Reproduction Block

Pathology Practicals

Objectives:

At the end of the practical classes, the medical students should be able to:

- Know the normal structure of the male and female genital systems.
- Acquire the knowledge about the gross appearances and histopathological features of the following diseases in the Male and Female genital systems and breast.

Contents:

1st Practical (Male Genital System):

- Testicular Atrophy.
- Seminoma of the testis.
- Embryonal carcinoma and teratoma of testis.
- Prostatic Hyperplasia.
- Adenocarcinoma of the prostate.

2nd Practical (Female Genital System):

- Uterine Leiomyomata.
- Endometrial hyperplasia and carcinoma.
- Endometriosis.
- Cervical dysplasia and carcinoma.
- Acute salpingitis.

3rd Practical (Ovarian & Breast diseases):

- Ovarian cysts and breast masses.
- Dermoid cysts (Teratoma) of the ovary.
- Breast diseases (Fibroadenoma, invasive ductal carcinoma and Paget's disease of the nipple)

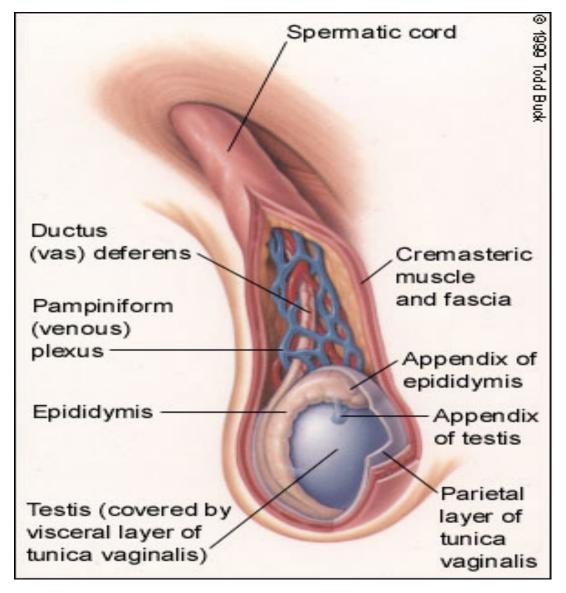
1st Practical Session

MALE GENITAL SYSTEM

TESTIS

Normal Anatomy and Histology

Diagram of Normal Testis

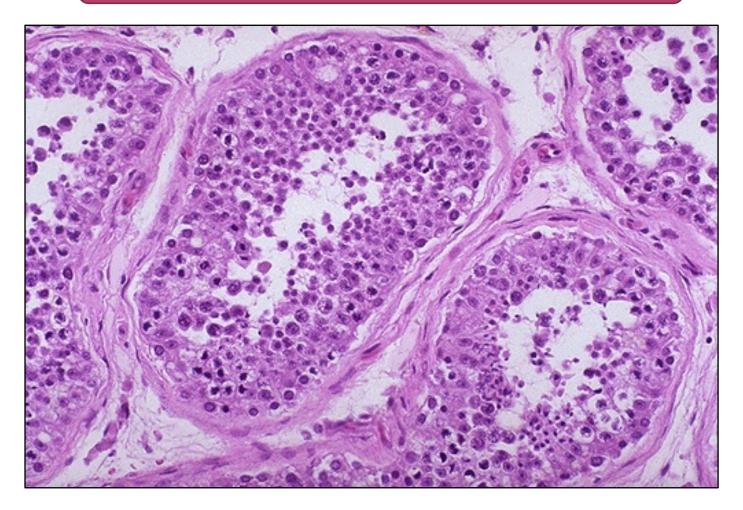


Anatomy of Normal Testis - Gross



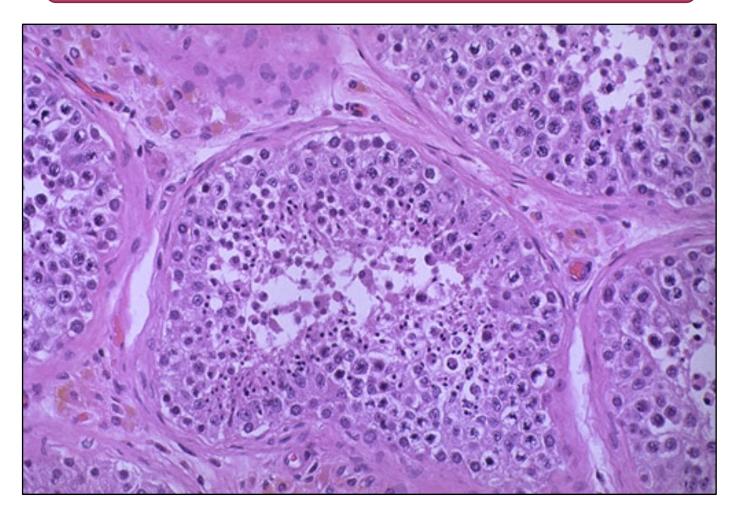
Here is a normal testis and adjacent structures. Identify the body of the testis, epididymis, and spermatic cord. Note the presence of two vestigial structures, the appendix testis and the appendix epididymis.

Histology of Normal Testis - LPF



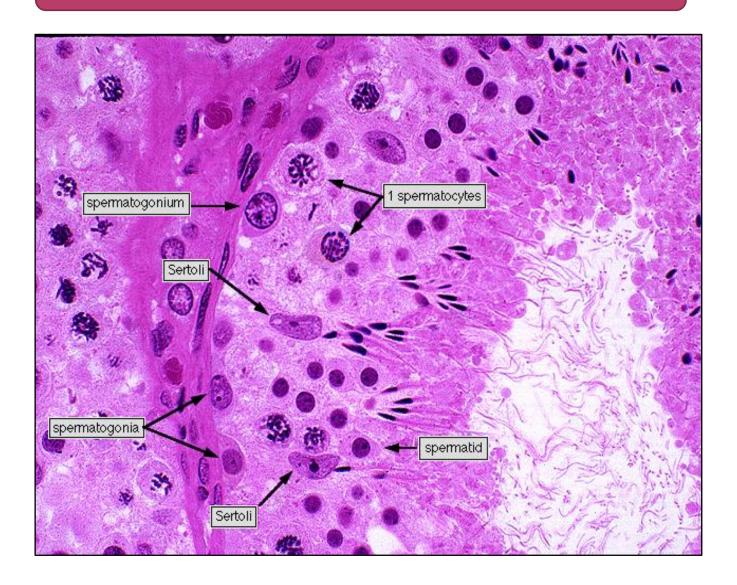
The seminiferous tubules have numerous germ cells. Sertoli cells are inconspicuous. Small dark oblong spermatozoa are seen in the center of the tubules.

Histology of Normal Testis - LPF



Pink Leyding cells are seen here in the interstitium. Note the pale golden brown pigment as well. There is active spermatogenesis.

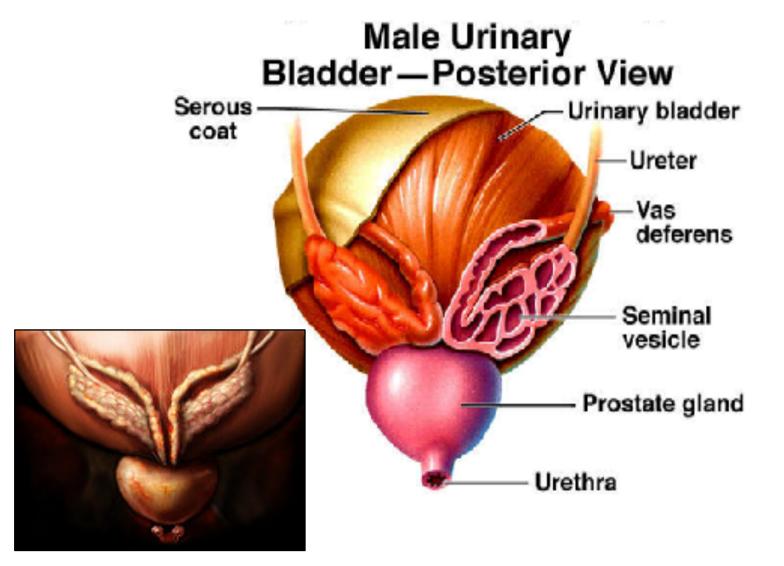
Histology of Normal Testis - HPF



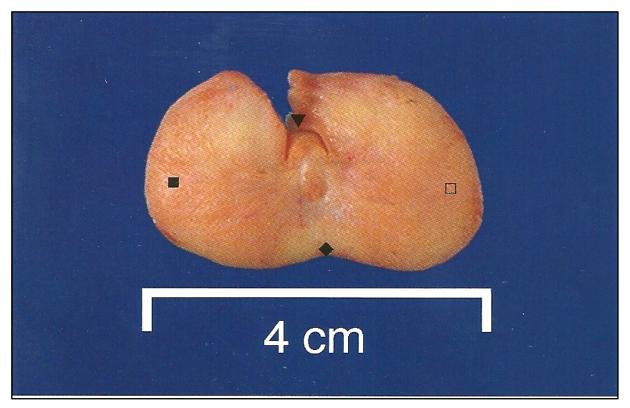
PROSTATE

Normal Anatomy and Histology

Diagram of Prostate and Seminal Vesicle



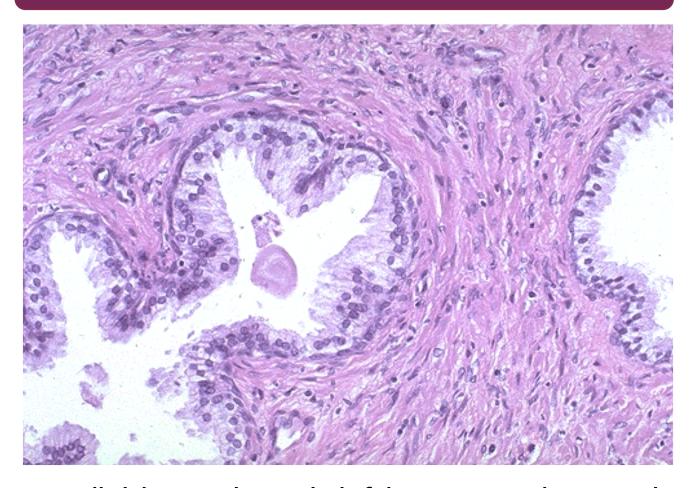
Normal Prostate - Gross



A normal prostate gland is about 3 to 4 cm in diameter.

This is an axial transverse section of a normal prostate. There is a central urethra(▼), at the depth of the cut made to open this prostate anteriorly at autopsy, with the left lateral lobe (■), the right lateral lobe (□), and the posterior lobe (♦). Consistency is uniform without nodularity.

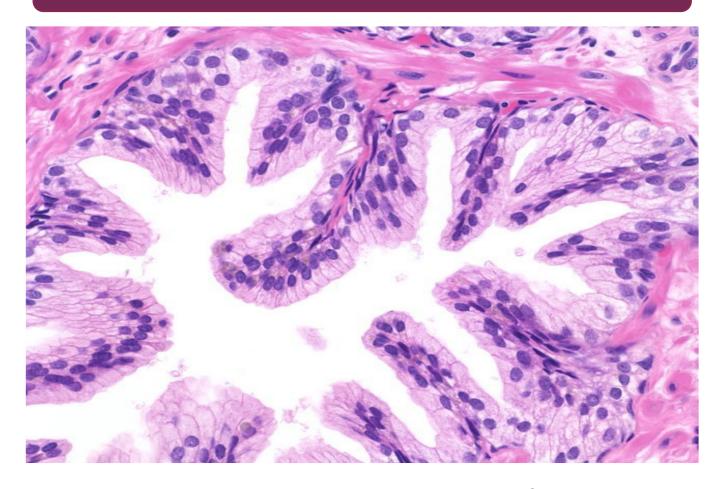
Normal Prostate Histology - LPF



A small pink concretion (typical of the corpora amylacea seen in benign prostatic glands) appears in the gland just to the left of center.

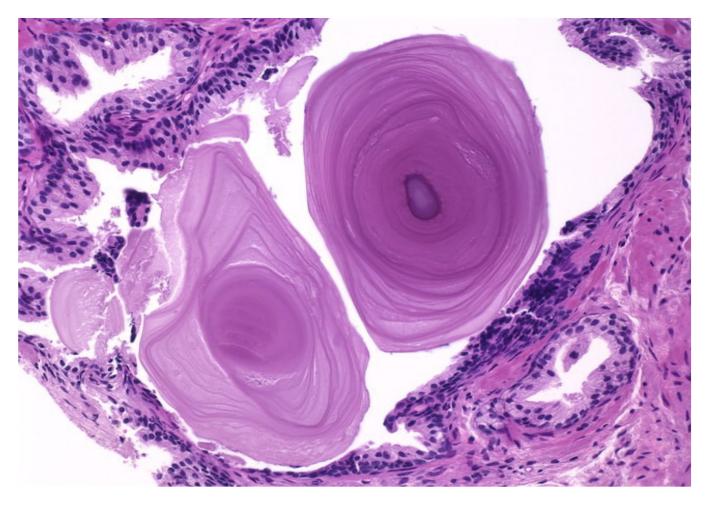
Note the well-differentiated glands with tall columnar epithelial lining cells. These cells do not have prominent nucleoli.

Normal Prostate Histology - HPF



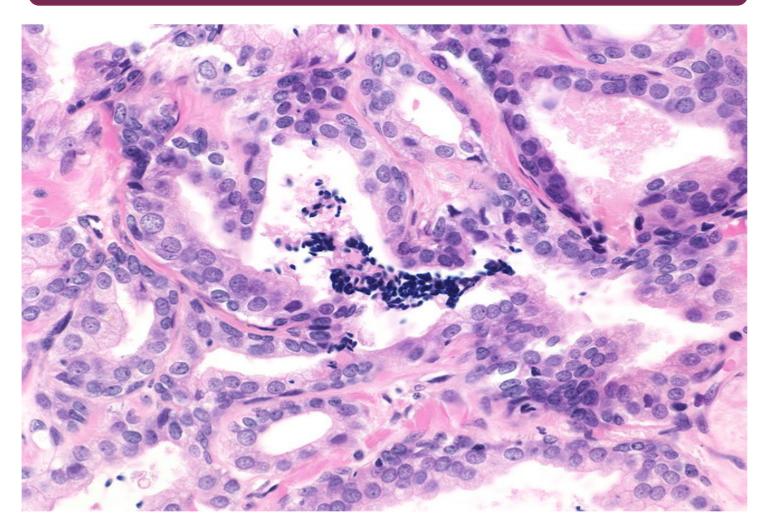
In this benign gland, the luminal contour shows tufts and papillary infoldings. The tall secretory epithelial cells have pale clear cytoplasm and uniform round or oval nuclei. Prominent nucleoli are not seen. Many basal cells can be identified

Corpora Amylacea in Prostate - HPF



Corpora amylacea are inspissated secretions that may have a lamellated appearance. Usually they are pink or purple in appearance. Sometimes they may be golden-brown

Sperms in Normal Prostate Biopsy – HPF

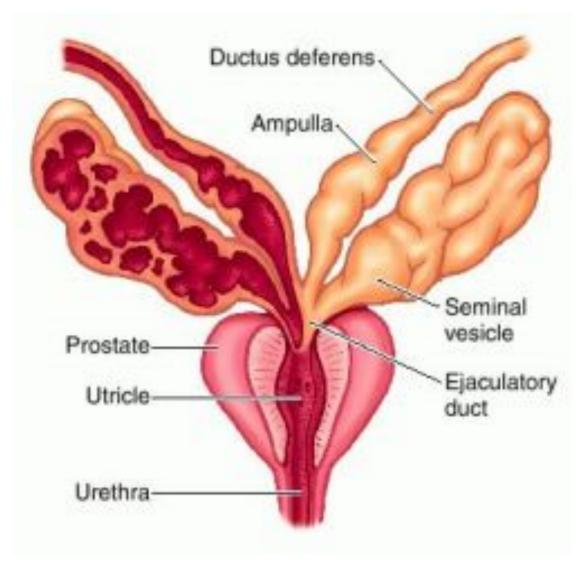


Spermatozoa are seen in approximately 1% of prostate needle biopsies (unpublished personal observation).

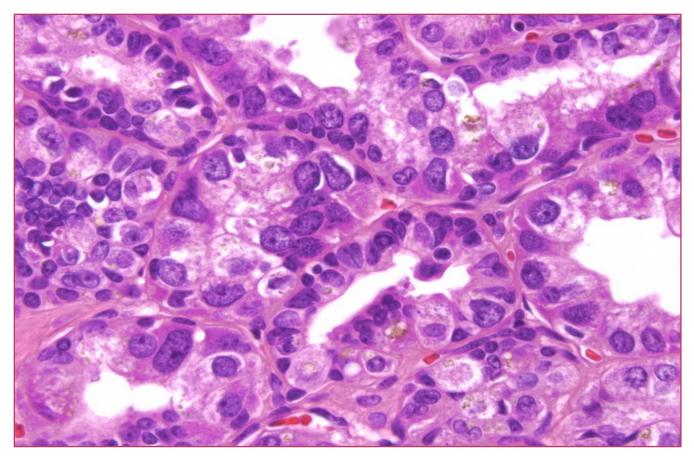
SEMINAL VESICLE

Normal Anatomy and Histology

Diagram of Seminal Vesicle



Normal Seminal Vesicle – HPF



Highly atypical cells are a normal finding in the seminal vesicles of about 80% of older men. The nuclei are large, irregular, hyperchromatic & show prominent nucleoli.

The atypia is degenerative and not observed in the seminal vesicles of young men

HISTOPATHOLOGY OF THE TESTIS

Testicular Atrophy

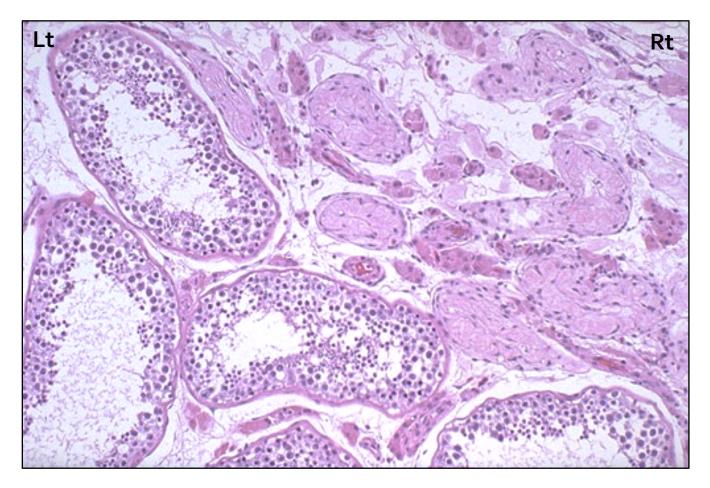
- refers to the shrinking of the actual testicles
- Symptoms before puberty: not developing secondary sexual characteristics, such as: facial hair pubic hair
- Symptoms after puberty : decreased sex drive, infertility and reduced muscle mass
 - It can be unilateral or bilateral

Normal vs Atrophied Testis - Gross



On the left is a normal testis. On the right is a testis that has undergone atrophy. Bilateral atrophy may occur with a variety of conditions including chronic alcoholism, hypopituitarism, atherosclerosis, chemotherapy or radiation, and severe prolonged illness.

Normal vs Atrophied Testis - Microscopic

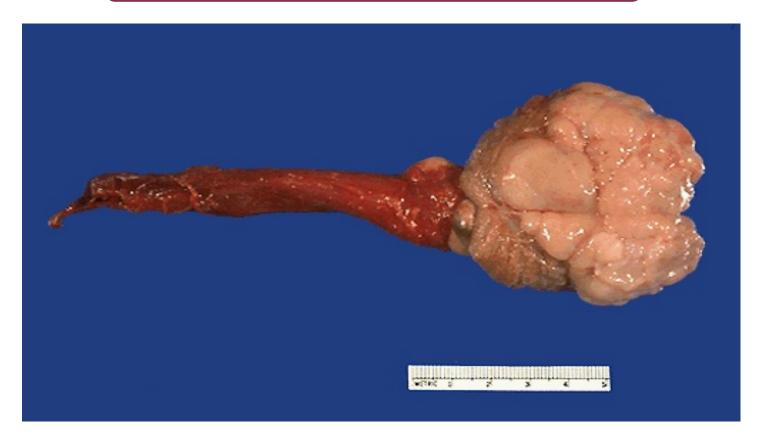


There is focal atrophy of tubules seen here to the upper right. The most common reason for this is probably childhood infection with the mumps virus, which produces a patchy orchitis

Seminoma of the Testis

- Is the most common pure germ cell tumor (GCT) of the testis, accounting for up to 50% of cases
- Mean age 40 years vs. 25 years for nonseminomatous germ cell tumors (NSGCT)

Seminoma of the Testis - Gross



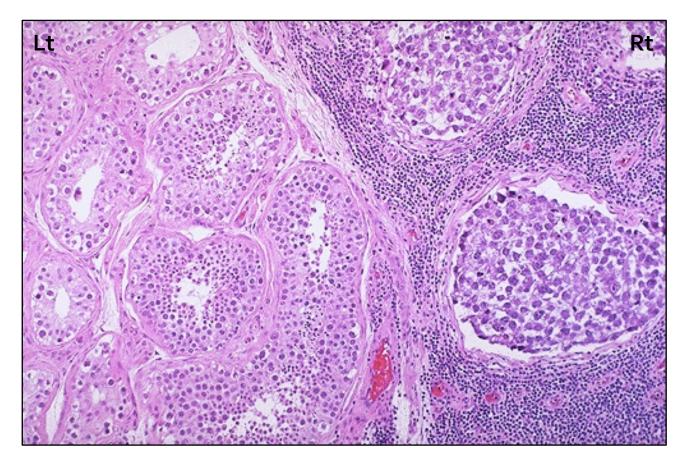
Here is a Seminoma that is larger yet. Normal testis appears to the left of the mass. Pale and lobulated testicular mass with bulging and potato like cut surface with attached and congested spermatic cord. Most important risk factor is cryptorchidism (undescended testicle).

Seminoma of the Testis - Gross



Seminoma: Germ cell neoplasms are the most common types of testicular neoplasm. They often have several histologic components: seminoma, embryonal carcinoma, teratoma & choriocarcinoma.

Seminoma vs Normal Testis - LPF

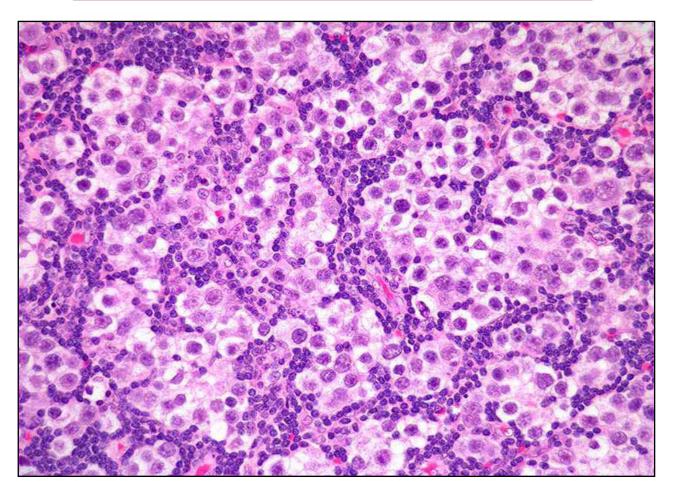


Normal testis appears at the left, and seminoma is present at the right.

Note the difference in size and staining quality of the neoplastic nests of cells compared to normal germ cells.

Note the lymphoid stroma between the nests of seminoma.

Seminoma of the Testis - HPF



Seminoma; a malignant tumour consisting of sheets of uniform malignant germ cells showing large vesicular nuclei, prominent nucleoli and clear cytoplasm.

Usually minimal mitotic figures

Embryonal Carcinoma & Teratoma of the Testis

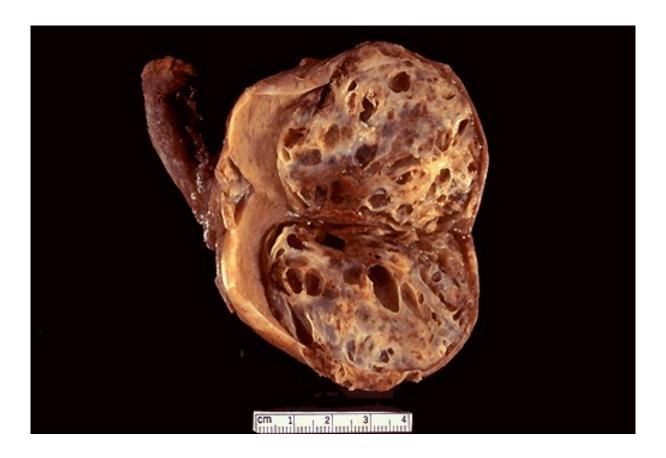
Embryonal Carcinoma

- Malignant germ cell tumor composed of primitive epithelial tumor cells
- Age at presentation: 30's
- Most commonly part of mixed germ cell tumor

Teratoma of the Testis

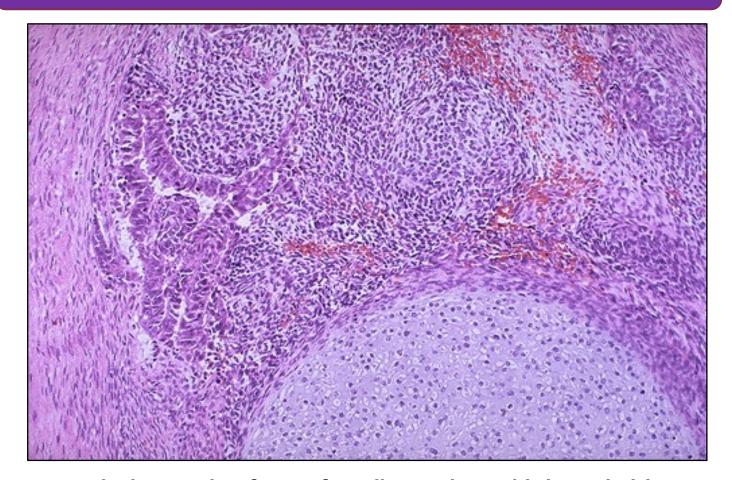
 Teratoma is second most common germ cell tumor type in pediatrics, after yolk sac tumor

Embryonal Carcinoma & Teratoma - Gross



Here is an embryonal carcinoma mixed with teratoma in which islands of bluish white cartilage from the teratoma component are more prominent. A rim of normal brown testis appears at the left.

Embryonal Carcinoma & Teratoma - HPF



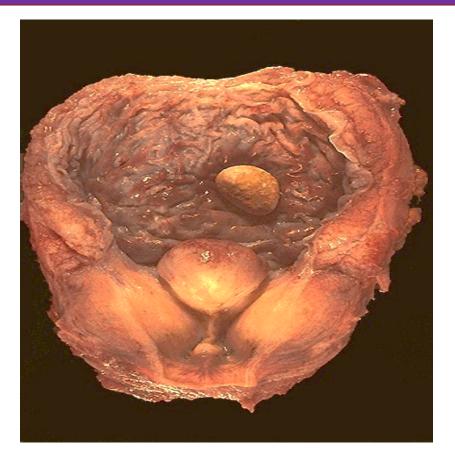
At the bottom is a focus of cartilage. Above this is a primitive mesenchymal stroma and to the left a focus of primitive cells most characteristic for embryonal carcinoma. This is embryonal carcinoma mixed with teratoma.

PROSTATE

Prostatic Hyperplasia

- Also known as benign prostatic hypertrophy (BPH)
- Present in 20% of men at age 40, 50% at age 50 and 70% at age 60

Prostatic Hyperplasia - Gross



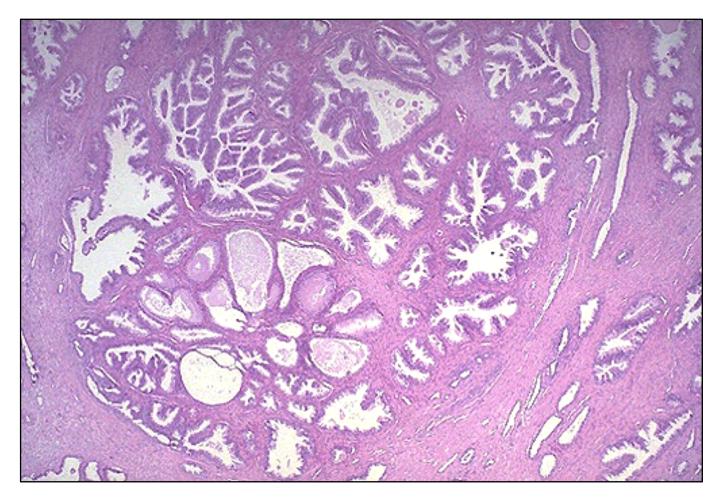
Enlarged lateral lobes, and median lobe that obstructs the prostatic urethra that led to obstruction with bladder hypertrophy, as evidenced by the prominent trabeculation of the bladder mucosa. Obstruction with stasis also led to the formation of the yellow-brown calculus (stone).

Prostatic Hyperplasia - Gross



Here is another example of benign prostatic hyperplasia.
Nodules appear mainly in the lateral lobes. Such an enlarged prostate can obstruct urinary outflow from the bladder and lead to an obstructive uropathy

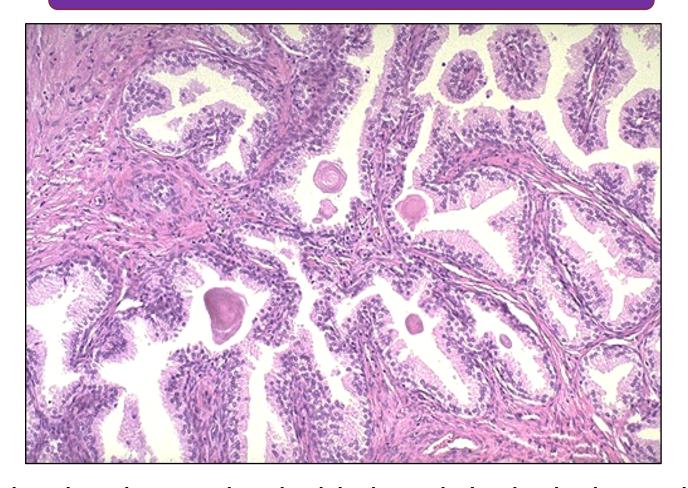
Prostatic Hyperplasia - LPF



Microscopically, benign prostatic hyperplasia can involve both glands and stroma, though the former is usually more prominent.

Here, a large hyperplastic nodule of glands is seen

Prostatic Hyperplasia - HPF



The enlarged prostate has glandular hyperplasia. The glands are well-differentiated and still have some intervening stroma. The small laminated pink concretions within the glandular lumens are known as corpora amylacea

Adenocarcinoma of Prostate

Clinical features

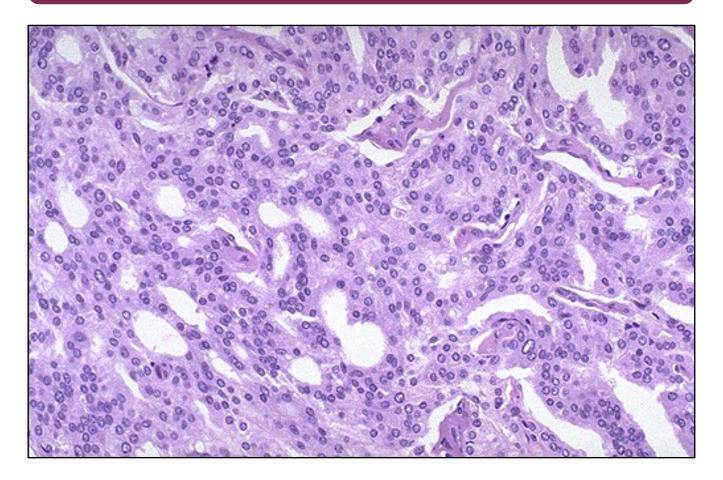
Prostate cancer is detected by digital rectal exam (DRE), transurethral ultrasound, or elevated PSA (either above 4 ng/dL or increasing over time)

Adenocarcinoma of the Prostate - Gross



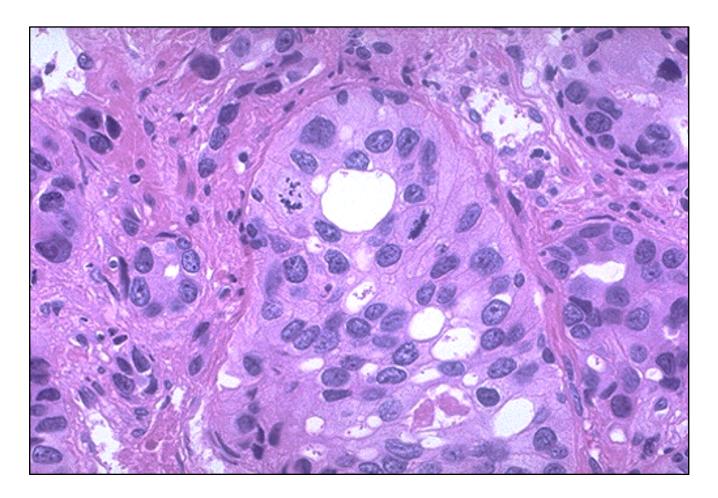
These sections through a prostate removed via radical prostatectomy reveal irregular yellowish nodules, mostly in the posterior portion (seen here superiorly). This proved to be prostatic adenocarcinoma

Adenocarcinoma of the Prostate - MPF



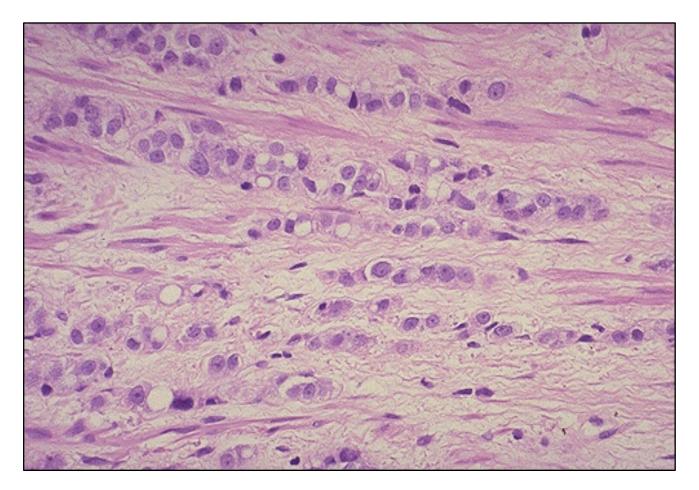
At high magnification, the neoplastic glands of prostatic adenocarcinoma are still recognizable as glands, but there is no intervening stroma and the nuclei are hyperchromatic.

Adenocarcinoma of the Prostate - HPF



At high magnification, this poorly differentiated prostatic adenocarcinoma demonstrates cells with nucleoli and mitotic figures.

Adenocarcinoma of the Prostate - HPF



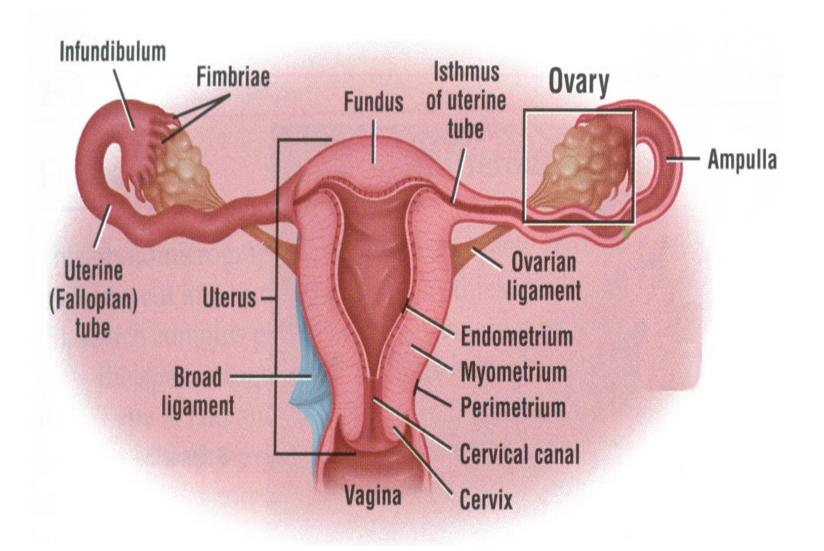
This adenocarcinoma of prostate is so poorly differentiated that no glandular structure is recognizable, only cells infiltrating in rows.

2nd Practical Session

FEMALE GENITAL SYSTEM



Female Reproductive System - Diagram



Female Reproductive System - Gross



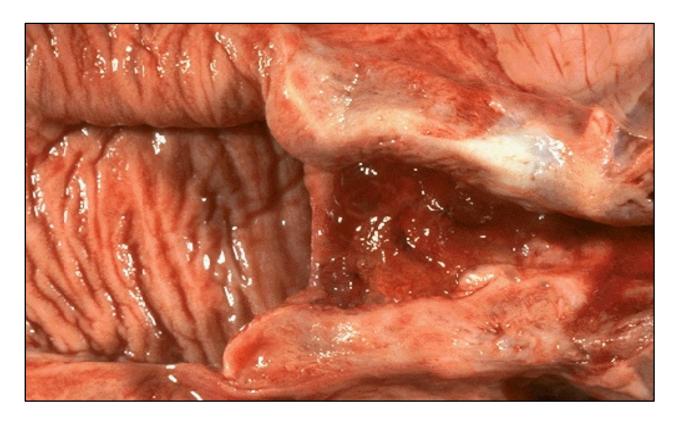
Uterus with Cervix, Ovaries and Fallopian Tubes

Normal Uterine Cervix - Gross



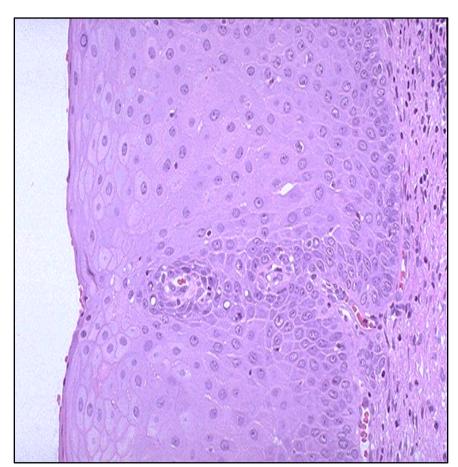
Normal cervix with a smooth, glistening mucosal surface. There is a small rim of vaginal cuff from this hysterectomy specimen. The cervical os is small and round, typical for a nulliparous woman. The os will have a fish-mouth shape after one or more pregnancies

Normal Vagina & Cervix - Gross Cut section

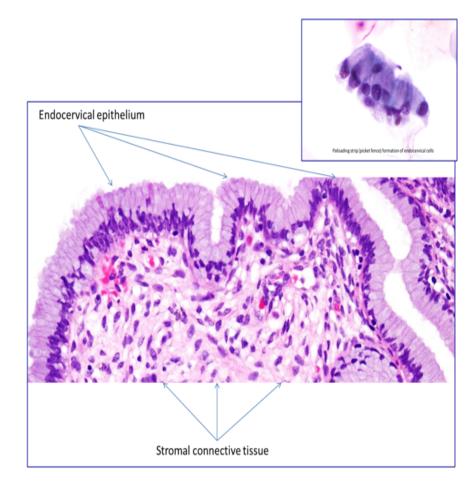


The normal adult vaginal mucosa with a wrinkled appearance that is seen in women of reproductive years appears at the left. The cervix has been opened to reveal an endocervical canal leading to the lower uterine segment at the right that has an erythematous appearance extending to the cervical os consistent with chronic inflammation.

Normal Cervical Mucosa - HPF



Ectocervix lined by non-keratinizing squamous epithelium. The squamous cells show maturation from the basal layer to the surface



Endocervix lined by simple columnar epithelium.
Squamocolumnar zone; zone of junction



Uterine Leiomyomata

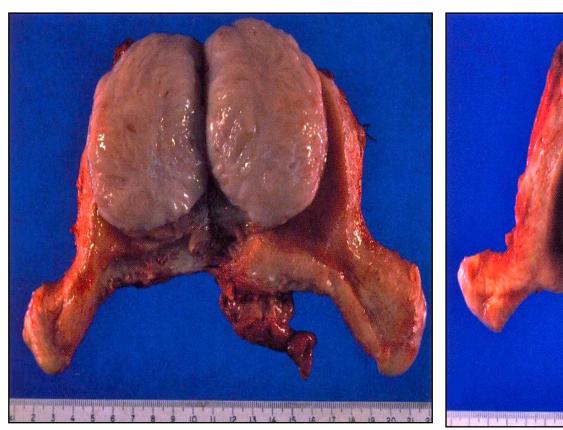
- Uterine leiomyoma is the most common tumor found in women of reproductive age group
- Also called fibroid, myofibroma, fibromyoma, leiomyofibroma, fibroma, myoma
- The clinical symptoms and severity usually depend upon the size, position, and number of fibroids present.
- Typically asymptomatic, but up to 30% of women experience abnormal uterine bleeding or lower abdomen pressure related symptoms

Multiple Uterine Leiomyomata - Gross



Smooth muscle tumors of the uterus are often multiple.
Seen here are submucosal, intramural, and subserosal leiomyomata of the uterus.

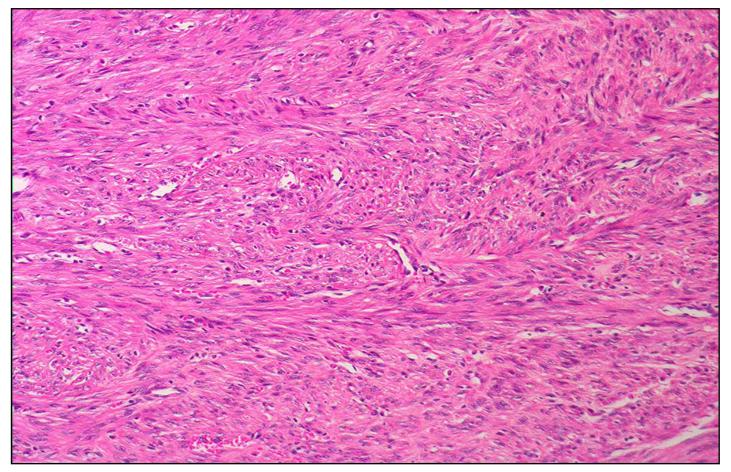
Multiple Uterine Leiomyomata - Gross





A well demarcated tumour mass in the muscle coat of uterus without a definite capsule.

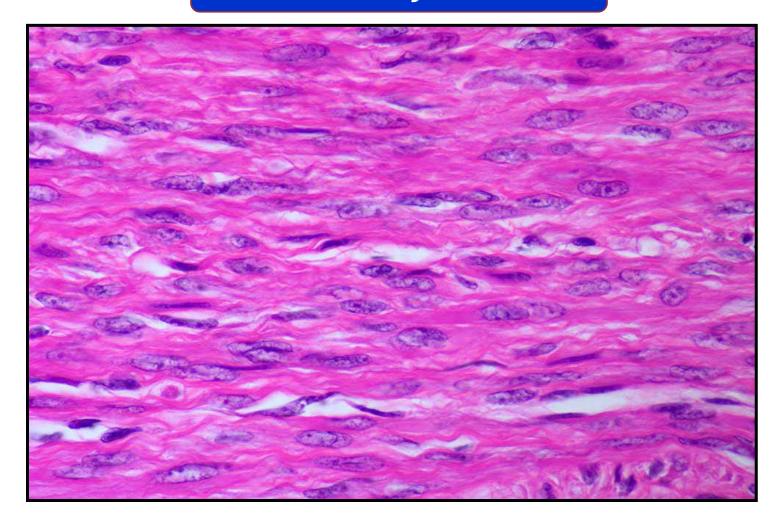
Uterine Leiomyoma – LPF



Tumour consists of interlacing (Whorled) bundles of smooth muscle separated by well vascularized connective tissue and fibrous tissue.

The muscle cells are spindle shaped with elongated nuclei and eosinophilic cytoplasm.

Uterine Leiomyoma – HPF

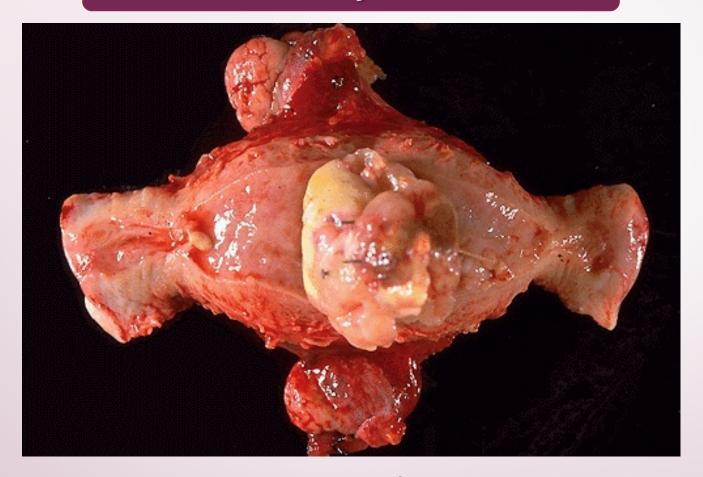


The muscle cells are spindle shaped with elongated nuclei and eosinophilic cytoplasm
Usually less than 5 mitotic figures per 10 high power fields in most mitotically active area, no significant atypia

Uterine leiomyosarcoma

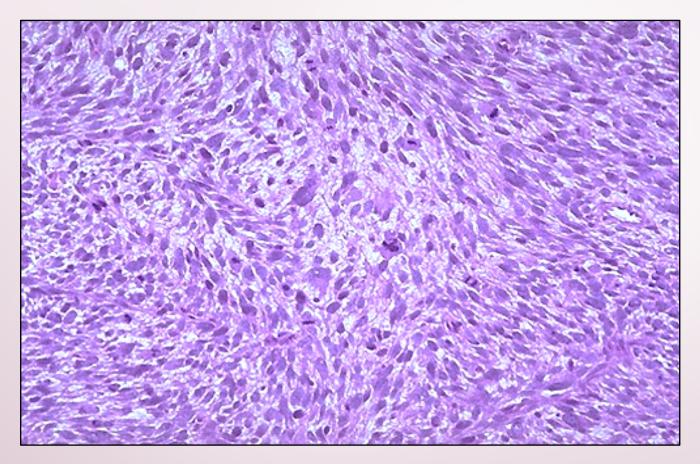
- 1% 2% of uterine malignancies, but most common uterine sarcoma
- The malignant transformation of a uterine leiomyoma is still debated and, if it occurs, it is very rare
- Very aggressive even when confined to uterus

Endometrial Leiomyosarcoma - Gross



This is a leiomyosarcoma protruding from myometrium into the endometrial cavity of this uterus that has been opened laterally so that the halves of the cervix appear at right and left. Fallopian tubes and ovaries project from top and bottom.

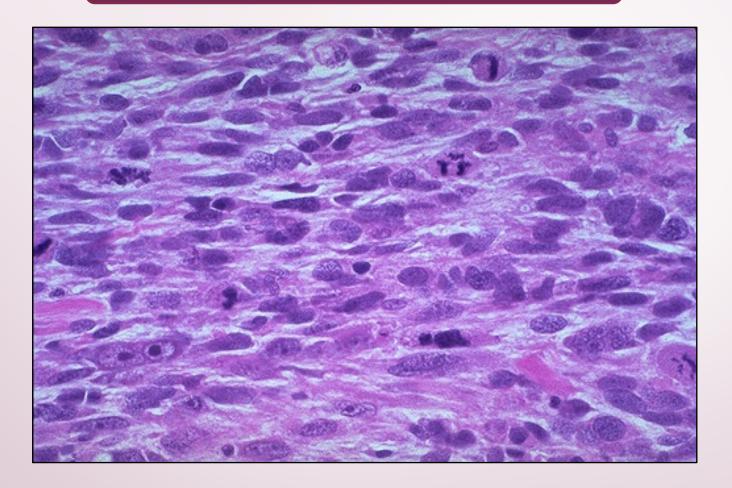
Endometrial Leiomyosarcoma - LPF



Here is the microscopic appearance of a leiomyosarcoma. It is much more cellular and the cells have much more pleomorphism and hyperchromatism than the benign leiomyoma.

An irregular mitosis is seen in the center

Endometrial Leiomyosarcoma - HPF



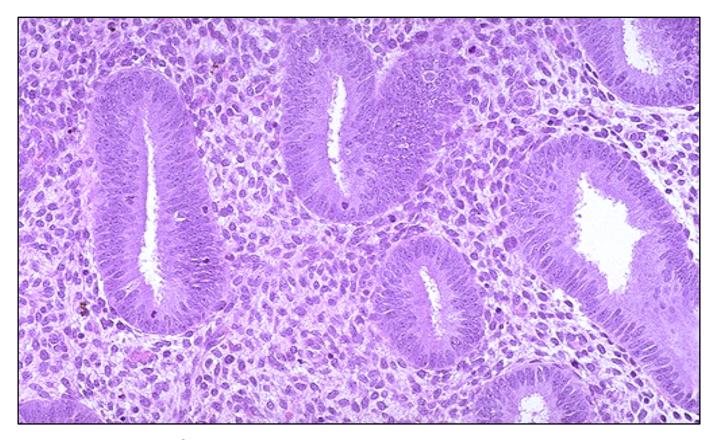
As with sarcomas in general, leiomyosarcomas have spindle cells.

Several mitoses are seen here (10+ mitotic figures per 10 high power fields (HPF)), just in this one high power field.

Endometrial Hyperplasia

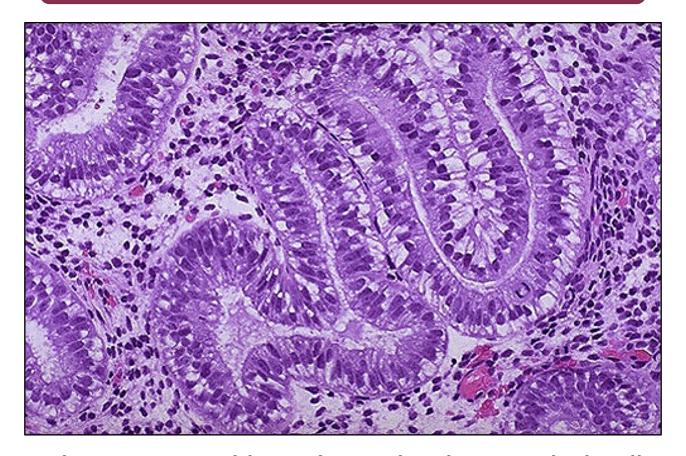
- Proliferation of endometrial glands with an increase in the gland to stroma ratio compared to proliferative endometrium (> 1:1, glands represent more than 50% of the surface area)
- Endometrial hyperplasia usually results with conditions of prolonged estrogen excess

Normal Proliferative Endometrium



Normal proliferative endometrium in the menstrual cycle. The proliferative phase is the variable part of the cycle. In this phase, tubular glands with columnar cells and surrounding dense stroma are proliferating to build up the endometrium following shedding with previous menstruation.

Early Secretory Endometrium



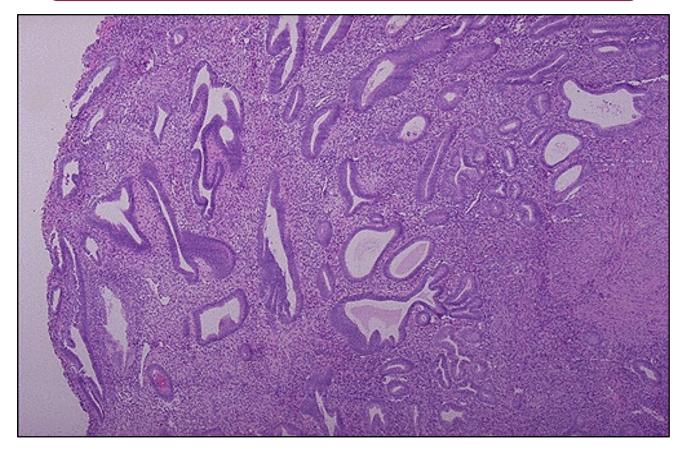
The appearance with prominent subnuclear vacuoles in cells forming the glands is consistent with post-ovulatory day 2 of luteal phase. The histologic changes following ovulation are quite constant over the 14 days to menstruation and can be utilized to date the endometrium.

Endometrial Hyperplasia - Gross



The endometrial cavity is opened to reveal lush fronds of hyperplastic endometrium. Endometrial hyperplasia usually results with conditions of prolonged estrogen excess and can lead to metrorrhagia (uterine bleeding at irregular intervals), menorrhagia (excessive bleeding with menstrual periods), or menometrorrhagia.

Endometrial Hyperplasia - LPF



This is endometrial cystic hyperplasia in which the amount of endometrium is abnormally increased and not cycling as it should. The glands are enlarged and irregular with columnar cells that have some atypia. Simple endometrial hyperplasias can cause bleeding, but are not thought to be premalignant.

Endometrial Carcinoma

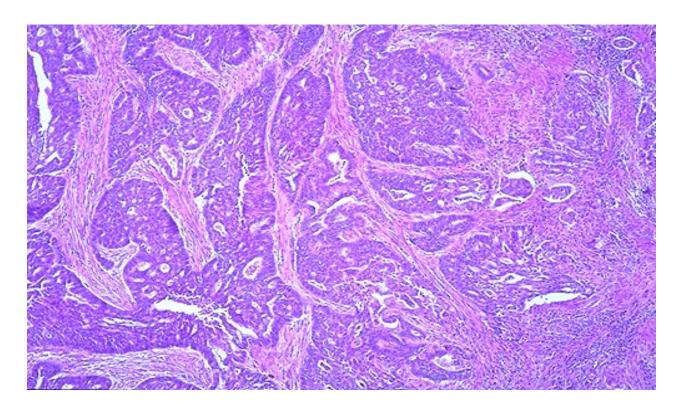
- Most common gynecologic malignancy in US
- 80% arise in postmenopausal women, and manifest with symptoms of bleeding

Endometrial Adenocarcinoma - Gross



This uterus is not enlarged, but there is an irregular mass in the upper fundus that proved to be endometrial adenocarcinoma on biopsy. Such carcinomas are more likely to occur in postmenopausal women. Thus, any postmenopausal bleeding should make you suspect that this lesion may be present.

Endometrial Adenocarcinoma - LPF

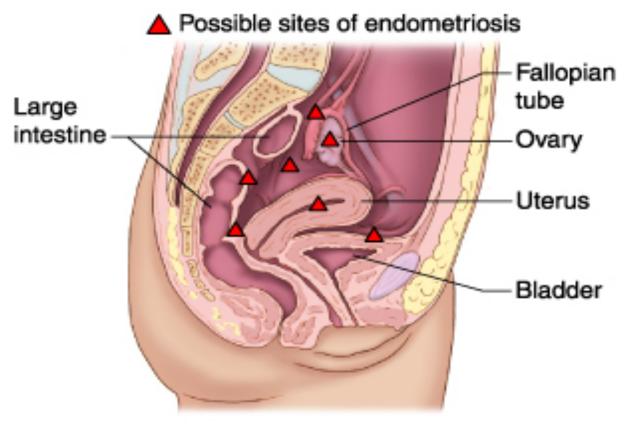


This is an endometrial adenocarcinoma which can be seen invading into the smooth muscle bundles of the myometrial wall of the uterus. This neoplasm has a higher stage than a neoplasm that is just confined to the endometrium

ENDOMETRIOSIS

• Incidence of endometriosis is estimated at 10% of women of reproductive age

Endometriosis sites - Diagram



Endometriosis, a chronic noncancerous disorder of the female reproductive system, develops when the endometrium grows outside the uterus.

Common sites for endometriosis include ovaries, fallopian tubes, external genitalia (vulva), ligaments supporting the uterus, intestine, bladder, cervix, and vagina.

Endometriosis - Gross



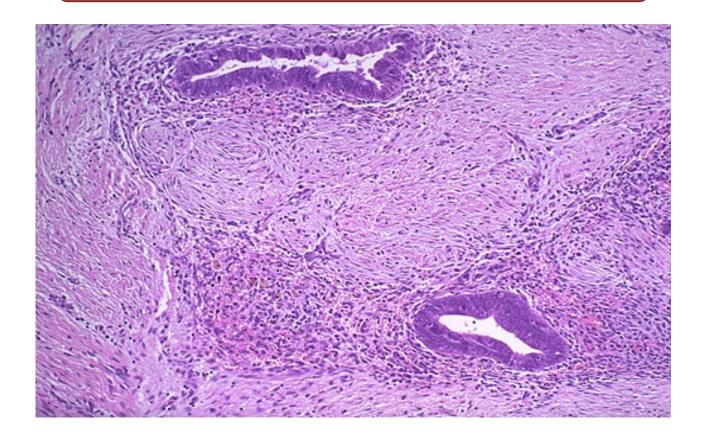
Grossly, in areas of endometriosis the blood is darker and gives the small foci of endometriosis the gross appearance of "powder burns". Small foci are seen here just under the serosa of the posterior uterus in the pouch of Douglas.

Endometriosis - Gross



Upon closer view, these five small areas of endometriosis have a reddish-brown to bluish appearance. Typical locations for endometriosis may include: ovaries, uterine ligaments, rectovaginal septum, pelvic peritoneum, and laparotomy scars

Endometriosis - HPF Microscopy



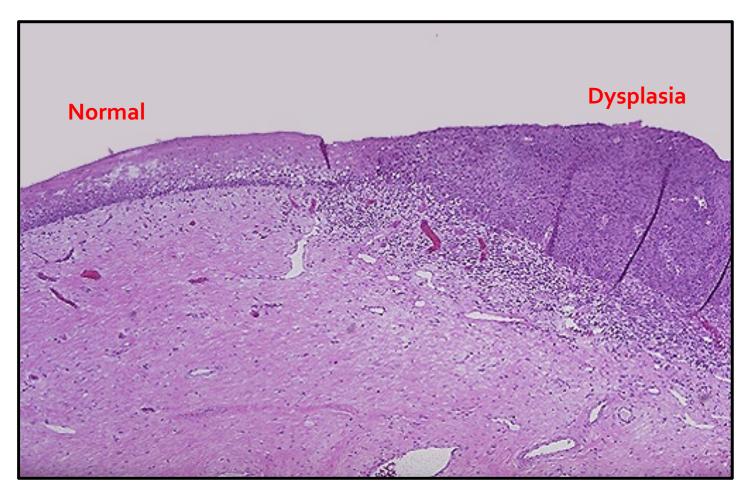
Endometrial glands along with stroma are seen at high magnification in the smooth muscle wall of the colon.

Endometriosis is symptomatic during reproductive years when patients may present with dysmenorrhea, pelvic pain, and infertility



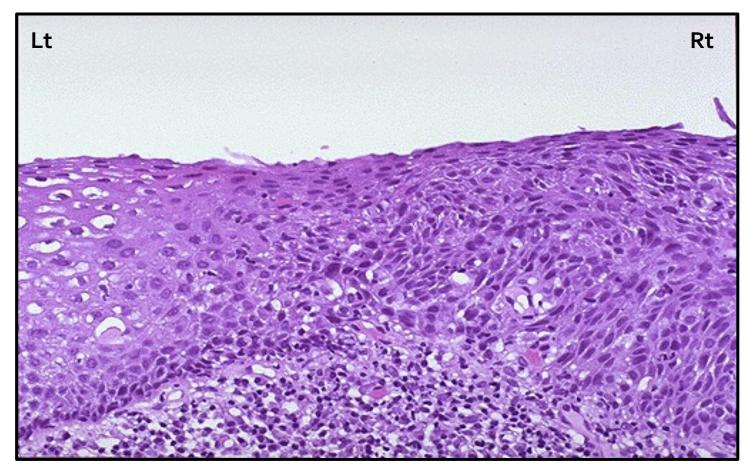
Cervical Dysplasia & Cervical Carcinoma

Normal and Dysplastic Cervical Squamous Epithelium



The normal cervical squamous epithelium at the left transforms to dysplastic changes on the right with underlying chronic inflammation

Endocervical Squamous Dysplasia



Cervical squamous dysplasia is seen at medium magnification, extending from the center to the right. The epithelium is normal at the left.

Note how the dysplastic cell nuclei at the right are larger and darker, and the dysplastic cells have a disorderly arrangement

Cervical Squamous Cell Carcinoma

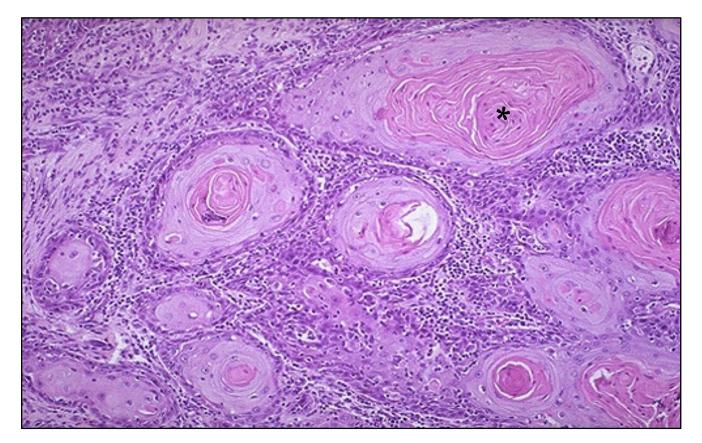




This is the gross appearance of a cervical squamous cell carcinoma that is still limited to the cervix (stage I).

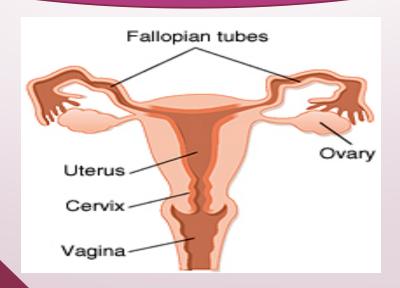
The tumor is a fungating red to tan to yellow mass.

Cervical Squamous Cell Carcinoma - HPF

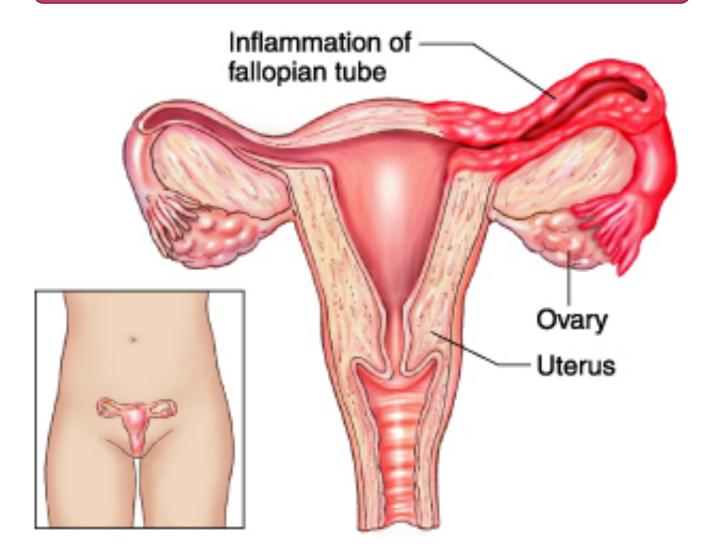


At high magnification, nests of neoplastic squamous cells are invaded through a chronically inflamed stroma. This cancer is well-differentiated, as evidenced by keratin pearls (*) within nests of tumor cells. However, most cervical squamous carcinomas are non-keratinizing.

FALLOPIAN TUBES



Normal vs Inflamed Fallopian Tube

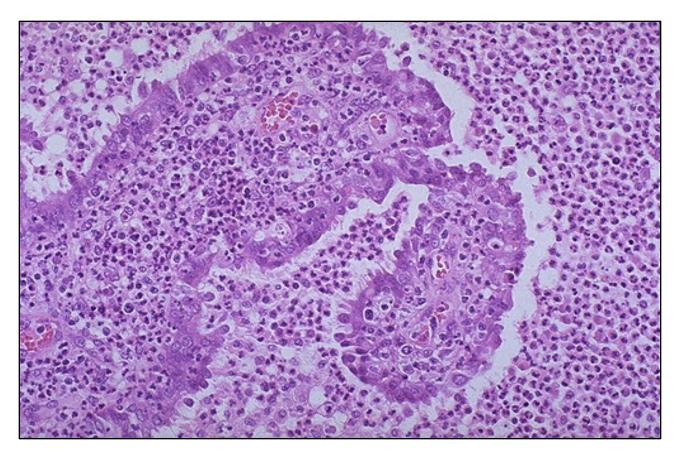


Acute Salpingitis - Gross



Acute salpingitis: Excised congested swollen fallopian tube with hemorrhagic patches

Acute Salpingitis - Microscopic



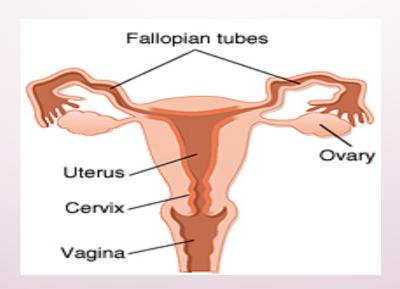
A remnant of tubal epithelium is seen here surrounded and infiltrated by numerous neutrophils. This is acute salpingitis.

Neisseria gonorrheae was cultured.

3RD PRACTICAL SESSION

Ovarian Cysts and Breast Masses

OVARIES





Benign Ovarian Cyst - Gross



Here is a benign cyst in an ovary. This is probably a follicular cyst. Occasionally such cysts may reach several centimeters in size and, if they rupture, can cause abdominal pain.

Serous Cystadenoma of the Ovary



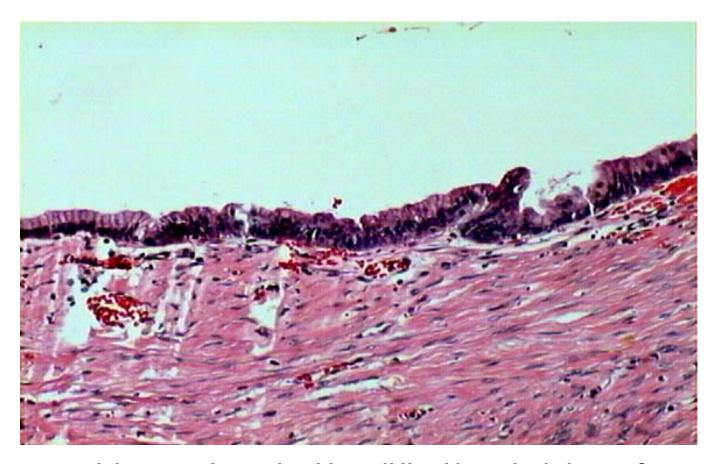
Benign epithelial tumors of the ovary can reach massive proportions. The serous cystadenoma seen here fills a surgical pan and dwarfs the 4 cm ruler.

Serous Cystadenoma of the Ovary - LPF



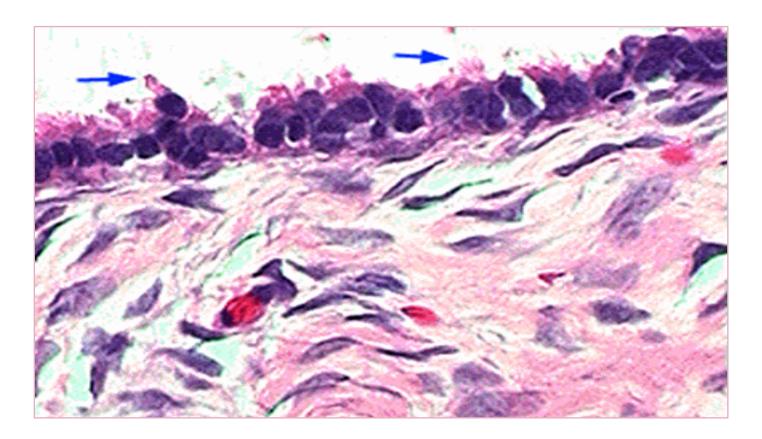
Microscopy shows the thin wall lined by a single layer of mucin-secreting columnar cells with a basally-placed spherical small nucleus

Serous Cystadenoma of the Ovary - HPF



High power shows the thin wall lined by a single layer of mucin-secreting columnar cells with a basally-placed spherical small nucleus

Serous Cystadenoma of the Ovary - HPF



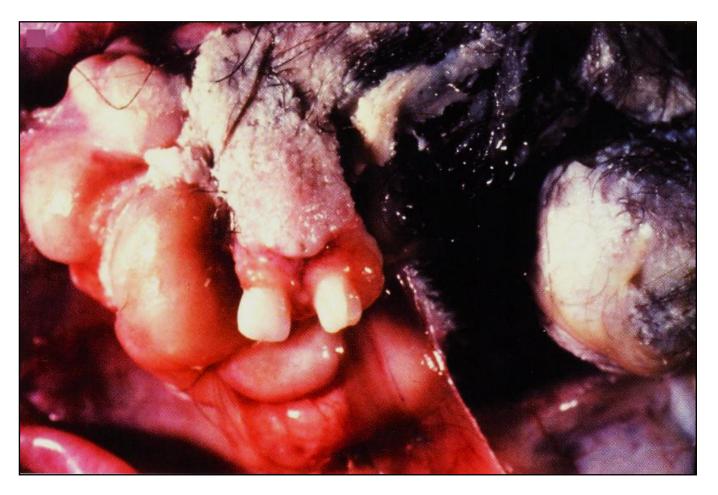
- The blue arrows point to cilia.
- The cells have dark nuclei without nucleoli or mitoses.
- The cytoplasm is eosinophlic and ciliated like tubal epithelium.

• The stroma contains spindly fibroblasts

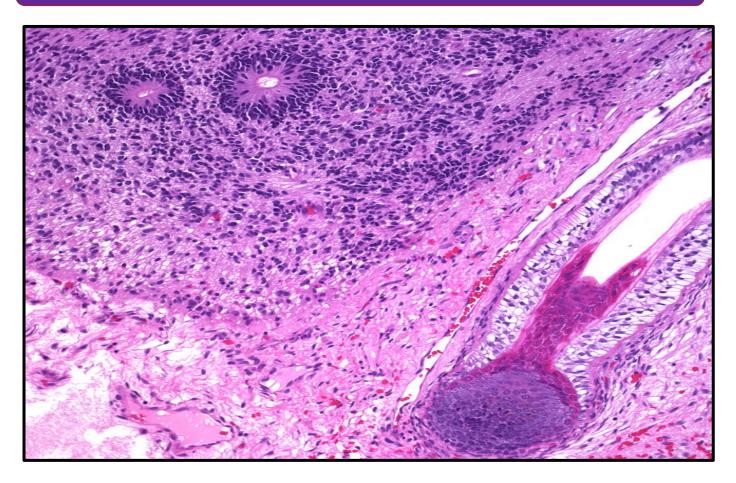




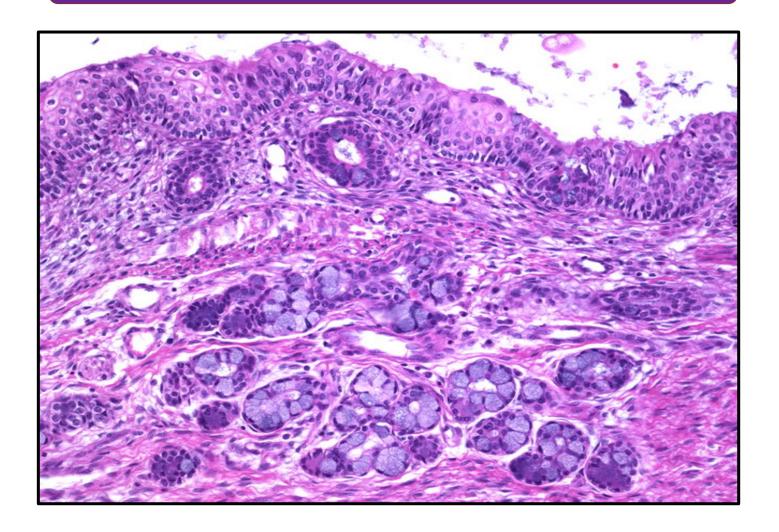
This 4.0 cm dermoid cyst is filled with greasy material (keratin and sebaceous secretions) and shows tufts of hair. The rounded solid area at the bottom is called Rokitansky's protruberance. Microscopically, it also showed foci of neural tissue.



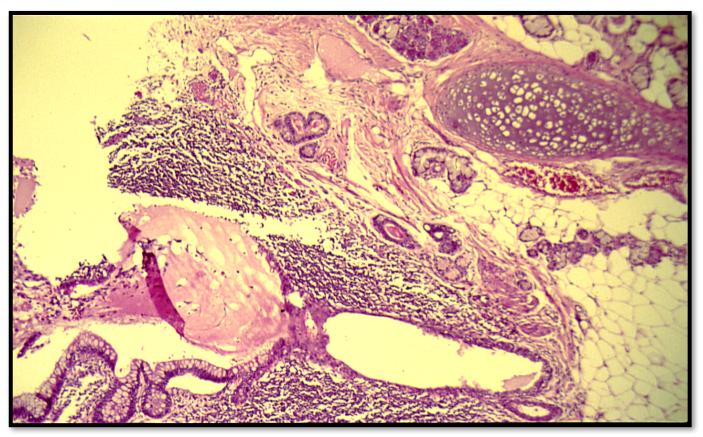
The picture shows cyst containing teeth and hairs with nail tissue and skin. It may be complicated by torsion infarction, struma ovarii and immature teratoma.



Ovarian teratoma showing neuroepithelial tubules and rosettes (immature component) adjacent to a hair follicle (mature component). They consist of epidermis, hair follicles, sweat and sebaceous glands and neuroectodermal derivatives



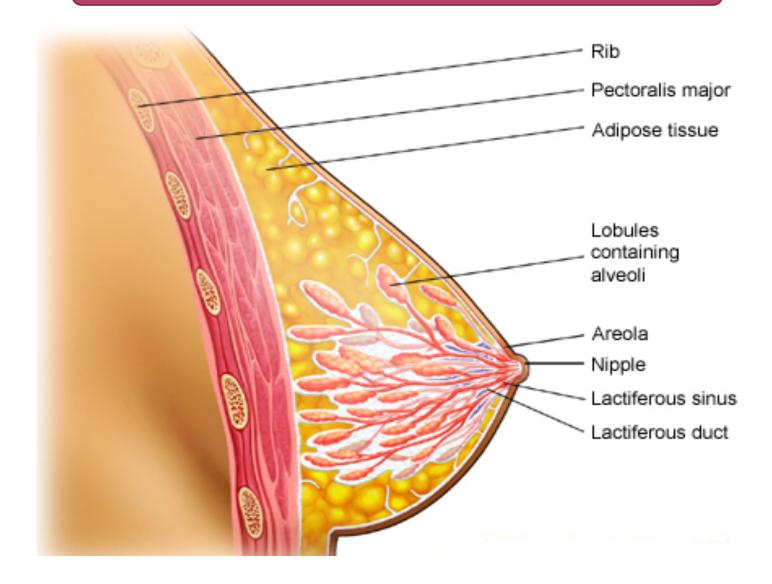
This image shows skin and mucinous glands in a mature solid teratoma of the ovary



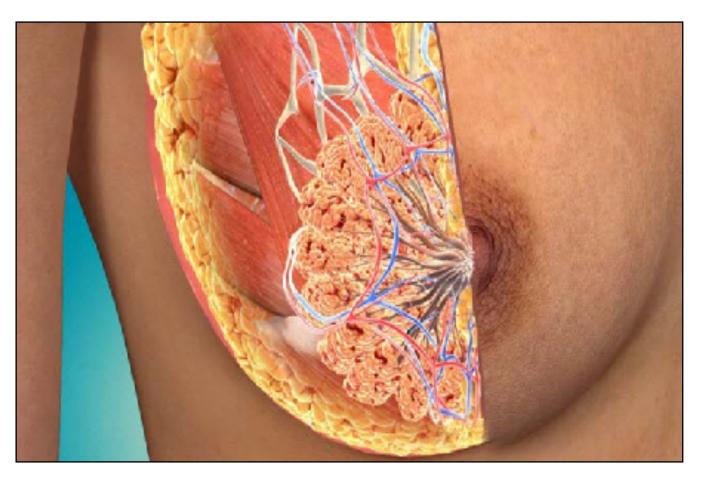
Stratified Squamous epithelium with underlying sweat glands, sebaceous glands, hair follicles, columnar ciliated epithelium, mucous and serous glands and structures from other germ layers such as bone and cartilage, lymphoid tissue, smooth muscle and brain tissue containing neurons and glial cells

Breast Diseases

Diagram of the Normal Breast

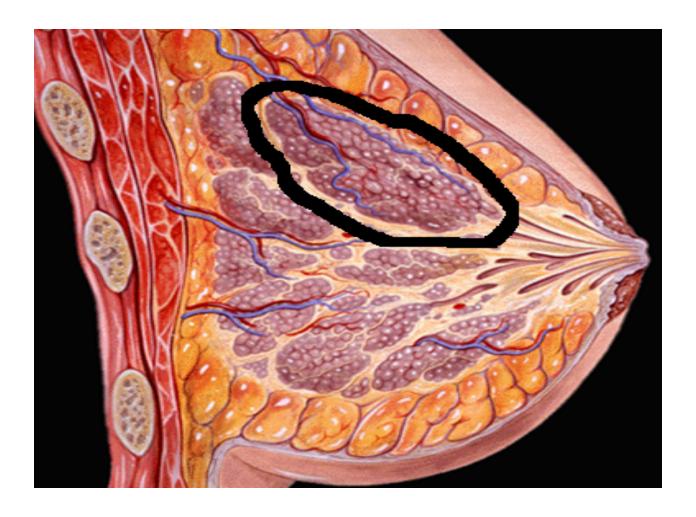


Anatomy of Normal Female Breast



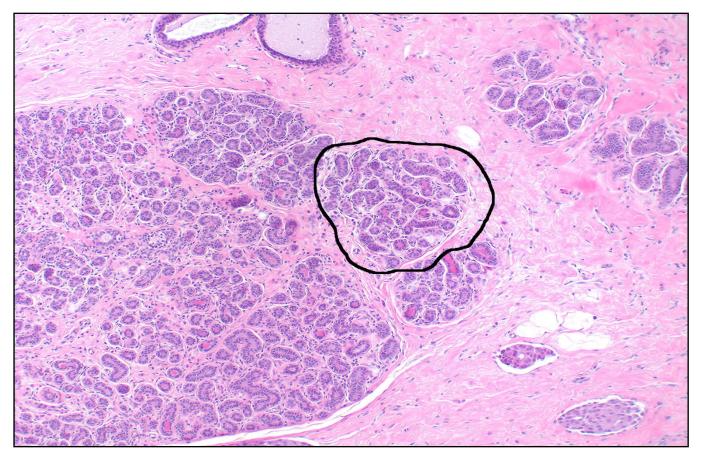
<u>From inside outwards</u>: Pectoralis muscles, Adipose tissue, Lobules containing alveoli (acini), Lactiferous ducts, Lactiferous sinus, Nipple, Skin covering the breast with dark colored Areola around the nipple.

Normal Breast Lobe



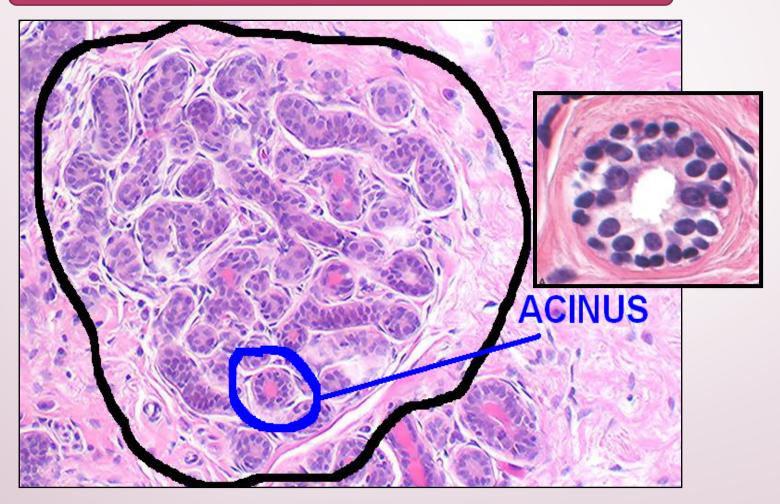
There are an average of about 10 LOBES per breast. The suspensory ligament separates lobes.

Normal Histology of Breast– LPF



Normal histology of breast tissue consists of the lobules. Within the lobules are small acini. Lobules are connected to intralobular ductules and interlobular ducts. Lobules are surrounded by loose connective tissue sensitive to sex hormones.

BREAST ACINUS – HPF Microscopy



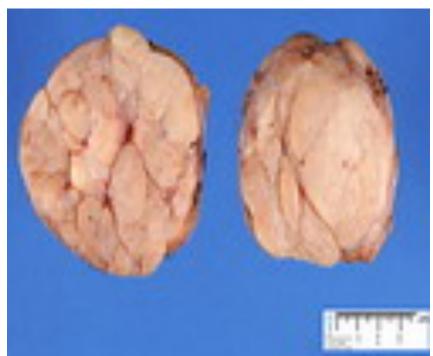
Each lobule contains several acini. Acini are also known as alveoli similar to pulmonary alveoli but the difference here it is secretory but in the lungs it is respiratory.

GROSS AND HISTOPATHOLOGY

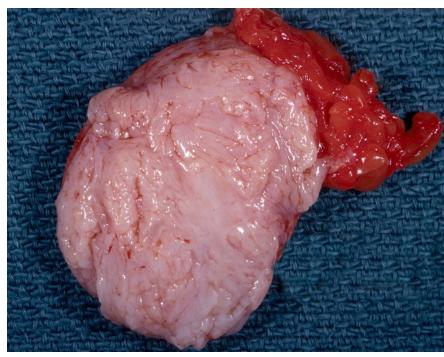
Fibroadenoma

Fibroadenoma of the Breast - Gross

Fibroadenoma of the breast has a benign behavior with good prognosis

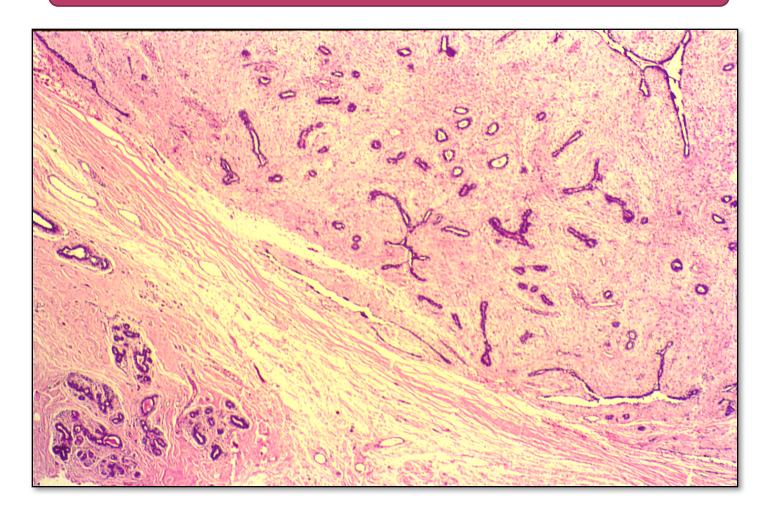


Multiple fibroadenomas with smooth, circumscribed borders



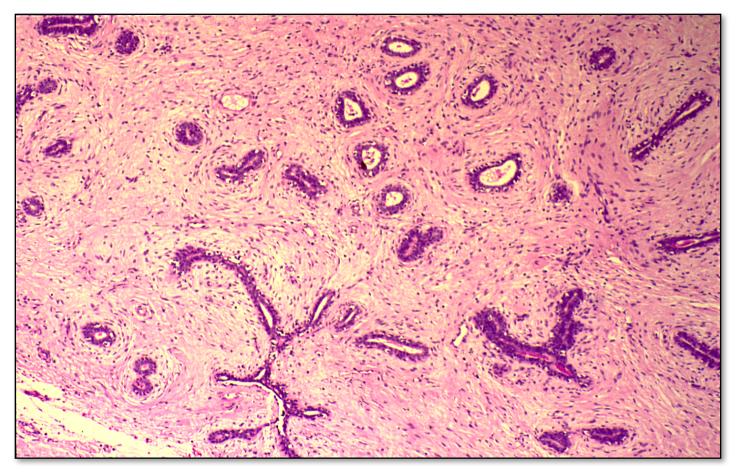
Well circumscribed and bulging white mass .The cut surface is lobulated with slit-like spaces

Fibroadenoma of the Breast-LPF



A tumour shows proliferation of both glandular tissue and fibrous tissue with intracanalicular and pericanalicular fibrous and ductular tissue growth pattern .

Fibroadenoma of the Breast- HPF



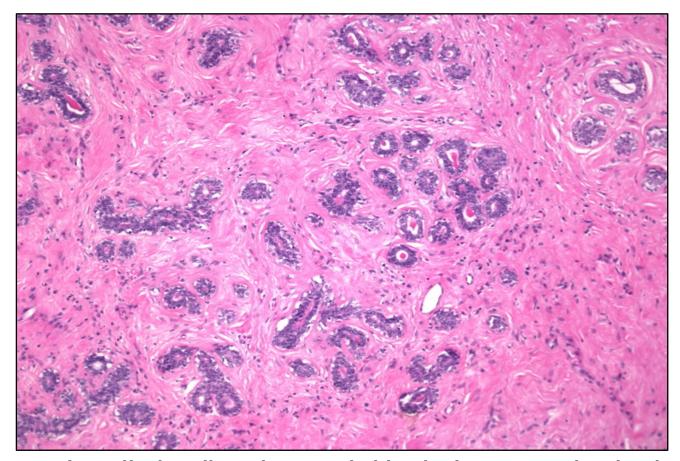
Proliferation fibrous tissue is invaginating the ducts causing elongation, compression and distortion of the ducts which have slit-like lumen (intracanalicular).

At places fibrous tissue is arranged around the ducts

(pericanalicular) and does not invaginate

Reproduction block

Pericanalicular Fibroadenoma of Breast



Pericanalicular Fibroadenoma: in histologic pattern, the glands maintain their round or oval profiles. There is no prognostic or clinical significance attached to the pericanalicular and intracanalicular patterns. Both may be seen within the same lesion

Carcinoma of the breast

Breast Cancer – Clinical Signs



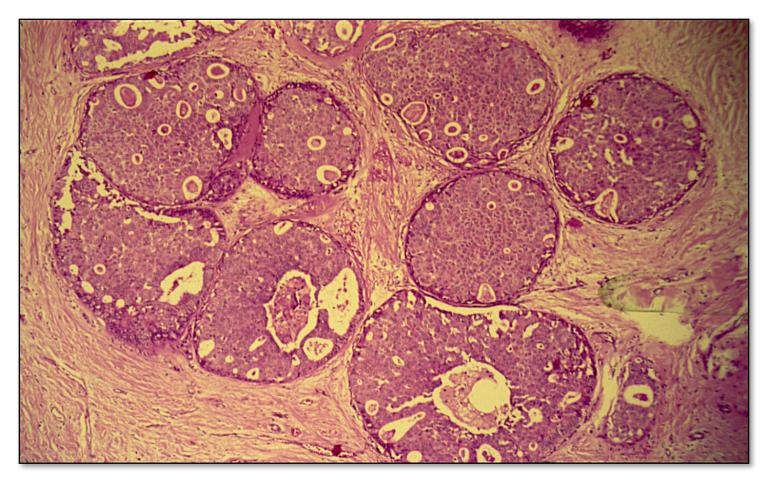
Breast cancer showing an inverted nipple, lump and skin dimpling

Breast Cancer – Gross Biopsy



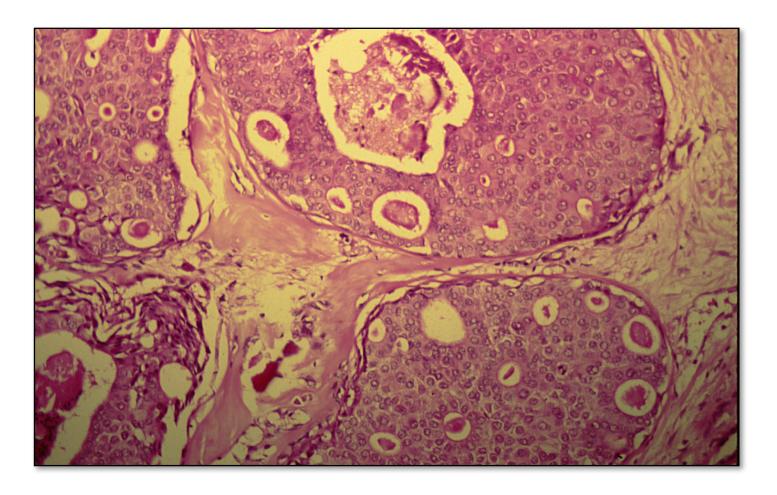
Ill-defined pale and firm nodule with overlying retracted nipple and surrounding skin .

Intraductal (In-situ) Carcinoma of the Breast-LPF



Cells are forming imperfect acini and shows a cribriform pattern. Small groups of cells in the center of many ducts are necrotic. No invasion of basement membrane of the ducts.

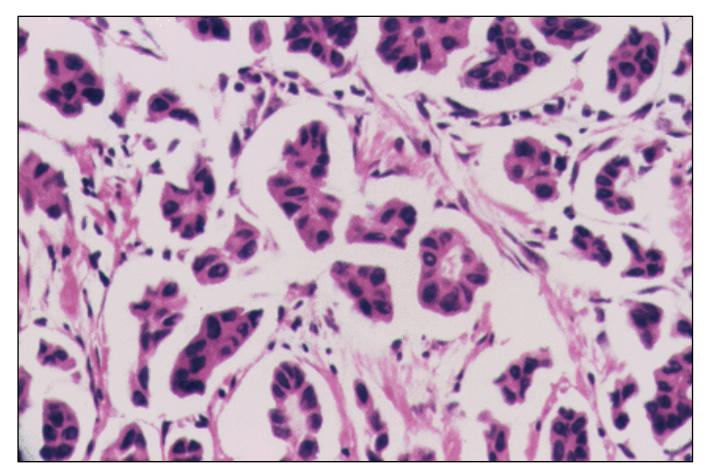
Intraductal Carcinoma of the Breast- HPF



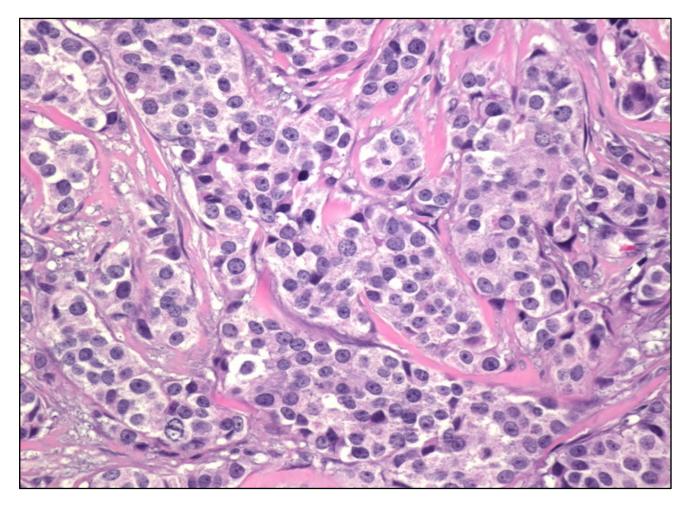
Large ducts are distended by neoplastic epithelial cells which are pleomorphic with large hyperchromatic nuclei and mitosis.



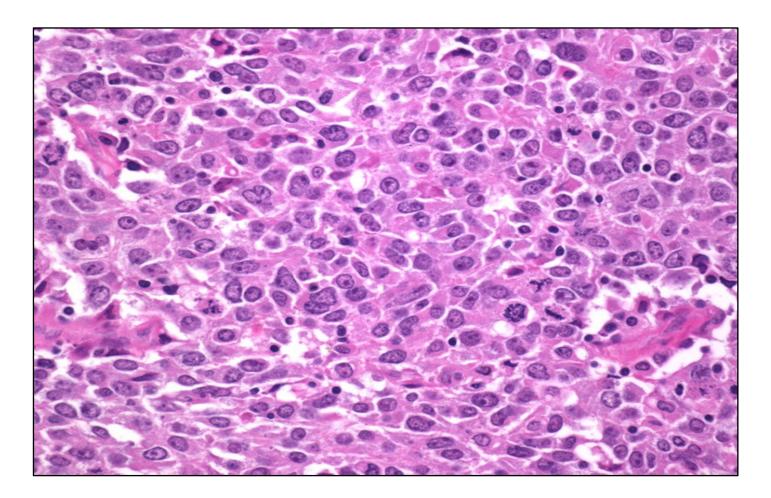
In a typical invasive ductal carcinoma, the tumor is firm and poorly circumscribed with a yellowish gray cut surface. It cuts with a gritty sensation. It may show strands radiating into the surrounding fat.



Microscopically, A well-differentiated ductal carcinoma made up of small acini and glands. Tumour cells are around to polygonal with deeply stained nuclei and occasional mitoses. Nuclear atypia is mild



Cords, sheets and nests of tumour cells surrounded by dense fibrous tissue stroma containing scattered lymphocytes



High grade invasive ductal carcinoma, The tumor cells are highly pleomorphic and show frequent mitotic figures with minimal tubular formation

Paget's Disease of the Nipple

Paget's Disease of the Nipple - Gross

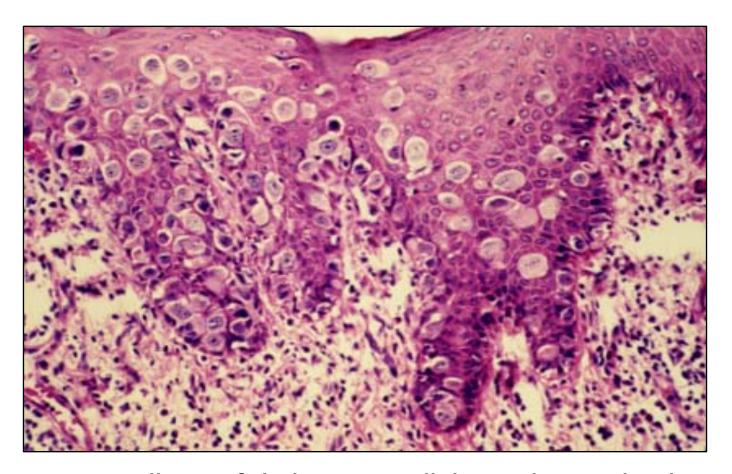






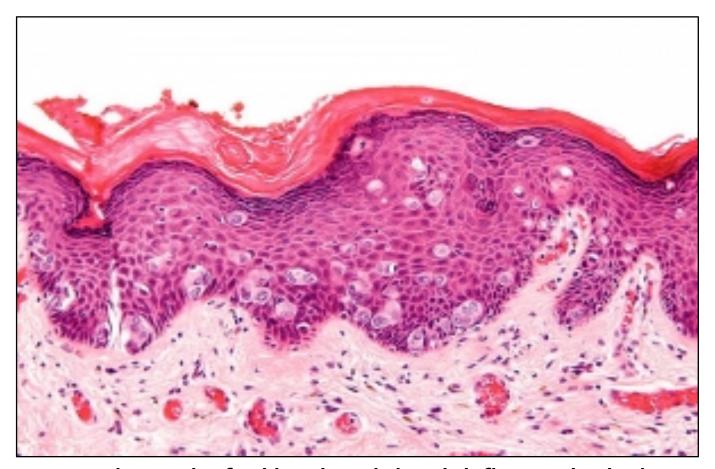
Paget's disease is a nipple lesion associated with underlying ductal carcinoma-in-situ with or without associated stromal invasion. Clinically, the lesion is eczema-like with hyperemia and erosion of the epidermis. Initially centered on the nipple, they may later involve the areola.

Paget's Disease of the Nipple- HPF



Paget's disease of nipple. Paget's cells have pale, vacuolated cytoplasm and large nuclei and migrate through the epidermis from parabasal cell layers upward. Notice the highest concentration in the deep layers of epidermis.

Paget's Disease of the Nipple- HPF



Hyperkeratosis of epidermis and chronic inflammation in the dermis are common. Ulceration and invasion of epidermis by ductal carcinoma cells (Paget cells), present between basal cells in elongated rete pegs.

GOOD LUCK