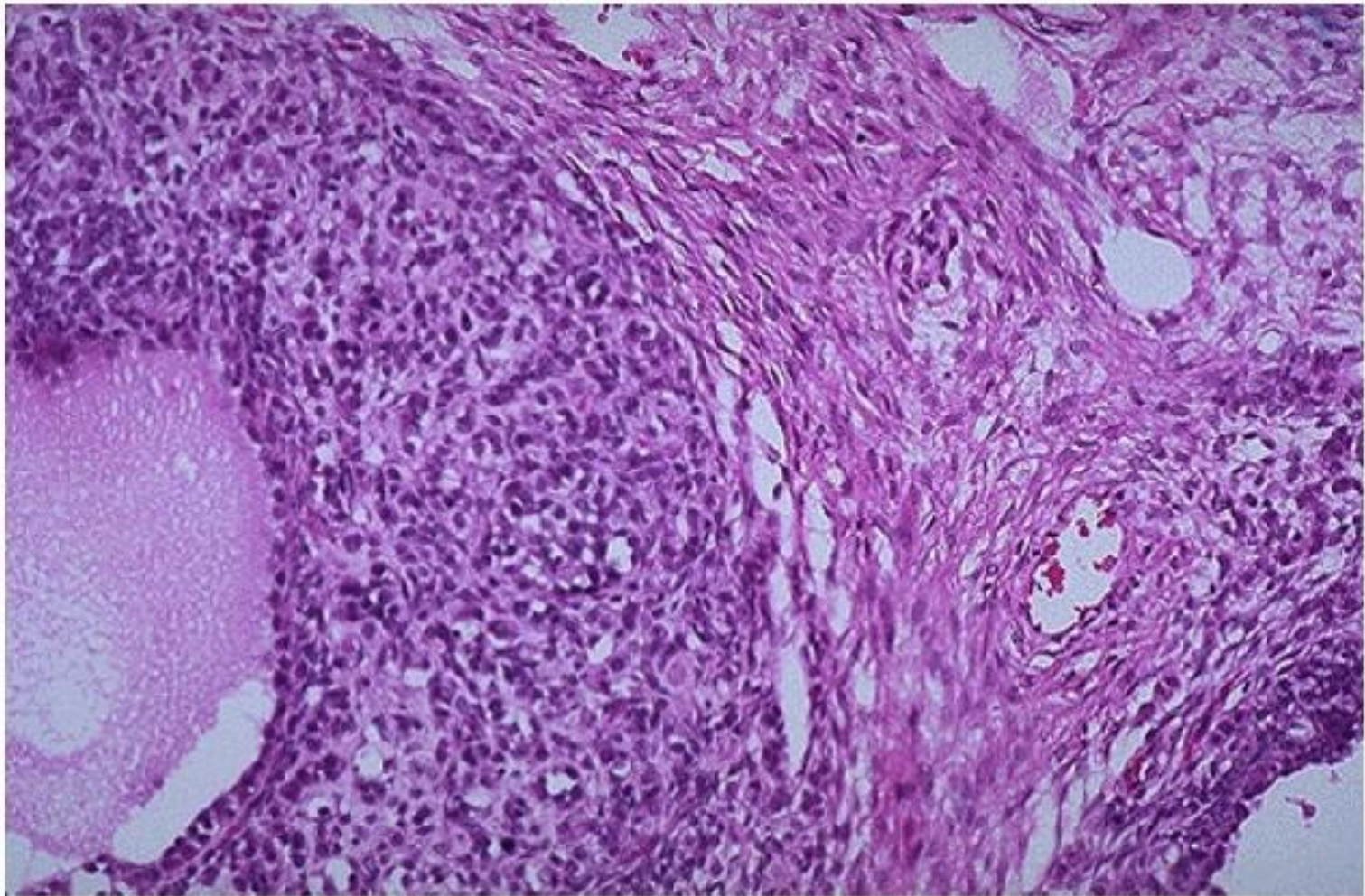
- Call-Exner bodies are present in some granulosa cell tumors and, when present, are a useful diagnostic feature.
- Call-Exner bodies consist of a radial aggregate of tumor cells about a central deposit of eosinophilic proteinaceous material.

- **Thecoma**

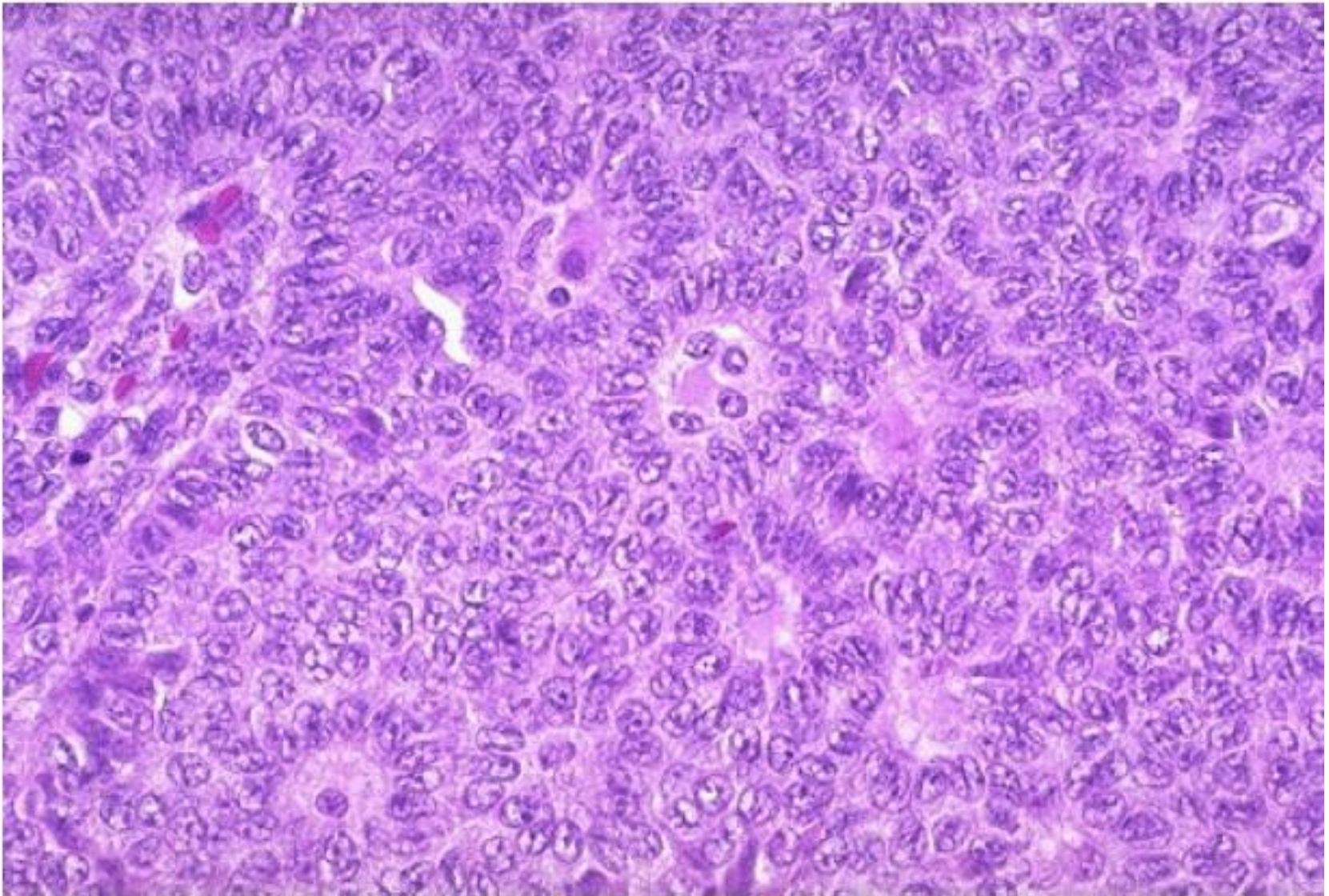
- Thecoma consists of irregular, loosely arranged unencapsulated aggregates of spindle shaped cells
- Individual cells have elongated nuclei, and the cytoplasm may contain lipid vacuoles, which are indicative of steroid hormone production.
- The distinction between a thecoma and mesenchymal tumors such as leiomyoma and fibroma can be difficult. However, a thecoma has the capacity to produce steroid hormones, elevated levels of which often can be detected in blood.
- Cytoplasmic lipid vacuoles in the cells of thecoma can be stained with fat stains such as Sudan Black.
- If necessary, histochemical or immunohistochemical staining can be used to identify muscle or collagen to distinguish thecoma from mesenchymal tumors



This is a granulosa cell tumor of ovary with a variegated cut surface. These tumors are derived from the ovarian stroma and often have a component of thecoma. They are often hormonally active and can produce large amounts of estrogen such that the patient may initially present with bleeding from endometrial hyperplasia.



Microscopically, the granulosa cell tumor attempts to form structures that resemble primitive follicles, as seen at the left. Most of these tumors are histologically benign, but some are malignant.



At higher magnification, an ovarian granulosa cell tumor has nests of cells which are forming primitive follicles.

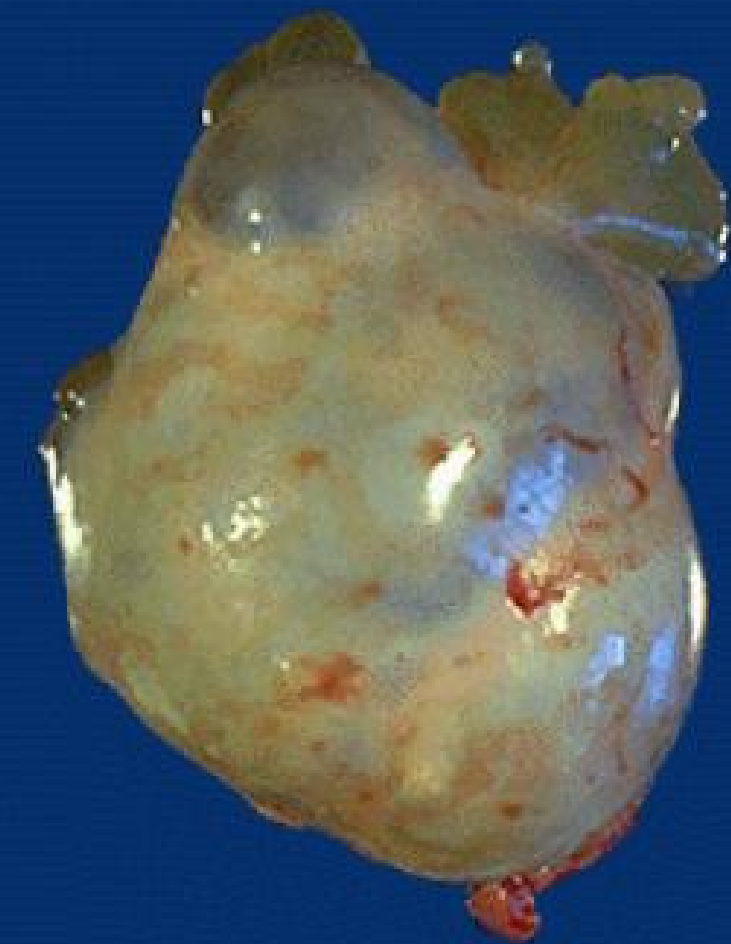
Epithelial Tumors

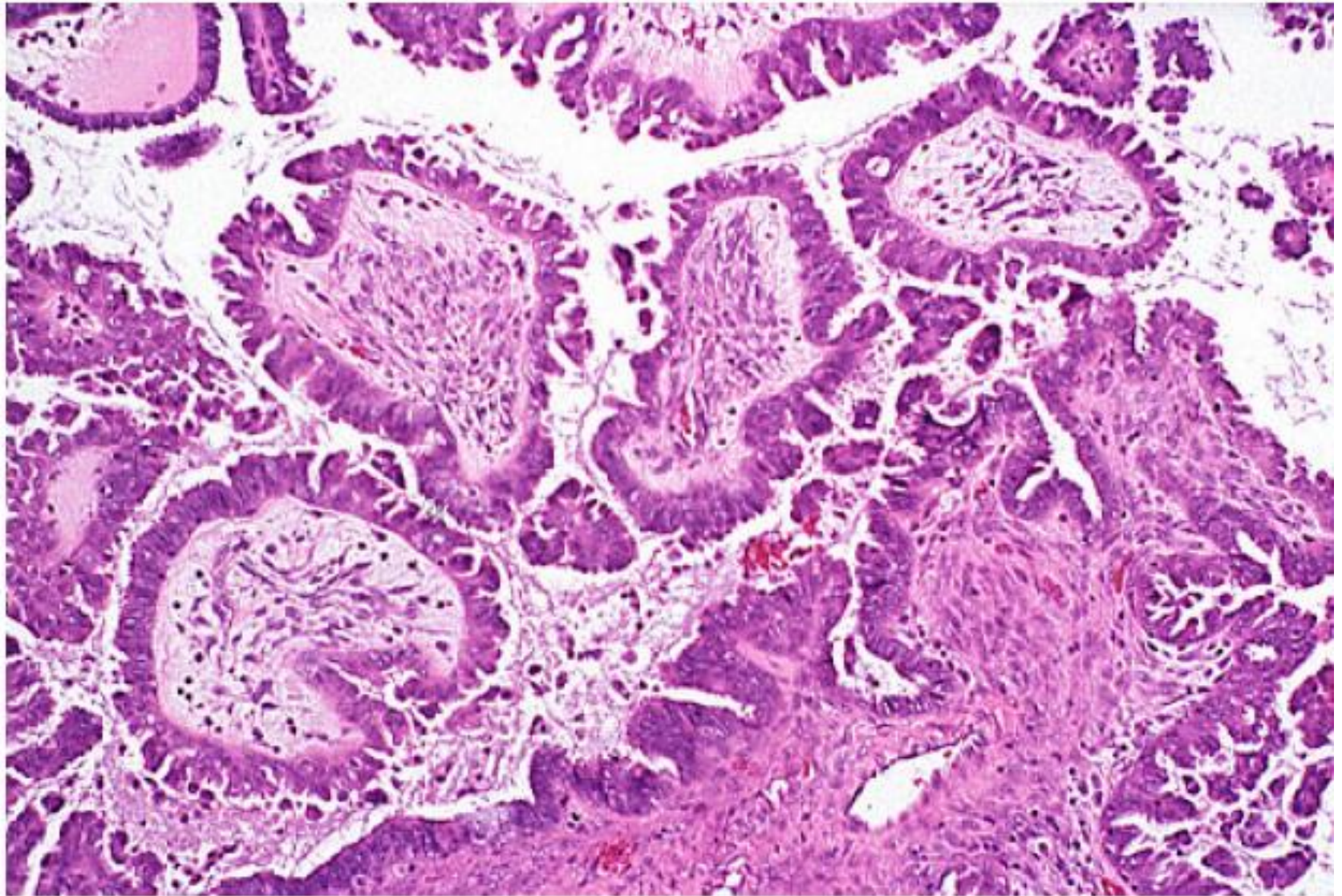
- Gross Morphology
- Epithelial tumors of the ovary can be either uni- or bilateral, and characteristically appear as cystic, multinodular enlargements.
- The cut surface typically has multiple cysts that contain thin yellow to brown fluid, interspersed between solid regions.
- Carcinomas also may appear as ***proliferative cauliflower-like*** growths that project from the surface of the ovary to involve adjacent structures

Histological Features

- Both adenomas and carcinomas of the ovary usually consist of arboriform papillae that project into the lumen of cystic cavities.
- They sometimes are further subclassified as papillary (papillary adenoma or carcinoma) or cystic (cystadenoma or cystadenocarcinoma).

- The papillae that characterize these tumors consist of connective tissue stalks that are lined by single or multiple layers of cuboidal or columnar epithelial cells that may or may not be ciliated
- Anaplastic carcinomas that lack the characteristic arboriform pattern occur occasionally and consist of broad, disorganized sheets of neoplastic cells.





Here is a serous cystadenocarcinoma in which there is more pronounced papillary growth with more hyperchromatic cells. 7

Tumors of germ cells

Dysgerminoma:- is a rare tumor that is comparable to the more common seminoma of testicle

It is usually unilateral (bitch, mare, cow & sow)

The tumor is smooth, or nearly so & relatively soft

The cut surface is gray & may have areas of hemorrhage or yellow patches of necrosis



Histologically:-

- it is composed of a uniform population of large rounded cells with a large chromatic central nuclei
- Mitotic figures & giant cells are frequent
- The pattern of growth is diffuse; the stroma is always scanty
- Just as in the canine testicular seminoma, accumulation of lymphocytes are present within the

Ovarian teratomas:-reported in bitch, sow, mare &
COW

Most are well differentiated & benign

They usually have solid & cystic areas containing
sebaceous materials & hair

A variety of other tissues including neural, adipose &
bone tissue may present



The cystic nature of a mature teratoma of ovary is seen here. The most common tissue element of these teratomas is skin, so large amounts of hair and sebum are produced, leading to

Pathology of the uterine (Fallopian) tube

Hydrosalpinx, pyosalpinx & salpingitis are the only ones of importance

Hydrosalpinx:-the uterine tube is distended, uniformly or irregularly with clear watery mucus that fluctuates

The tube is also increased & tortuousity & is thin walled

Histologically there may be extensive multilocular cyst formation in the mucosa with obliteration of the lumen

In some chronically inflammed uterine tubes, there is extensive interstitial fibrosis

Salpingitis

- ⌘ It is usually bilateral, is usually not detectable macroscopically
- ⌘ May show serous, catarrhal, or fibrinous inflammation
- ⌘ Congestion of the mucosal vessels, mononuclear infiltration, loss of epithelial cilia, & some desquamation of epithelium
- ⌘ Severe case:
 - ⌘ Catarrhal exudates collects in the lumen, the mucosal folds are thickened by cellular infiltration & congestion & the epithelium is largely destroyed

Pathology of the uterus

Torsion

- ♣ In almost all cases twisted uteri are pregnant but may also occur with pyometra & hydrometra
- ♣ Minor torsion (90°) are fairly common in cows but resolve themselves but torsion of 180° or greater cause dystocia
- ♣ Veins are obstructed before arteries & then uterus become congeste & edematous
- ♣ Edema of placenta & death of fetus

Prolapse:-occurs commonly in ruminants

- ⌘ The pathologic sequence of prolapse are congestion & edema followed by hemorrhage, necrosis & sepsis.
- ⌘ Gangrene may supervene

Pathology of the endometrium

Hyperplasia

- ⌘ Endometrial hyperplasia is common(bitch) & usually involves cystic distension of endometrial glands
- ⌘ Is called cystic endometrial hyperplasia & if extensive, results in accumulation of endometrial secretions in the uterine lumen
- ⌘ Infection may follow & **cystic endometrial hyperplasia-pyometra syndrome** may develop
- ⌘ Cystic endometrial hyperplasia can involve either a single or a few glands, or endometrial glands extending along segments of endometrium
- ⌘ Sometimes, the entire endometrial surface is involved. Individual endometrial glandular cysts can become quite large

Endometrial polyp

- ⌘ Most commonly seen in bitch & queen and is striking when the polyps are large
- ⌘ Polyps can be confused with tumors of the myometrium (leiomyoma), chronic pyometra, pregnancy or site of fetal resorption or segmental cystic endometrial hyperplasia
- ⌘ The true polyp contains substantial connective tissue stroma in addition to dilated glands, is pedunculated
- ⌘ Polyps may provide sufficient mass that uterine contractions can mechanically force prolapse of the affected horn

Hydrometra & mucometra

- ♣ The two conditions are considered together as the difference is probably only in physical
- ♣ The accumulation of thin or viscid fluid in the uterus is concurrent with the development of endometrial hyperplasia or is proximal to an obstruction of uterus, cervix or vagina
- ♣ Grossly, there is uniform distension of the uterus
- ♣ If hydrometra/mucometra persists for long time, the endometrium becomes markedly attenuated & will atrophy

Inflammatory diseases of the uterus

Inflammation limited in extent to the endometrium is termed **endometritis**

- of the entire thickness of the wall is **metritis**
- of the serosa, **perimetritis**
- of the suspensory ligament, **parametritis**

The classification is to some extent a use full index of the severity of reaction & of the pathogenesis

Endometritis: the endometrium or uterine mucosa is mainly involved

Mild endometritis may not be overtly evident clinically (a slight

Histologically :-the changes are not striking & consist for most part of a diffuse but light infiltration of inflammatory cells with slight desquamation of the superficial epithelium

- ⌘ The best indication of mild endometritis in all species consists of accumulations of plasma cells & foci of lymphocytes in the stroma

Severe endometritis of cow (common to the puerperium):-

- ⌘ The uterus is enlarged, flabby & collapsed rather than firm & contracted
- ⌘ The lumen contains chocolate-colored slightly tenacious lochia

- ⌘ With the admixture of inflammatory exudates & placental debris it becomes progressively dirty gray-yellow
- ⌘ The endometrium is congested & swollen
- ⌘ The intercotyledonary areas are ragged & tattered with shred of mucosa free in the lumen
- ⌘ Small hemorrhage are common in the congested mucosa, & there is a prominent leukocyte infiltration massing at the surface involving all mucosal elements, including the glands

Chronic endometritis

- θ Recovery from the acute results in chronic endometritis
- θ With greater or less degrees of endometrial destruction & replacement by granulation scar tissue, the uterus takes a fistulous tract
- θ Thickening of the endometrium is by inflammatory tissue
- θ The glands are depleted; those that survived are atrophic, flattened, attenuated or cystic due to periglandular fibrosis
- θ The lining mucosa may be intact, denuded in places, or show
foci of polypoid hyperplasia or squamous metaplasia (chronic

- ♣ Inflammatory changes essentially of productive fibrosis & leukocytosis in which lymphocytes & plasma cells predominate

Metritis :-all layers of the uterine wall show evidence of inflammation

Thickened & friable wall of the uterus

The serosa is dull & finely granular with “paintbrush” hemorrhages & a thin deposition of fibrin

Microscopically:- the subserosal CT are edematous & infiltrated with leukocytes

Leukocytes mass on the mucosal surface & are associated with extensive hemorrhage, necrosis, & sloughing

Invasion of blood vessels aggravates the lesion

Thrombosis may extend to the vessel of

Pyometra :- is acute or chronic suppuration infection of the uterus with accumulation of puss in the uterus

- **In less advanced cases-** the uterus may be slightly enlarged with mild endometrial hyperplasia & inflammation
- **In more advanced case-**remarkable distension of the uterine horns & occupy most of the peritoneal cavity
- The serosal surface is dark & vessels are congested & prominent
- The wall is friable & either rupture or perforated(peritonitis)
- The exudate is thick, viscid, tenacious, opaque, red-brown & with characteristic fetid odor (E.coli & Proteus)

- The mucosa is irregular in thickness, necrotic & ulcerated in portions with irregular superficial hemorrhages
- In other portions obviously hyperplastic, dull-white, & dry in appearance with small cysts visible in these hyperplastic areas
- Microscopically-*the most significant feature is the remarkable endometrial hyperplasia & progestational proliferation in almost all cases*
- *The cells of such progestation epithelium are enlarged, columnar, vacuolated, & have small pyknotic nuclei*
- In some cases, the normal single layer of cells piles up to

- Masses of neutrophils collect in the uterine lumen & in the glands
- The migrating leukocytes collect near the surface & then penetrate the epithelium
- In much more cases in the endometrial stroma there are all the exudate phenomena of acute inflammation
- The blood vessels are very congested, thrombosed & with diapedesis or large hemorrhage
- The stroma is edematous & numerous neutrophils infiltrate the stroma & collect in the lumen
- It is clear that most cases of pyometra in the bitch are associated with endometrial hyperplasia (progesterone effect)

PLACENTAL PATHOLOGY

└ **Retained fetal membrane**

- ⌘ Cows >12 hours

- ⌘ Infectious, nutritional, hormonal, circulatory

└ **Inflammation**

- ⌘ **Brucellosis**

- Mononuclear cells infiltration in the
intercotyledonary area

- ⌘ **Listeriosis**

- Diffuse necrotizing & suppurative inflammation
(cotyledon plus intercotyledonary area)

⌘ **Enzootic abortion (Chlamydia)**

Cotyledons more severely affected than the intercotyledonary area

⌘ **Toxoplasmosis**

White (1-2mm) foci of inflammation, necrosis and mineralization in cotyledons

⌘ **Neospora caninum infections**

Foci of mononuclear inflammatory cells in many organs (fetus and the dam)

Pathology of male genital system

∞ Is composed of a production unit (testis), a maturation & maintenance unit (epididymis), & a transportation unit(various ducts & accessory genital glands)

- **TUMORS OF THE UTERINE TUBE (OVIDUCT) AND UTERUS**
- **Epithelial Tumors**
- **Tumors of the Uterine Epithelium**
- Epithelial tumors of both the uterus and oviduct are rare in domestic animals.
- **Uterine Carcinoma:** also is rare in domestic animals
 - Among the domestic species, it is most often reported in the cow, and it is fairly common in older cows at slaughter. There are a number of reports of similar tumors in the mare,

- Uterine carcinomas in cattle manifest as discrete, firm enlargements of the uterus that are composed of very firm, dense, white to yellow tissue. Widespread metastasis also can occur.
- These tumors tend to be solitary and develop in the uterine horn. The histological appearance of these tumors is characterized by nests and cords of anaplastic epithelium in a dense and abundant fibrous connective tissue stroma.
- The tumor develops deep in the endometrium and often extends into the myometrium early in the disease

Mesenchymal Tumors

- A variety of mesenchymal tumors occur in the uterus of domestic animals, including leiomyoma, fibroma, fibroleiomyoma and, far less commonly, their malignant

TUMORS OF THE CERVIX, VAGINA, AND VULVA

- **Epithelial Tumors**

- Primary epithelial tumors of the cervix are extremely uncommon in domestic animals, in contrast to the frequency of these tumors in women.
- Carcinomas of the vagina and vulva, on the other hand, are relatively common, particularly squamous cell carcinomas in ruminants and carcinomas of urinary epithelial (urothelial) origin in the vestibule of the bitch.

Squamous Cell Carcinoma

- Squamous cell carcinoma of the vulva is well recognized in sheep, goats, and cattle in areas where they are exposed to high levels of solar irradiation.
- These lesions in the vulva may be either ulcerative or proliferative, and histologically are typical squamous cell carcinomas..

Male RT

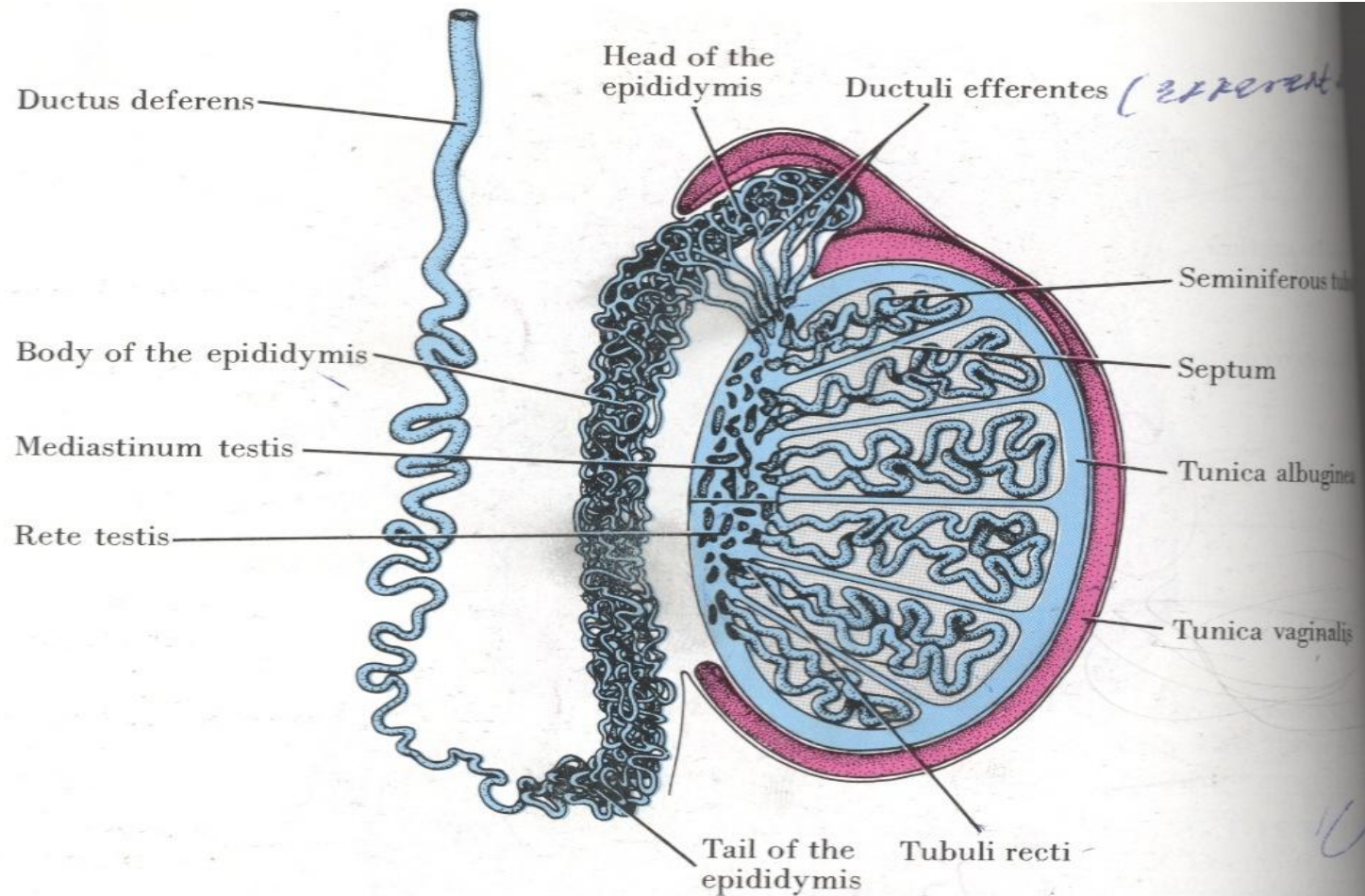


FIGURE 21-2. Schematic diagram of a longitudinal section through the human testis. The genital duct system, which includes the tubuli recti, rete testis, ductuli efferentes, ductus epididymidis, and ductus deferens, is also shown. (Modified from M. Dym, 1977.)

- **Scrotum**

- The scrotum is an outpouching of perineal skin and is lined by evaginations of the peritoneum.

- **Tunica vaginalis**

- *is an extremely thin mesothelium continuous with and structurally similar to the peritoneum* (parietal/ scrotum and visceral/testis/ separated by the cavity of the tunica vaginalis).

Hydrocele: accumulation of fluid (ascites, anasarca or local lymphedema).

- Hydrocele may lead to quite severe testicular degeneration on the involved side and to lesser damage on the opposite side, mostly in response to impaired thermoregulation.

- Scrotal hydrocele, with diminished sperm quality, has

- **Hematocoele:** accumulation of blood in the cavity (mostly the result of trauma/ common in housed together)
- Inflammatory changes in the tunica vaginalis may be part of disseminated infection, with lesions typical of the infection (feline infectious peritonitis, tuberculosis, caseous lymphadenitis).
- Suppurative inflammation also occurs as an extension of scrotal injury or from epididymitis

Testis and epididymis

- **Cryptorchidism**
- *Is incomplete descent of the testes and associated structures*
- Descent of the testes, epididymides, and spermatic cord (artery, vein and the ductus deferens)
- *is one of the most common abnormalities of the male reproductive system, and is the most common genital abnormality of the male cat and horse.*

- Retained testes are smaller than their normal counterparts.
- This is because of the deleterious effect of body temperature on spermatogenesis.
- The seminiferous tubules are smaller than normal and often present with the 'Sertoli cell only' pattern.
- Degenerative changes such as interstitial fibrosis and thickening of basement membranes superimpose on the hypoplastic appearance.
- In extreme forms, the outlines of distorted basement membranes are seen in a sclerotic tissue⁸⁰

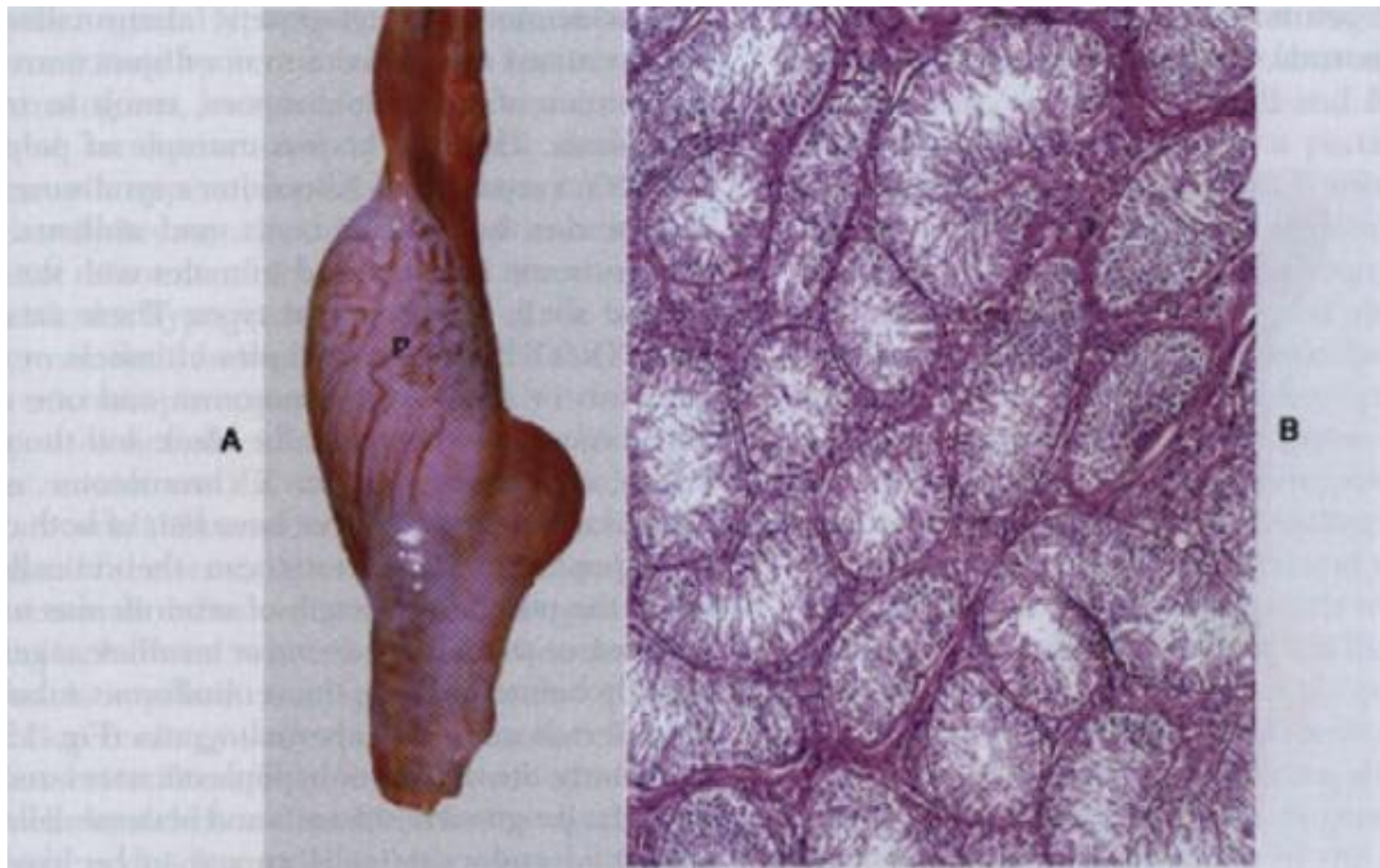


Fig. 19-12 Cryptorchid testis. **A**, Cryptorchid testis and epididymis, bull calf. The testis and epididymis are hypoplastic and are barely larger than the pampiniform plexus above (*P*). There are no attachments to the tunica vaginalis. **B**, Cryptorchid testis, dog. There is complete absence of spermatogenesis; however, the Sertoli cells are normal. H&E stain. (**A**, Courtesy Dr. R.A. Foster, Ontario Veterinary College, University of Guelph. **B**, Courtesy Dr. J.A. Ramos-Vara, College of Veterinary Medicine, Michigan State University; and Noah's Arkive, College of Veterinary Medicine, The University of Georgia.)

- **Testicular hypoplasia**
- Hypoplastic testes have failed to grow to a normal size.
- It can be unilateral or bilateral, and the small size is because of a reduction in the amount of the seminiferous epithelium.
- An affected testis is grossly similar to a normal testis in almost every way, except size
- The small size is because of an abnormally small number, length or diameter of tubules, or one or more combinations of these.

- Microscopic abnormalities include a total lack of germ cells, arrested spermatogenesis in all tubules, or arrested spermatogenesis that varies from tubule to tubule (low germ cell resistance).
- Hypoplastic testes with a total lack of germ cells are very small and fail to enlarge from their size at birth.
- Those testes with arrested development of all tubules fail to progress beyond a certain stage of spermatogenesis.

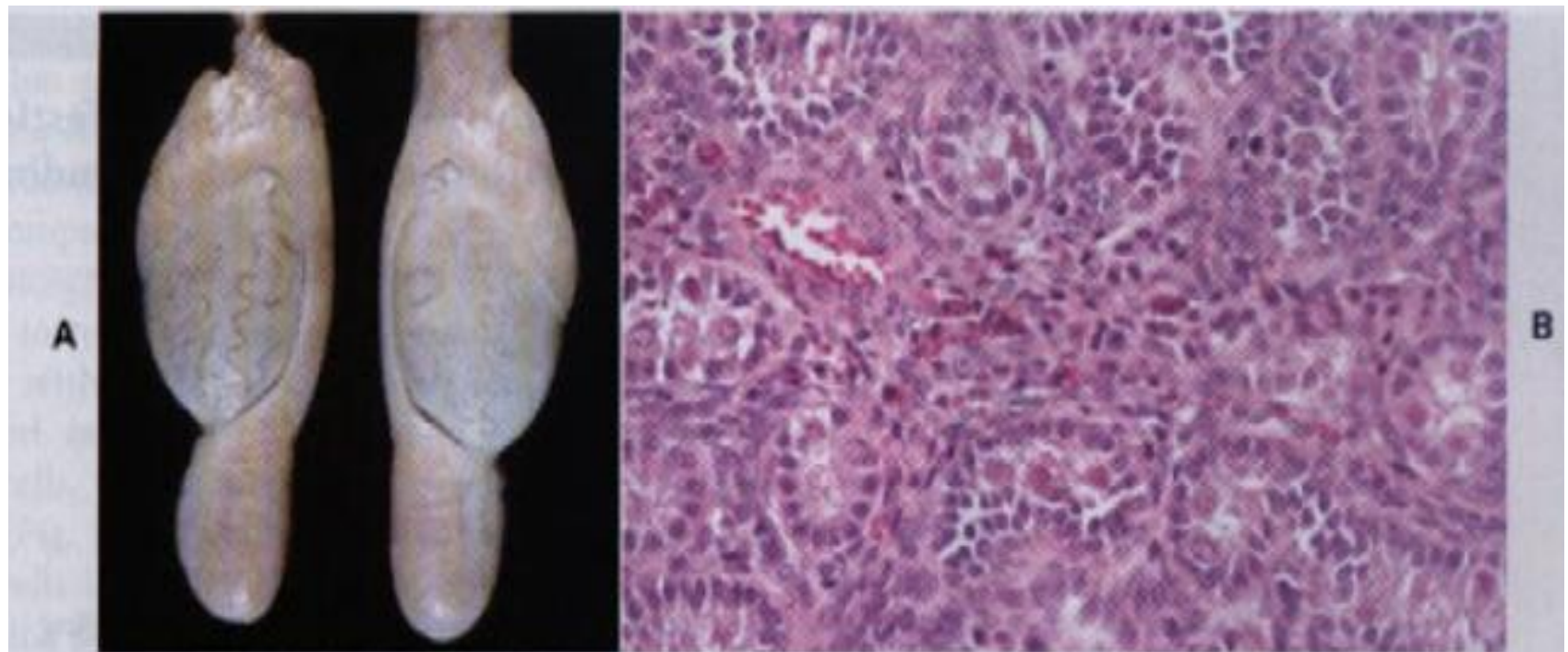


Fig. 19-14 Bilateral hypoplasia, testes, yearling ram. **A**, Both testes and epididymides from this yearling ram are very small compared with normal age-matched controls. **B**, The seminiferous tubules are lined only by Sertoli cells, and there is no spermatogenesis. H&E stain. (A and B, Courtesy Dr. R. A. Foster, Ontario Veterinary College, University of Guelph.)

- **Testicular Degeneration**
- *Testicular degeneration is manifested clinically and grossly as atrophy, mineralization, and fibrosis.*
- Many potential causes.
- Testes undergoing degeneration are usually reduced in size.
- In early or rapidly progressing degeneration, the testis is soft and flabby, lacks turgor, and the cut surface does not bulge.
- Wrinkling of the tunica albuginea may be apparent.

- With ongoing loss of fluid and reduction in the germinal epithelium relative to the stroma, the result is a small testis of firm consistency.
- The substance of the testis takes on a darker color that is often brown.
- Since the epididymis usually is less affected than the testis, it ultimately will appear to be disproportionately large.
- With continued degeneration and fibrosis, the testis becomes increasingly hard and variable mineralization may occur

- **Histological changes**

- In the early stages, Sertoli cells develop either a fine basal vacuolation or a more dramatic vacuolation of the apical cytoplasm.
- There also is disorganization and exfoliation of germ cells.
- In some cases there may be failure of release of germ cells from Sertoli cells (spermiation) and spermatozoa are phagocytized by Sertoli cells.

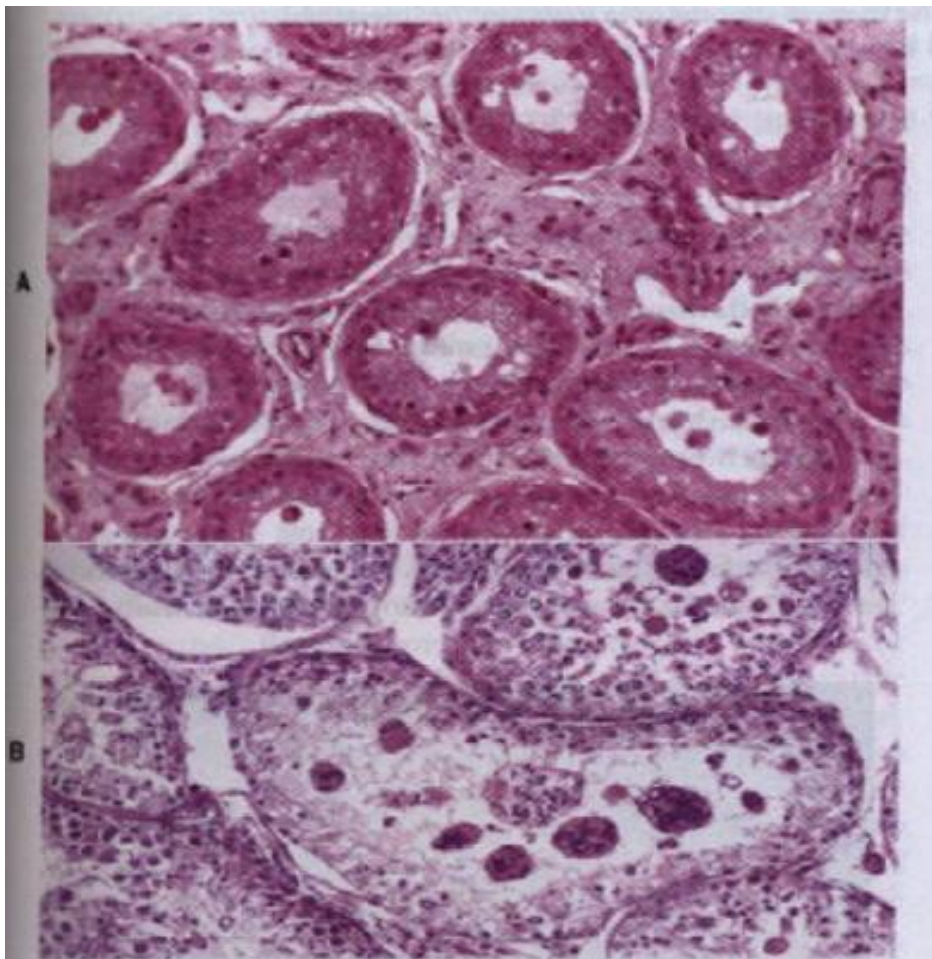


Fig. 19-16 Testicular degeneration, testis. A, Ram. There is interstitial fibrosis that separates the seminiferous tubules. Spermatogenic arrest at the spermatocyte stage, vacuolation of Sertoli cells, and a wavy basement membrane due to a reduction in tubular diameter are present. H&E stain. **B, Dog.** In addition to reduced spermatogenesis, there is formation of multinucleated spermatids (*centrally*) as a result of failure of spermatids to separate. This is a common change in testicular degeneration. (A and B, Courtesy Dr. R. A. Foster, Ontario Veterinary College, University of Guelph.)

- Early changes in the germ cells include failure of maturation of spermatozoa and degeneration of spermatids
- many spermatids are necrotic and others produce characteristic spermatidic multinuclear giant cells.
- When the degeneration is more advanced, the affected areas are more extensive and degenerative changes appear in the precursors of spermatids.
- Depending on the insult, there may be cytoplasmic vacuolation and nuclear pyknosis, or apoptotic bodies are seen.

- Progression of the changes results in loss of germinal cells, and eventually, loss of even the resistant Sertoli cells.
- Basement membrane thickening is a frequent finding, and as a result of shrinkage and collapse of tubules, it becomes wavy and buckled.
- The PAS stain clearly accentuates the basement membrane change.
- *Mineralization* is a common sign of degeneration, and it may involve all or part of one seminiferous tubule, or whole regions.

- **Inflammation of the testis and epididymis**
- ***Orchitis***
- Apart from bulls in areas endemic for *Brucella abortus* or tuberculosis, orchitis is a rare and sporadic disease in domesticated animals
- 3 major categories of orchitis; interstitial, intratubular or granulomatous, and necrotizing orchitis.

- **Interstitial orchitis**

- May not be recognized macroscopically
- histologically it is characterized by *lymphocytic infiltration of intertubular stroma, with concurrent or subsequent fibrosis.*

- **Intratubular or granulomatous orchitis**

- probably results from *ascending infection.*
- Macroscopically, solitary or multiple white-yellow foci of up to ~1 cm diameter are seen.

-

- Histologically, the tubule outline is retained in the affected area, but the seminiferous epithelium is obliterated and replaced by numerous macrophages and multinucleated giant cells that surround neutrophils and debris
- The pathogenesis of this granulomatous orchitis is comparable to sperm granuloma formation in the epididymis. Sertoli cell hyperplasia and mineralization may accompany these changes

- **Necrotic orchitis**

- Necrotizing orchitis is characteristic of *brucellosis* but may result from other infections, or conditions causing severe trauma or ischemia of the testis.
- Severe periorchitis may reduce blood supply to the testis so that it dies and becomes a necrotic mass encased within the markedly thickened tunics.

- Necrotic areas are dry, yellow, often laminated and slightly mineralized.
- Histologically: coagulative necrosis bordered by fibrosis and inflammatory cells.
- Abscessation and fistulation through the scrotum may accompany necrotizing or other forms of orchitis.

- **Epididymitis**

- *is one of the more common inflammatory diseases of the genitalia, but frequently it is diagnosed clinically as 'orchitis'.*
- Regardless of cause, damage to the epididymal duct is complicated by the formation of sperm granulomas and subsequent development of epididymitis (exception is prepubertal animals).
- **Lesion.**
- Acute stage with edematous enlargement followed by abscess and sperm granuloma formation, sometimes with perforation, periorchitis and peritonitis, and increasing fibrosis

- Macroscopically, an increased epididymal size and ***dissymmetry*** in shape is apparent (in unilateral / in comparison).
- Fibrinous and then fibrous adhesions may be present between affected epididymis and adjacent tunics.
- Consistency will depend on duration of inflammation and the development of sperm granulomas

- In chronic epididymitis, the marked increase in fibrous tissue both within the epididymis and between the epididymis and tunics results in atrophy of epithelial elements
- The epididymis becomes hard and nodular, perhaps enclosing dilated remnants of epididymal duct.
- Distinct hard “sperm stones”, the end products of spermiostasis, may be present within such ducts.
- Concurrent testicular atrophy will also result in the epididymis appearing disproportionately large in relation to the testis.

Histologically

- Affected epididymal ducts contain fibrin, neutrophils, and spermatozoa in various stages of disintegration
- Damaged epithelium, macrophages and multinucleate giant cells, many of which contain spermatozoa in ducts.
- Other features of sperm granuloma, with prominent interstitial accumulation of lymphocytes and plasma cells, become apparent

- Epithelial hyperplasia, with the development of intra-epithelial lumina.
- In chronic epididymitis, squamous metaplasia of epithelium may also occur in affected ducts in association with progressive fibrosis
- Hypertrophy of smooth muscle surrounding ducts.

- **Neoplasm**

- The three main testicular neoplasms are the Sertoli cell tumor, the interstitial (endocrine) cell tumor, and the seminoma
- The fourth most common, but still rare, is a mixed germ cell and stromal cell neoplasm.

- Lesions
- Most neoplasms cause enlargement of the testis.
- In general, seminomas are white, soft and usually bulge on cut section.
- Sertoli cell tumors induce fibrous tissue so they are white and are tough.
- The interstitial cell tumor is yellow, often contains areas of hemorrhage, and is soft.

Sertoli cell tumor

- Sertoli cell tumor is common in dogs, especially in cryptorchid testicles, but also has been reported in the stallion, ram, cat, and bull.
- Approximately 20 to 30% of dogs with Sertoli cell tumor manifest signs of hyperestrinism (feminization, gynecomastia, atrophy of the contralateral testicle, alopecia, and bone marrow atrophy)

Gross Morphology

- are very firm, discrete nodular or multinodular tumors that are well demarcated within the affected testicle.
- They can become quite large and cause
- The Sertoli cell tumor is much firmer than seminoma, interstitial cell tumor, and other common tumors of testicle

- On cut surface the tumor is white or gray, and it sometimes has tan or yellow areas of hemorrhage.
- Histological Features
- Sertoli cell tumors are subdivided on the basis of their **histological appearance** (intratubular and diffuse forms).
- Cells within the tumor:
 - variably resemble Sertoli cells that normally populate the seminiferous tubules
 - are arranged into islands or tubular structures that are separated by an abundant stroma of dense, mature fibrous connective tissue

- The tumor cells are elongate, with small, round to elongate nuclei and have either vacuolated or dense eosinophilic cytoplasm that frequently contains lipochrome pigment granules.
- In the intratubular form the tumor consists of well-formed tubules that are lined by multiple layers of neoplastic Sertoli cells.
- The tumor cells are arranged perpendicularly to the basement membrane.
- In contrast, the diffuse form lacks an orderly tubular architecture, and the neoplastic Sertoli cells are present in broad sheets or islands divided by dense fibrous stroma. The cells in such tumors are more irregular in their size and

- **Interstitial (Leydig) Cell Tumor**
- They are most common in the dog, but also occur in the bull, cat, and stallion
- **Gross Morphology**
 - The gross appearance of interstitial cell tumors is distinctive. They normally are small, frequently producing little or only subtle distortion of the affected testicle.
 - They are yellow/brown, soft, well circumscribed, and sharply delineated from the adjacent testicle.
 - They tend to bulge on cut surface, and some contain areas of hemorrhage or cysts.

- **Histological Features**

- The tumor cells are round to polyhedral, with cytoplasm that varies from finely granular to vacuolated, and containing prominent lipid accumulations.
- Nuclei typically are small, dark, and round, and mitotic figures are extremely unusual.
- The tumor cells can be arranged in ***solid sheets or an irregular acinar (glandular) pattern***, and they have a supporting fine stroma of connective tissue and blood vessels.
- Cysts lined by tumor cells are present in some tumors

- **Seminoma**

- Gross Morphology

- The tumor is soft or somewhat firm, but markedly less so than Sertoli cell tumor
- Has a homogeneous glistening gray/white appearance on cut surface.
- Some tumors include obvious areas of discoloration that reflect hemorrhage or necrosis-

Histological

- Seminomas are subdivided into intratubular and diffuse forms
- intratubular consists of aggregates of germ cells that fill the lumen of affected seminiferous tubules, replacing the normal lining of spermatogenic and Sertoli cells.
- The appearance of the tumor cells is highly characteristic:

- Mitotic figures are numerous and frequently bizarre.
- In the diffuse form, tumor cells are not confined to the seminiferous tubules; instead they form broad sheets.
- Necrosis of individual cells produces a “starry sky” effect within the neoplasm.

Prostate

→ Prostatitis

- Caused by E. coli, and Proteus invasion from the urethra or by blastomycosis (granulomatous type)
- Hyperplasia and metaplasia
- Common in old dogs
- They can cause hydronephrosis and constipation
- It is hormone related (removal of androgen by castration is therapeutic)
- Administration of estrogen can cause enlargement of the prostate
- Sertoli cell tumors can cause hyperplasia

→ Adenocarcinoma