



MALE GENITAL TRACT PATHOLOGY

IN THE FOLLOWING LECTURES, WE WILL CONSIDER THE MOST COMMON MALFORMATIONS, INFLAMMATORY CONDITIONS, & NEOPLASMS INVOLVING THE PENIS & SCROTUM, PROSTATE, & TESTES.

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PENIS

Malformations

The most common malformations are abnormalities in the location of the urethral orifice:

- **Hypospadiasis** (HYP) is abnormal opening of the distal urethra orifice anywhere along the ventral aspect of the shaft of the penis. The orifice may be constricted, resulting in obstruction with an increase risk of UTI.
- **Epispadias** indicates the presence of the urethral orifice on the dorsal aspect of the penis, may produce obstruction or result in urinary incontinence. It is commonly associated with the congenital malformation of the bladder called **extrophy**.

PENIS

Inflammatory Lesions

1. mostly caused by Sexually Transmitted Diseases
2. local inflammatory processes unrelated to STDs
3. several other systemic inflammatory diseases may, on occasion, produce penile lesions

Local inflammation of the (1) Glans penis is called **Balanitis**; (2) glans penis + the overlying prepuce is called **balanoposthitis**. Most cases occur as a consequence of poor local hygiene **in uncircumcised males**.

Grossly, the distal penis is typically **inflamed, red, swollen, & tender**; & a **purulent discharge may be present**.

PENIS INFLAMMATION LESION

Balanopthitis the inflammation of the foreskin and glans in uncircumcised males, balanoposthitis occurs over a wide age range and may have any of multiple bacterial or fungal origins or be caused by contact dermatitides

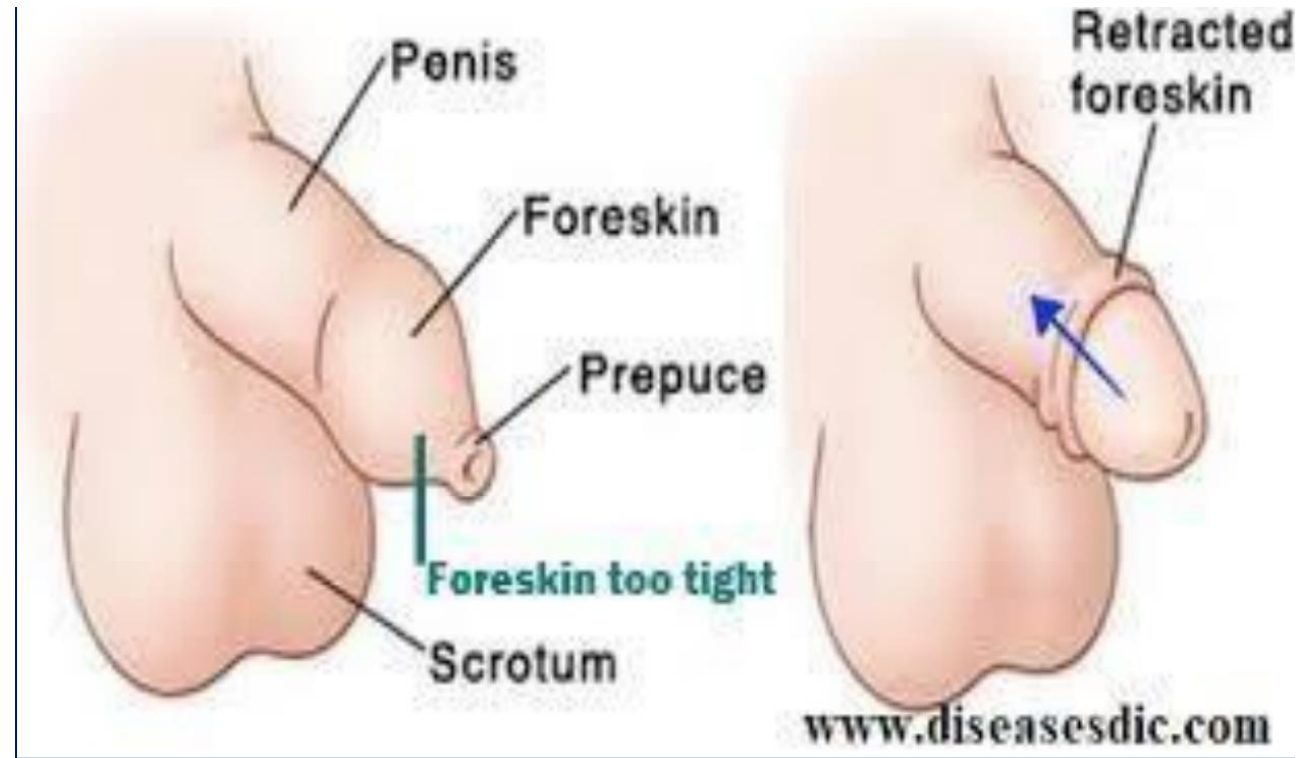


PENIS INFLAMMATION LESION

Phimosis

a condition in which the prepuce cannot be retracted easily over the glans penis.

Some cases are congenital anomaly, but most cases are acquired from scarring of the prepuce secondary to previous episodes of balanoposthitis.



PENIS NEOPLASM

- More than 95% of penile tumors are squamous cell carcinomas (SCC), uncommon in the US, accounting for about 0.4% of all cancers in males. In developing countries, however, penile SCCa occurs at much higher rates.
- Most cases occur in:
 - (1) uncircumcised Patients older than 40 years of age. Several factors have been implicated in the pathogenesis of the penis SCC
 - (2) poor hygiene (with resultant exposure to potential carcinogens in smegma),
 - (3) smoking
 - (4) infection with HPV, particularly types 16 & 18

PENIS NEOPLASM

- SCC of the penis (as with other body sites) is generally preceded by the appearance of malignant cells confined to the epidermis, termed intraepithelial neoplasia or carcinoma in situ.
- Three clinical variants of carcinoma in situ, all strongly associated with HPV infection, occur on the penis:

(I) Bowen disease (which may also occur elsewhere on the skin & mucosal surfaces, including the vulva & oral mucosa) occurs in older uncircumcised males & appears grossly as a solitary, plaque like lesion on the penis shaft.

Histopathology: there are malignant cells throughout the epidermis with no invasion of the underlying stroma (in situ ca).

Bowen disease involving the penis progresses to invasive SCC in 33% of cases

PENIS NEOPLASM: BOWEN DISEASE

Bowen disease (Ca in situ) penis. The epithelium above the intact basement membrane (which is not seen in this picture) shows hyperchromatic, dysplastic, dyskeratotic epithelial cells with scattered mitoses above the basal layer



PENIS NEOPLASM

- **(II) Erythroplasia of Queyrat** when Bowen disease presents as an erythematous patch on the glans penis.
- **(III) Bowenoid papulosis** occurs in young, sexually active males & is identical to Bowen disease. **Histologically**, but clinically it presents with **multiple reddish brown papules on the glans** & is most often transient, with only rare progression to carcinoma in immunocompetent patients.



Fig. 13.39 Erythroplasia of Queyrat.

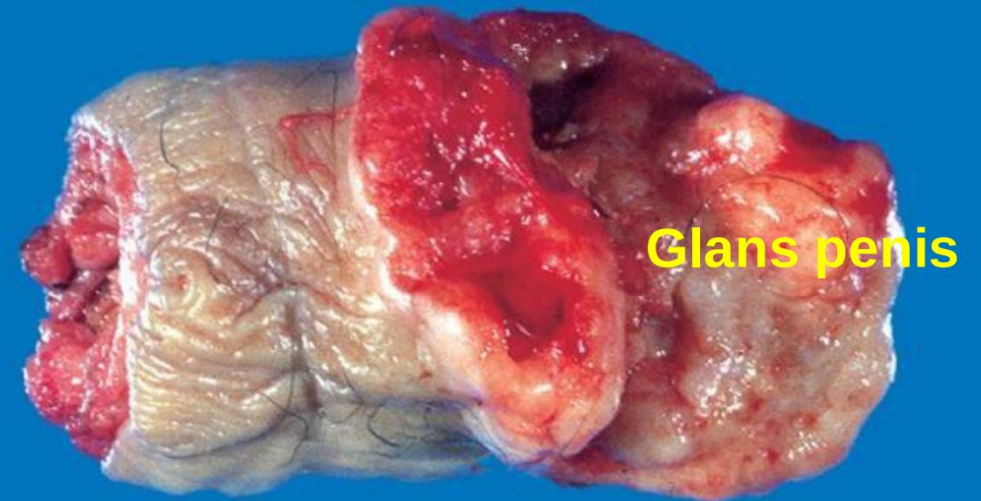
PENILE SQUAMOUS CELL CA

- Penis SCC appears as a **gray, crusted, papular** lesion, most commonly on the glans penis or prepuce.
- It may infiltrate the underlying connective tissue producing an indurated ulcer with irregular margins
- Histopathology , it is usually an **infiltrating keratinizing SCC**.
- Verrucous carcinoma is a variant of SCC characterized by a papillary architecture, less striking cytological atypia, & rounded, pushing deep margins.
- Most cases of SCC of the penis are indolent, locally infiltrative lesions.
- Regional inguinal LN metastases are present in 25% of patients at the time of diagnosis.
- Distant metastases are relatively uncommon,& the overall 5-year survival rate averages 70%.

PENILE SQUAMOUS CELL CA

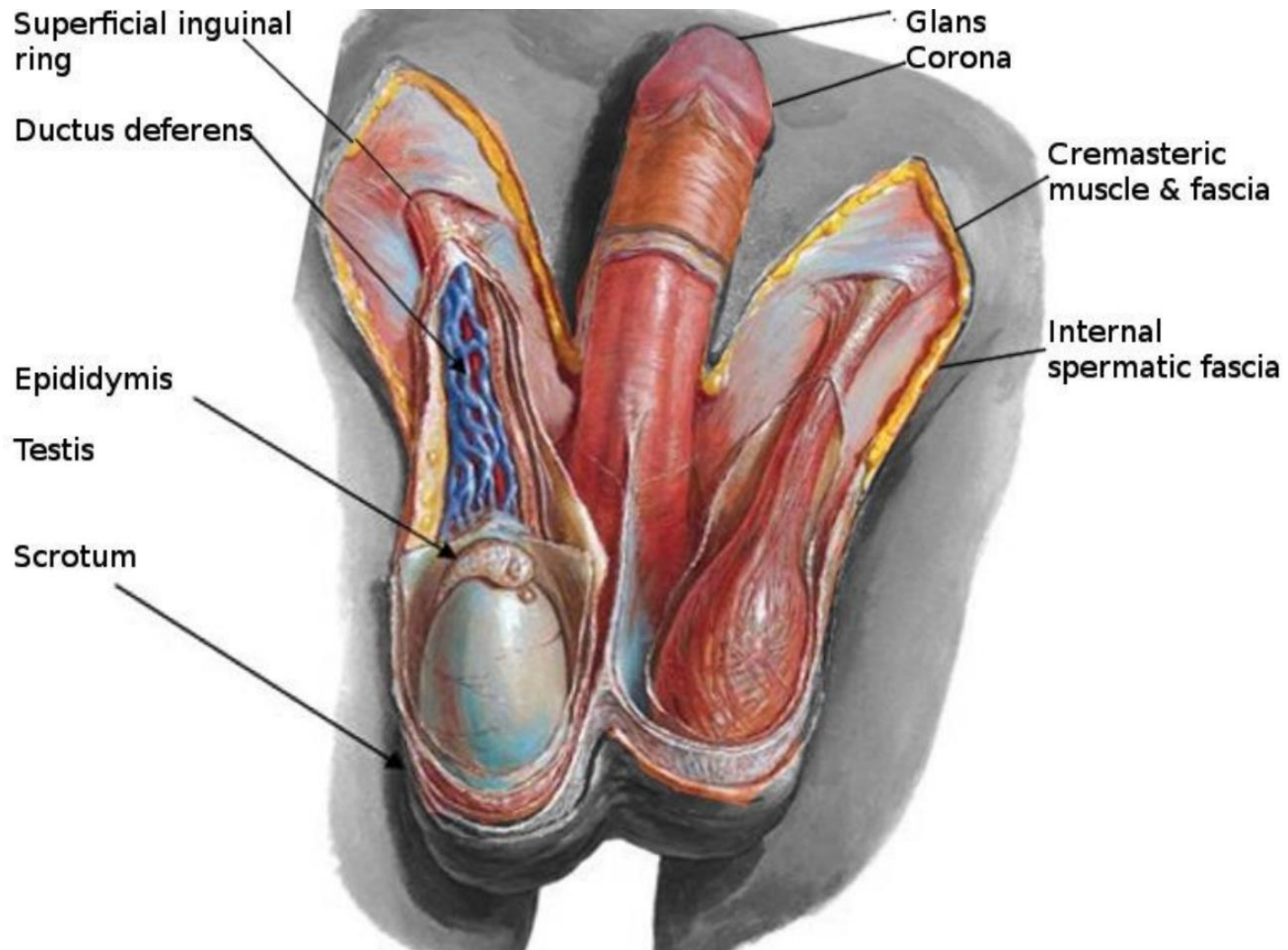
- Carcinoma of the penis. The glans penis is deformed by a firm, ulcerated & infiltrating cancer.

**Proximal
resection**



SCROTUM

- Scrotum: The bag of skin that holds and helps to protect the testicles.
- The testicles make sperm and, to do this, the temperature of the testicles needs to be cooler than the inside of the body. This is why the scrotum is located outside of the body.
- Each testicle produces hormones, the main one being testosterone, with the help of parts of the brain like the hypothalamus and pituitary gland.
- Epididymis is located on the top of each testicle.
- Spermatic cord
- Cremaster muscle

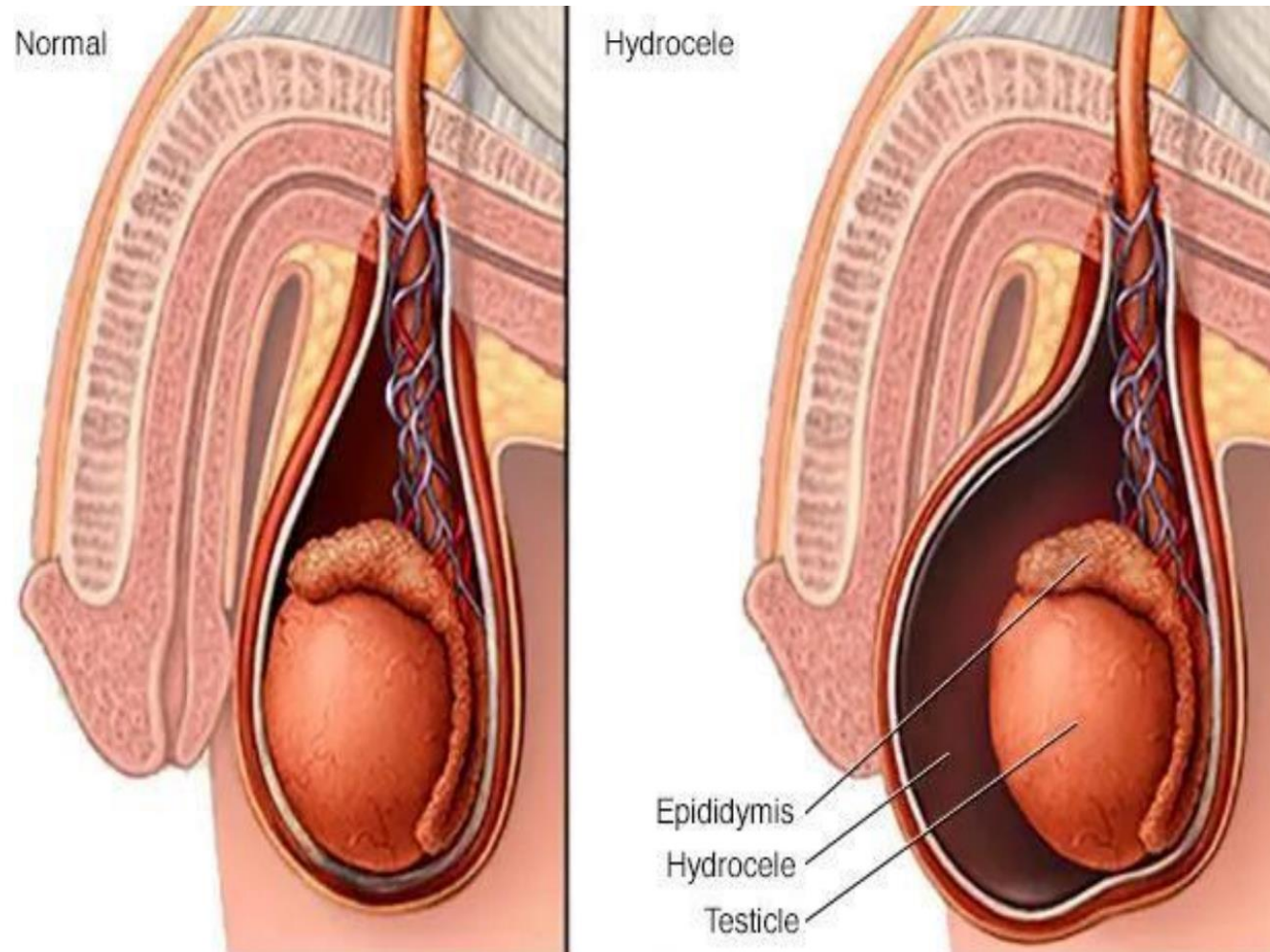


SCROTUM

- The most common cause of scrotal enlargement is:
- **Hydrocele** an accumulation of serous fluid within the tunica vaginalis, which can be idiopathic or arise in response to neighboring infections or tumors; A hydrocele must be distinguished from a true testicular mass, and **transillumination** may help, because the hydrocele will transilluminate but a testicular mass will be opaque.
- less common causes of scrotal enlargement are: Accumulation of blood (Hematocele) or lymphatic fluid (chylocele) within the tunica vaginalis

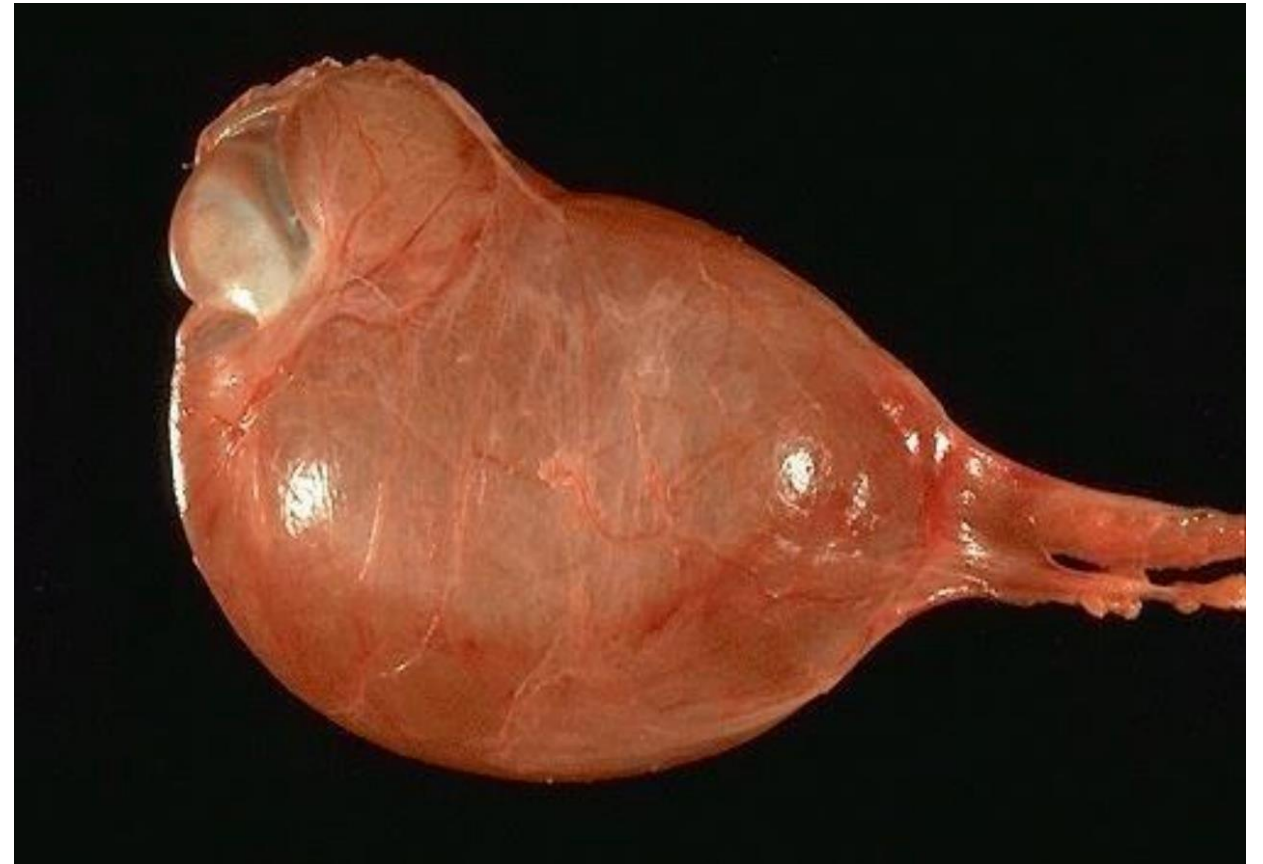
SCROTUM HYDROCELE

Hydrocele.
An abnormal accumulation
of serous fluid in the sac of
tunica vaginalis.



SCROTUM HYDROCELE

- large hydrocele of the testis. Such hydroceles are fairly common, though most do not reach this size.
- Clear fluid accumulates in a sac of tunica vaginalis lined by a serosa.
- It is a remnant of the embryologic processus vaginalis.
- It may arise in association with a variety of inflammatory and neoplastic conditions.
- A hydrocele must be distinguished from a true testicular mass, and transillumination may help, because the hydrocele will transilluminate but a testicular mass will be opaque



TESTIS & EPIDIDYMIS

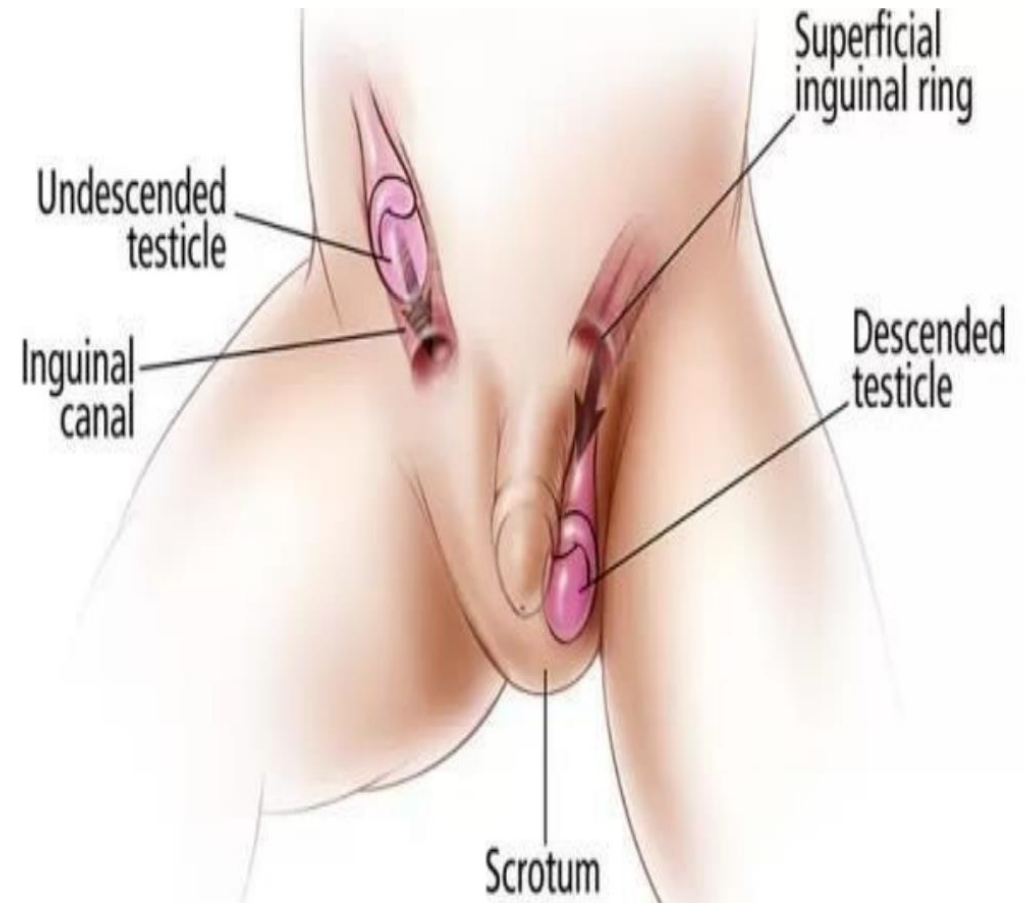
- Testicular diseases may be
- Congenital, Inflammatory, Neoplastic.
- They may manifest themselves as infertility, atrophy, enlargement, & local pain.
- Cryptorchidism & Testicular Atrophy.

CRYPTORCHIDISM

- Cryptorchidism is failure of testicular descent into the scrotum
- **Normally**, the testes descend from the coelomic cavity into the pelvis by the 3rd month of gestation & then through the inguinal canals into the **scrotum during the last 2 months of intrauterine life.**
- Because complete testicular descent into the scrotum is not always present at birth, the diagnosis of cryptorchidism is difficult to establish with certainty before 1 year of age, particularly in premature infants,
- **By 1 year of age: Cryptorchidism is present in 1% of the male population.**
- **Approximately 10% of these cases are bilateral.**
- In the vast majority, the cause of the cryptorchidism is **unknown!**
- Rarely, **hormonal abnormalities, intrinsic testicular abnormalities, & mechanical problems,** may interfere with normal testicular descent, resulting in mispositioning of the gonad.

CRYPTORCHIDISM

Undescended testis
(Cryptorchidism).
The testis is situated within the
commencement of the inguinal
canal at the pelvic brim.



CRYPTORCHIDISM

Effects of cryptorchidism

- Bilateral cryptorchidism causes **sterility**
- Unilateral cryptorchidism may be associated with **atrophy of the contralateral** descended gonad & may also lead to **sterility**.
- associated with a 3-to 5-fold increase risk of testicular **cancer**.
- Individuals with unilateral cryptorchidism are also **at increase risk for the development of cancer in the contralateral normally descended testis**, suggesting that **some intrinsic abnormality**, rather than simple failure of descent, may be responsible for the increase risk.
- Surgical placement of the undescended testis into the scrotum (orchiopexy) **before puberty decrease the likelihood of testicular atrophy & reduces (but does not eliminate) the risk of cancer & infertility**.

CRYPTORCHIDISM MORPHOLOGY

- Cryptorchidism involves the **right testis** somewhat more commonly than the left. In **10% of cases**, the condition is **bilateral**. The cryptorchid testis may be of normal size early in life, although some degree of atrophy is usually present by the time of puberty
- Histologically: cryptorchid testes show evidence of:
 - (1) **tubular atrophy** by 5 to 6 years of age, **hyalinization** is present by the time of puberty,
 - (2) accompanied by **Leydig cell hyperplasia**.
 - (3) foci of **intratubular germ cell neoplasia** may be present in cryptorchid testes & may be the source of subsequent testicular cancers.
- Similar tubular atrophy may be caused by several other conditions, **حفظ** including:
Chronic ischemia, Trauma, Chronic hyperestrogenism (e.g., cirrhosis), Radiation, Anti-neoplastic chemotherapy

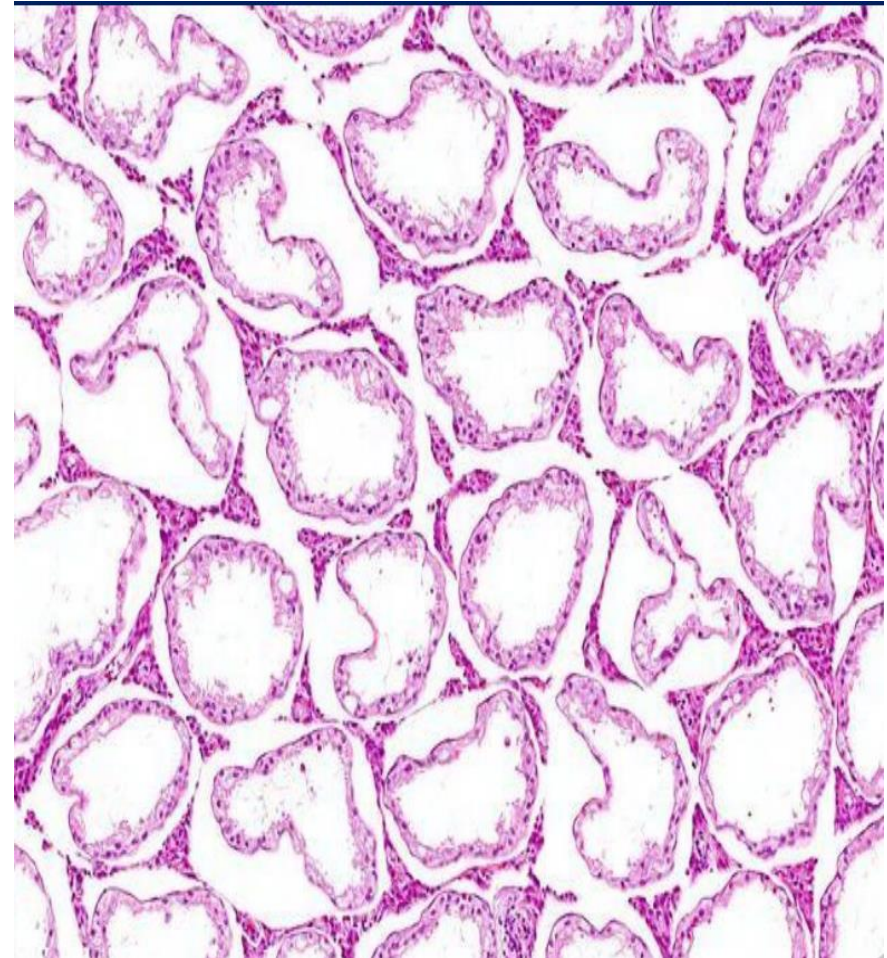
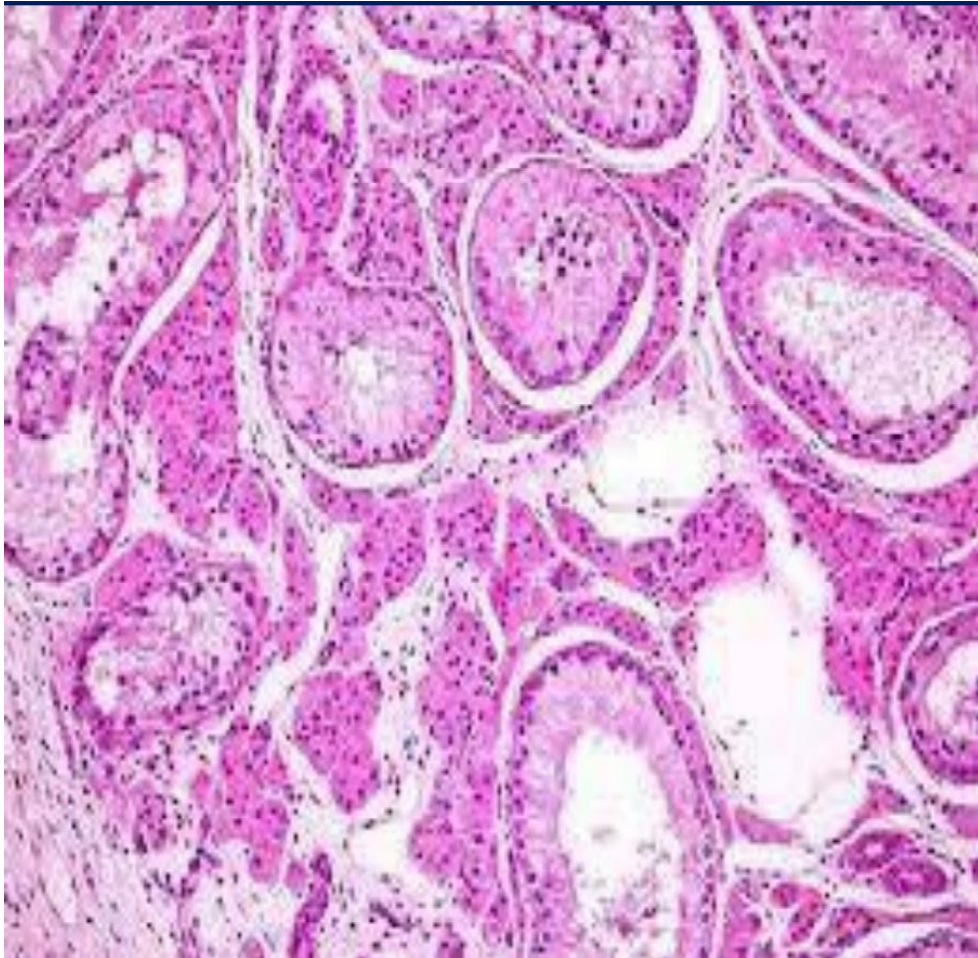
NORMAL TESTIS

This is the microscopic appearance of the **normal testis**.

- The seminiferous tubules have numerous germ cells. Sertoli cells, with cytoplasm that extends between the germ cells, are inconspicuous.
- Small dark oblong spermatozoa are seen toward the center of the tubules



ATROPHIC TESTISIN BOTH PICTURES



TESTIS INFLAMMATION LESIONS

- Inflammatory lesions of the testis are more common in the epididymis than in the testis proper. Some of these are associated with STD (venereal) disease. Other causes of testicular inflammation include nonspecific epididymitis & orchitis, mumps, & tuberculosis.

(I) Nonspecific epididymitis & orchitis, begin usually as a primary UTI with secondary ascending infection to the testis through the vas deferens or lymphatics of the spermatic cord. The involved testis is typically swollen, tender & contains a predominantly neutrophilic cell infiltrate.

(II) Orchitis complicates mumps infection in roughly 20% of infected adult males but rarely occurs in children.

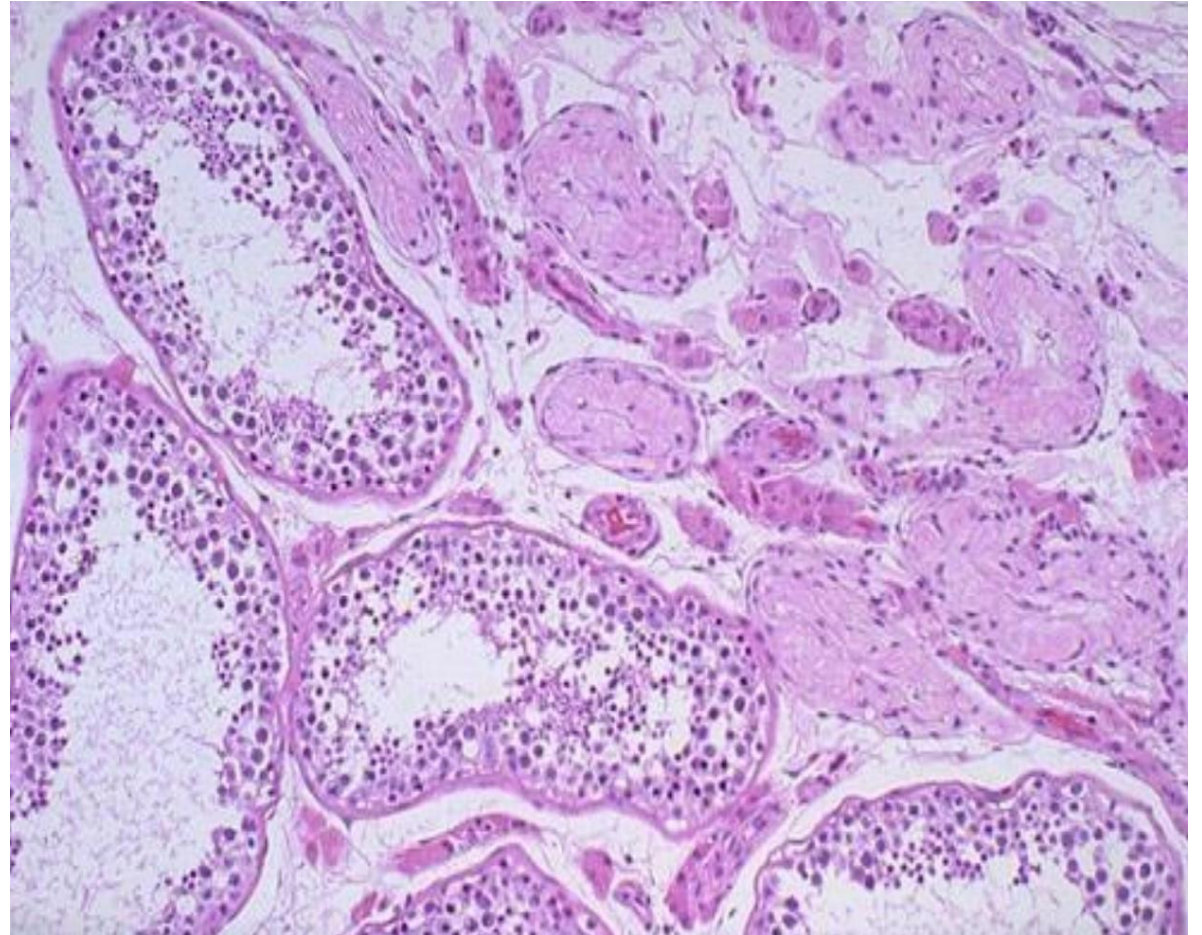
- The affected testis is edematous & congested & contains a predominantly lymphoplasmacytic cell infiltrate. Some cases associated with atrophy, fibrosis, & sterility.

(III) Granulomatous inflammation of the testis may be caused by some infections & autoimmune disease, of which TB is the most common. Testicular TB generally begins in the epididymis, with secondary involvement of the testis.

- Histologically, there is caseous granulomatous inflammation.

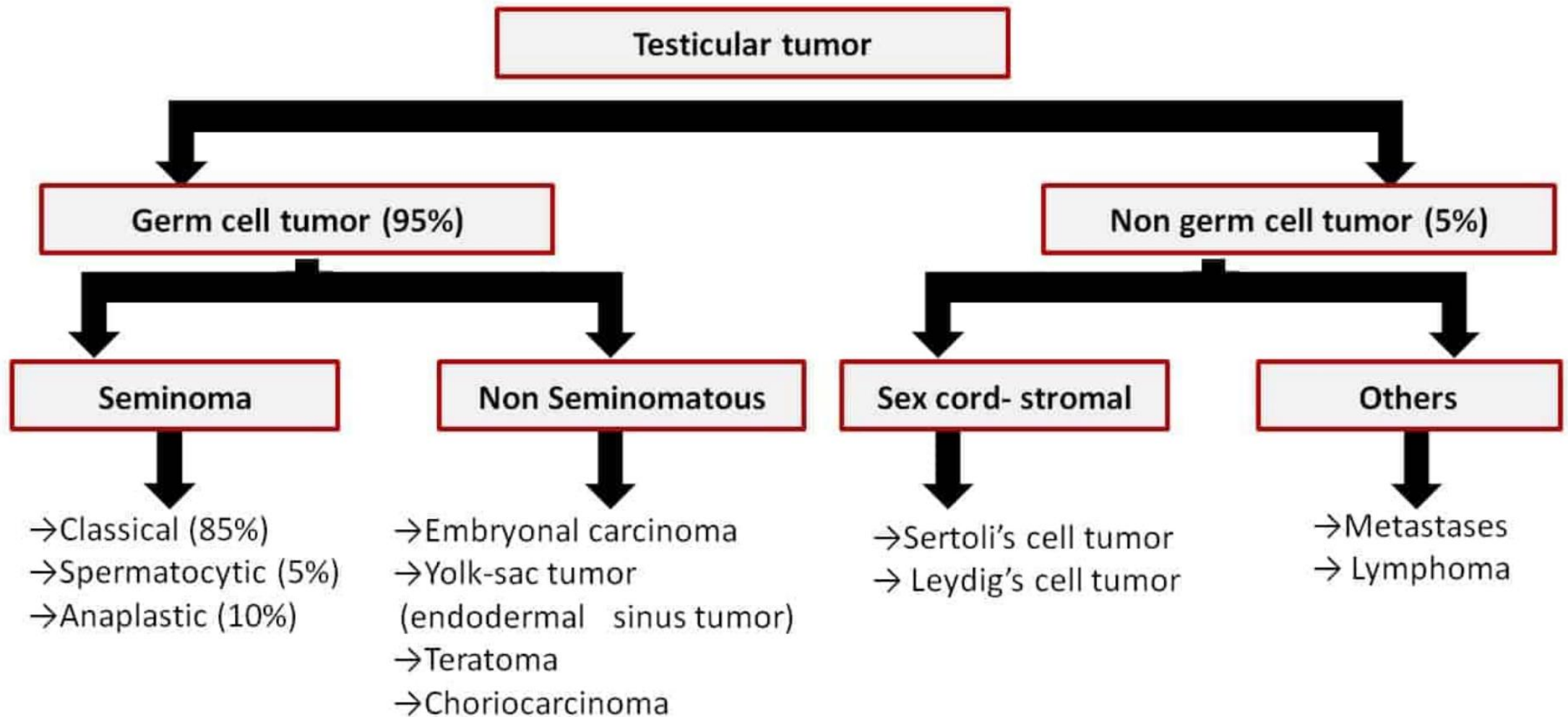
TESTIS INFLAMMATORY LESIONS

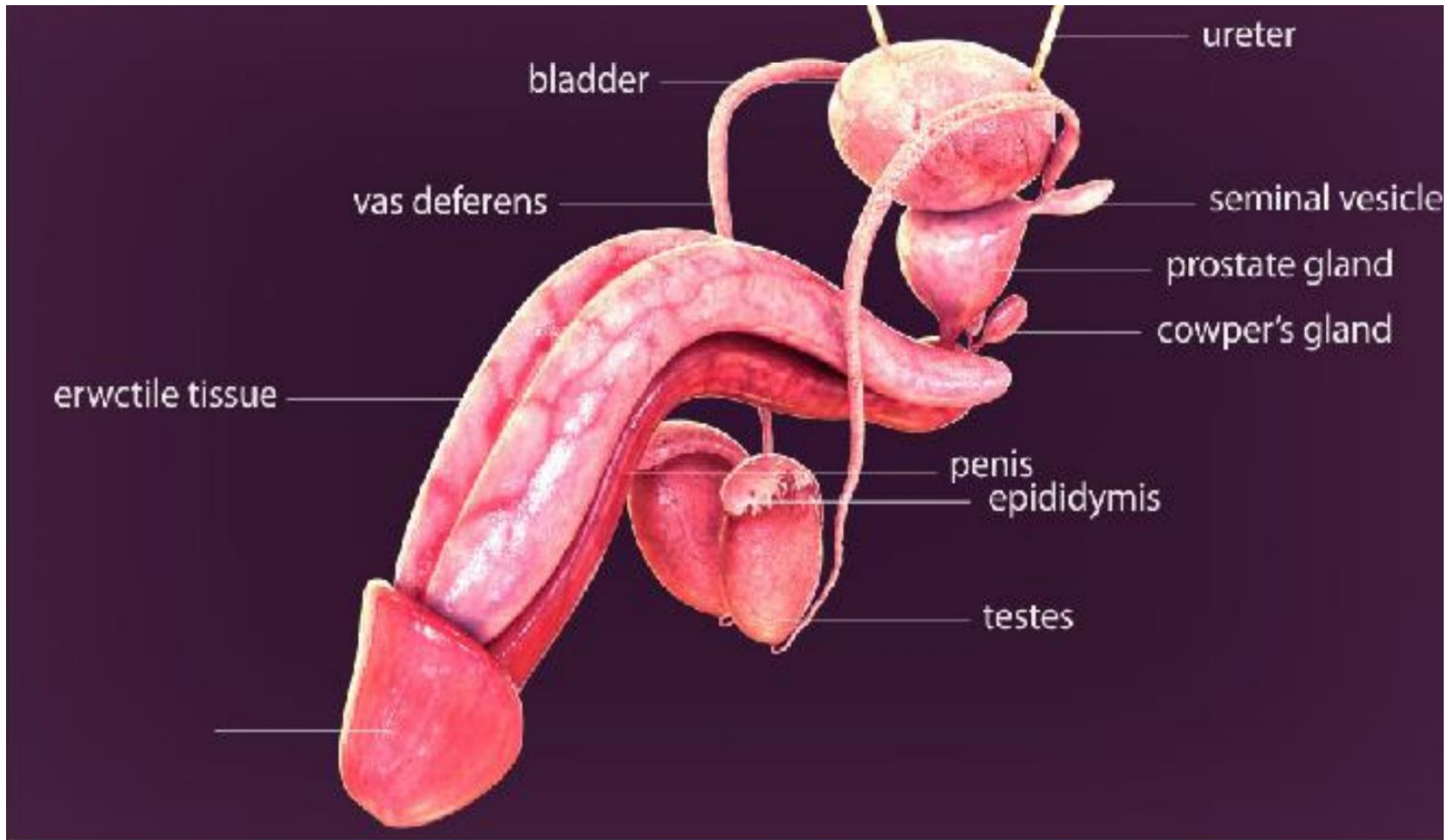
- There is focal atrophy of tubules seen here to the upper right.
- The most common reason for this is probably childhood infection with the mumps virus, which produces a patchy orchitis.
- However, it is unusual for this infection to cause enough atrophy to significantly affect the sperm count.



TESTICULAR TUMORS (T)

- Testicular T are the most important cause of firm, painless enlargement of the testis with a peak incidence in 20-34 years age group.
- In adults, 95% of testicular T arises from germ cells & all are malignant. Sertoli or Leydig cells T (sex cord/stromal tumors) are uncommon & are usually benign.
- Cryptorchidism is associated with a 3-to 5-fold increase risk of cancer. In the undescended testis, as well as increase risk of cancer in the contralateral descended testis,
- Intersex syndromes, including androgen insensitivity syndrome & gonadal dysgenesis, are also associated with an increase frequency of testicular cancer.
- For unknown reasons, the risk of cancer is increase in siblings of males with testicular cancers.
- Testicular T are more common in whites than in blacks & the incidence has increase in Caucasian populations in recent decades.
- Cytogenetic studies show a wide range of abnormalities in testicular germ cell T, **the most common of these is an isochromosome of the short arm of chromosome 12**, but their role in the pathogenesis of these cancers remains unclear.





CLASSIFICATION & HISTOGENESIS OF TESTICULAR TUMORS

- In the WHO classification, which is the most widely used in the US the germ cell T of the testis are divided into two broad categories, based on whether they contain a single histologic pattern (60% of cases) or multiple histologic patterns (40% of cases).
- WHO Classification of Testicular Germ Cell T:
- **Tumors with One Histologic Pattern (60% of cases)**
 - (I) Seminoma,
 - (II) Non-seminomatous T including: • Embryonal carcinoma, • Yolk sac tumor, • Choriocarcinoma, • Teratomas – Mature & Immature & with malignant transformation of somatic elements.

CLASSIFICATION & HISTOGENESIS OF TESTICULAR TUMORS

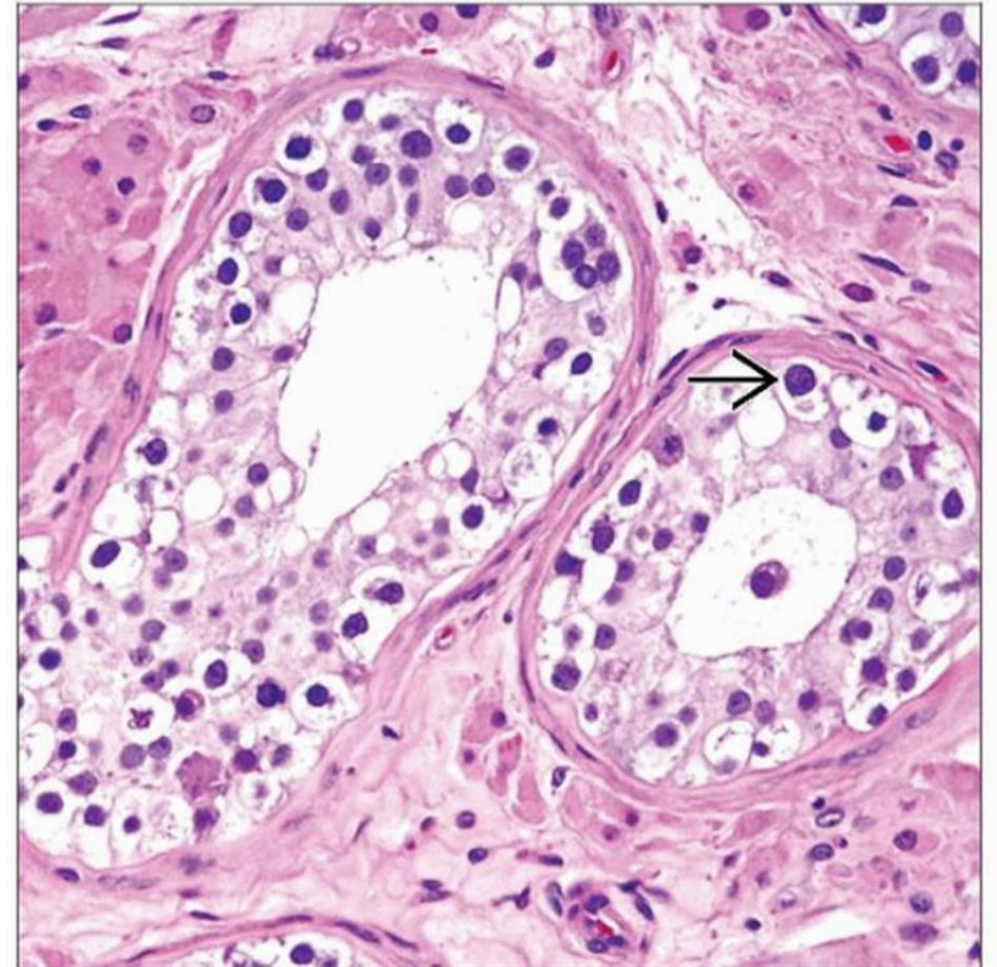
- **Tumors with More Than One Histologic Pattern (40%)**
- This classification is based on the view that testicular germ cell T arise from primitive cells that may either differentiate along
 - (I) Gonadal lines to produce seminomas.
 - (II) Transform into a totipotential cell population, giving rise to non- seminomatous germ cell T. Such totipotential cells:
 - (a) may remain undifferentiated to form embryonal ca, or (b) may differentiate along extra-embryonic lines to form yolk sac tumors& choriocarcinomas. (c) may differentiate along somatic cell lines to produce teratomas.

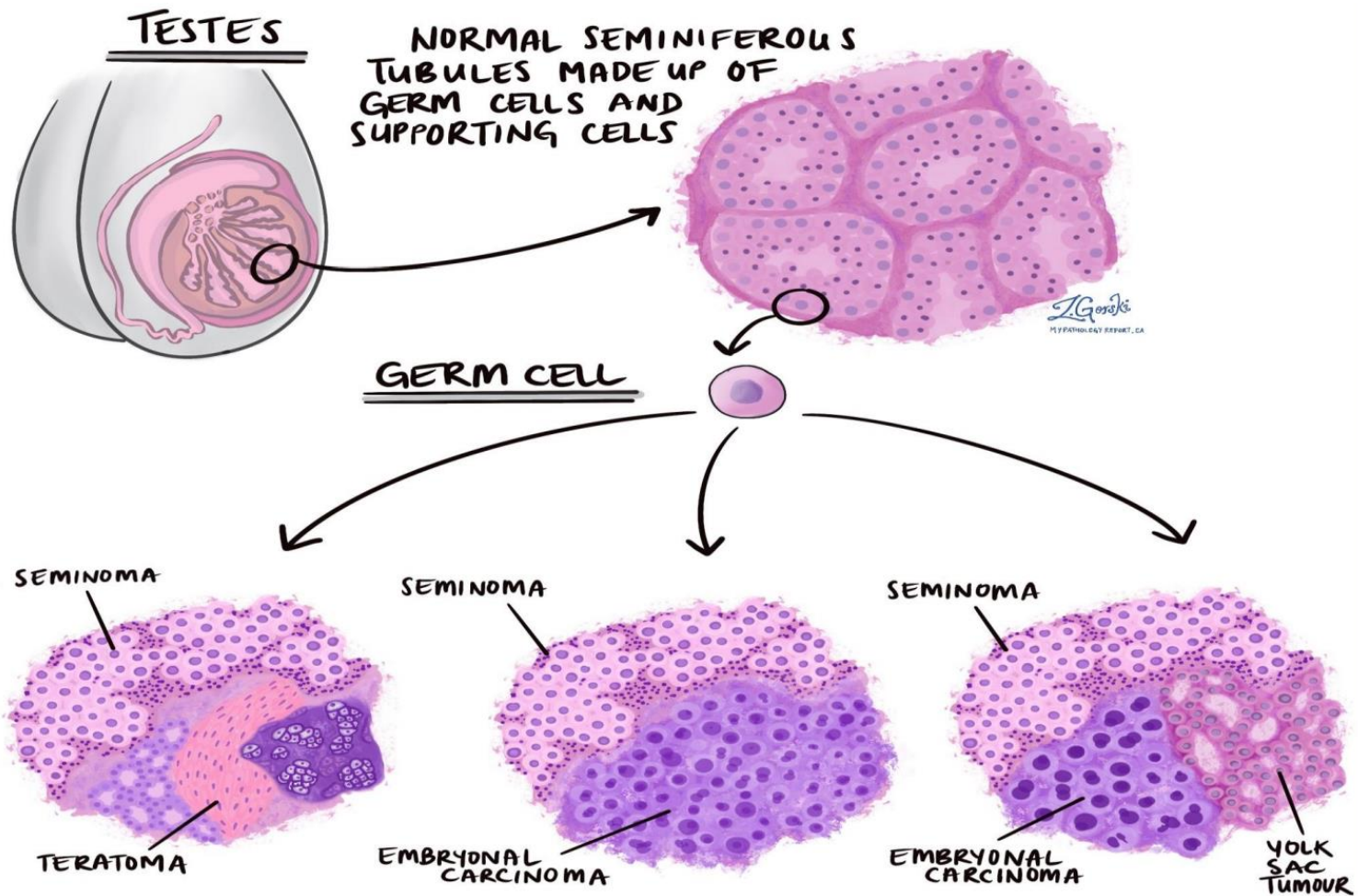
CLASSIFICATION & HISTOGENESIS OF TESTICULAR TUMORS

- Testicular germ cell tumors (TGCTs) demonstrate a wide variety of histopathologic, genetic, pathogenetic, and immunocytochemical characteristics and various clinical-biologic profiles and prognoses.
- Most TGCTs arise from an intratubular precursor cell referred to as germ cell neoplasia in situ (GCNIS), which is an embryonic germ cell with the potential to differentiate into a plethora of embryonic and extraembryonic lineages.

HISTOGENESIS OF TESTICULAR TUMORS

- Intratubular germ cell neoplasia(IGCN): Beautiful picture showing cells (within seminiferous tubule) having enlarged nuclei, prominent nucleoli, and clear cytoplasm along the basal aspect of a seminiferous tubules lacking spermatogenesis. Sertoli cells are displaced toward the lumen.
- The TGCT of young adults originate from a common precursor, germ cell neoplasia in situ (GCNIS), initially termed carcinoma in situ (CIS) testis .
- GCNIS is considered to originate from developmentally arrested immature germ cells (gonocytes) that fail to differentiate to spermatogonia



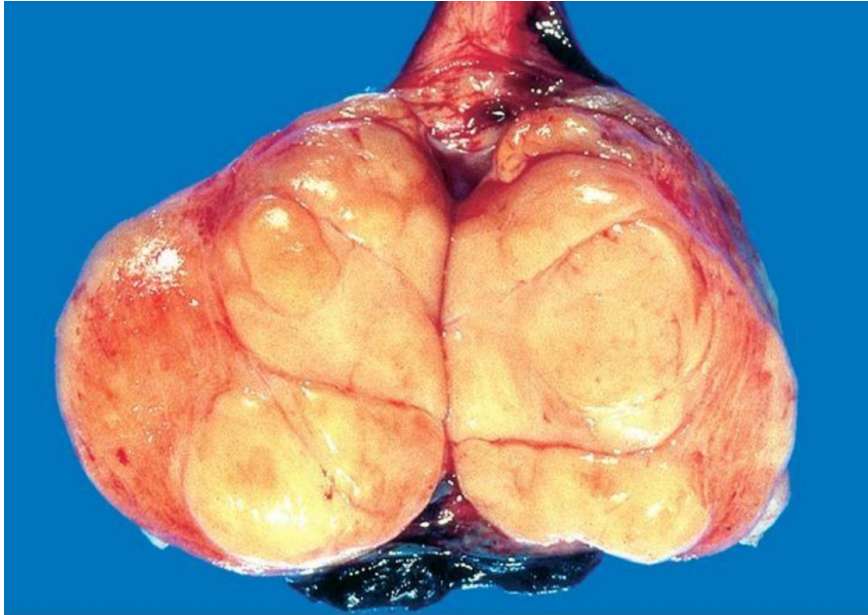


EXAMPLES OF MIXED GERM CELL TUMOURS

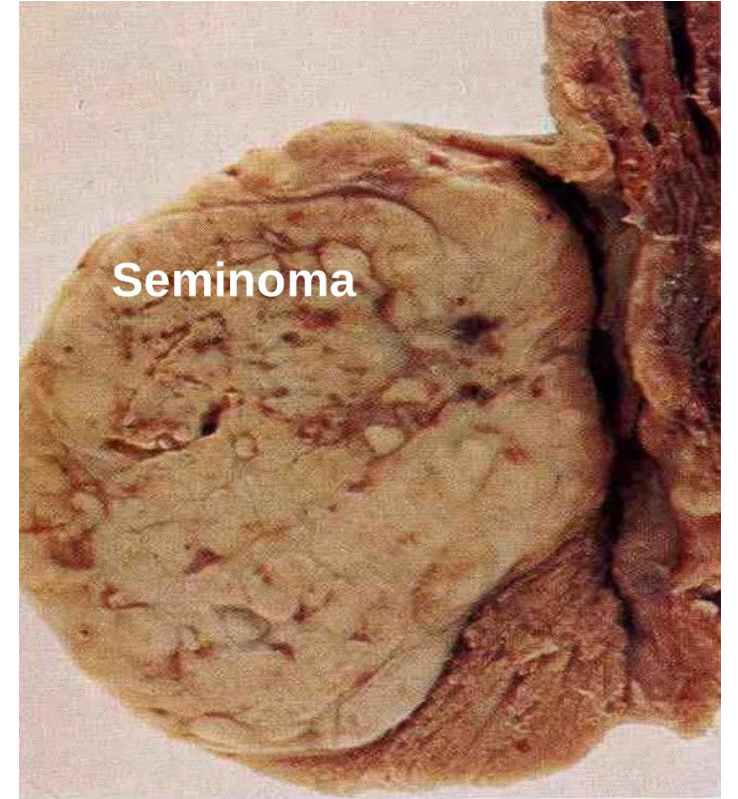
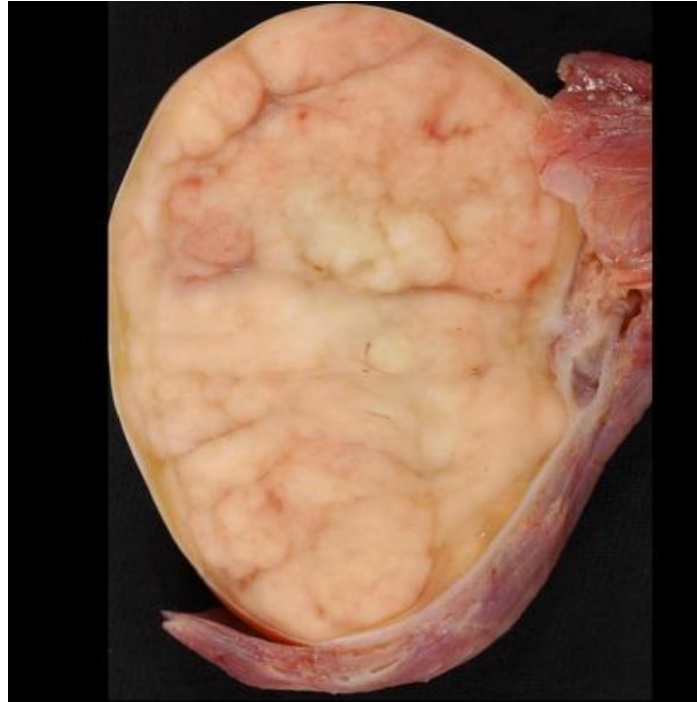
SEMINOMAS "CLASSIC"

- Seminomas "classic" حفظ
- Seminomas account for 50% of testicular germ cell T.
- They are histologically identical to ovarian dysgerminomas & to germinomas occurring in the CNS & other extra-gonadalsites.
- **GROSSLY**, seminomas are "potato "like, large, soft, well-demarcated, homogeneous, gray-white T that bulge from the cut surface of the affected testis, typically confined to the testis by an intact tunica albuginea.
- Large seminoma may contain foci of coagulation necrosis, usually without hemorrhage; But the presence of hemorrhage should prompt careful scrutiny (examination) for an associated non-seminomatous germ cell component to the T.

SEMINOMAS CLASSIC GROSSLY



Well circumscribed, pale, fleshy, homogenous mass.

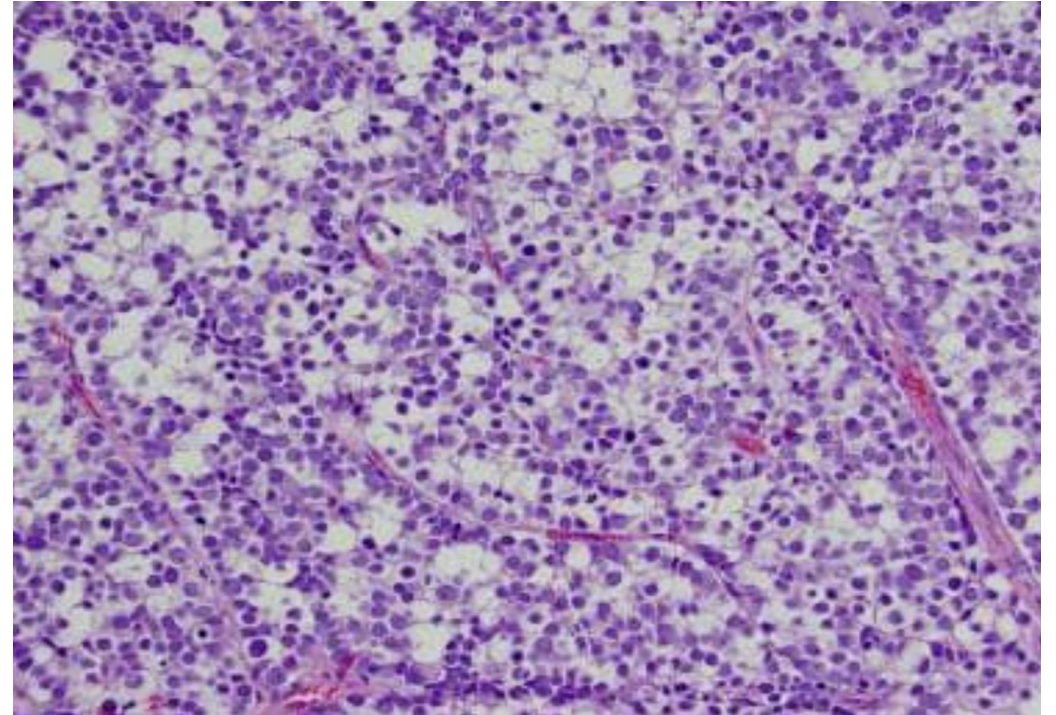
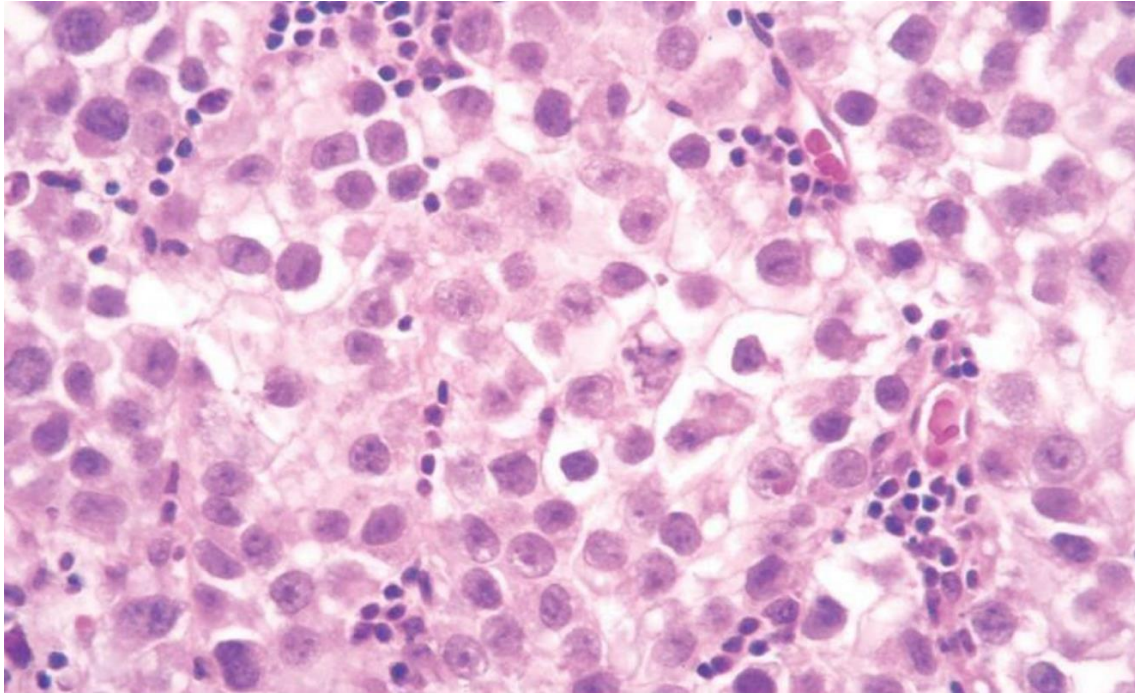


A lobulated, pale grey opaque tumor of the testis, which is firm & "potato" looking on section

SEMINOMAS CLASSIC HISTOLOGICALLY

1. seminomas composed of large, uniform cells with distinct cell borders, clear, glycogen-rich cytoplasm, & round nuclei with conspicuous nucleoli.
2. Cells are arranged in small lobules with intervening fibrous septa infiltrated by lymphocytes.
3. A granulomatous inflammatory reaction may also be seen.
4. In as many as 25% of cases, cells staining positively for human chorionic gonadotropin (hCG).
5. These hCG-expressing cells are morphologically similar to syncytiotrophoblasts, & they are presumably the source of the elevated serum hCG concentrations that may be encountered in some males with pure seminoma.

SEMINOMAS CLASSIC HISTOLOGICALLY



Seminoma of the testis. HP showing large cells with distinct cell borders, pale nuclei, prominent nucleoli, & a sparse lymphocytic infiltrate

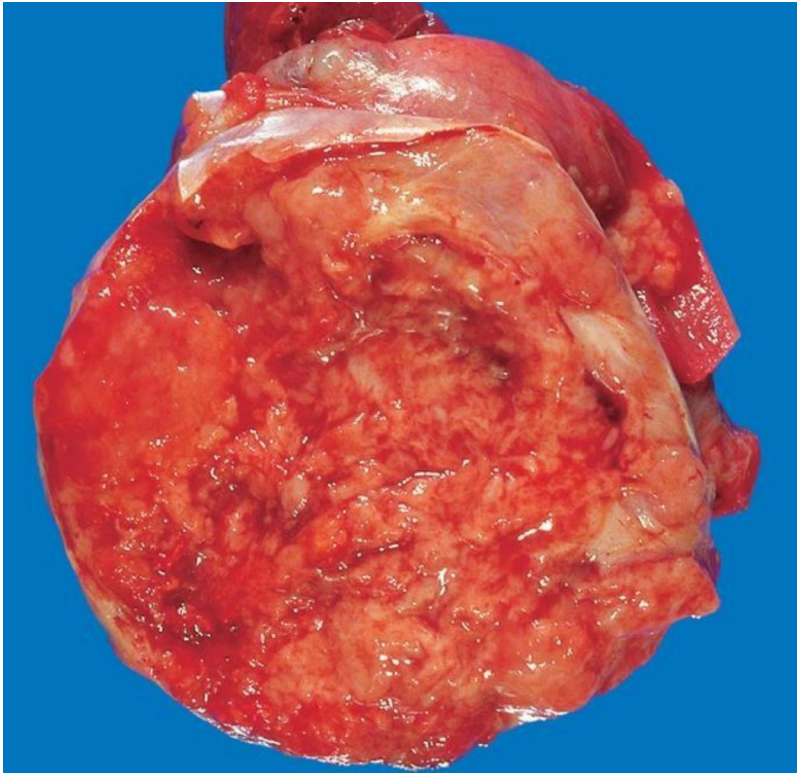
SPERMATOCYTTIC SEMINOMA

- Spermatocytic seminoma is a less common morphologic variant of seminoma, which tend to occur in: حفظ
- Older patients
- It contain a mixture of medium-sized, large uninucleate or multinucleate T cells, & small cells with round nuclei that are reminiscent of secondary spermatocytes.
- In contrast to the behavior of classic seminoma,
 - 1)there is no association with intratubular germ cell neoplasia.
 - 2) metastases are exceedingly rare,

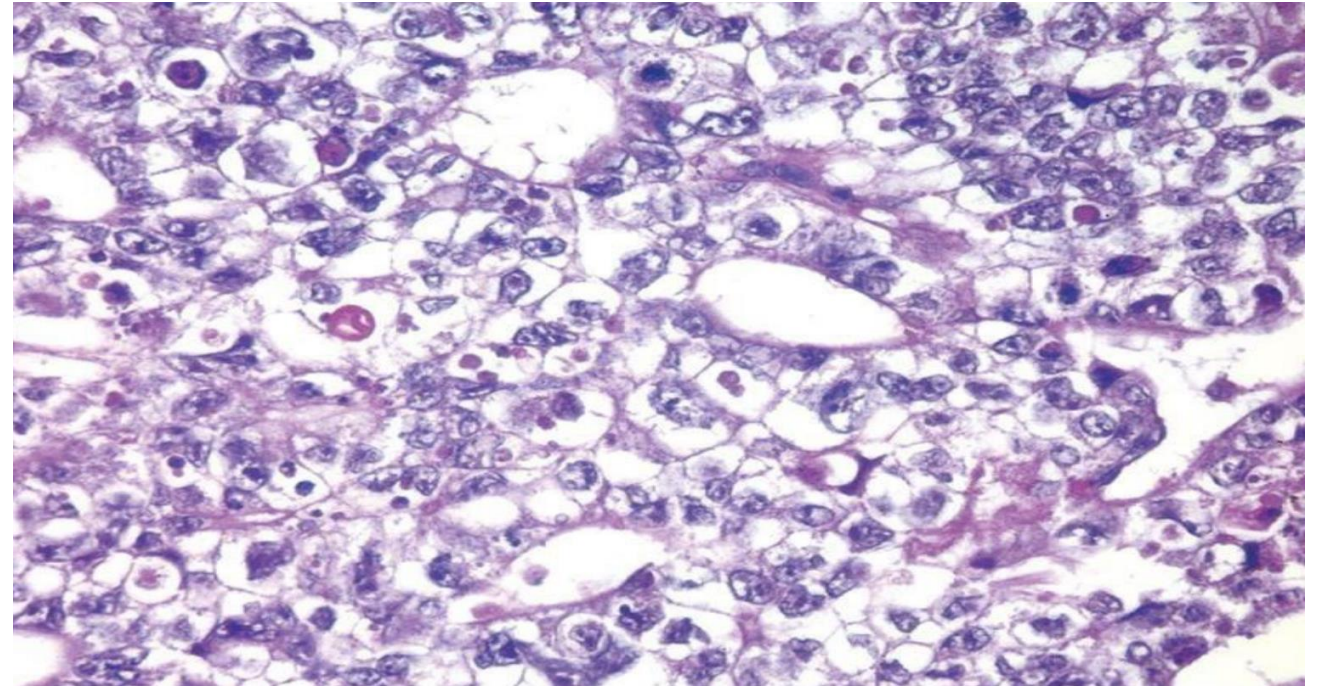
EMBRYONAL CARCINOMAS

- highly malignant, ill-defined, invasive T containing foci of hemorrhage & necrosis .
- The primary lesions may be small, even in patients with systemic metastases. Larger lesions may invade the epididymis & spermatic cord.
- **Histologically :**
 - 1. the T cells are large & primitive looking, with basophilic cytoplasm, indistinct cell borders, & large nuclei with prominent nucleoli.
 - 2. Tumor cells may arranged in undifferentiated solid sheets or may contain glandular structures & irregular papillae .
 - 3. In most cases of embryonal carcinoma, other patterns of germ cell T (e.g., teratoma, yolk sac ca, choriocarcinoma) are admixed with the embryonal areas.
 - 4. Pure embryonal carcinomas are rare, comprise 2% to 3% of all testicular germ cell T.

EMBRYONAL CARCINOMA OF THE TESTIS.



In contrast to the seminoma, the embryonal carcinoma is a hemorrhagic mass



Sheets of undifferentiated cells, as well as primitive glandular differentiation. The nuclei are large & hyperchromatic

EMBRYONAL CARCINOMA OF THE TESTIS.

- Here is an even larger testicular neoplasm. It is composed mostly of embryonal carcinoma, but there are scattered firmer white areas that histologically are teratoma.
- Thus, this testicular neoplasm is mixed embryonal carcinoma plus teratoma (sometimes called teratocarcinoma).
- Embryonal carcinoma is more aggressive than seminoma.



EMBRYONAL CARCINOMA OF THE TESTIS.

- A small testicular carcinoma is shown here. There is a mixture of bluish cartilage with red and white tumor tissue. This neoplasm microscopically contained mainly teratoma, but areas of embryonal carcinoma were also present.

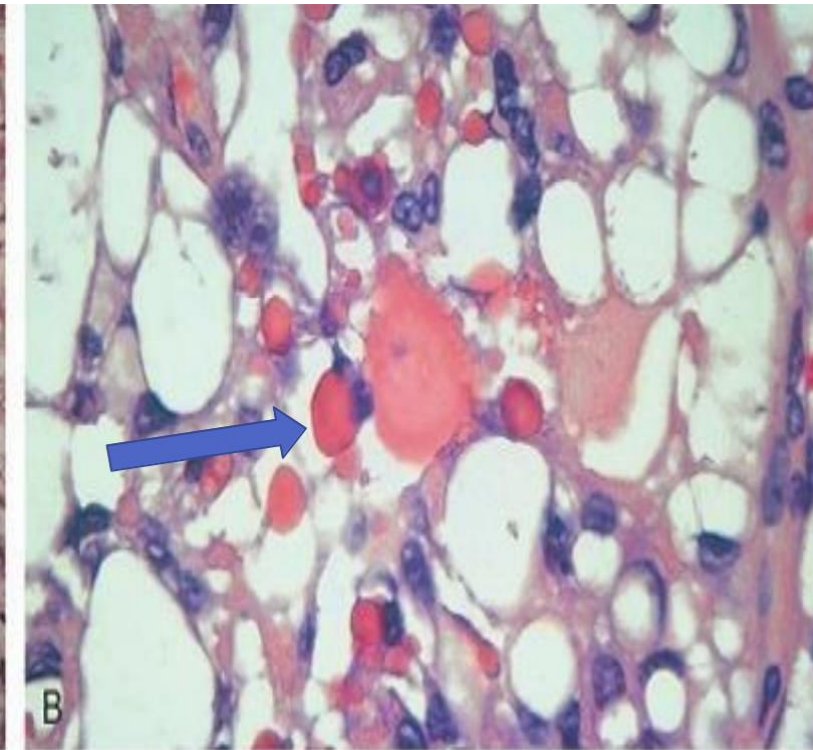
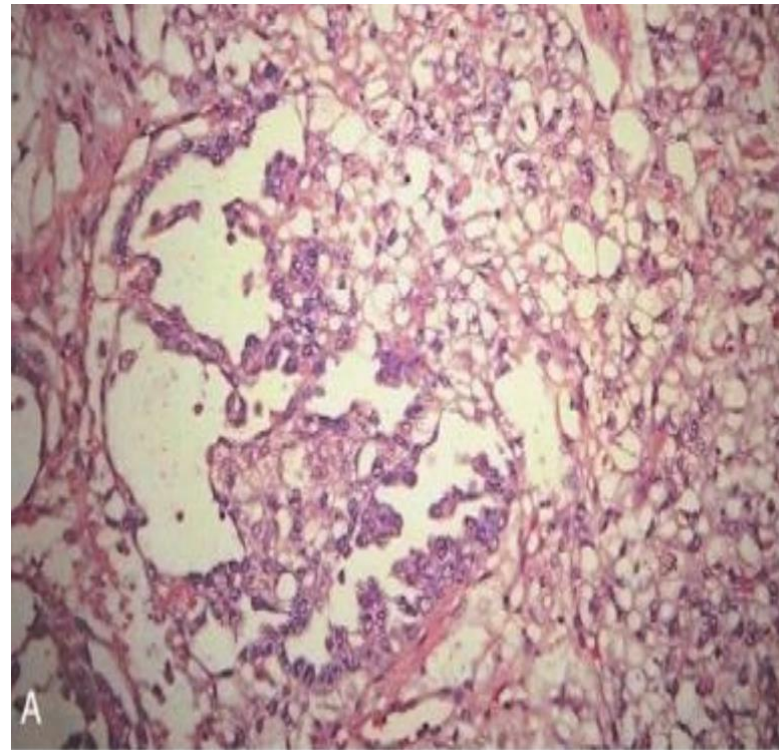


YOLK SAC TUMORS

- Represents endodermal sinus differentiation of totipotential neoplastic cells, hence the other name endodermal sinus T. They are the **most common primary testicular cancer in children younger than 3 years of age**. In adults, they are mostly seen admixed with embryonal ca.
- **Grossly**, these T are often large & may be well demarcated.
- **Histologically** :
 - 1. cuboidal to columnar epithelial cells forming microcysts, sheets, glands, & papillae, often associated with eosinophilic hyaline globules.
 - 2. A distinctive feature is the presence of structures resembling primitive glomeruli, the so-called **Schiller-Duvall bodies**.
 - 3. **α -fetoprotein (AFP)** can be demonstrated within the cytoplasm of the T cells by immunohistochemical techniques.

YOLK SAC TUMOR “CARCINOMA”.

- A, LP view showing areas of loosely textured, microcystic tissue & papillary structure resembling a developing glomerulus (Schiller-Duval body)
- B, HP view showing characteristic hyaline droplets within the microcytic areas of the tumor. **Alpha-fetoprotein** is present within the droplets.

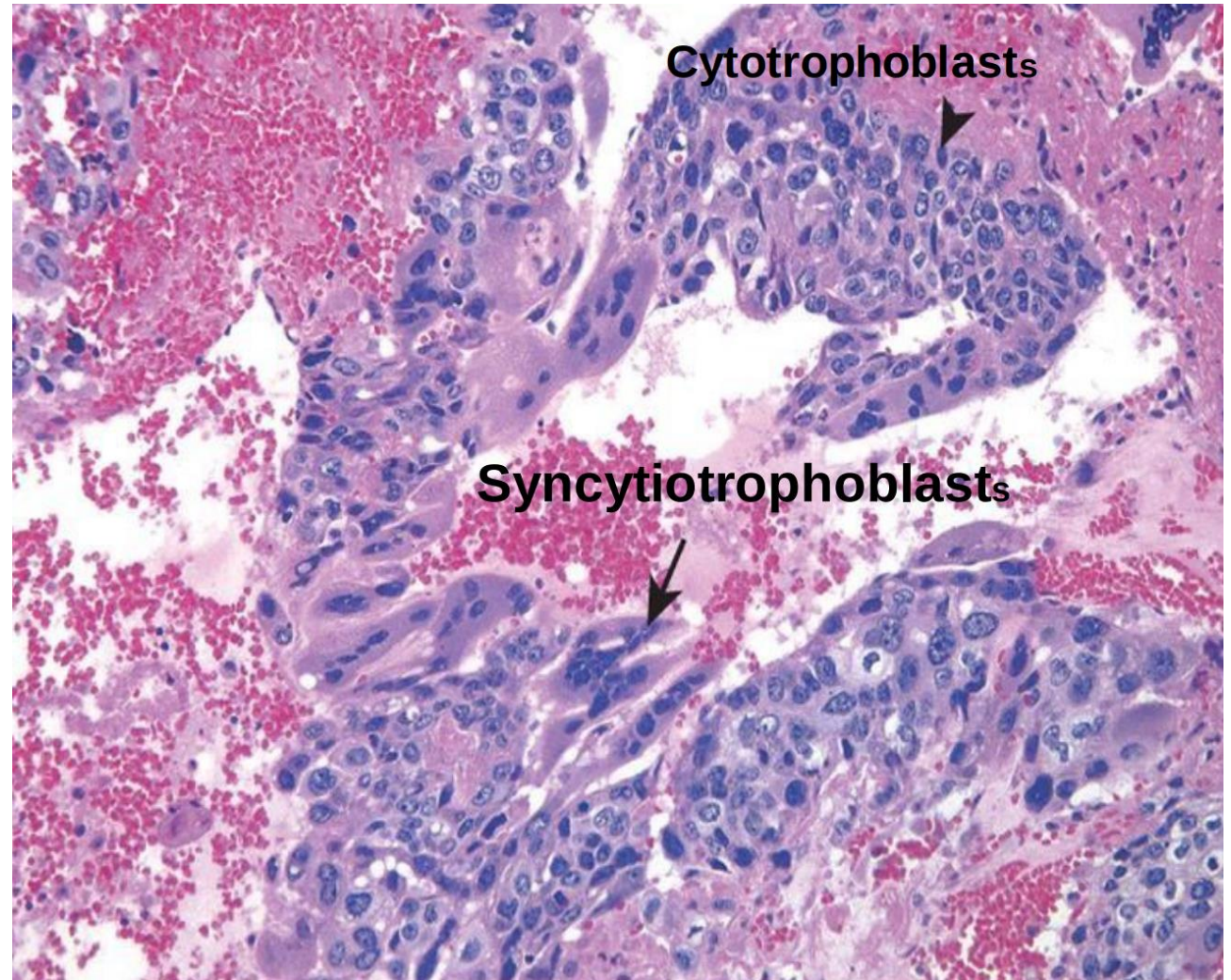


CHORIO- CARCINOMAS

- represent differentiation of pluripotential neoplastic germ cells along trophoblastic lines.
- **Grossly**, the primary T are often small, non palpable lesions, even with extensive systemic metastases!
- **Histologically** composed of
 - (1) cytotrophoblasts; sheets of small cuboidal cells capped by
 - (2) Syncytiotrophoblasts ; large, eosinophilic syncytial cells containing multiple dark, pleomorphic nuclei.
 - Well-formed placental villi are never seen.
 - hCG hormone can be identified by immunohistochemical staining, particularly within the cytoplasm of the syncytiotrophoblastic elements.

CHORIOCARCINOMA

- (1) cytotrophoblastic cells with central nuclei &
- (2) syncytiotrophoblastic cells with multiple dark nuclei in the cytoplasm, in which HCG can be identified. hemorrhage & necrosis are prominent.

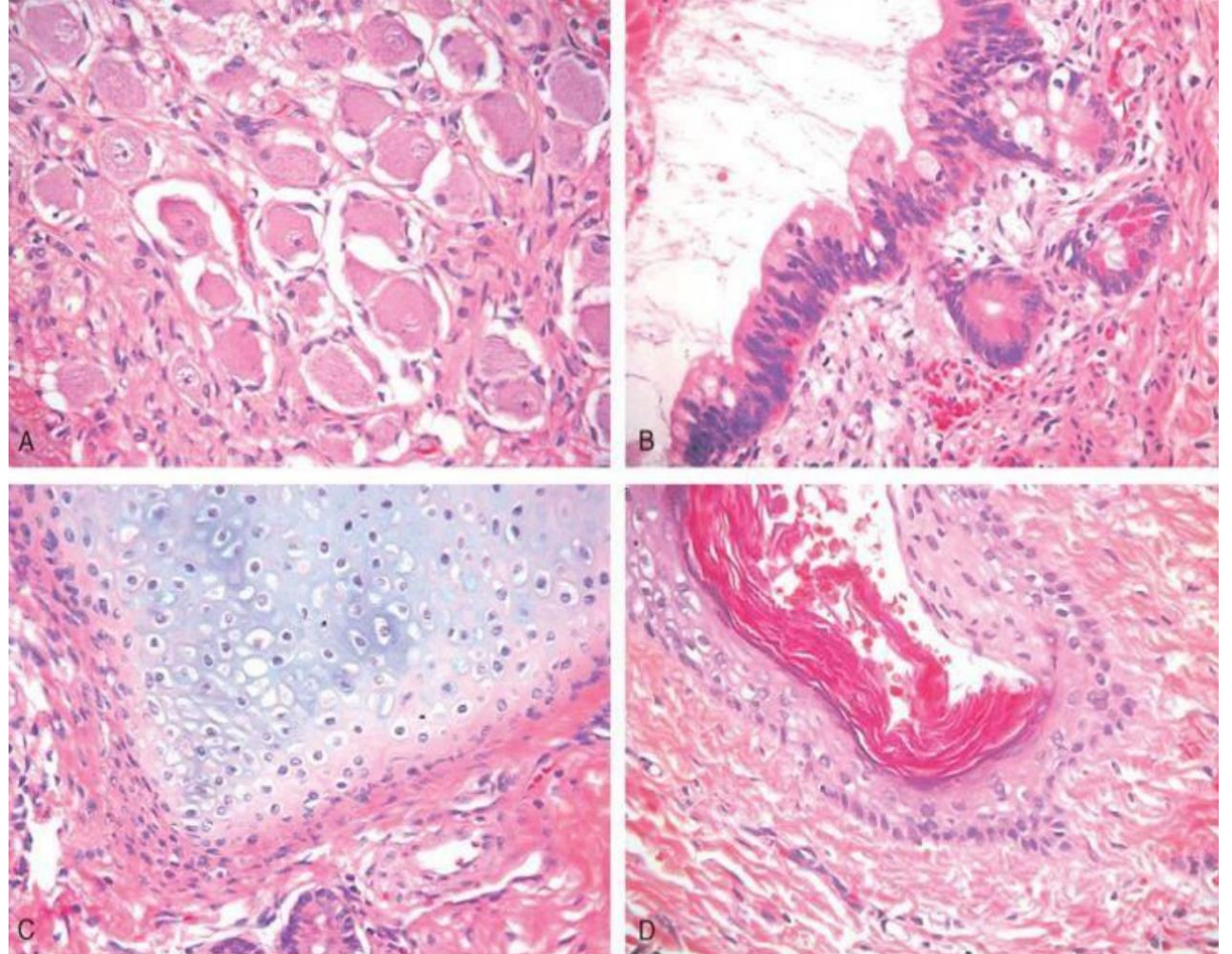


TERATOMAS (TT)

- Represent differentiation of pluripotential neoplastic germ cells along somatic cell lines.
- TT form firm masses that on cut surface, often contain cysts & areas of cartilage.
- **Histologically** : 3 major variants of pure teratomas are recognized:
 - (I) Mature TT contain fully differentiated tissues from one or more germ cell layers (neural tissue, cartilage, adipose tissue, bone, & epithelium) in a haphazard array.
 - (II) Immature TT ,contain immature somatic elements reminiscent of those in developing fetal tissue.
 - (III) TT with somatic-type malignancies are characterized by the development of frank malignancy (usually in the form of a SCCa or adenocarcinoma) in preexisting TT elements.
- Pure TT in prepubertal males are usually benign, BUT... All testicular TT in adults should be regarded as malignant T because they are: (1) often contain other malignant germ cell elements & (2) they metastasize in 37% of cases.

TERATOMA

- Mature testicular teratoma {Rare tumor}.
- 4 different fields from the same tumor, containing cells derived from ectoderm both
- (A)neural &
- (D)squamous epithelium}; endoderm
- (B)glandular; & mesodermal
- (C)cartilage lines.



TERATOMA

- Teratoma: testis, from a man aged 44years.
- Solid testicular mass, 6X4 cm.
- C/S is pinkish-white with yellow areas of necrosis & hemorrhage. No cysts are present.



11.22 Teratoma: testis

MIXED GERM CELL TUMORS

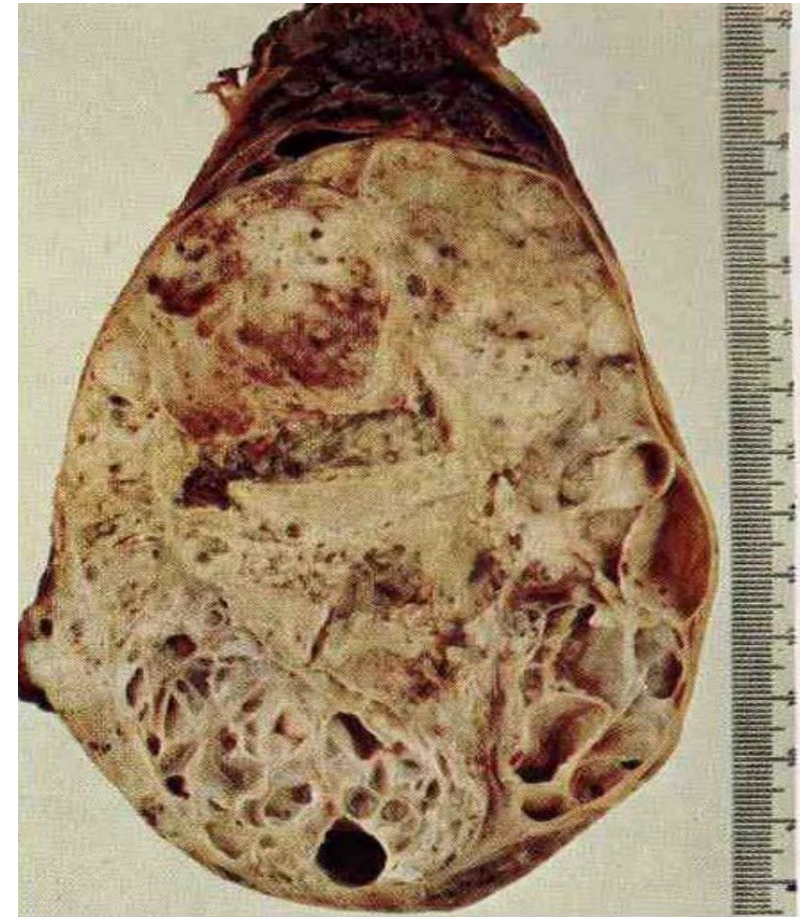
- Account for 40% of all testicular germ cell T. Combinations of any of the described patterns may occur in mixed T. The most common of which is a combination of teratoma, embryonal carcinoma, & yolk sac tumors.
- **Clinical Features:** All testicular germ cell T present mostly
 - (1) painless enlargement of the testis.
 - (2) Unfortunately some T, especially nonseminomatous germ cell T, may present with widespread metastases at diagnosis, in the absence of a palpable testicular lesion!

MIXED GERM CELL TUMORS

- **Clinically**, it is best to consider testicular germ cell T under 2 broad categories:
 - Seminomas & non-seminomatous T.
- Seminomas often remain confined to the testis for long time & may reach considerable size before diagnosis.
- Lymphatic metastases are most commonly encountered in the iliac & para-aortic LN, particularly in the upper lumbar region.
- Hematogenous metastases occur later.
- In contrast, nonseminomatous germ cell T tend to metastasize earlier, by both blood (most commonly to the liver & lungs) & by lymphatics.
- Seminomas have good prognosis, as they are very radiosensitive, & respond well to chemotherapy.

COMBINED TESTICULAR SEMINOMA & TERATOMA

- A large ,ovoid mixed tumor, with:
- (1) seminomatous, yellowish-white solid element, with necrosis & hemorrhages in the upper 2/3 of tumor
- (2) an almost entirely cystic teratomatous element in the lower



11.21 Teratoma: testis

MIXED GERM CELL TUMORS

- Nonseminomatous germ cell T prognosis is generally poor, but it has improved dramatically in some cases with the introduction of platinum-based chemotherapy regimens.
- **Testicular germ cell T are staged in to:**
- Stage I: T confined to the testis.
- Stage II: Regional LN metastases only.
- Stage III: Non-regional LN &/or distant organ metastases

- Assay of tumor markers secreted by T cells is important in the clinical evaluation & staging of germ cell T
- **(I) hCG,**
 - 1. produced by neoplastic syncytiotrophoblastic cells, is always elevated in patients with choriocarcinoma.
 - 2. Germ cell tumors, including seminoma, may also contain foci of syncytiotrophoblastic cells (without cytotrophoblastic element) & hence may elaborate hCG. Approximately 10% to 25% of seminomas elaborate hCG.
- **(II) α -fetoprotein (AFP)** is a glycoprotein normally synthesized by the fetal yolk sac & several other fetal tissues

- Nonseminomatous germ cell T containing elements of yolk sac (endodermal sinus) often produce AFP (AFP is also elevated in hepatocellular ca); & in contrast to hCG
- The presence of AFP is a reliable indicator of the presence of a nonseminomatous component in the germ cell T, as yolk sac elements are not found in pure seminomas.
- As mixed patterns are common, most nonseminomatous T have elevations of both hCG & AFP.
- Serial determinations of hCG & AFP are useful in the (A) primary diagnosis (B) staging (C) monitoring patients with testicular germ cell T for persistent or recurrent T after therapy