Male Genital Tract Pathology 2024

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The Male Genital System

In the following lectures, we will consider the most common malformations, inflammatory conditions, & neoplasms involving the penis & scrotum, prostate, & testes

❑ 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 increased 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 are

(I) mostly caused by Sexually Transmitted Diseases,
(II) local inflammatory processes unrelated to STDs, &
(III) several other systemic inflammatory diseases may, on occasion, produce penile lesions.

- Local inflammation of the

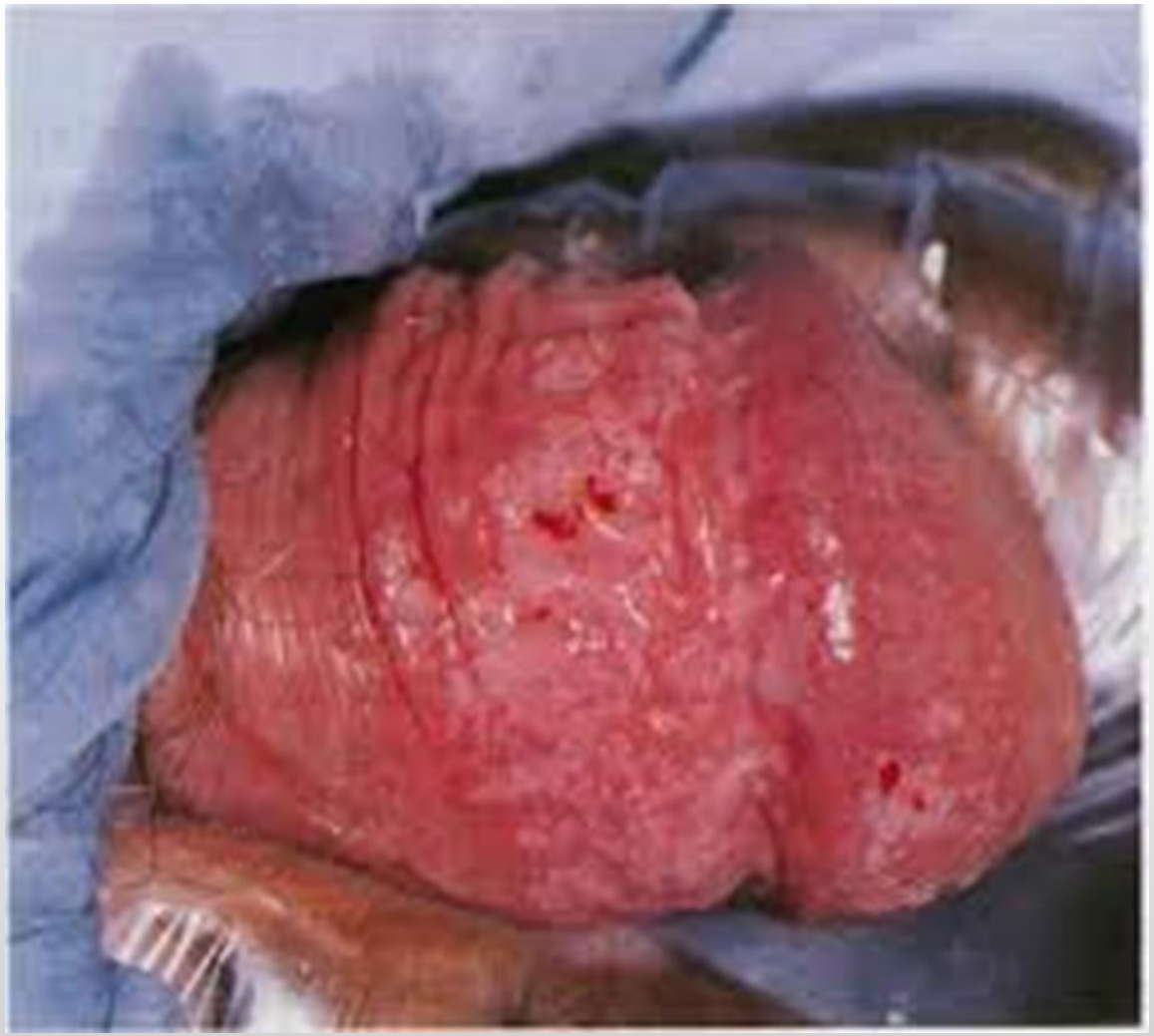
(1) Glans penis is called Balanitis

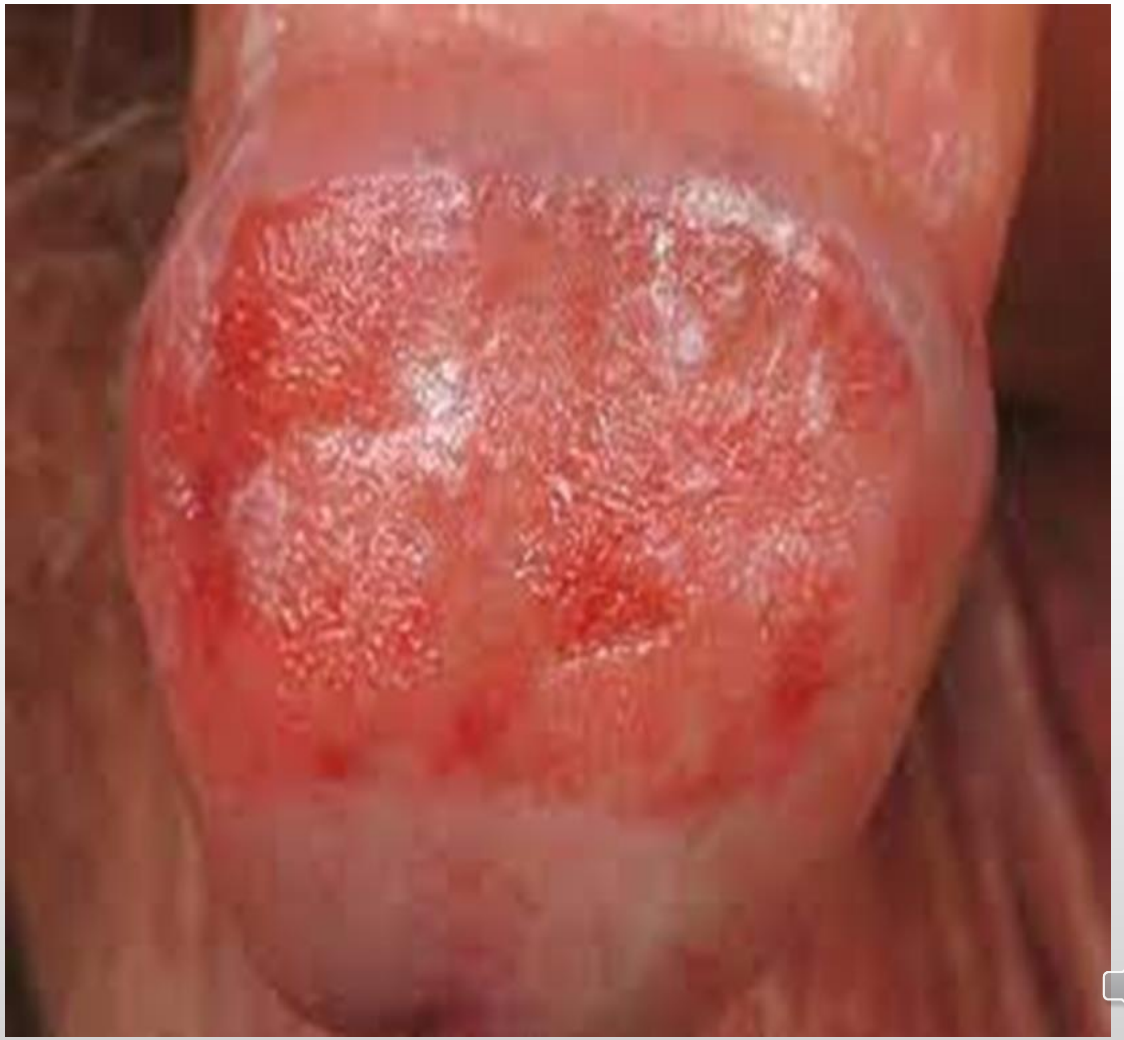
2) glans penis + the overlying prepuce is called balanoposthitis.

- 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.

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

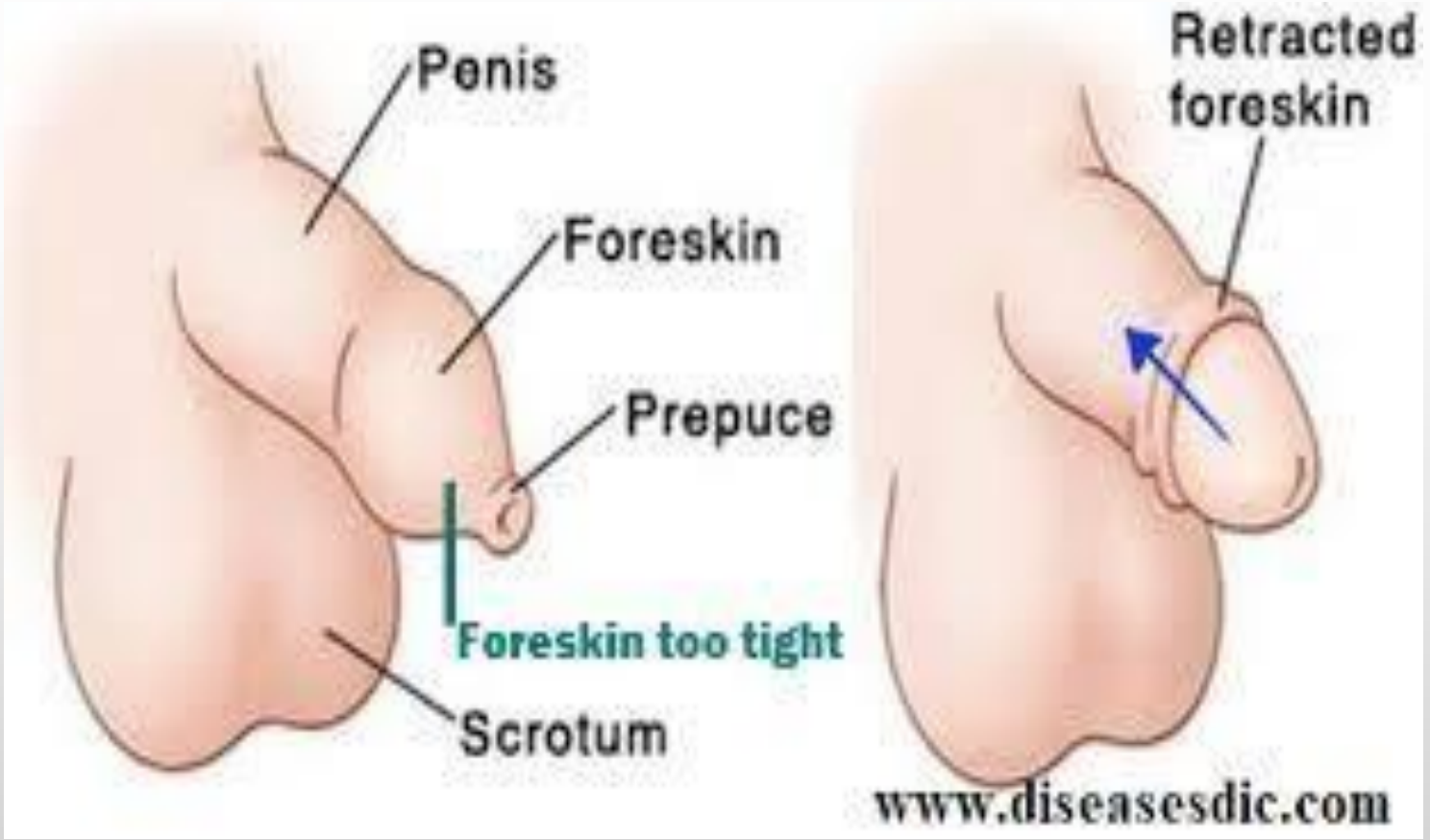




Phimosis

- 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.



Neoplasms of the penis

- 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, including:

(2)poor hygiene(with resultant exposure to potential carcinogens in smegma), (3) smoking,& (4) **infection with** HPV, particularly types 16 & 18.

- 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**.

(II) When Bowen disease presents as an erythematous patch on the **glans penis**, it is called **Erythroplasia of Queyrat.**

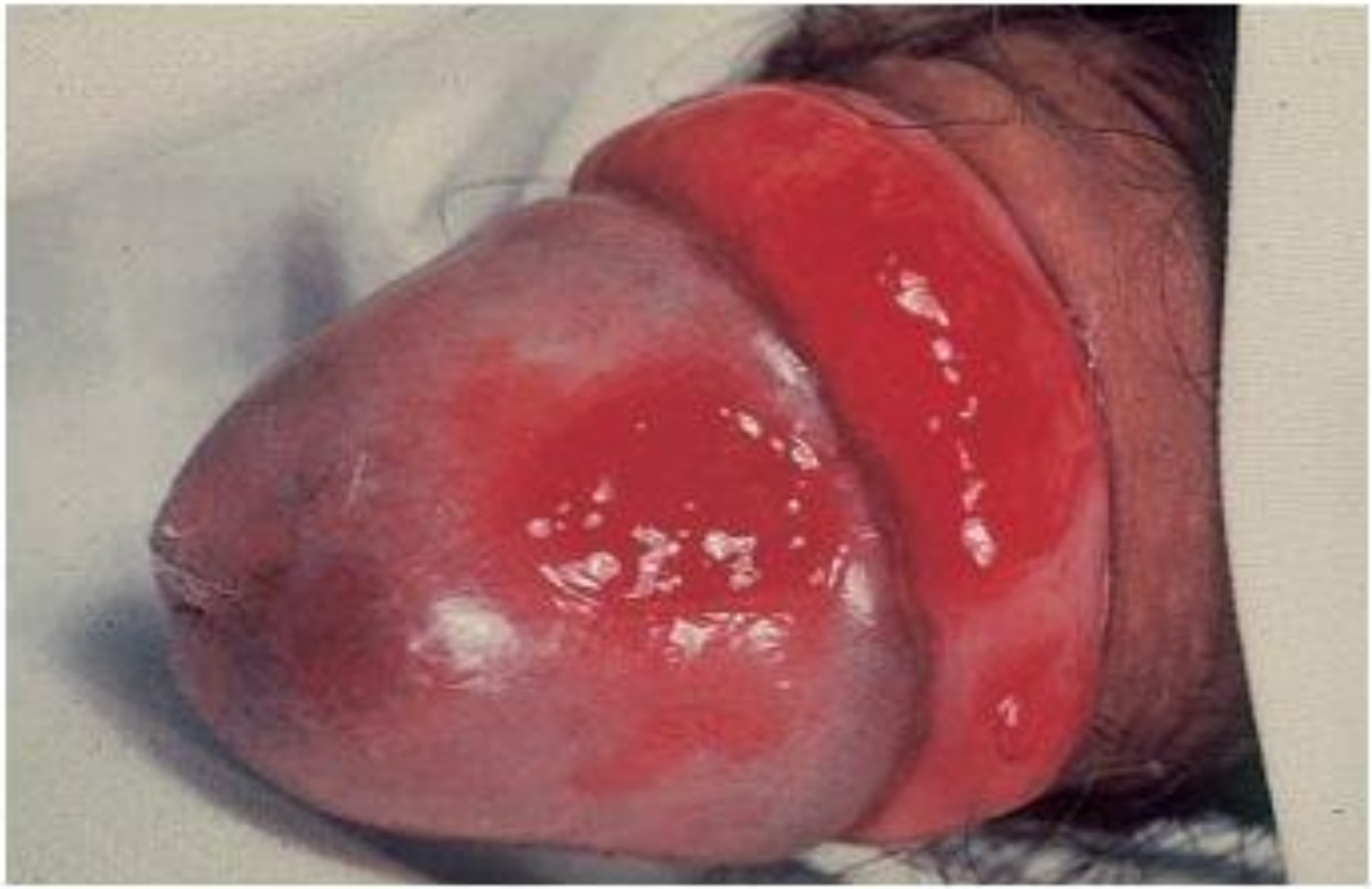
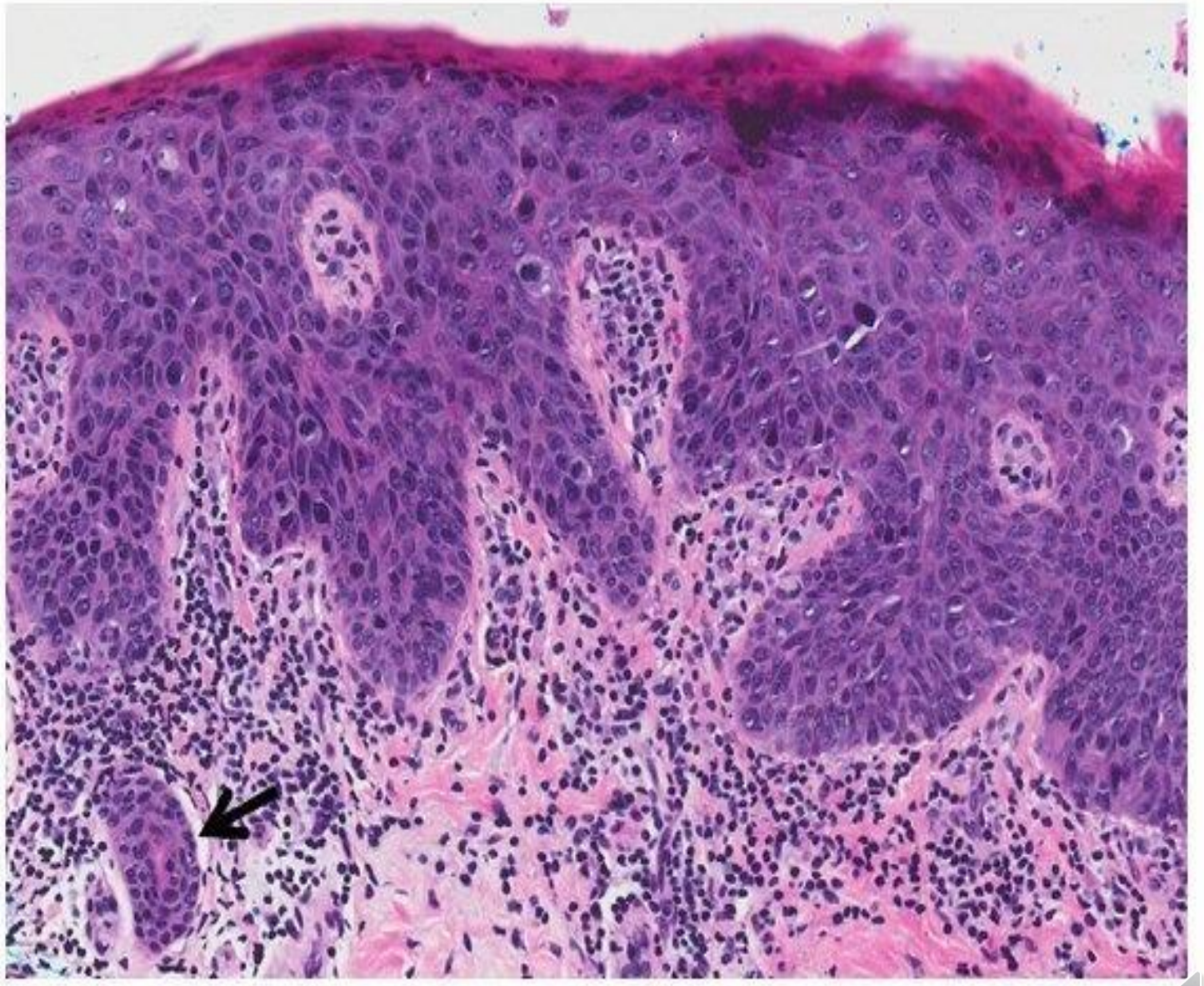


Fig. 13.39 Erythroplasia of Queyrat.

- 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



(III) Bowenoid papulosis occurs in young, sexually active males & is **identical to Bowen disease histologicaly, 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.

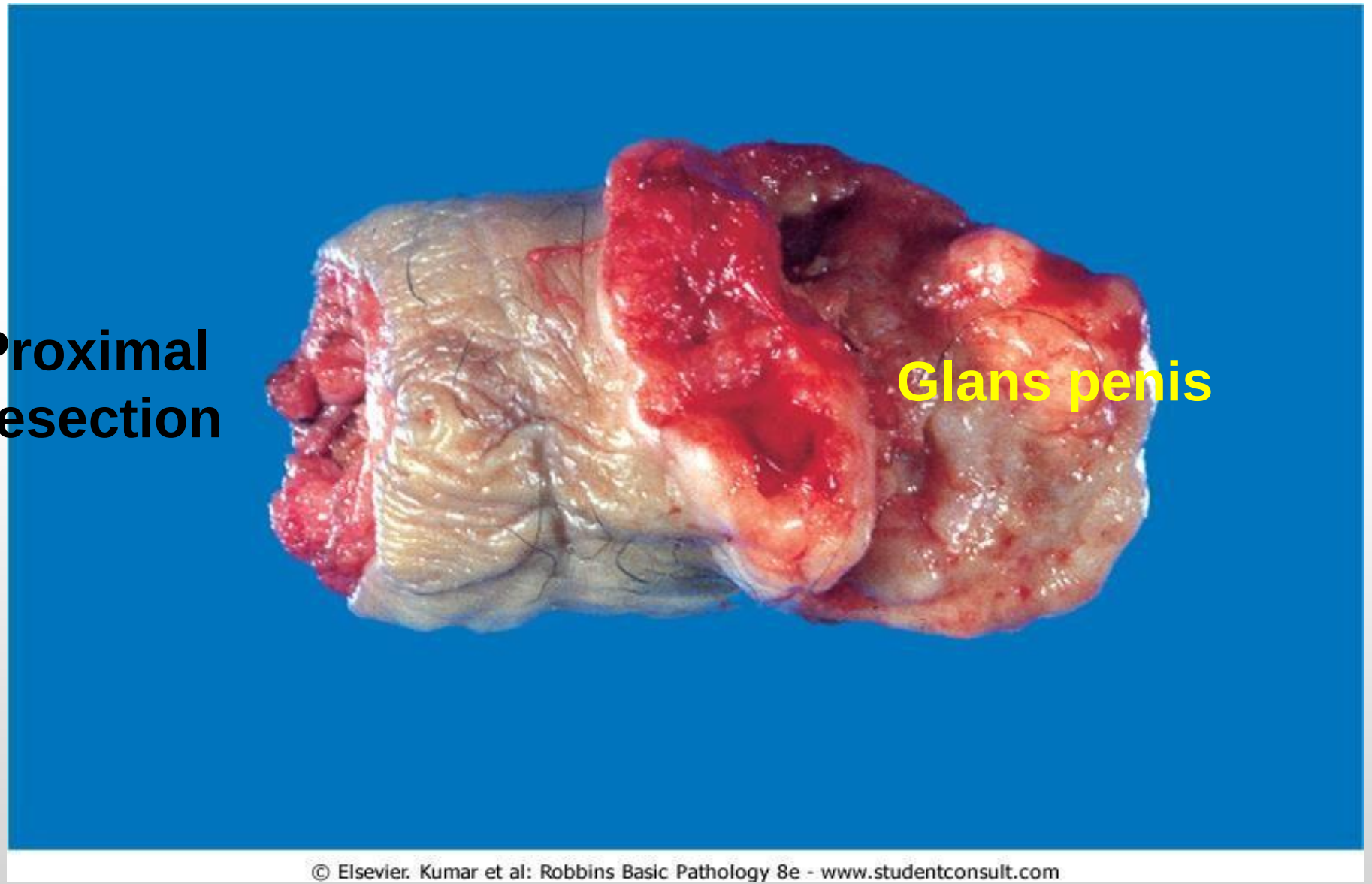
Penile Squamous cell ca

- Penis SCC appears as a gray, crusted, popular lesion, most commonly on the glans penis or prepuce.
- It may infiltrate the underlying connective tissue producing an indurated ulcer with irregular margins

- Histopathologty , 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.

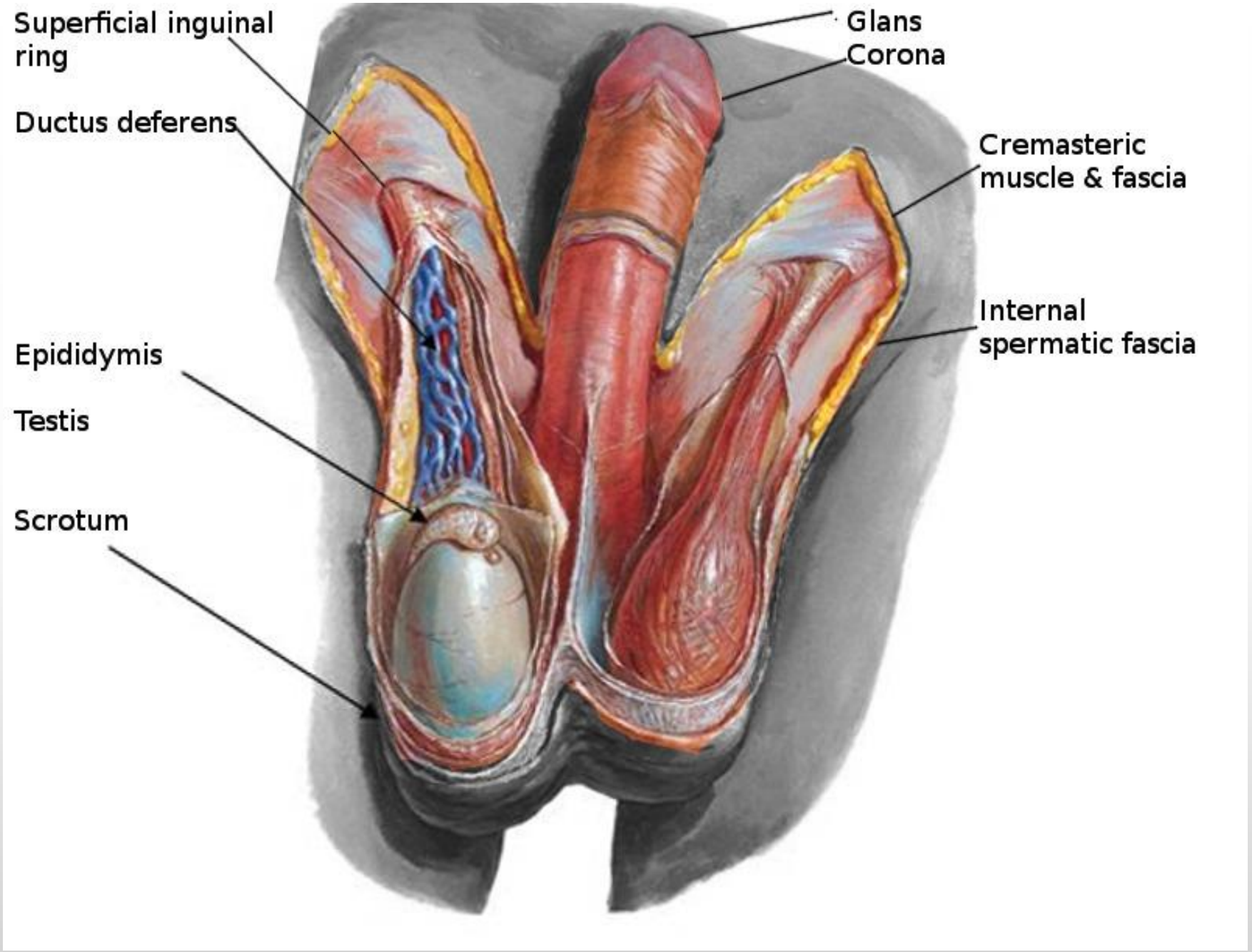
- Distant metastases are relatively uncommon, & the overall 5-year survival rate averages 70%.

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



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.
- Testicle. Each testicle produces hormones, the main one being testosterone, with the help of parts of the brain like the hypothalamus and pituitary gland. ...
- Epididymis. An epididymis is located on the top of each testicle. ...
- Spermatic cord. ...
- Cremaster muscle.


Superficial inguinal ring
Ductus deferens
Epididymis
Testis
Scrotum
Glans
Corona
Cremasteric muscle & fascia
Internal spermatic fascia

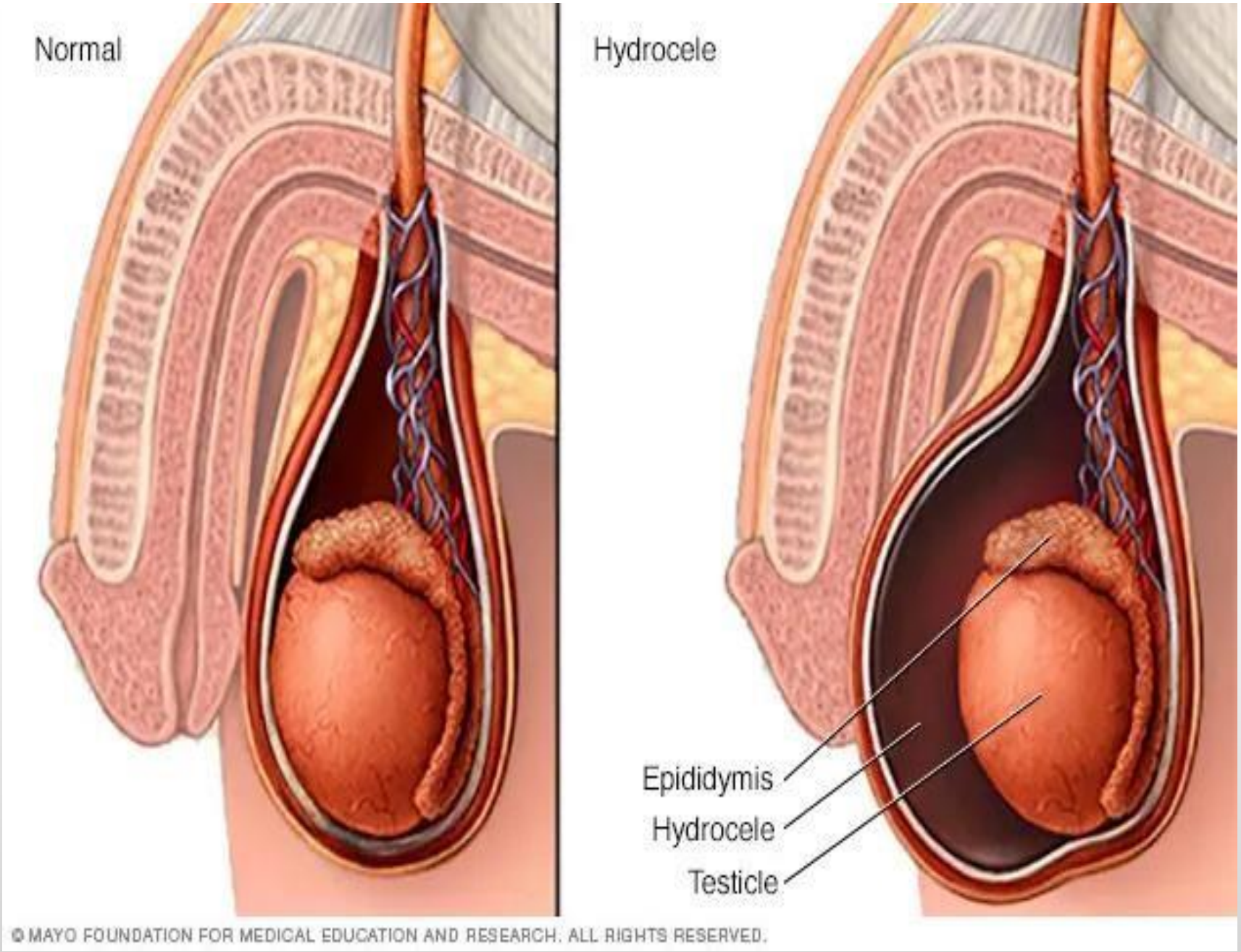
➢ The most common cause of scrotal enlargement is:

- **Hydrocele** an accumulation of serous fluid within the tunica vaginalis, which can be idiopathic or arise in response to neighboring infections or tumors;

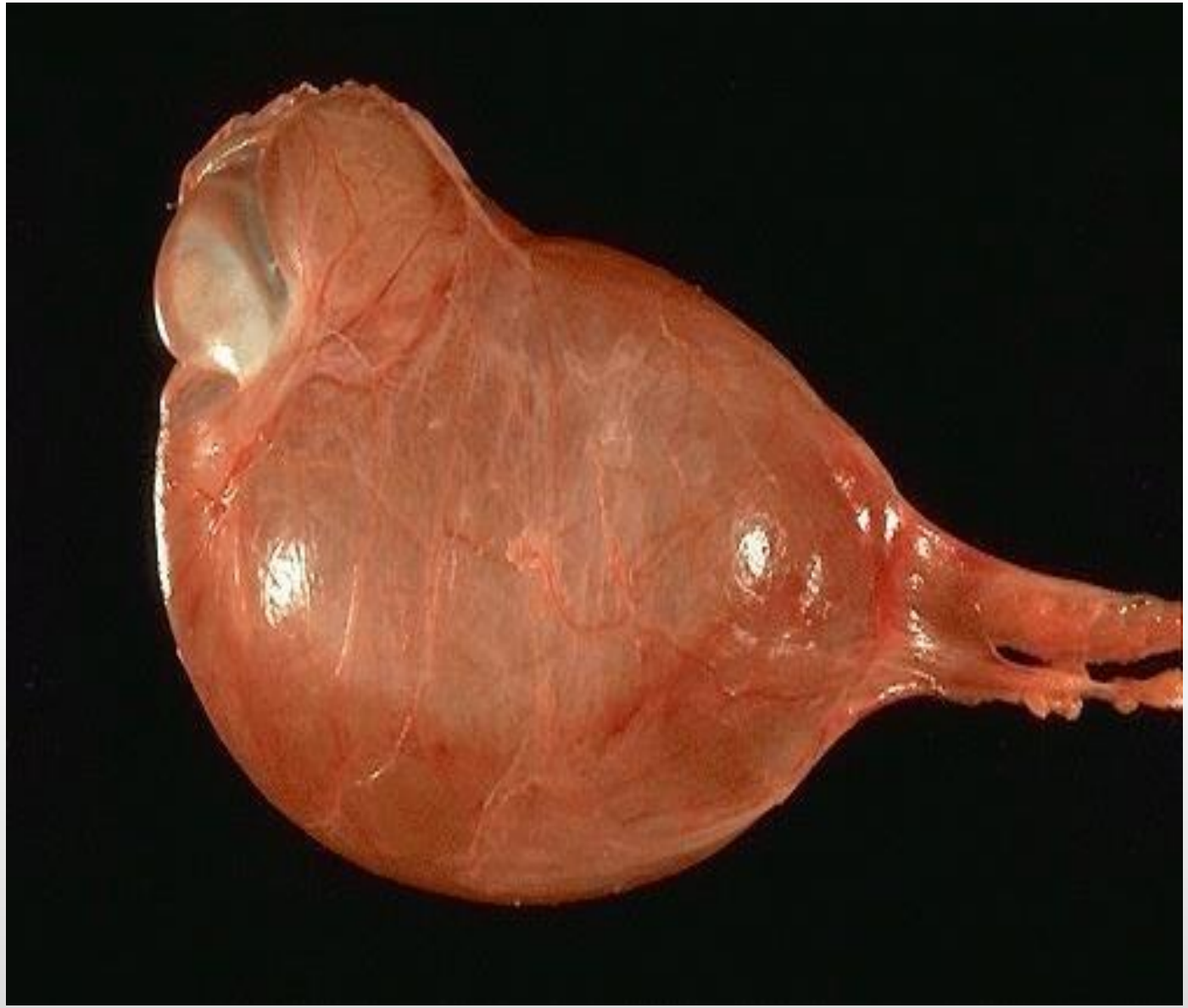
  A hydrocele must be distinguished from a true testicular mass, and transillumination may help, because the hydrocele will transilluminate but a testicular mass will be opaque.

  less common causes of scrotal enlargement are:

- Accumulation of blood (Hematocele) or lymphatic fluid (chylocele) within the tunica vaginalis



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



- 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

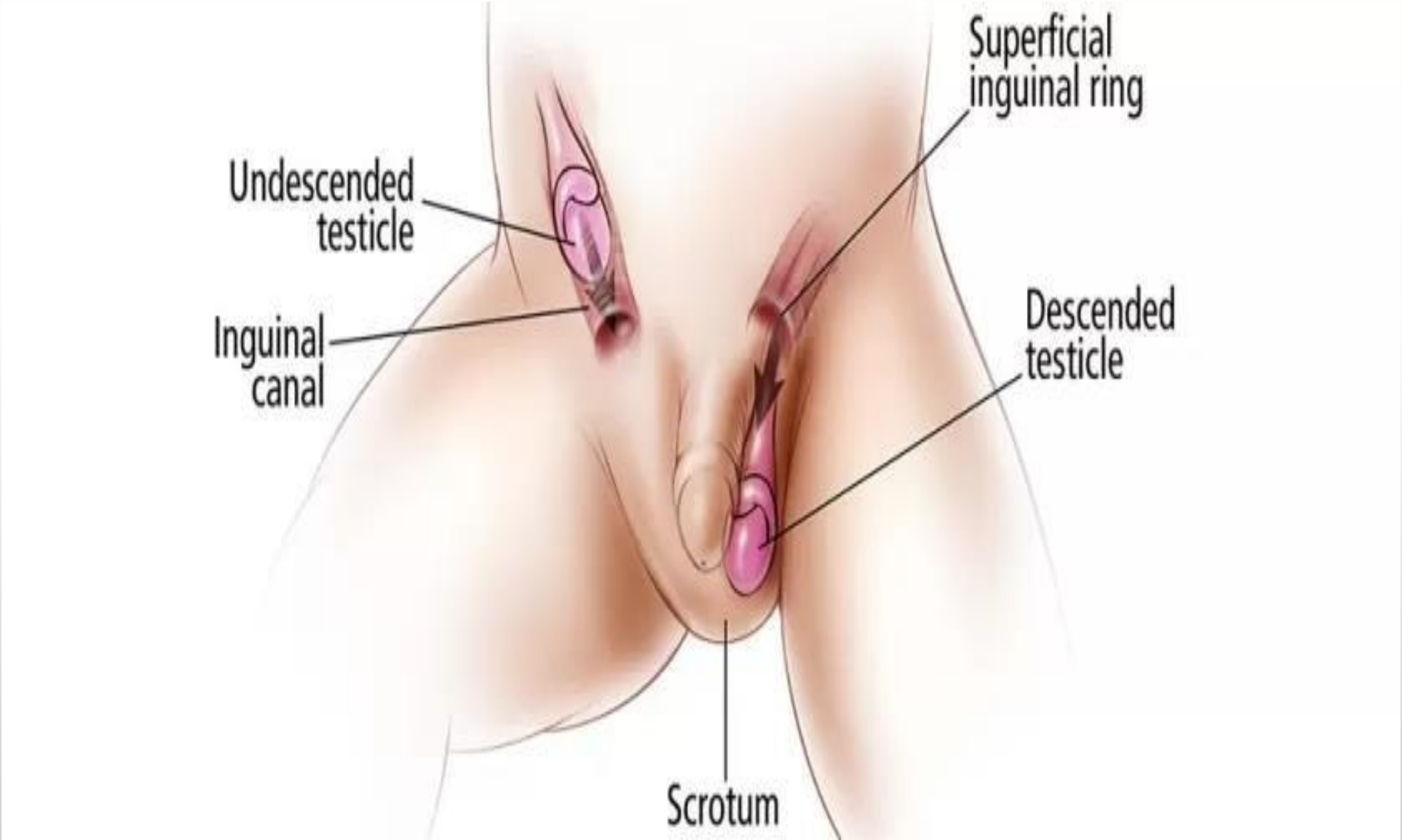
- infertility, - atrophy, - enlargement, & - local pain.

Cryptorchidism & Testicular Atrophy.

Cryptorchidism 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 malpositioning of the gonad.

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



Effects of cryptorchidism

(I)Bilateral cryptorchidism causes sterility

(I)Unilateral cryptorchidism may be associated with atrophy of the contralateral descended gonad& may also lead to sterility.

(II)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.

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.

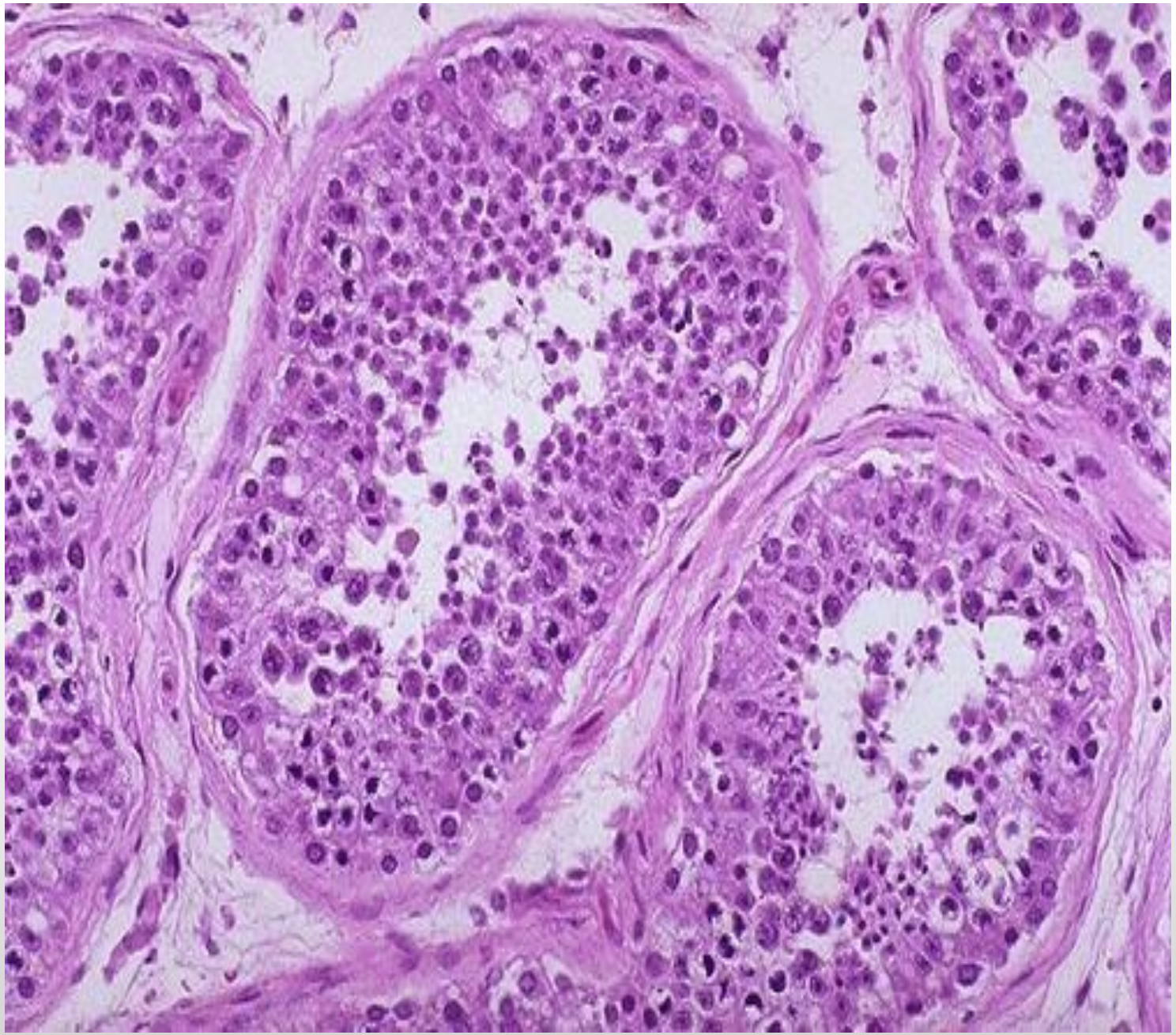
❖ Histologically (حفظ)

- cryptorchid testes show evidence of

(1) tubular atrophy by 5 to 6 years of age, hyalinization is present by the time of puberty,

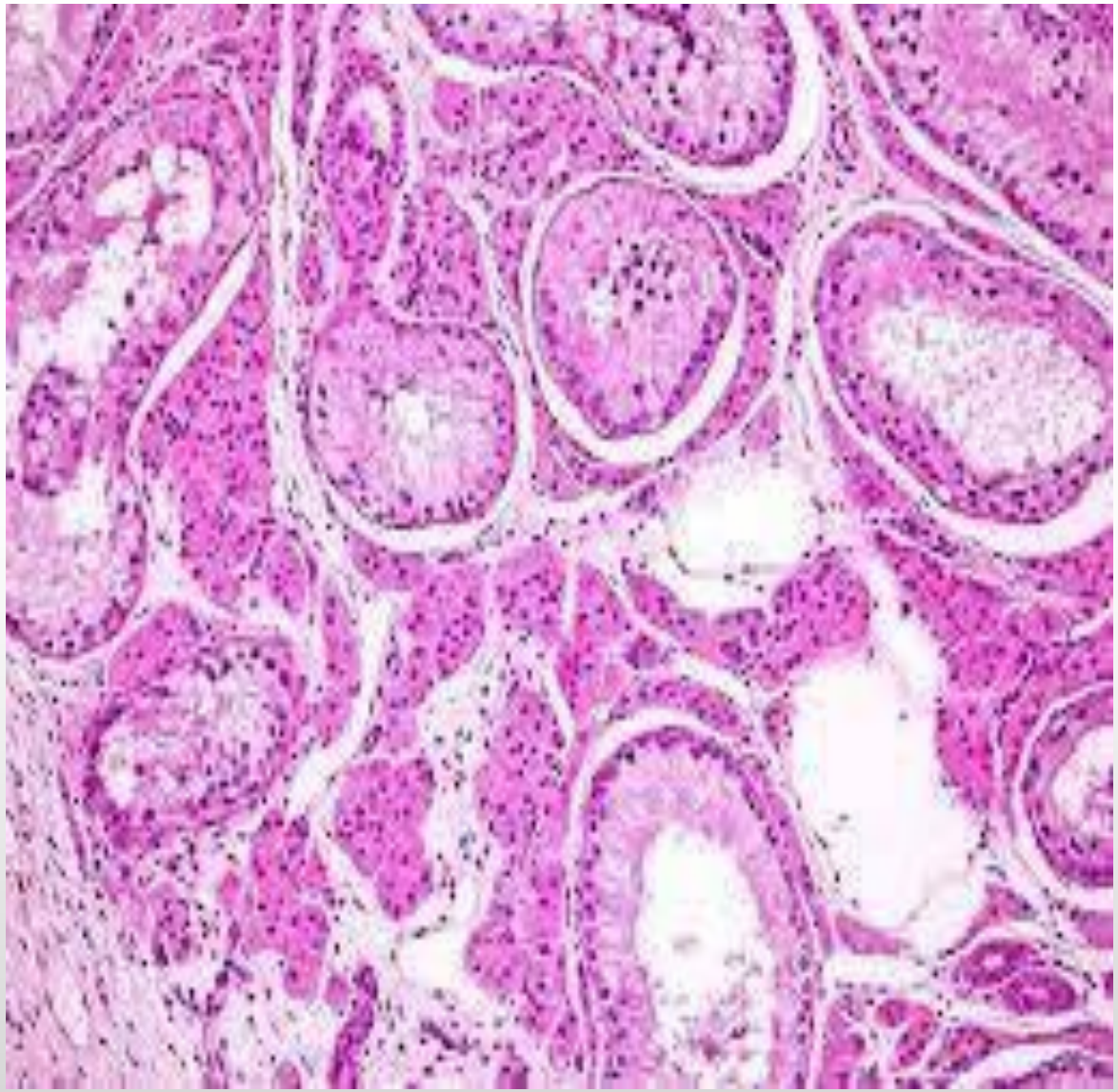
(2) accompanied by Leydig cell hyperplasia.

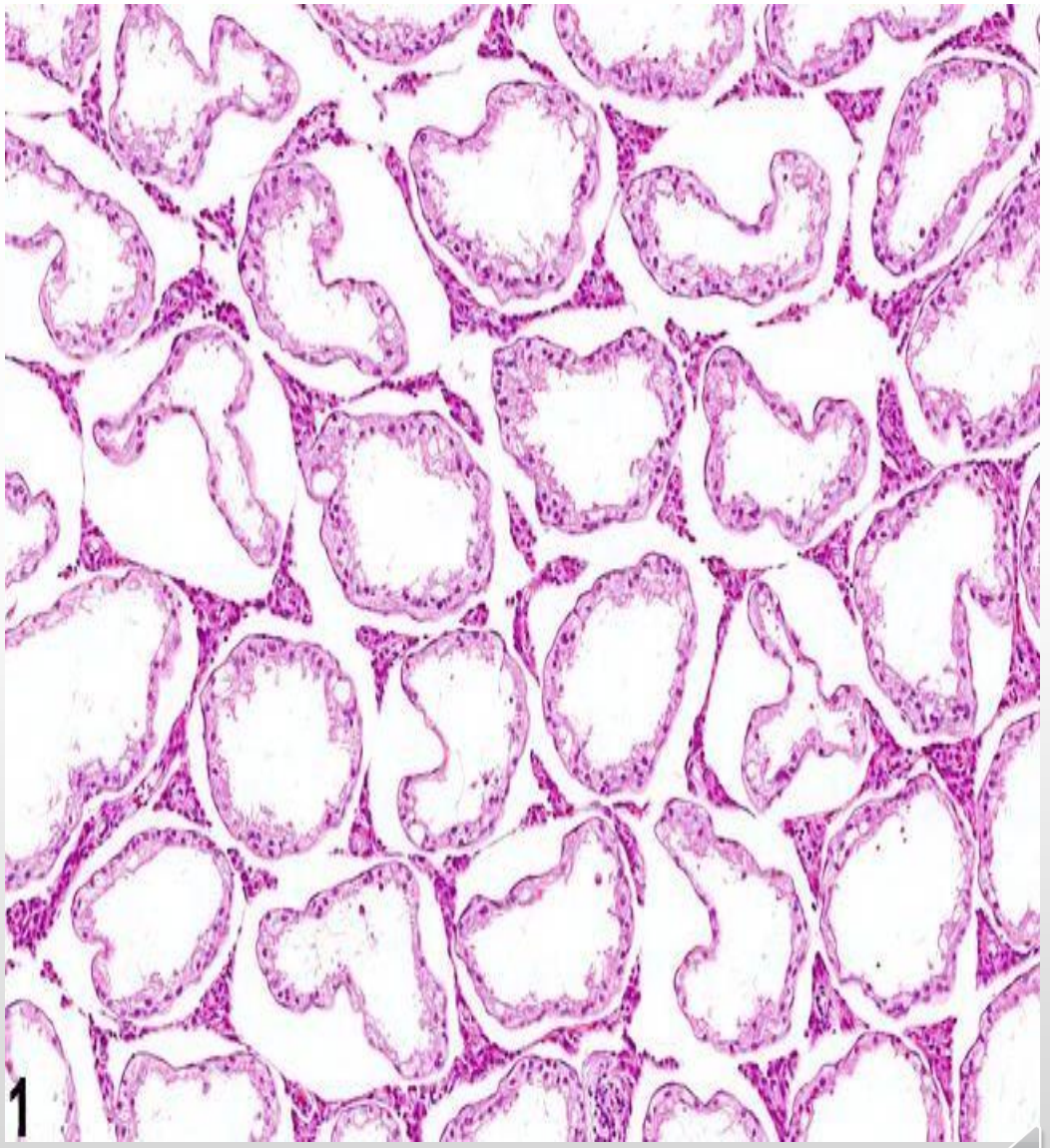
(3) foci of intratubular germ cell neoplasia may be present in cryptorchid testes & may be the source of subsequent testicular cancers.



- 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 Testis in both pictures





- Similar tubular atrophy may be caused by several other conditions, including☹ حفظ
  - Chronic ischemia.
  - Trauma.
  - Chronic hyperestrogenism (e.g., cirrhosis)
  - Radiation
  - Anti-neoplastic chemotherapy.

Inflammatory 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.

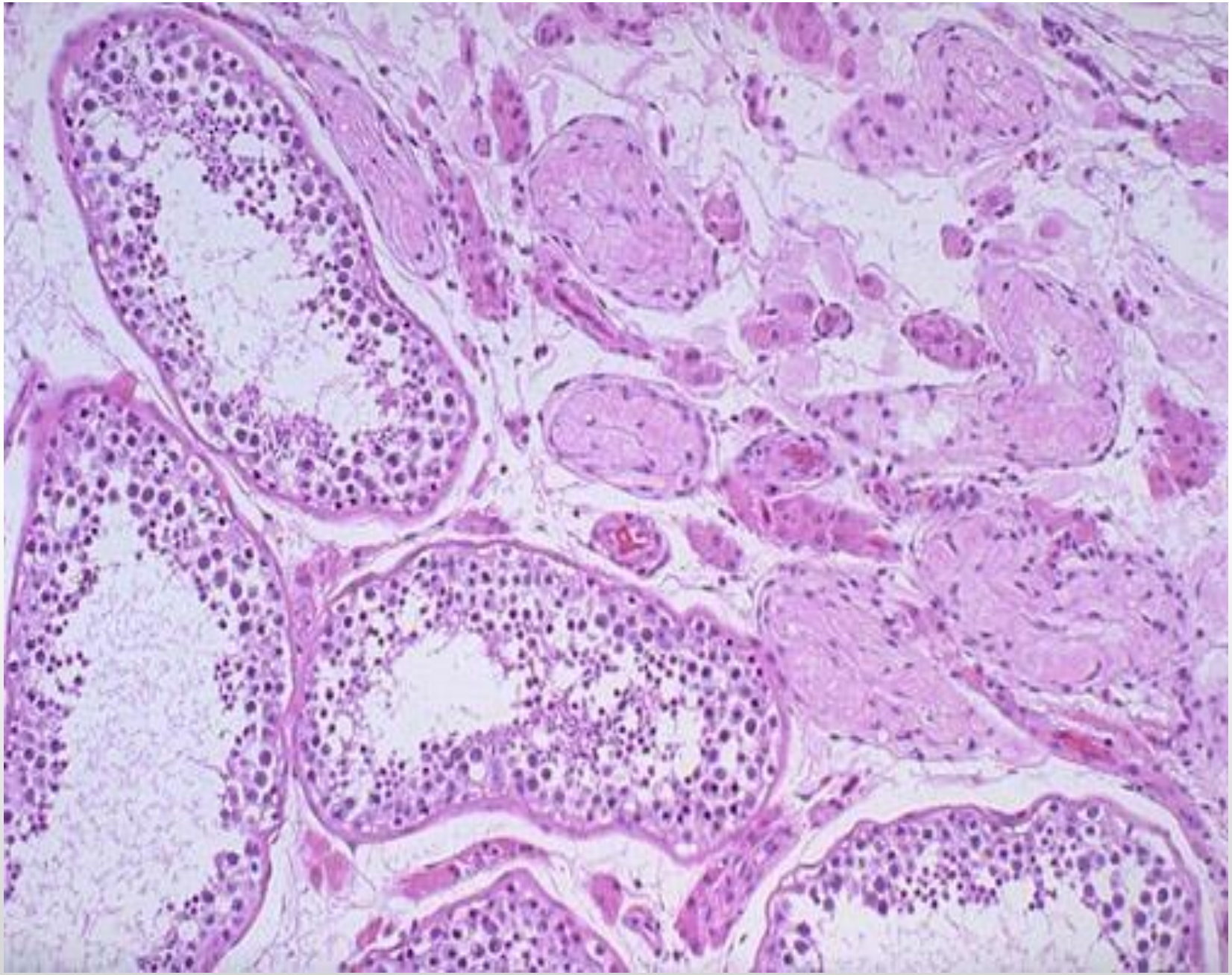
(I) Nonspecific epididymitis& orchitis, begin usually as a primary UTI with secondary ascending infection to the testis through the vas deferens or lymphatics of the spermatic cord. The involved testis is typically **swollen, tender**& contains a predominantly neutrophilic cell infiltrate.

(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**.

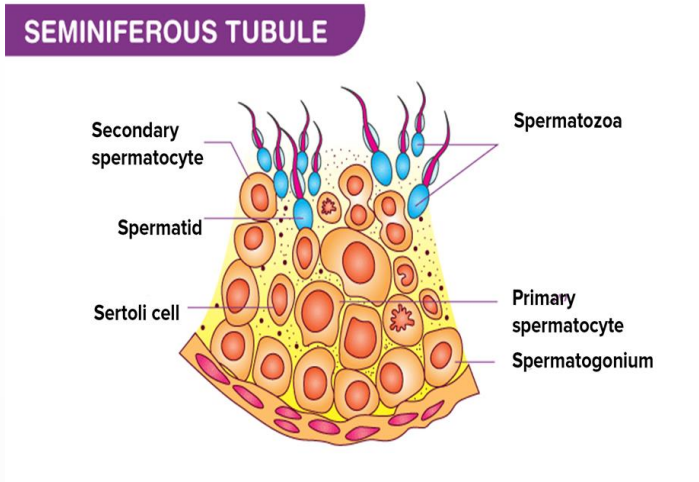
(III) Granulomatous inflammation of the testis may be caused by some infections & autoimmune disease, of which **TB is the most common.** Testicular TB generally begins in the epididymis, with secondary involvement of the testis.

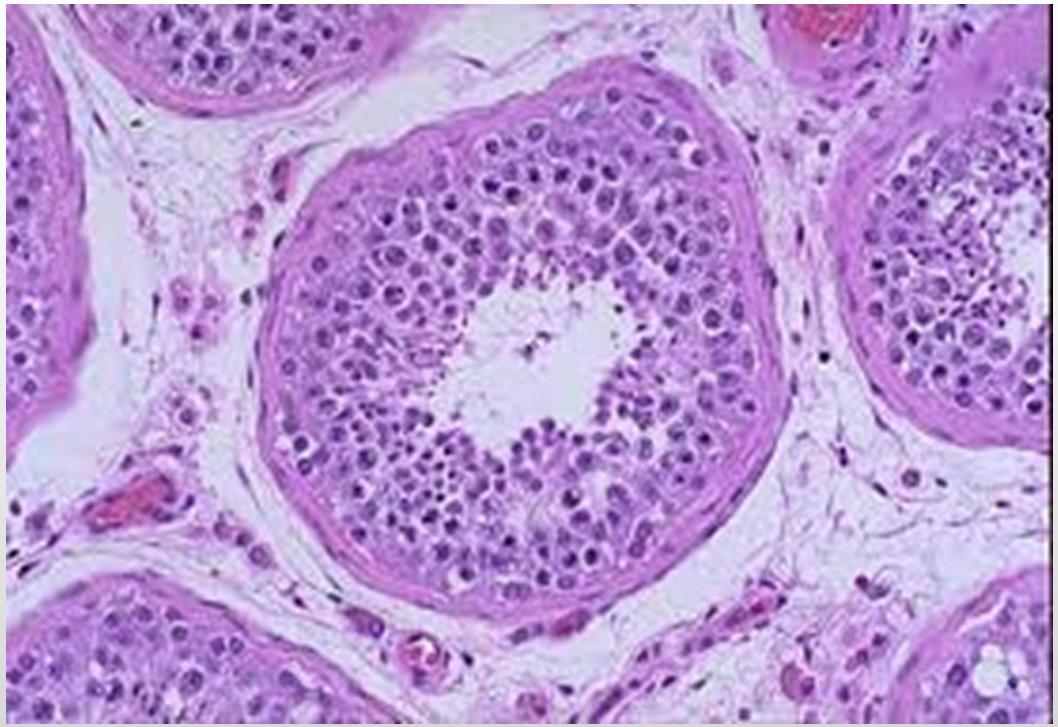
- Histologically , there is caseous granulomatous inflammation.

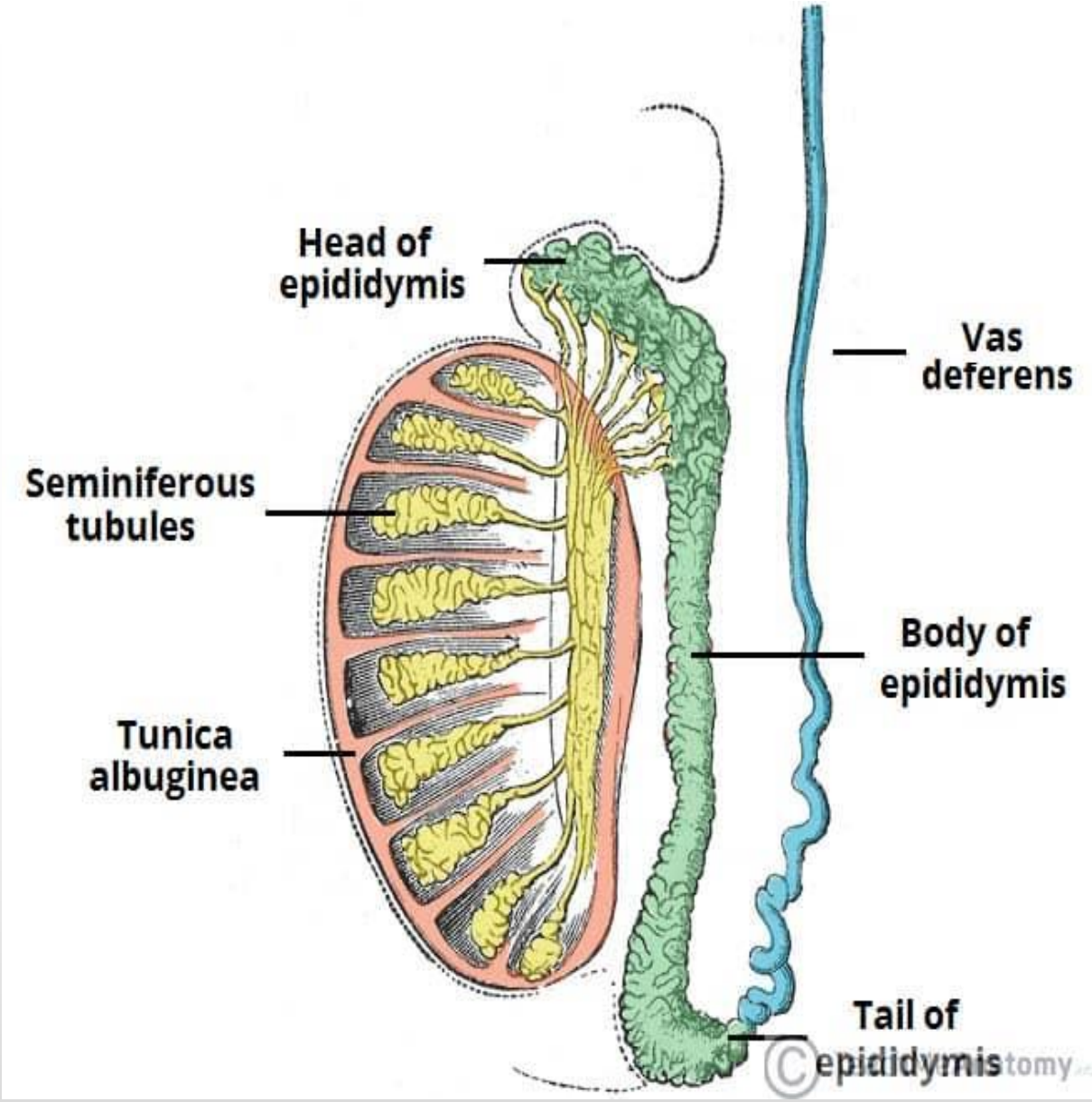


- There is **focal atrophy** of tubules seen here to the upper right.
- The most common reason for this is probably childhood infection with the mumps virus, which produces a patchy orchitis.
- However, it is unusual for this infection to cause enough atrophy to significantly affect the sperm count.

TESTIS


SEMINIFEROUS TUBULE
Secondary spermatocyte
Spermatid
Sertoli cell
Spermatozoa
Primary spermatocyte
Spermatogonium




Head of epididymis
Vas deferens
Seminiferous tubules
Body of epididymis
Tunica albuginea
Tail of epididymis

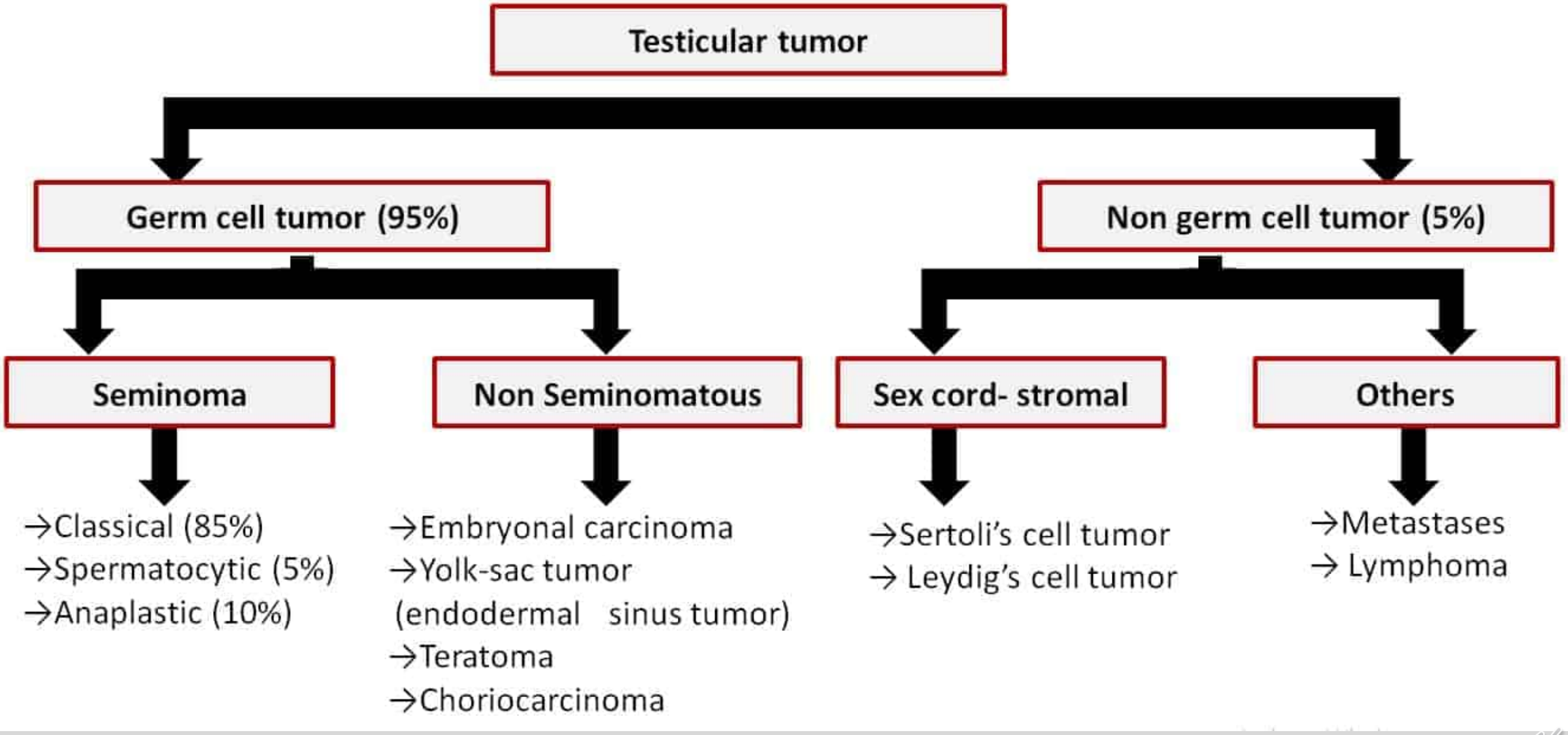
Testicular tumors (T)

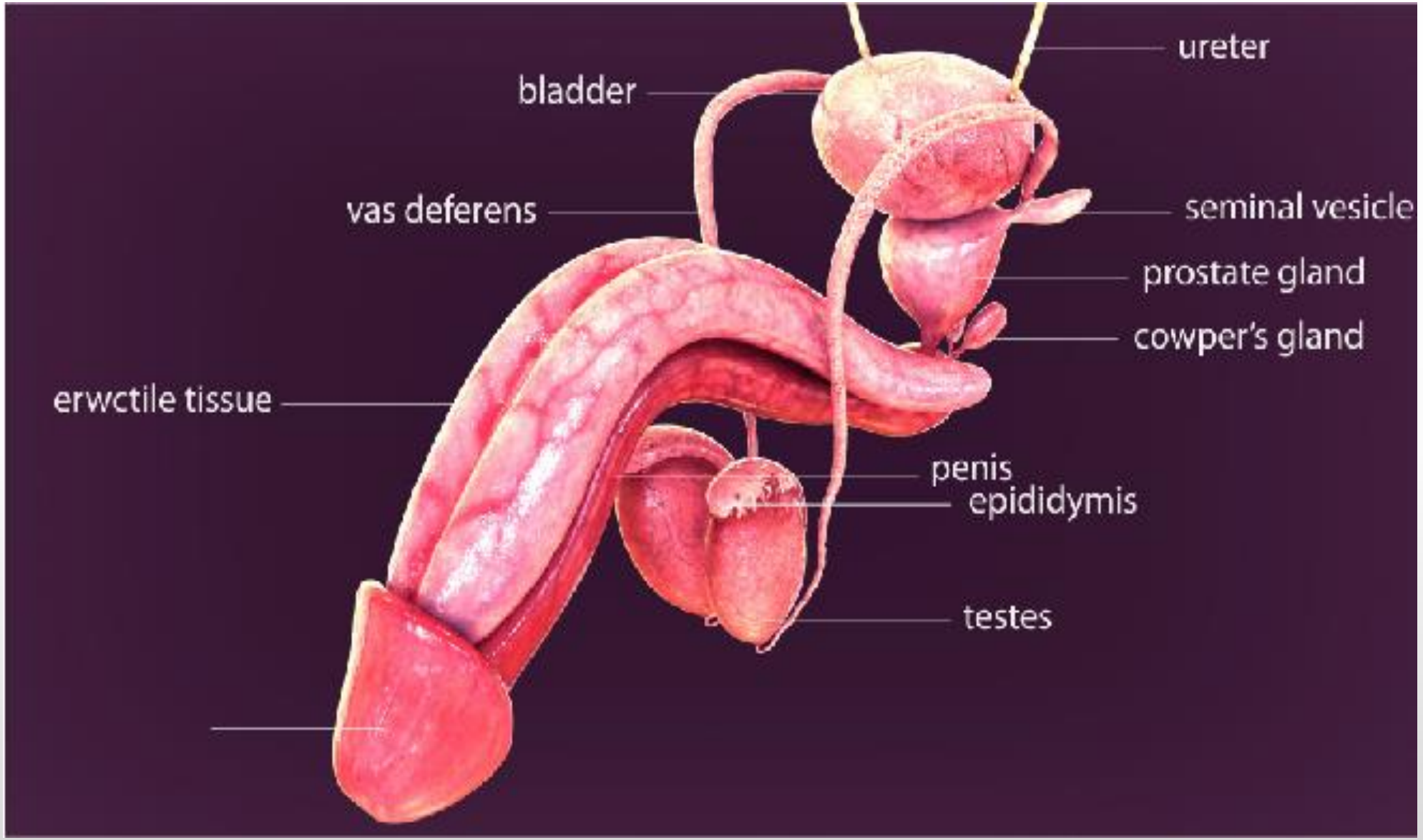
- Testicular T are the most important cause of firm, painless enlargement of the testis with a peak incidence in 20-34 years age group.

- **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.**
- **Cryptorchidismis 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 chromosome12, but their role in the pathogenesis of these cancers remains unclear.


Testicular tumor
Germ cell tumor (95%)
Non germ cell tumor (5%)
Seminoma
Non Seminomatous
Sex cord- stromal
Others
→Classical (85%)
→Spermatocytic (5%)
→Anaplastic (10%)
→Embryonal carcinoma
→Yolk-sac tumor
(endodermal sinus tumor)
→Teratoma
→Choriocarcinoma
→Sertoli's cell tumor
→ Leydig's cell tumor
→Metastases
→ Lymphoma


ureter
bladder
vas deferens
seminal vesicle
prostate gland
cowper's gland
erwctile tissue
penis
epididymis
testes

Classification & Histogenesis

- In the WHO classification, which is the most widely used in the US the germ cells 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.

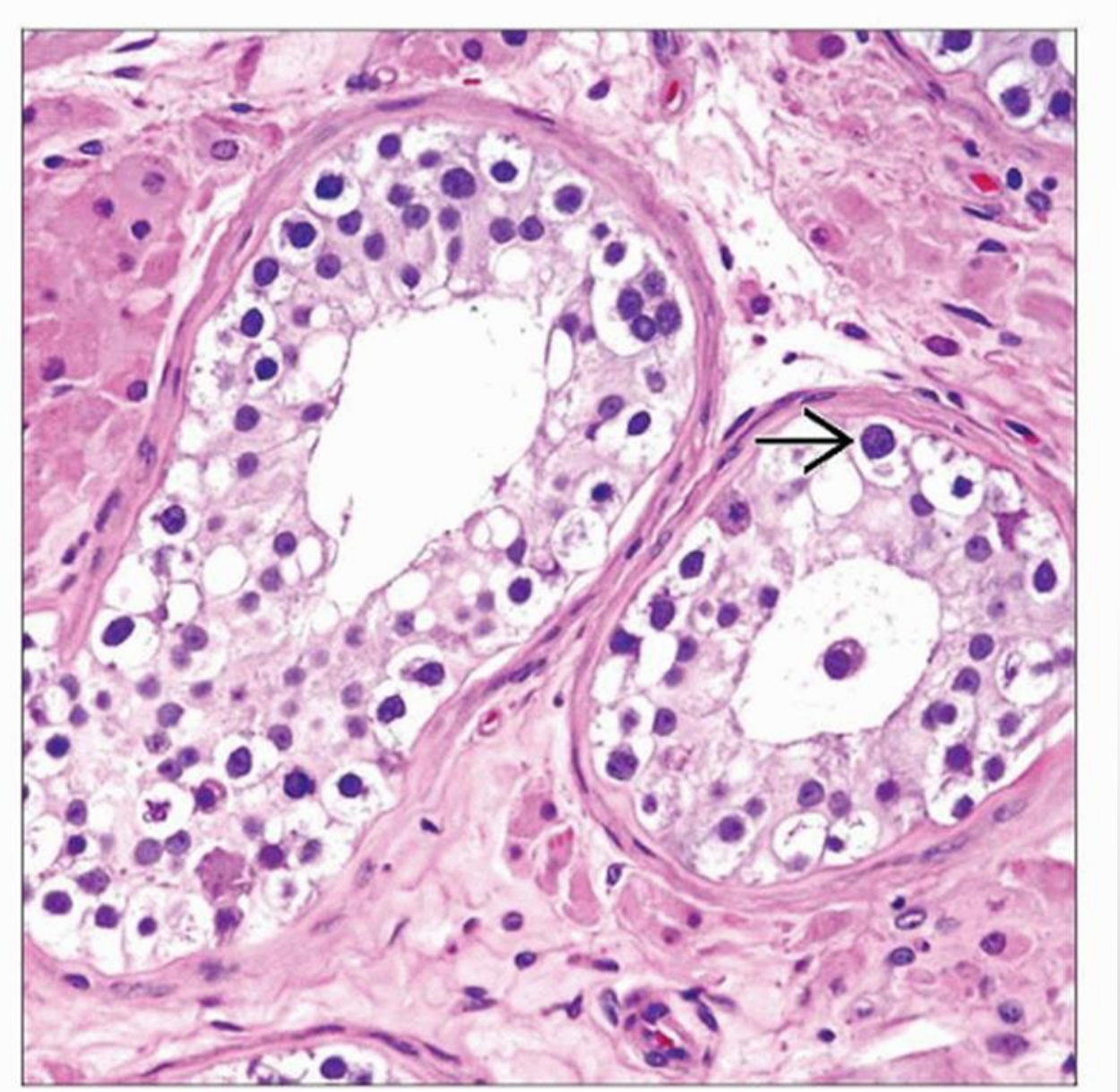
- **Tumors with More Than One Histologic Pattern (40%)**
- This classification is based on the view that testicular germ cell T arise from primitive cells that may either differentiate along

(I) Gonadal lines to produce seminomas.
(II) Transform into a totipotential cell population, giving rise to non- seminomatous germ cell T.Such totipotential cells:

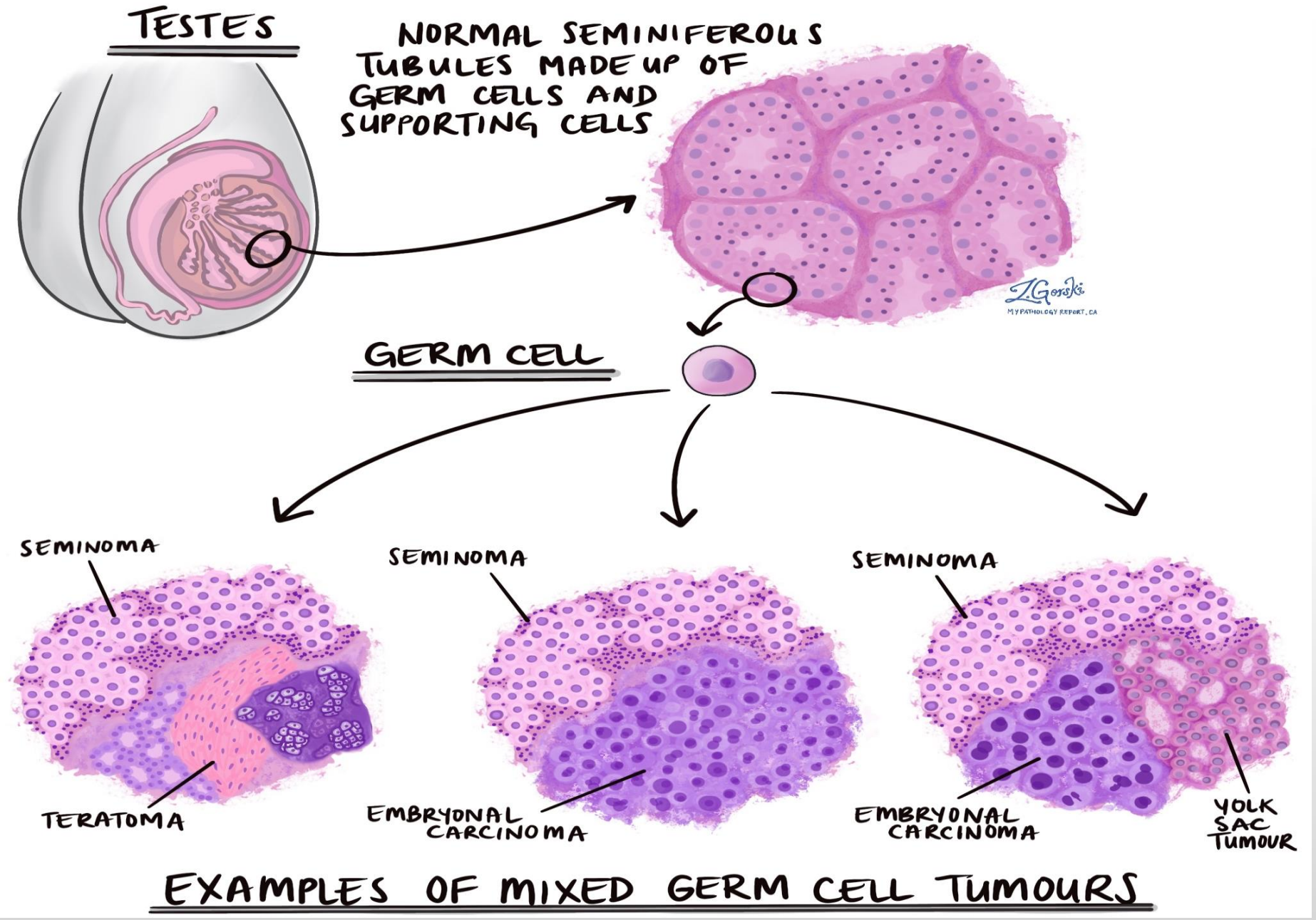
(a) may remain **undifferentiated** to form embryonal ca,or
(b) may **differentiate along extra-embryonic** lines to form yolk sac tumors& choriocarcinomas.
(c) may **differentiate along somatic cell** lines to produce teratomas.

- 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.



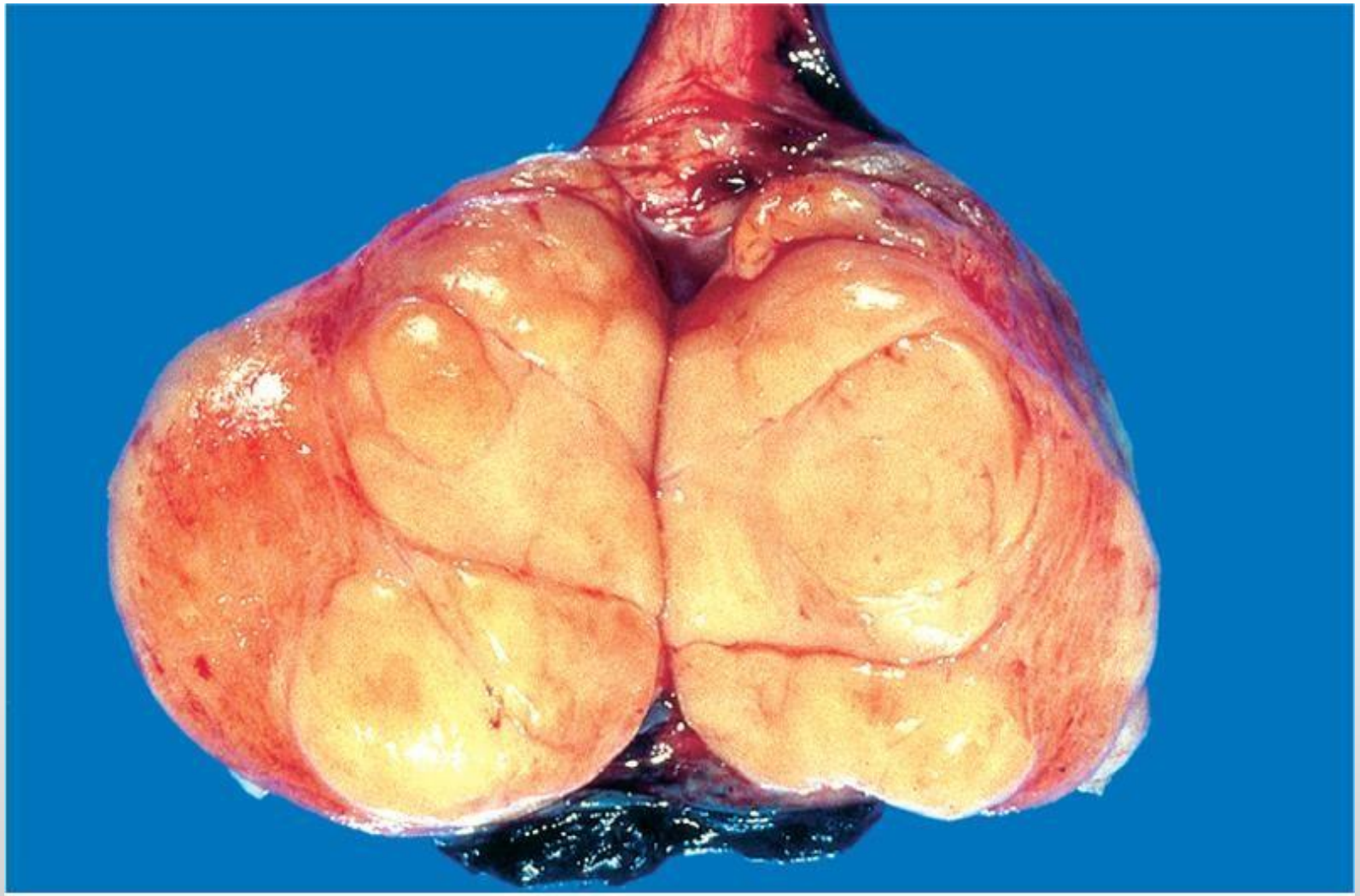
- intratubular germ cell neoplasia(IGCN): Beautiful picture showing cells (within seminiferous tubule) having enlarged nuclei, prominent nucleoli, and clear cytoplasm along the basal aspect of a seminiferous tubules lacking spermatogenesis. Sertoli cells are displaced toward the lumen.
- The TGCT of 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 .


TESTES
NORMAL SEMINIFEROUS TUBULES MADE UP OF GERM CELLS AND SUPPORTING CELLS
L.Gorski
MYPATHOLOGYREPORT.CA
GERM CELL
SEMINOMA
TERATOMA
SEMINOMA
EMBRYONAL CARCINOMA
SEMINOMA
EMBRYONAL CARCINOMA
YOLK SAC TUMOUR
EXAMPLES OF MIXED GERM CELL TUMOURS

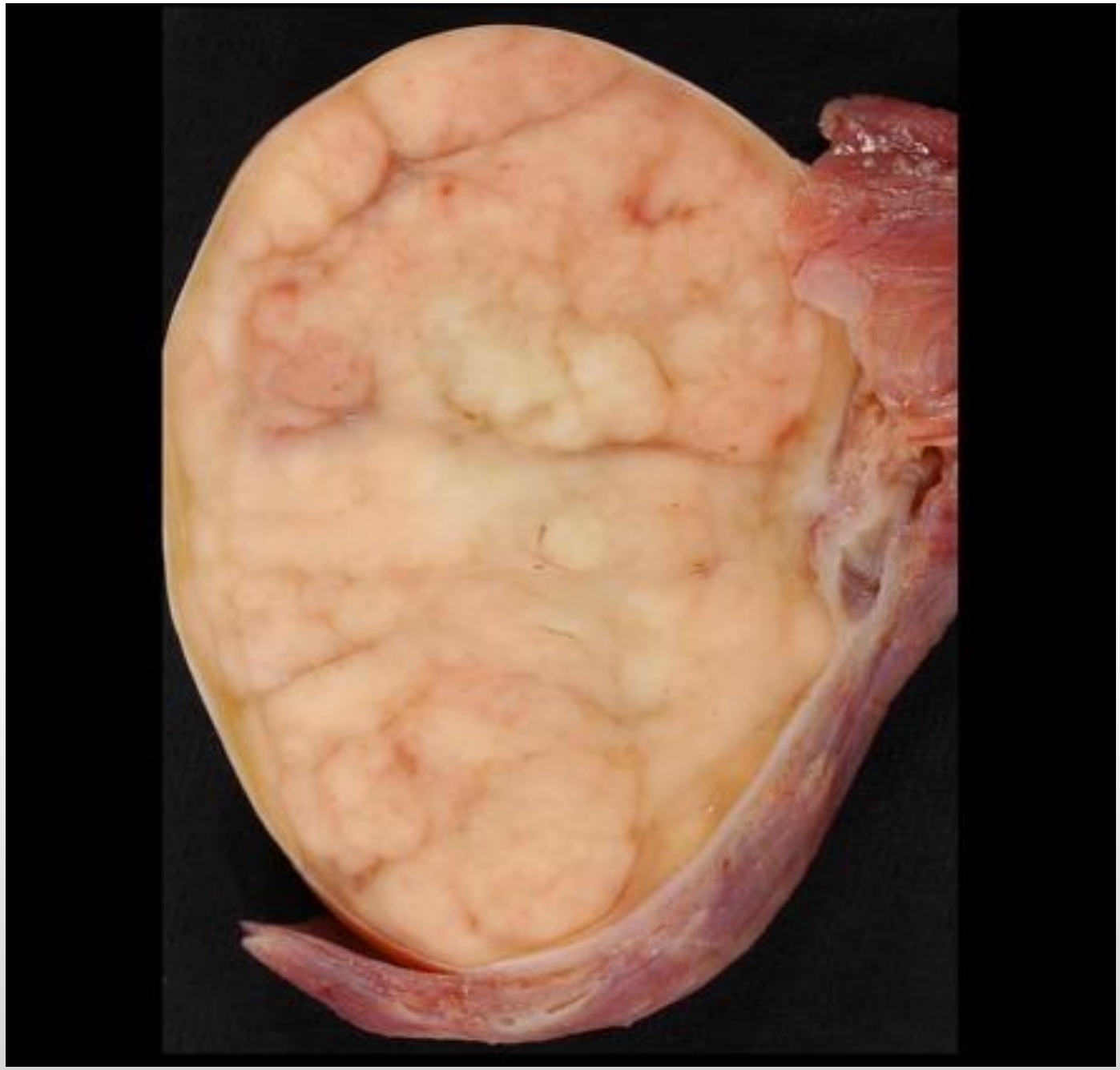
Seminomas "classic“ حفظ

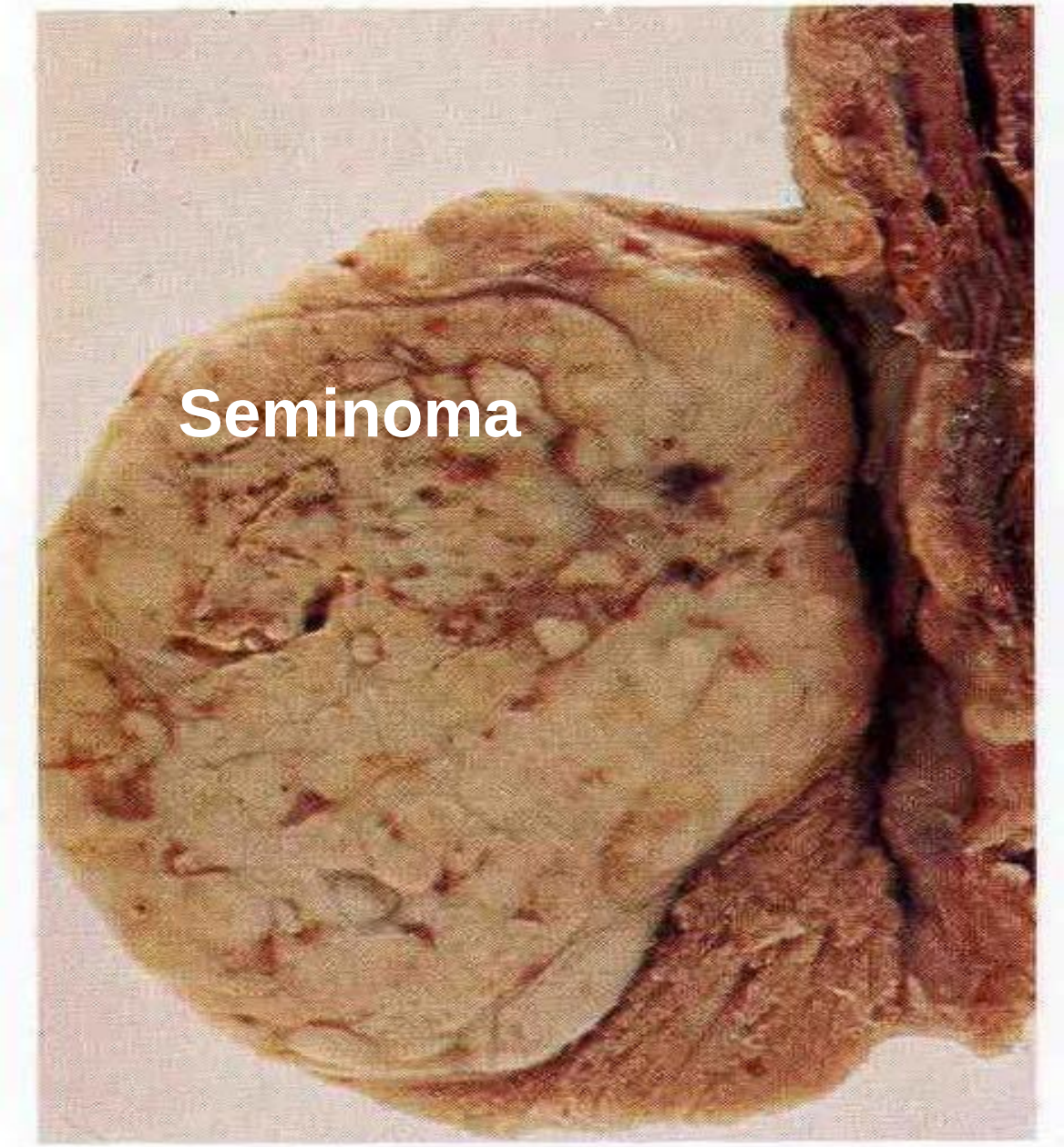
- Seminomas account for 50% of testicular germ cell T.
- They are histologicaly identical to ovarian dysgerminomas & to germinomas occurring in the CNS & other extra-gonadal sites.
- GROSSLY, seminomas are “potato "like, large, soft, well-demarcated, homogeneous, gray-white T that bulge from the cut 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.

Seminoma of the testis. Well circumscribed, pale, fleshy, homogenous mass.



Seminoma: testis.





11.23 Seminoma: testis

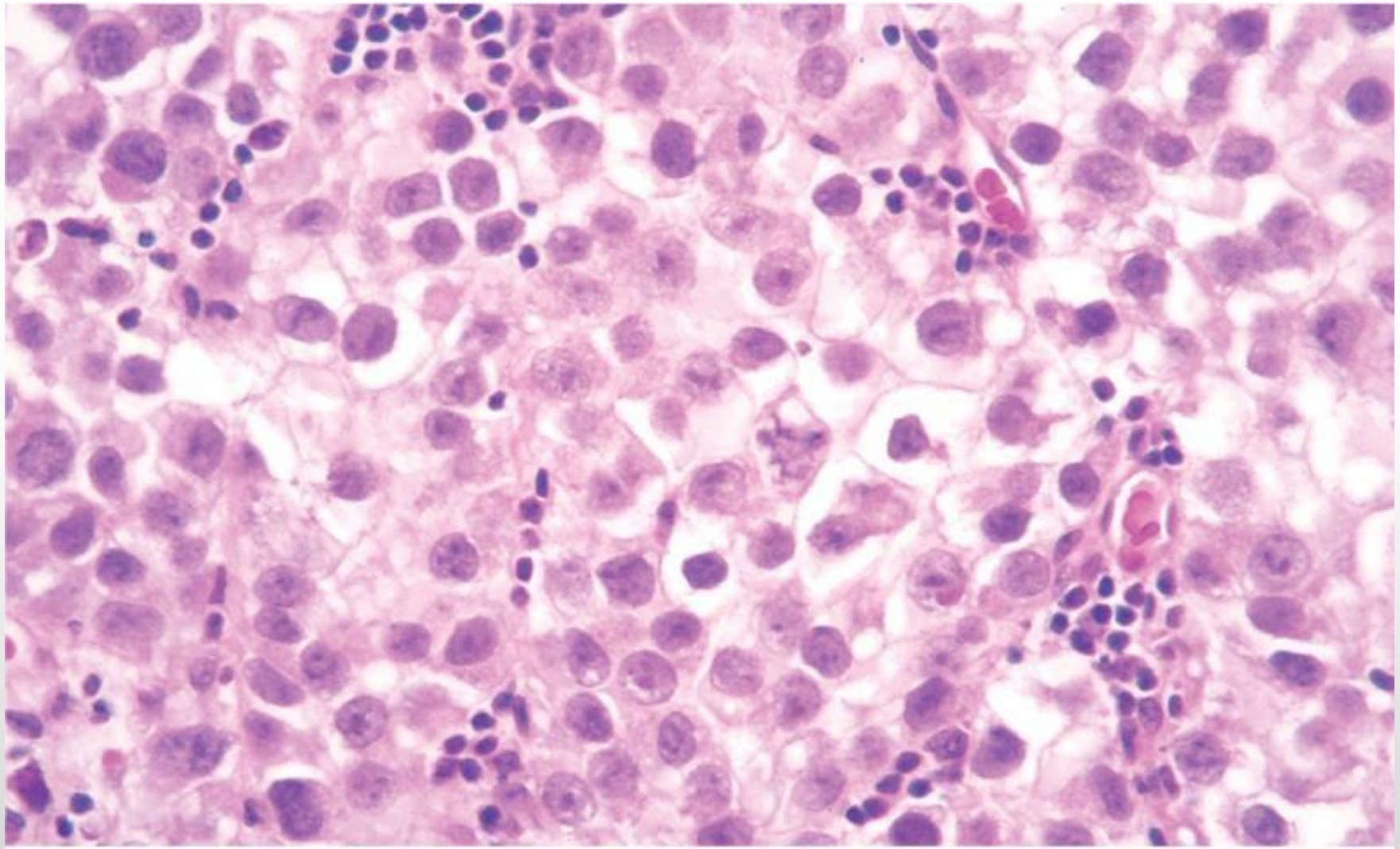
Seminoma: testis.

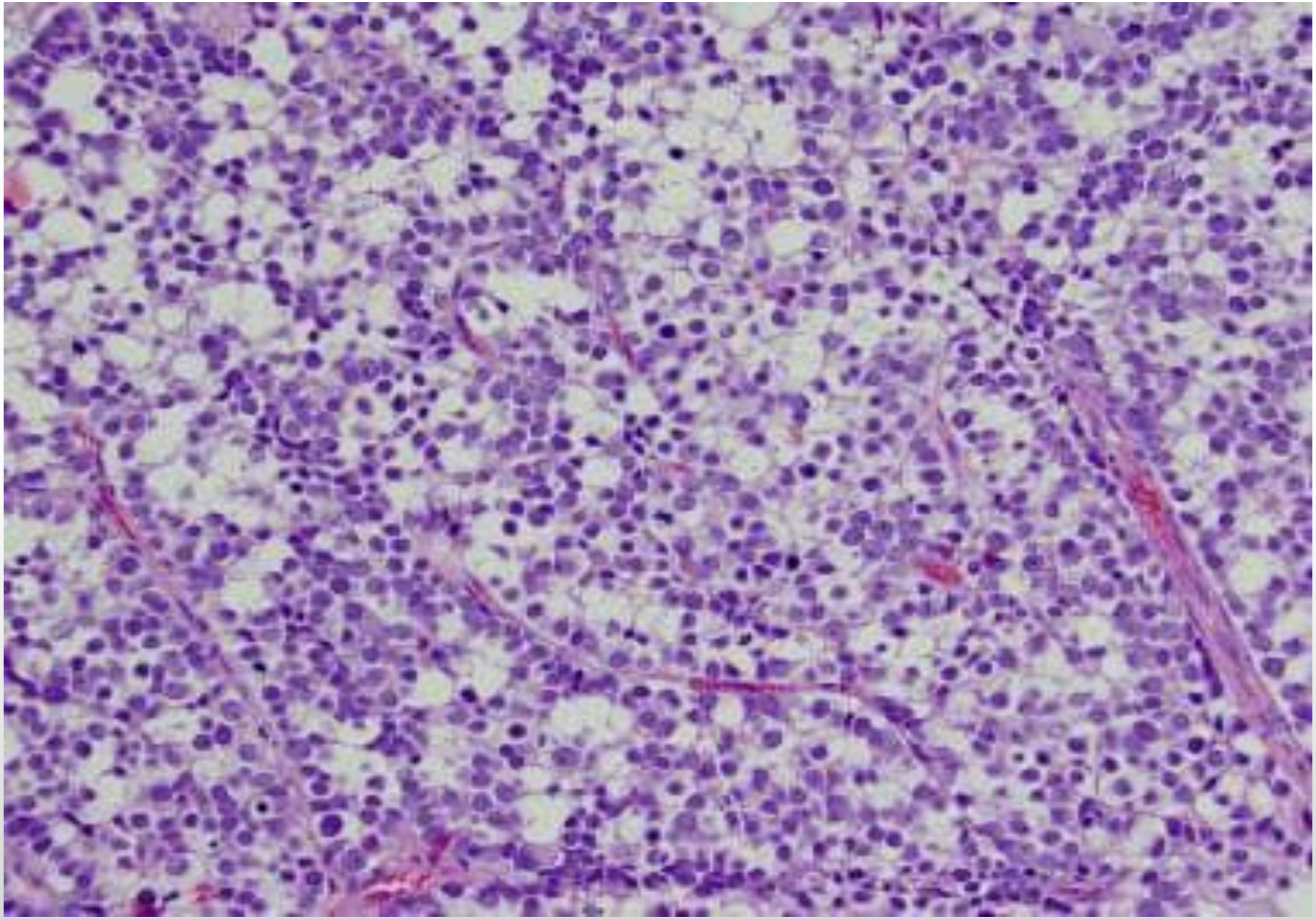
- A lobulated, pale-grey opaque tumor of the testis, which is firm &“**potato "looking** on section.

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.

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





❖ Spermatocytic seminoma is a less common morphologic variant of seminoma, which tend to occur in: حفظ

1. Older patients
2. It contain a mixture of medium-sized, large uninucleate or multinucleate T cells, & small cells with round nuclei that are reminiscent of secondary spermatocytes.
3. In contrast to the behavior of classic seminoma,

1)there is no association with intratubular germ cell neoplasia.

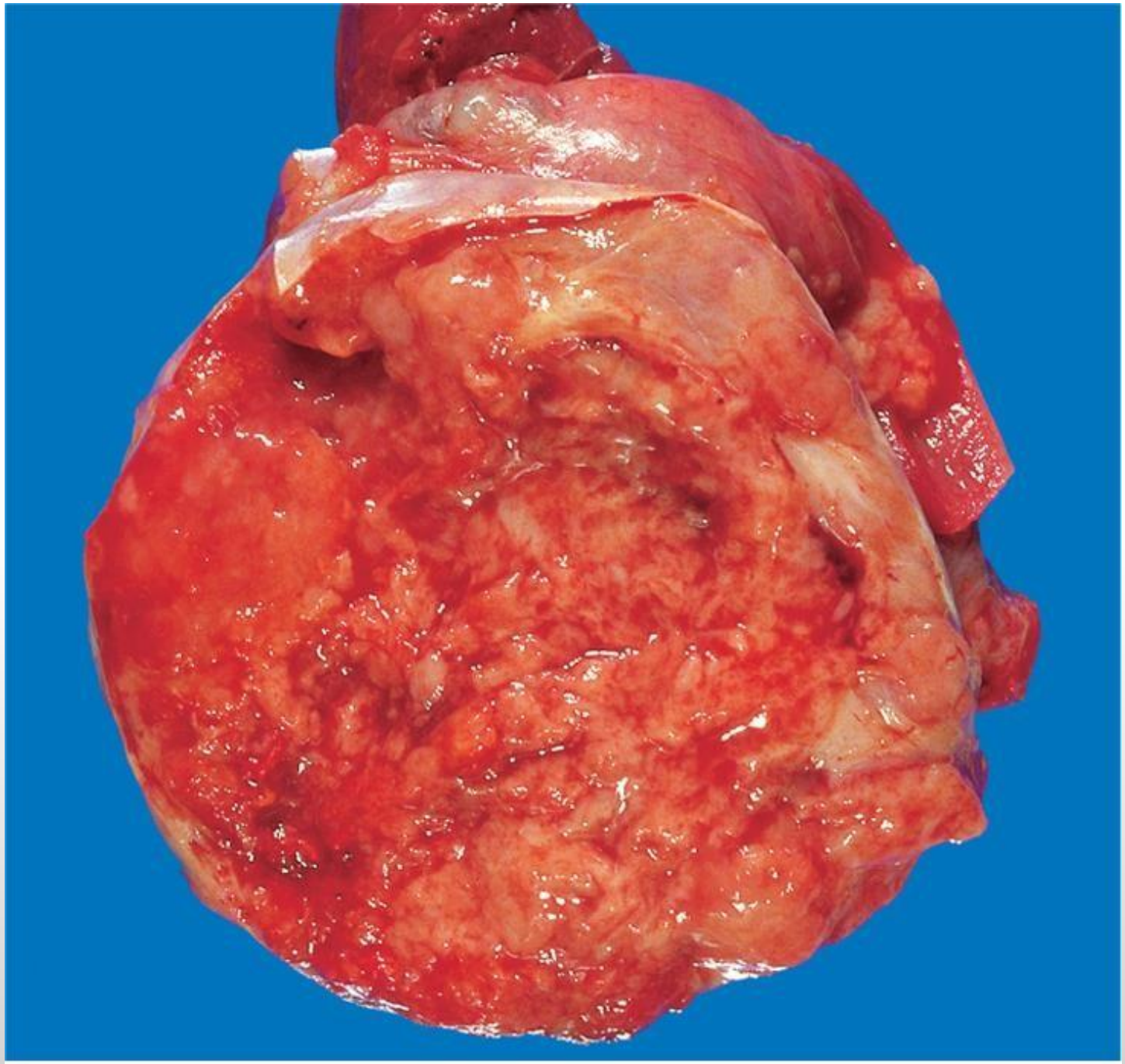
2) metastases are exceedingly rare,

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 :

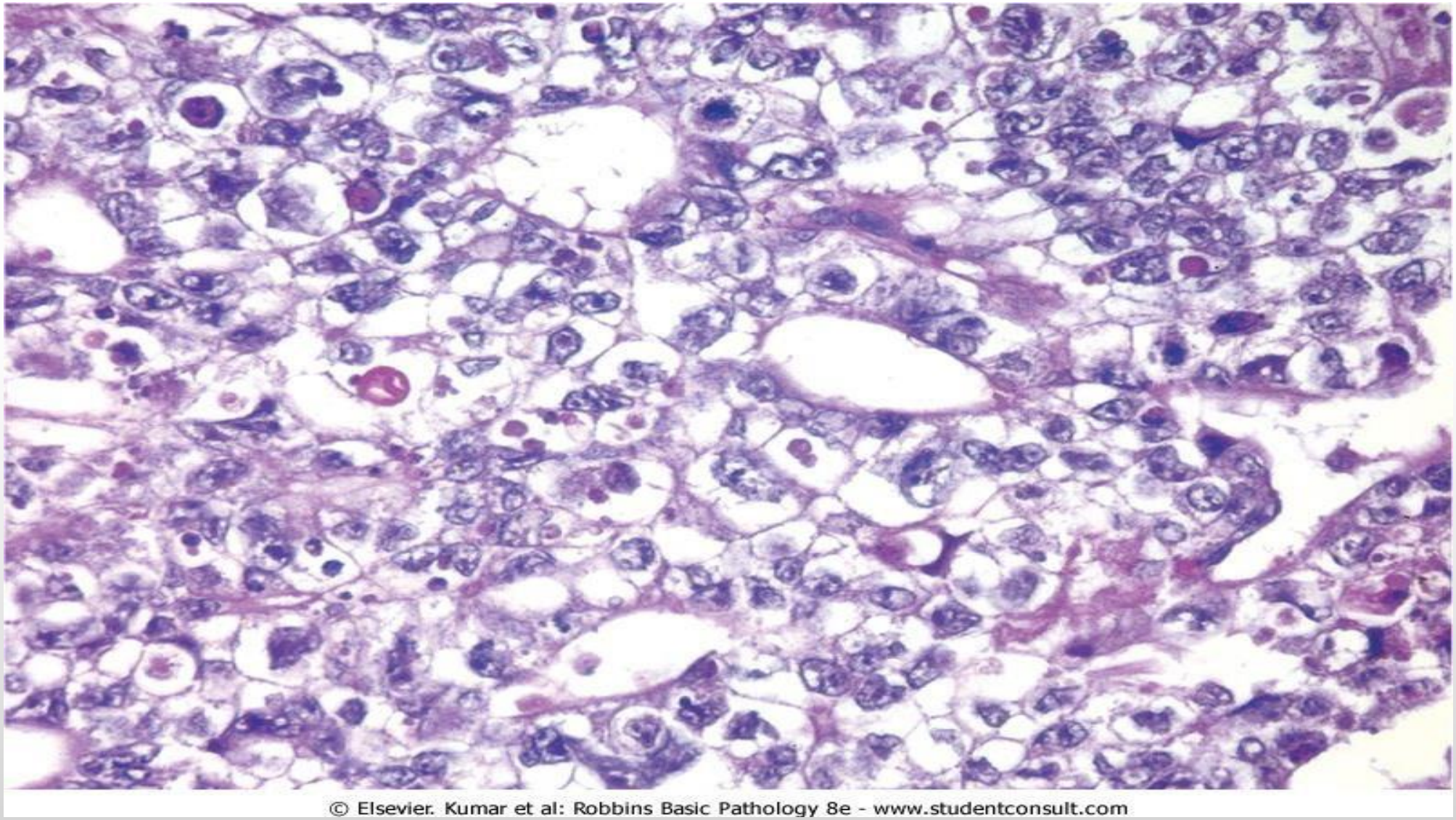
1. the T cells are large & primitive looking, with basophilic cytoplasm, indistinct cell borders, & large nuclei with prominent nucleoli.
2. Tumor cells may arranged in undifferentiated solid sheets or may contain glandular structures & irregular papillae .
3. In **most cases of** embryonal carcinoma, 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.

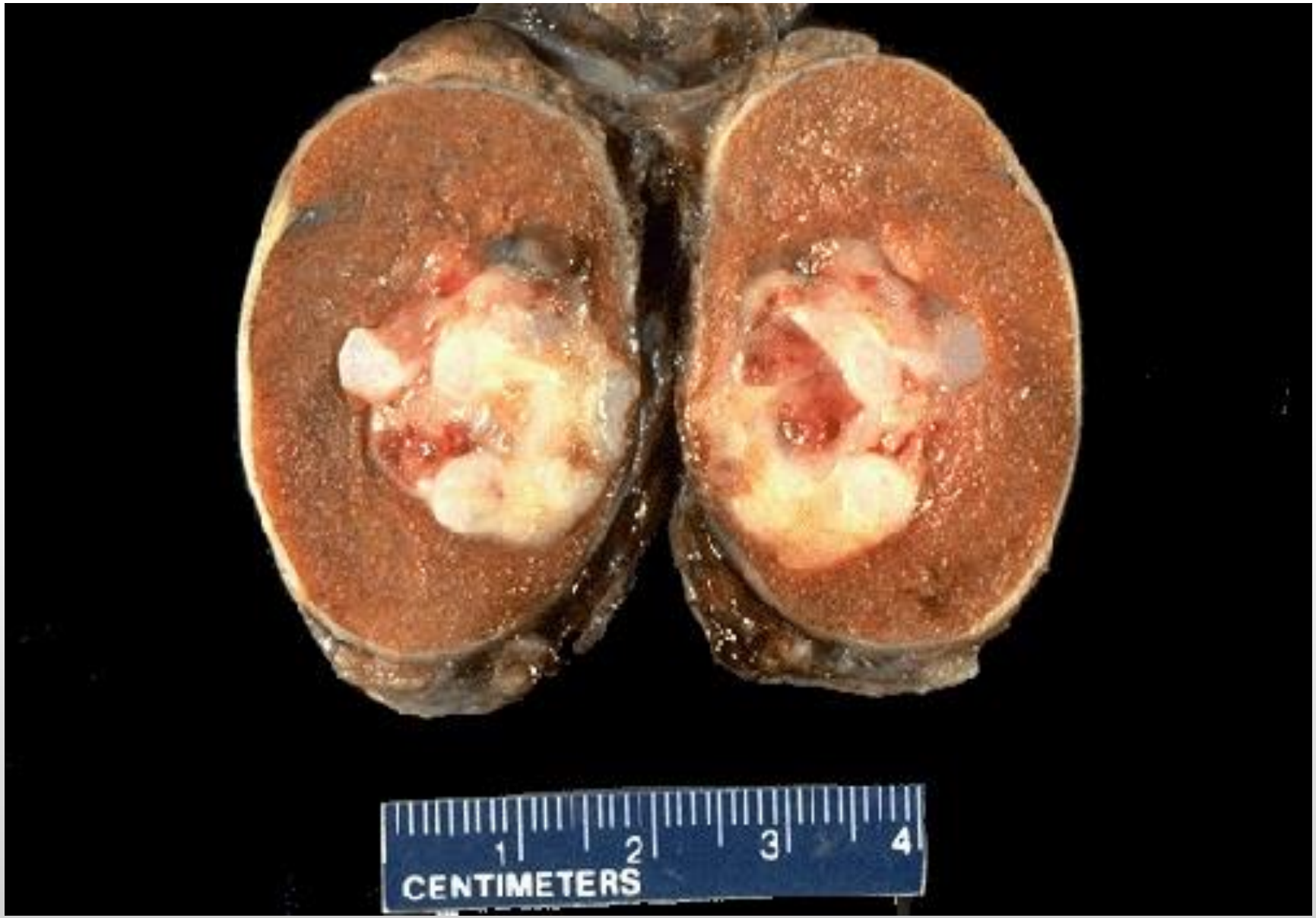
In contrast to the seminoma, the embryonal carcinoma is a **hemorrhagic** mass

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



- 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.

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

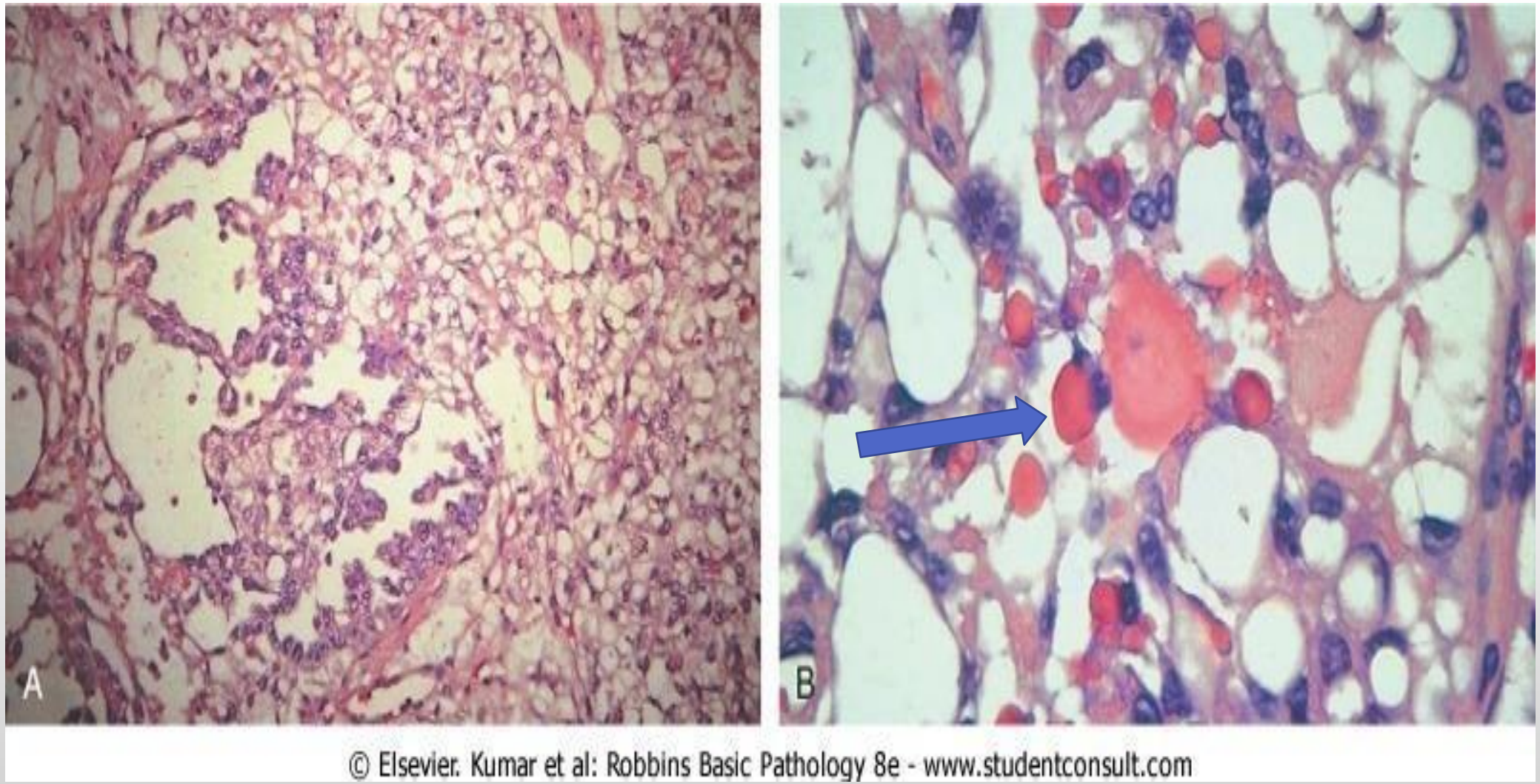
- Represents **endodermal sinus** differentiation of totipotential neoplastic cells, hence the other name **endodermal sinus T.**
- They are the **most common** primary testicular cancer **in children younger than 3 years of age**•
- In adults, they are mostly seen admixed with embryonal ca.

➢ **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-Duvallbody)**
B,HP view showing characteristic hyaline droplets within the microcytic areas of the tumor. **Alfa-fetoprotein** is present within the droplets.

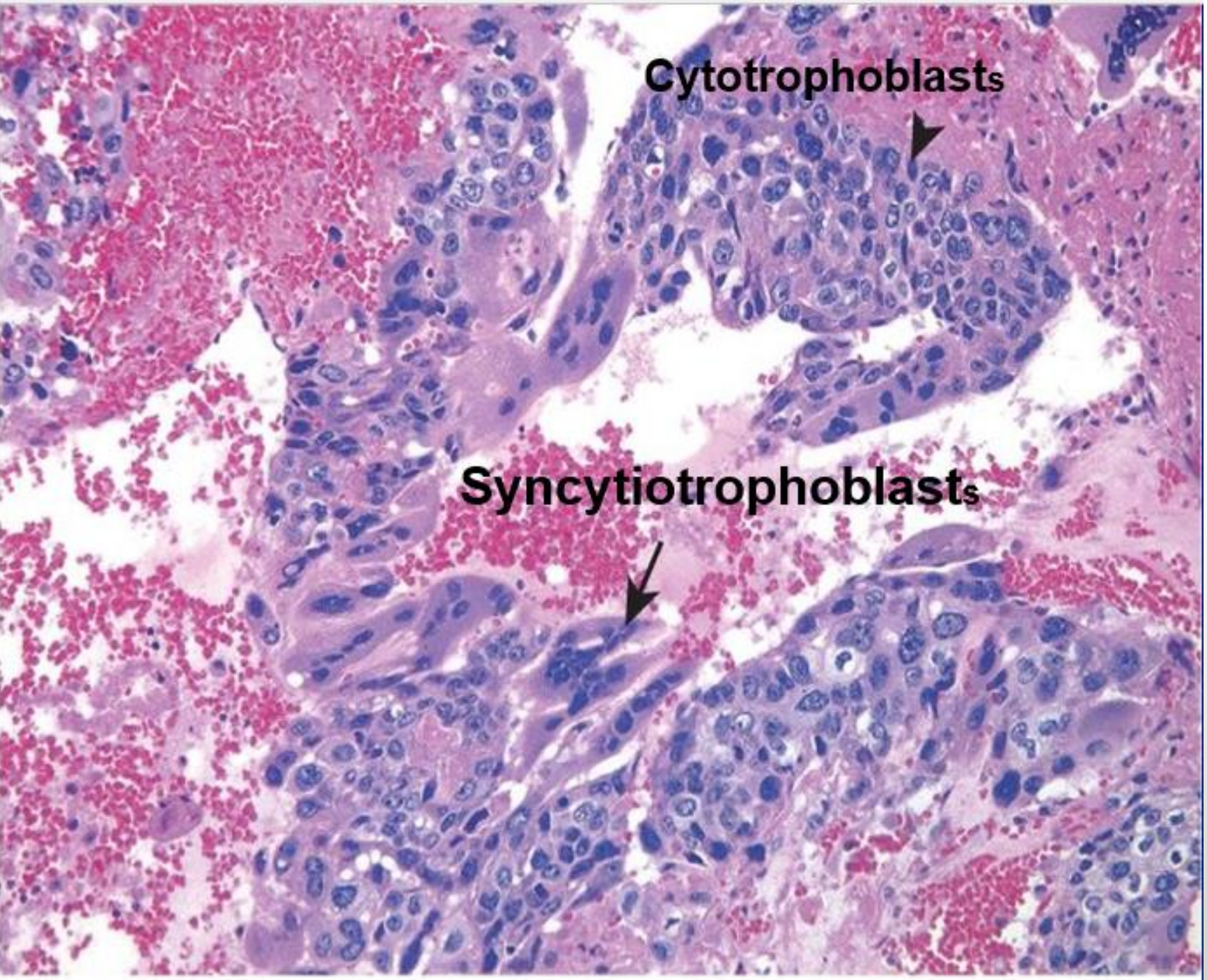


Choriocarcinomas

- represent differentiation of pluripotential neoplastic germ cells along trophoblasticlines.
- 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

shows:

(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**.

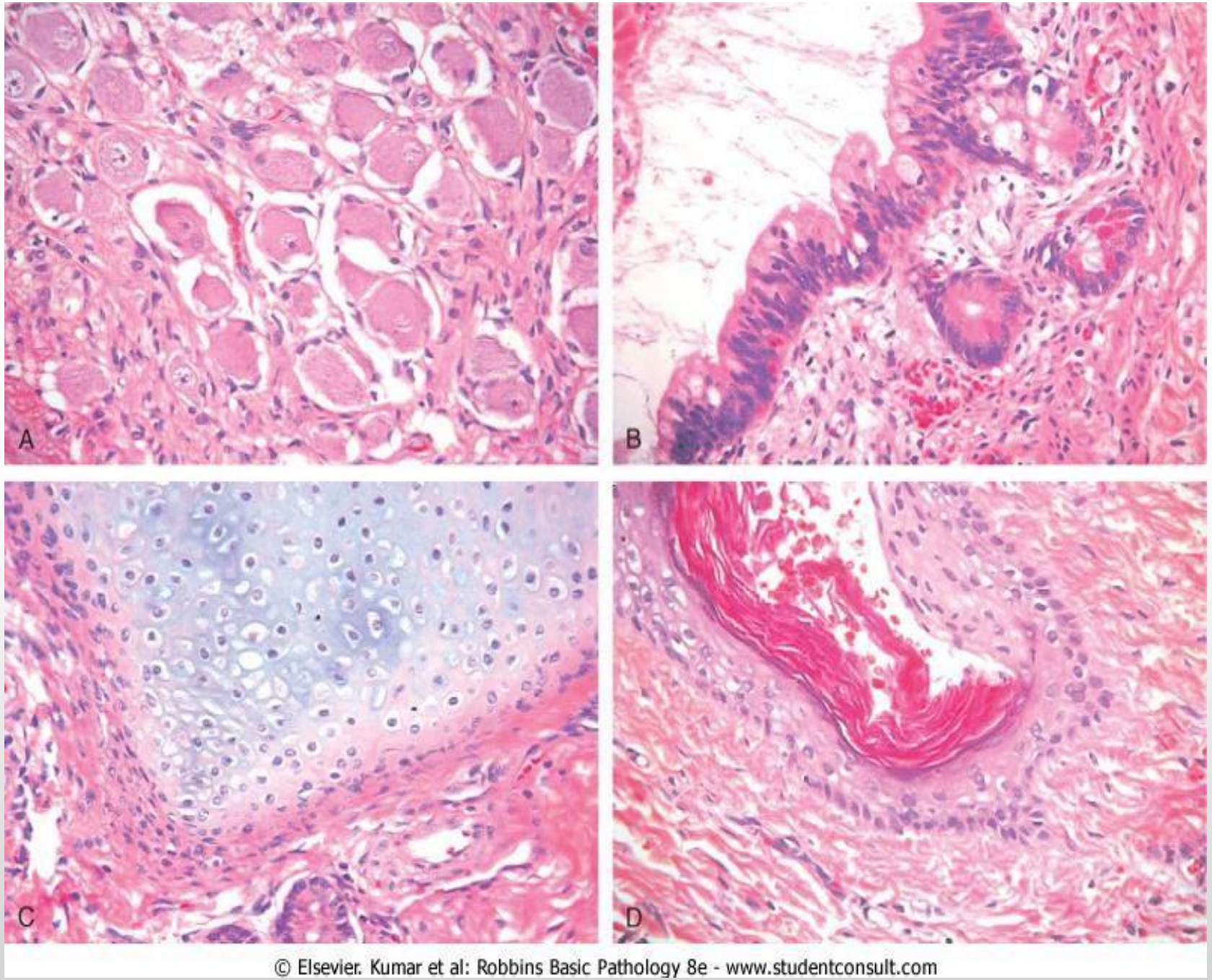
Histologically : 3 major variants of **pure** teratomas are recognized:

(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.

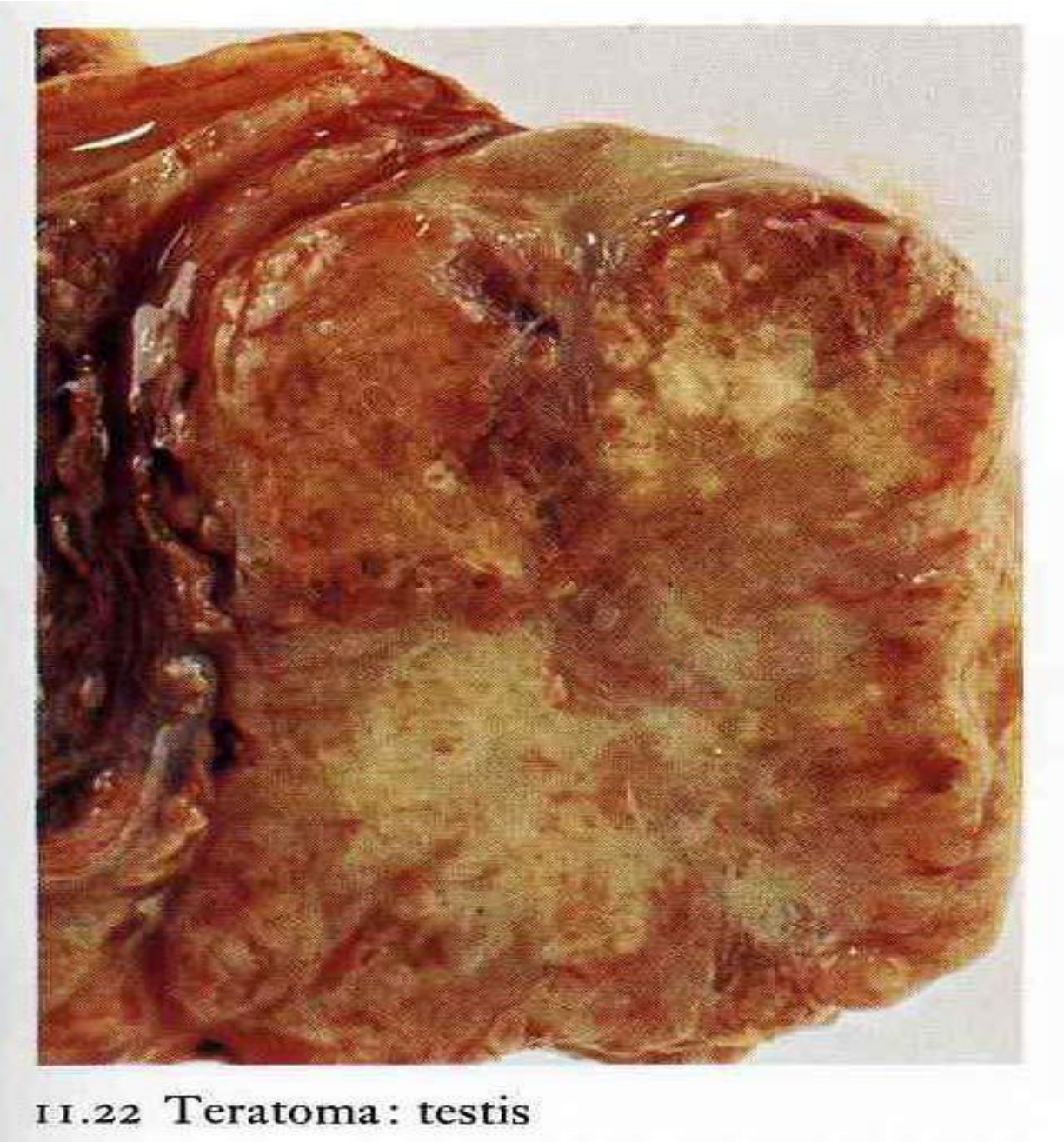
(ii) **Immature TT ,**contain **immature** somatic elements reminiscent of those in developing fetal tissue.

(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.



- **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.



11.22 Teratoma: testis

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.

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

1. All testicular germ cell T present mostly as a

- (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!
- **Clinically,**it is best to consider testicular germ cell T under 2 broad categories:

Seminomas & non-seminomatous T.

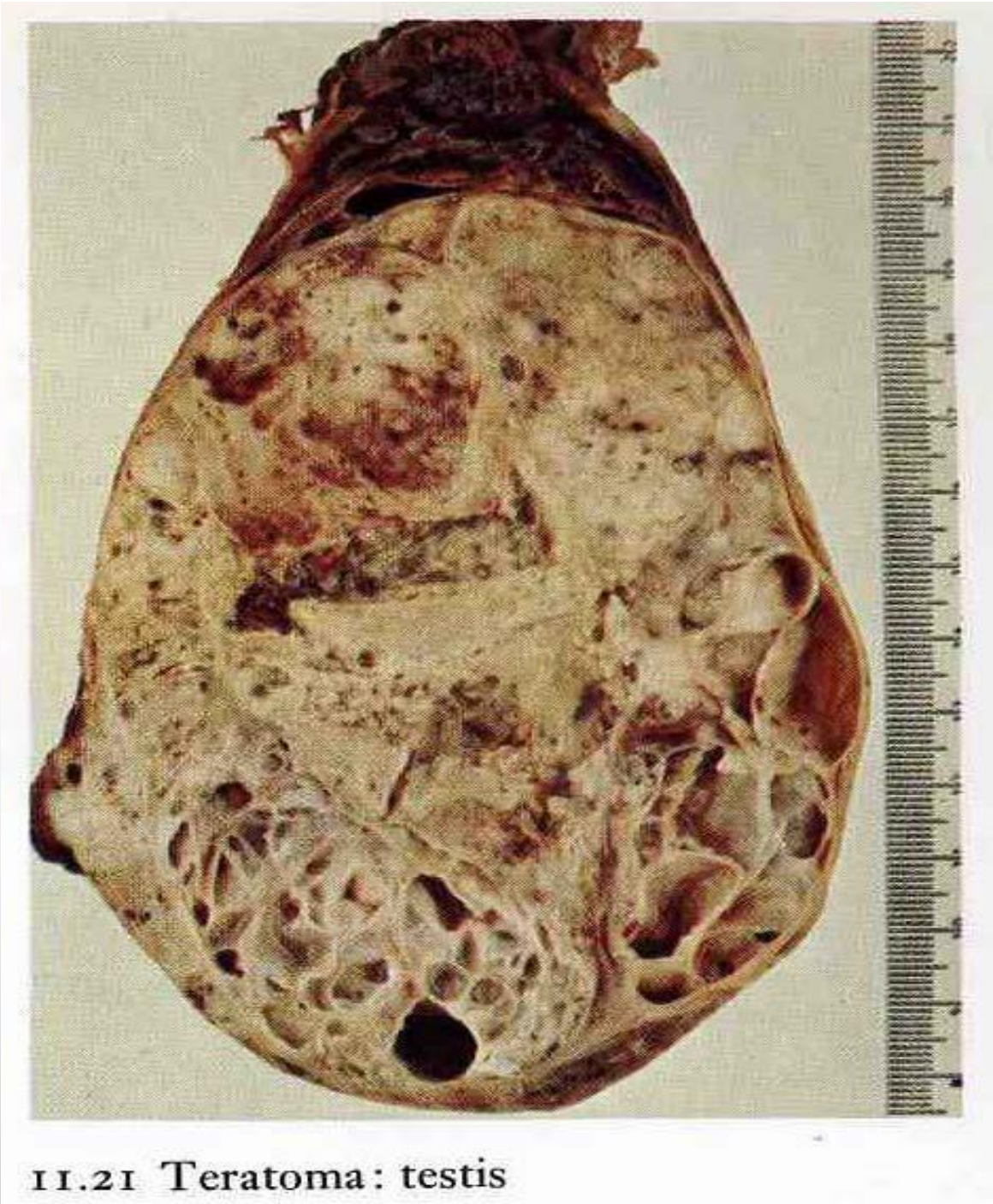
- Seminomas often remain confined to the testis **for long time** & may reach considerable size before diagnosis.

- 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.



11.21 Teratoma: testis

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

- 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.**

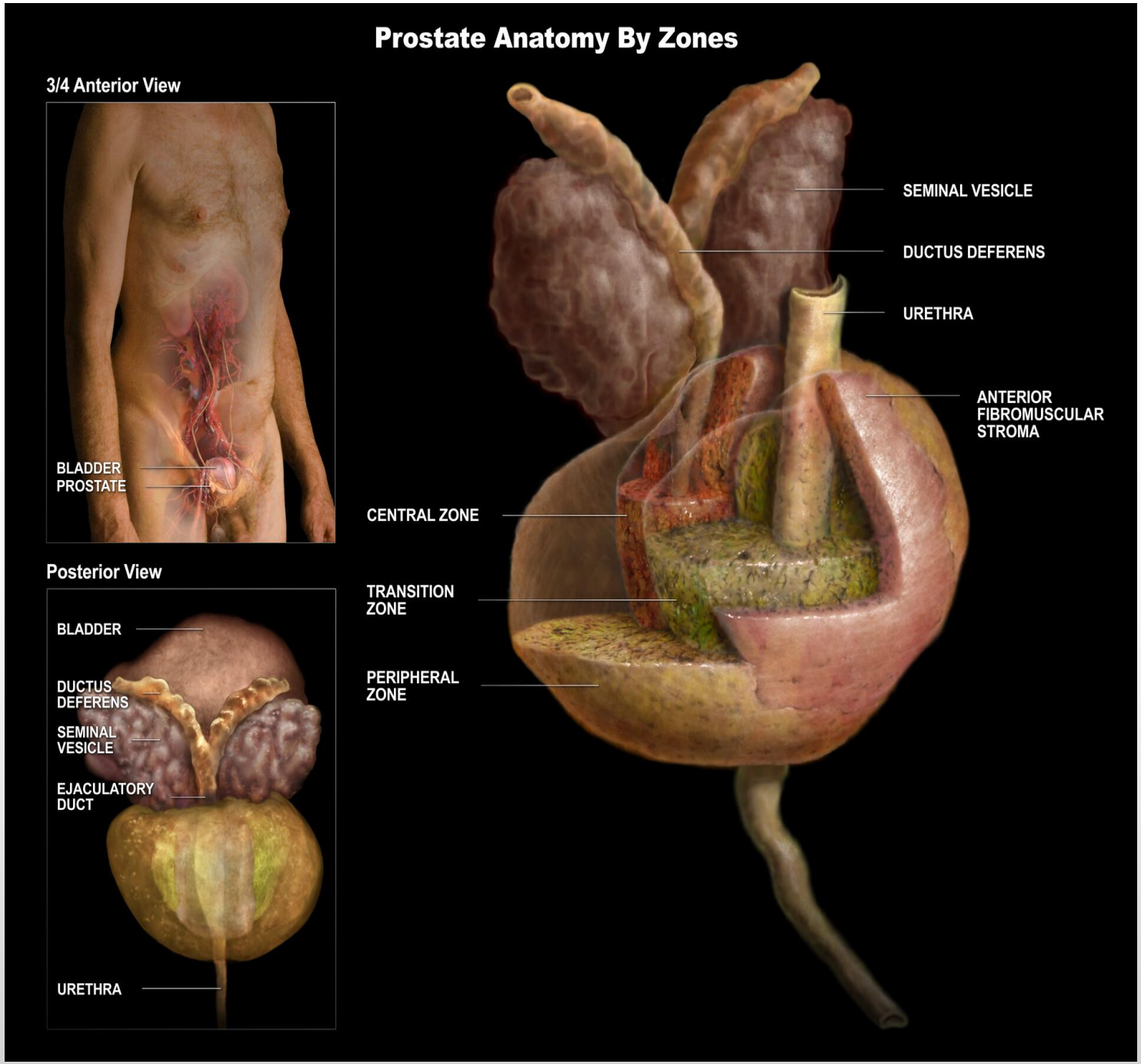
(II) α-fetoprotein (AFP)

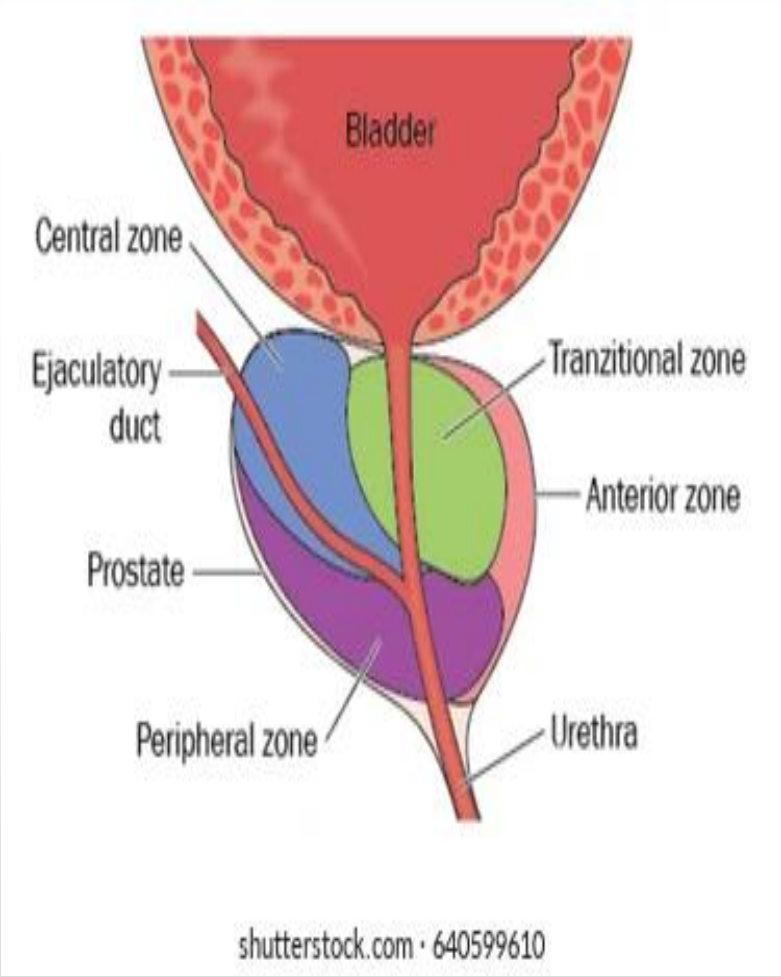
is a glycoprotein normally synthesized by the fetal yolk sac & several other fetal tissues.

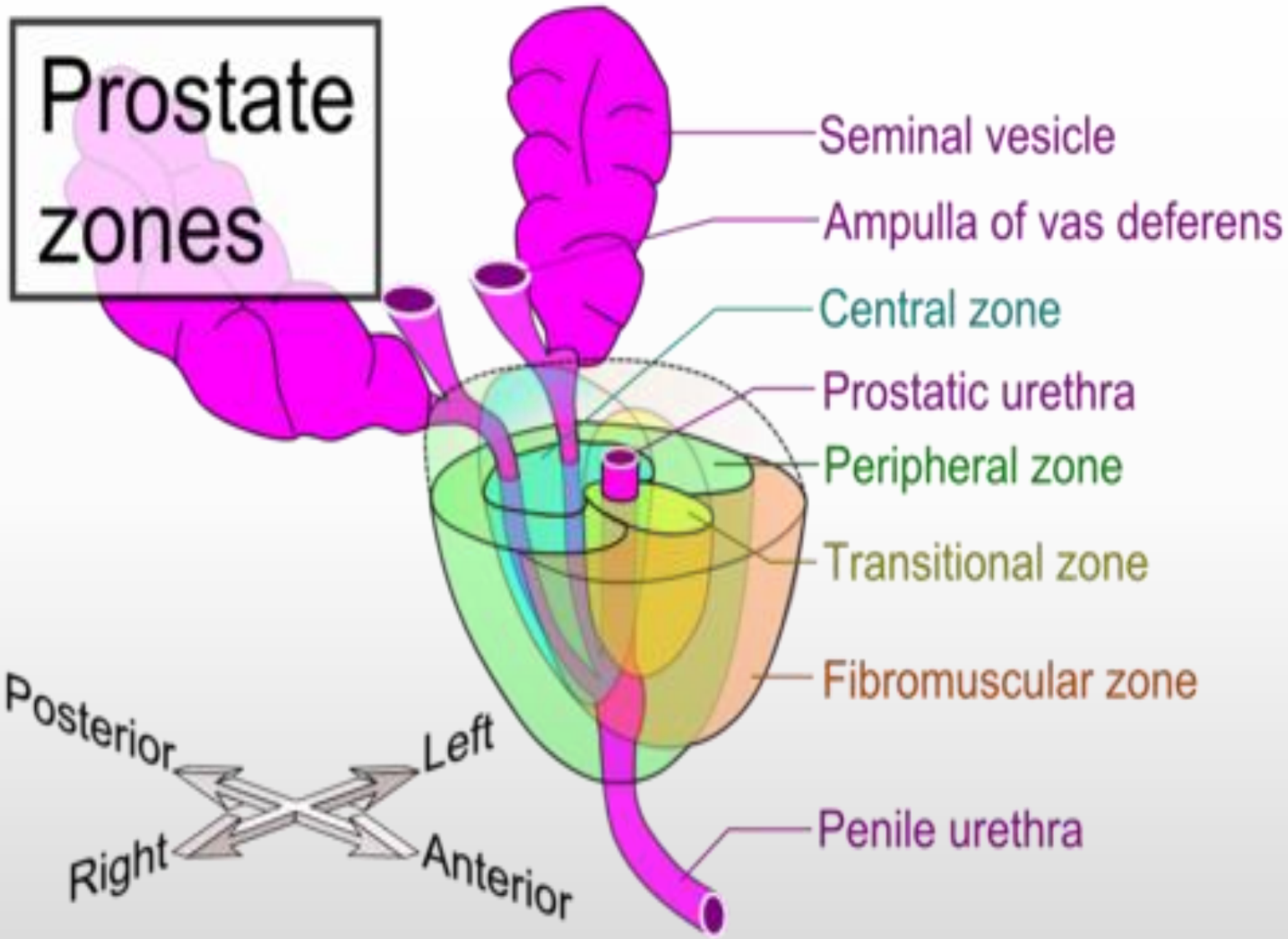
1. Nonseminomatous germ cell T containing elements of yolk sac (endodermal sinus) often produce AFP (AFP is **also elevated in hepatocellular ca**);& in contrast to hCG,…
2. The presence of AFP is a reliable indicator of the presence of a nonseminomatous component in the germ cell T, as yolk sac elements are not found in pure seminomas.
3. As mixed patterns are common, most nonseminomatous T have elevations of both hCG & AFP.
4. 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

Prostate


Prostate Anatomy By Zones
3/4 Anterior View
BLADDER
PROSTATE
Posterior View
BLADDER
DUCTUS DEFERENS
SEMINAL VESICLE
EJACULATORY DUCT
URETHRA
SEMINAL VESICLE
DUCTUS DEFERENS
URETHRA
ANTERIOR FIBROMUSCULAR STROMA
CENTRAL ZONE
TRANSITION ZONE
PERIPHERAL ZONE


Bladder
Central zone
Ejaculatory duct
Tranzitional zone
Anterior zone
Prostate
Peripheral zone
Urethra
shutterstock.com · 640599610


Prostate zones
Seminal vesicle
Ampulla of vas deferens
Central zone
Prostatic urethra
Peripheral zone
Transitional zone
Fibromuscular zone
Penile urethra
Posterior
Left
Right
Anterior

PROSTATE

❖ **Prostatitis** may be acute or chronic.

- **Acute bacterial prostatitis** is caused by the same organisms associated with other acute UTI, particularly **E. coli & other gram-negative rods**.
- Most patients with acute prostatitis have concomitant infection of the urethra & bladder; in which organisms may **reach** the prostate by **direct extension** from the urethra or bladder or, by **vascular channels** from more distant sites.

- **Chronic prostatitis.**

(1) may follow clinical episodes of acute prostatitis,
(2) may develop insidiously, without previous episodes of acute infection.

❑ In **some cases** it is (1) chronic bacterial prostatitis, in which there is an increase number of WBCs in prostatic secretions together with bacteria (similar to those responsible for acute bacterial prostatitis) which can be isolated, however…

(2) most cases are chronic abacterial prostatitis, with only an increase number of WBCs in prostatic secretions; but bacteriologic findings are negative.

Morphology

Histopathology :Acute prostatitis characterized by congestion, edema & acute neutrophilic inflammatory infiltrate; initially most conspicuous within the prostatic glands, but, as the infection progresses, the inflammatory infiltrate destroys glandular epithelium & extends into the surrounding stroma, resulting in the formation of **microabscesses.**

Grossly

visible abscesses are uncommon but can develop with extensive tissue destruction, e.g. in DM.

chronic prostatitis features are nonspecific & include lymphoid infiltrate, glandular injury, fibroblastic proliferation &, frequently, concomitant acute inflammatory changes.

Granulomatous prostatitis is may be encountered with systemic inflammatory processes (e.g., TB, sarcoidosis, & fungal infections).
It may also occur as a nonspecific reaction to inspissated prostatic secretions & after transurethral resection (TUR) of prostatic tissue.

❑ Clinical Features

- The clinical manifestations of prostatitis include

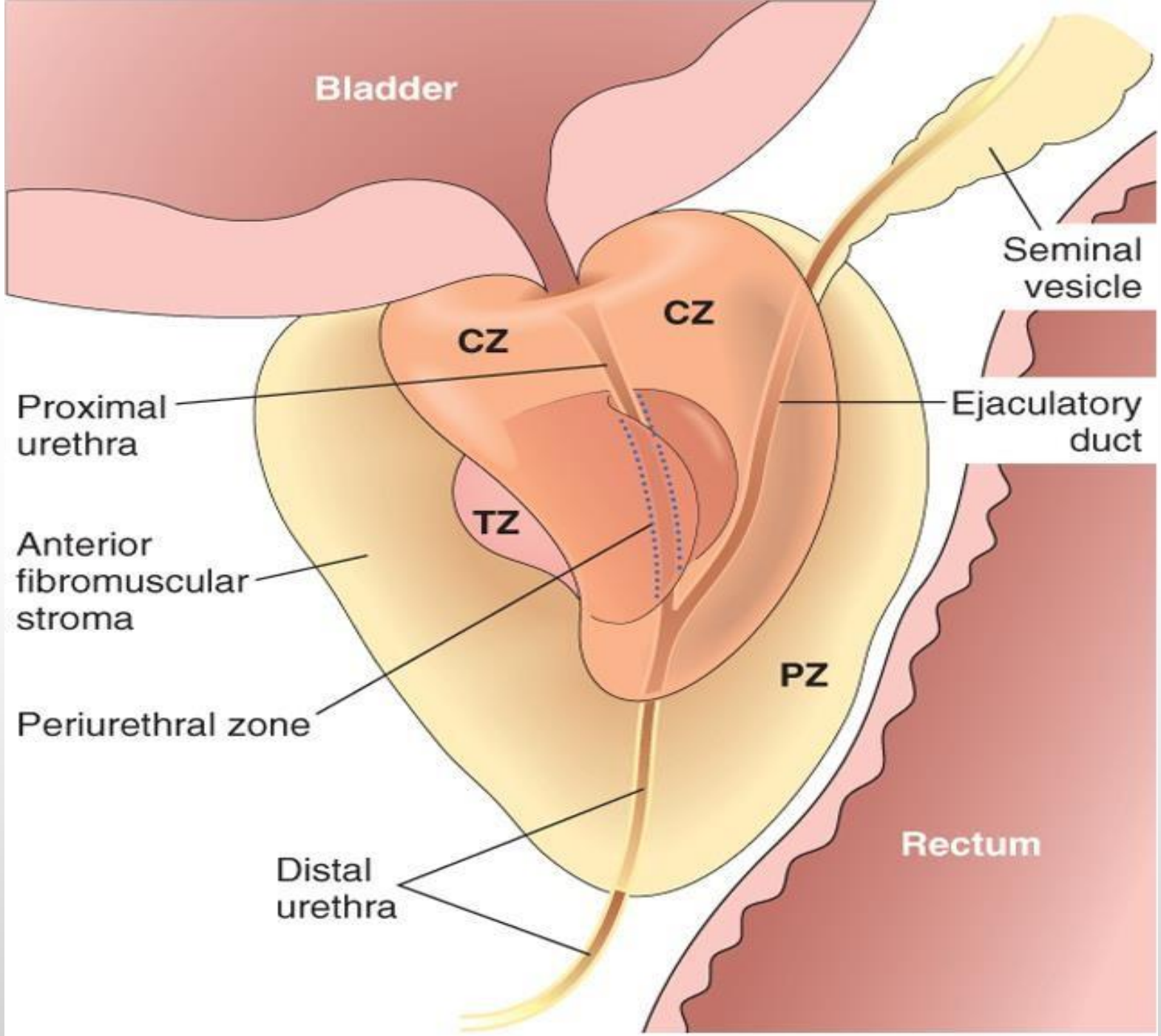
dysuria, urinary frequency, lower back pain,& poorly localized suprapubic or pelvic pain.

❑ On Per-Rectal (PR) examination, the prostate may be enlarged& tender, particularly in acute prostatitis, in which local symptoms are often accompanied by fever & leukocytosis.

❑ Complications: Chronic prostatitis, even if asymptomatic, may serve as a reservoir for organisms capable of causing UTI. Chronic bacterial prostatitis, therefore, is one of the most important causes of recurrent UTI in men.

Nodular Hyperplasia (NH) of the Prostate (P)

- Normal Prostate consists of glandular & stromal elements surrounding the urethra.
- It can be divided into periurethral, central, transitional, & peripheral, zones.
- Most (70%-80%) carcinomas arise in the peripheral zones;
- Most NH lesions arise in the central & inner transitional zones of the Prostate.
- NH is an extremely common abnormality of the P, frequency rises progressively with age reaching 90% by the eighth decade.
- NH is is characterized by proliferation of both stromal & epithelial elements, with resultant enlargement of the P gland which in some cases UT obstruction



Adult prostate

Z = zone.

CZ: central: NH,

TZ: transitional,

PZ: peripheral from which most carcinomas arise.

❖ Pathogenesis:

- although the cause of **NH** remains incompletely understood, it is clear that **androgens have a central role in its development, as:**

(1) **NH** does **not occur** **in males castrated before the onset of puberty** or in men with genetic diseases that block androgen activity.

(2) **Dihydrotestosterone (DHT),** an androgen derived from testosterone through the action of 5α-reductase, & its metabolite, 3α-androstanediol seems to be major hormonal stimuli for stromal & glandular proliferation in men with **NH**.

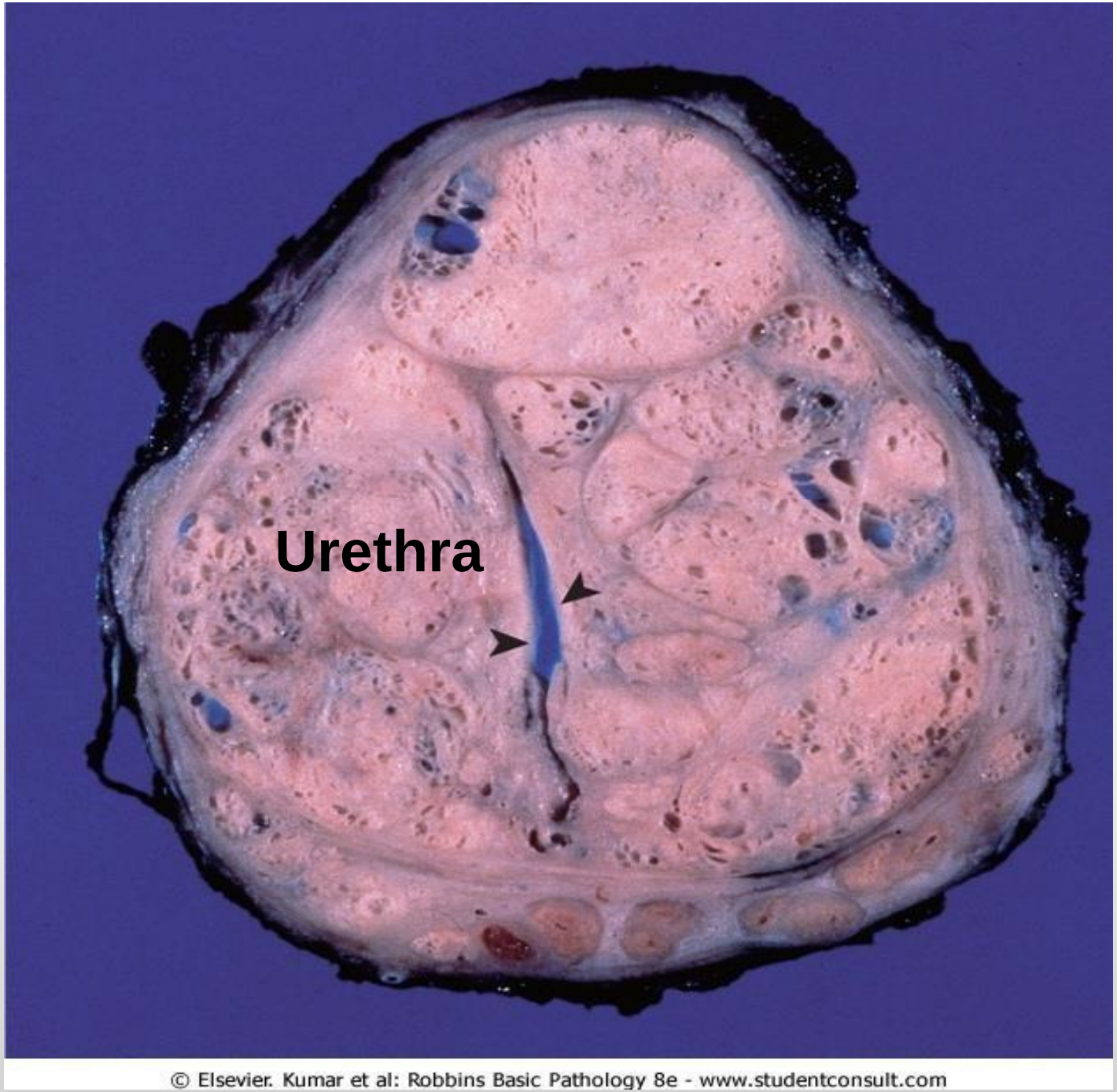
- DHT binds to nuclear androgen receptors stimulating the synthesis of DNA, RNA, GFs, & other cytoplasmic proteins, leading to hyperplasia.
- This forms the basis for the current use of 5α-reductase inhibitors in the treatment of symptomatic NH

❖ Morphology of NH

- GROSSLY, NH arises most commonly in the inner, periurethral glands of the P, particularly from those that lie above the verumontanum.
- The P is enlarged from its normal 20 gm to 300 gm or more in severe cases.
- Prostate C/S shows many well-circumscribed nodules that bulge from the cut surface , most pronounced in the inner(central & transitional) region.
- Nodules may be solid or may contain cystic spaces (due to the dilated glandular elements seen histologically).
- The urethra is usually compressed by the hyperplastic nodules, often to a slit like orifice.

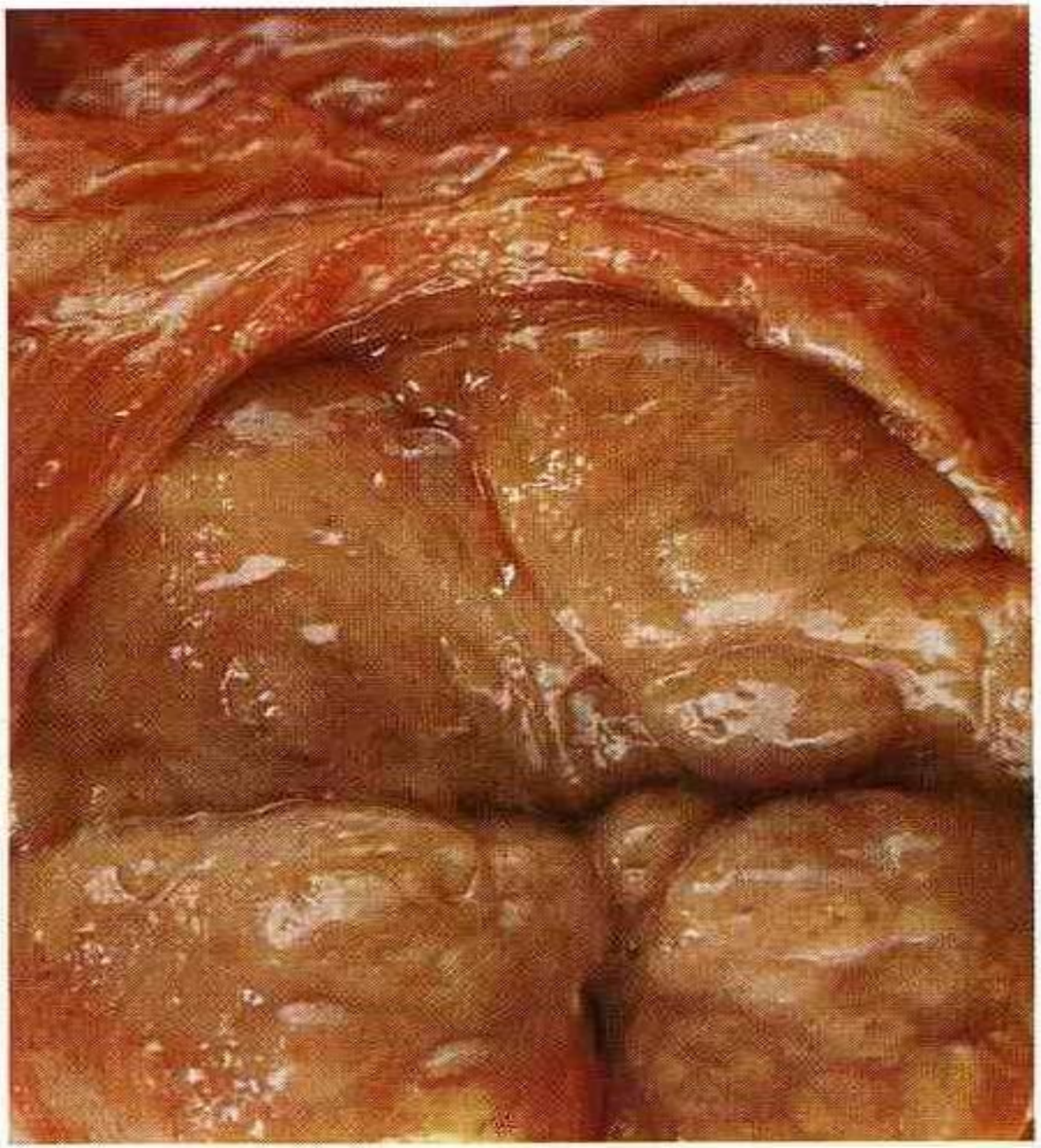
- Microscopically : the hyperplastic nodules composed of:

  (1) hyperplastic glands lined by characteristic dual (double)cell population, a central tall columnar epithelial cells; crowding of which results in the formation of papillary projections& a peripheral layer of flattened basal cells.
- The glandular lumina often contain inspissated, proteinaceous secretory material, termed corpora amylacea.
- The hyperplastic glands are surrounded by proliferating stromal elements.
- Some nodules composed predominantly of spindle-shaped stromal cells & connective tissue.



Nodular hyperplasia (NH) of the prostate

Well-defined nodules, with cystic spaces, compress the urethra (arrowheads) into a slitlike lumen.



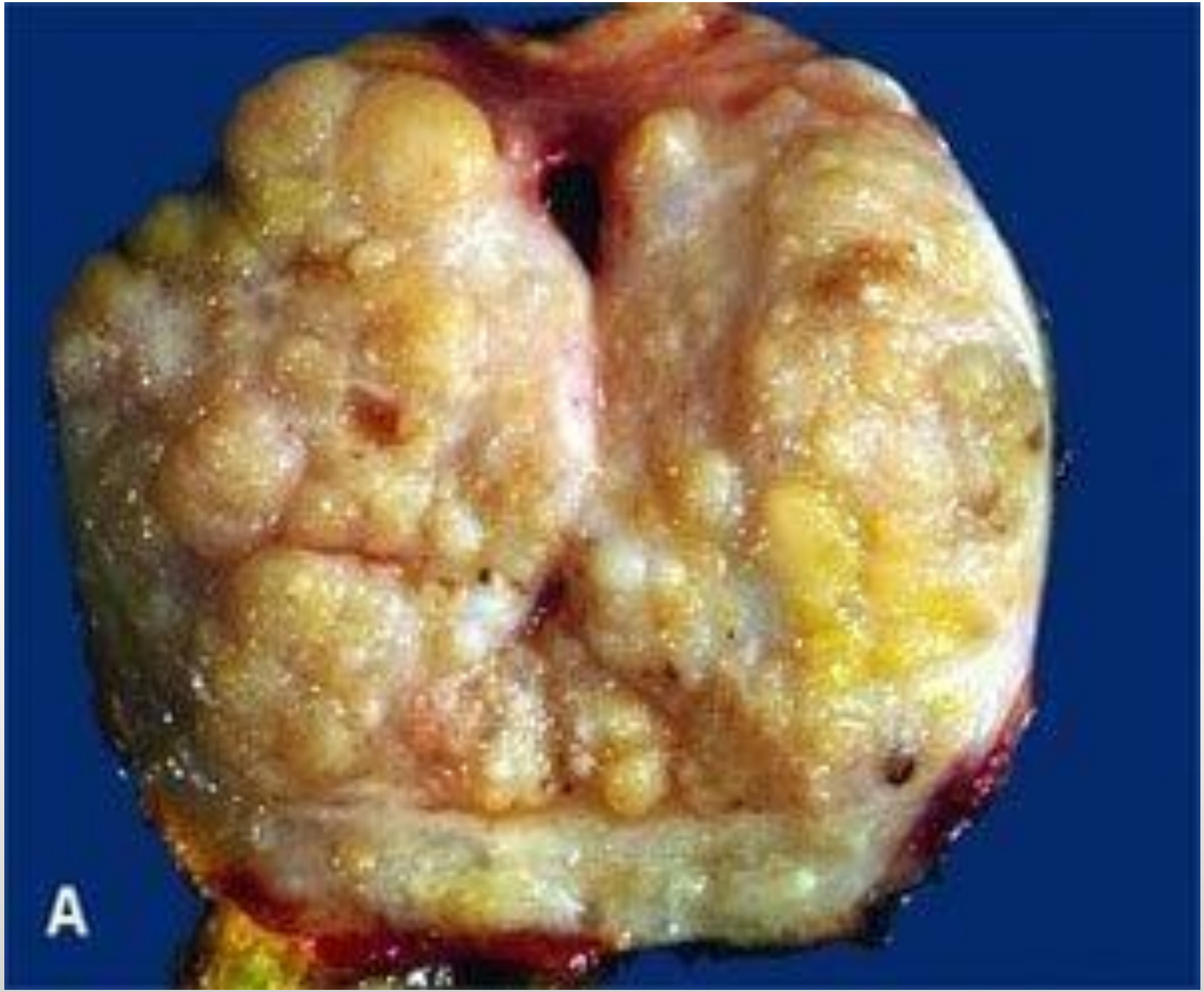
11.6 Adenomatous hyperplasia: prostate

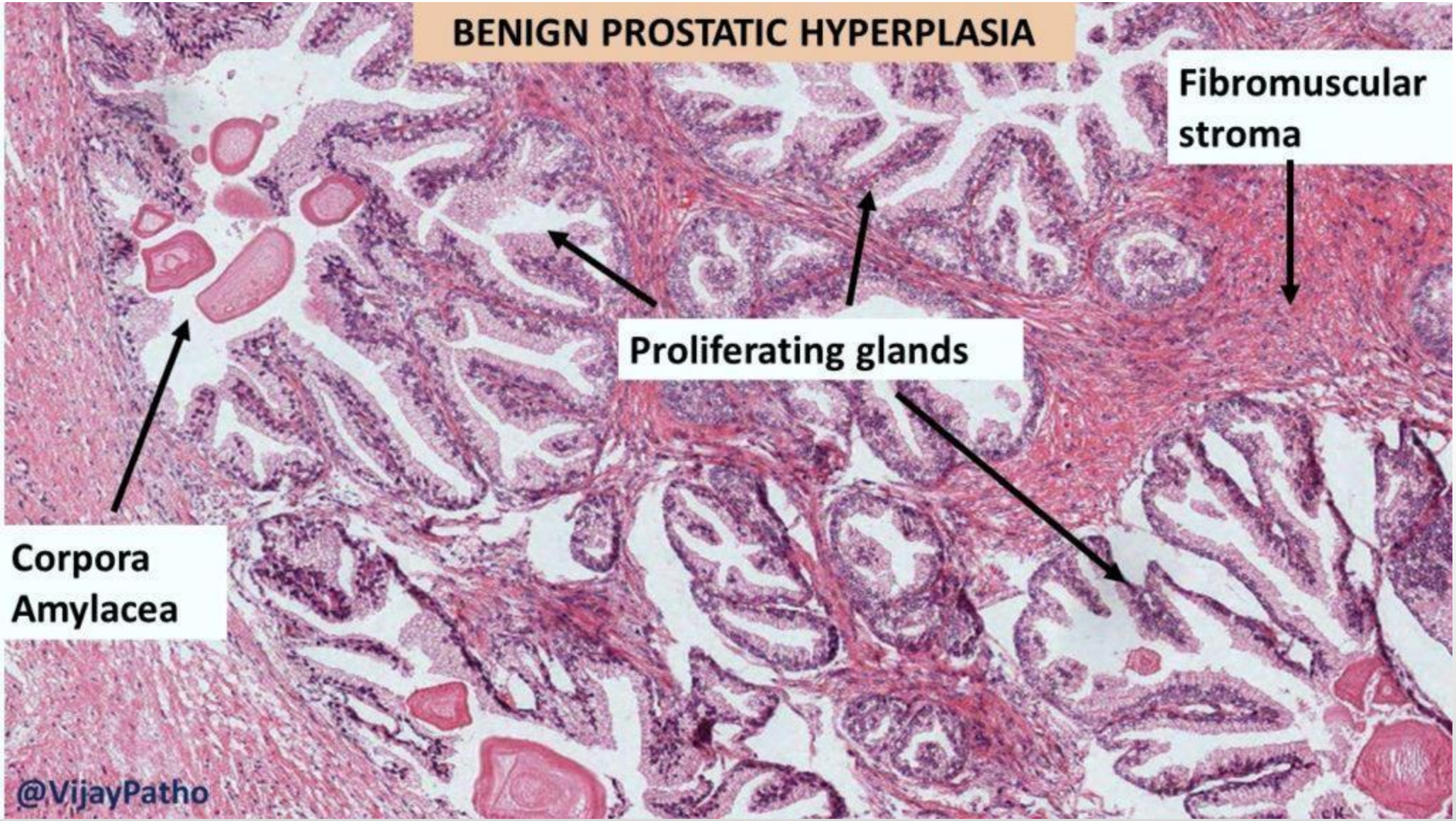
Adenomatous hyperplasia: Prostate.

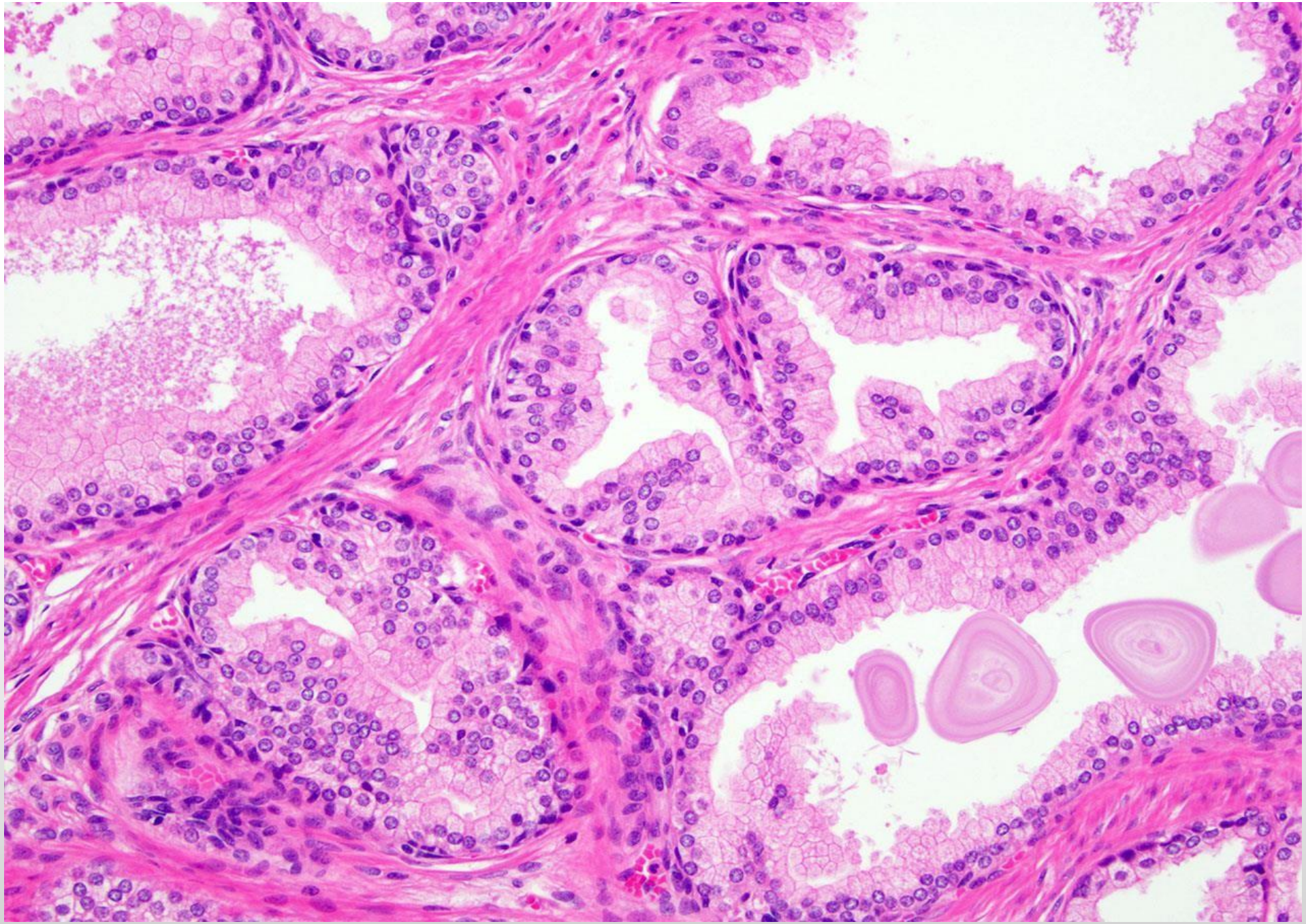
C/S of both lateral lobes of a very nodular prostate.

The creamy-white nodules vary in size & are separated by delicate greyish-white septa. The spongy hyperplastic nodules have compressed the surrounding gland into a ‘capsule’ (top).

Benign prostatic hyperplasia




BENIGN PROSTATIC HYPERPLASIA
Fibromuscular stroma
Proliferating glands
Corpora Amylacea
@VijayPatho



Nodular prostatic hyperplasia.

- Clinical manifestations of P NH occur in only about 10% of men with the disease.

Diagnosis is based primarily on digital rectal examination and symptoms; cystoscopy, transrectal ultrasonography, urodynamics, or other imaging studies may also be needed. As NH preferentially involves the inner portions of the P, NH most common manifestations are those of lower UT obstruction;

including difficulty in starting the stream of urine (hesitancy) & intermittent interruption of the urinary stream while voiding .

- ❑Some men may develop complete urinary obstruction, with resultant painful distention of the bladder, if neglected, bilateral hydronephrosis & RF.
- ❑Urinary urgency, frequency, & nocturia, all indicative of bladder irritation.
- ❑The combination of chronic obstruction and residual urine in the bladder increase the risk of UTI.
- ❑ Treatment options include 5 alpha-reductase inhibitors, alpha-blockers, tadalafil, and surgery.

Prostatic carcinoma(Pca)

- P ca is the most common visceral cancer in males (in the West), & ranks 2nd (after ca lung) as the most common cause of cancer-related deaths in men older than 50 y.

- **P ca is a disease of older males, with a peak incidence between the ages of 65 & 75 years.**
- Latent (Hidden) P ca are even more common than the clinically apparent P ca, with an overall frequency of more than 50% in men older than 80 years of age.

- Although the cause of Prost ca remains unknown, clinical & experimental observations suggest that **hormones, genes, & environment** all have a role in its pathogenesis.
- Hormones: **the androgens contribution to the development of P ca is suggested by:**

- (1) Prost ca **does not** develop in males **castrated** before puberty.
- (2) the fact that the growth of many Prost ca can be **inhibited by orchiectomy** or by the **administration of estrogens** such as diethylstilbestrol.

- **Hereditary: there is ↑ risk of P ca among first-degree relatives of patients with P ca**
- **Racial:** Symptomatic Prost ca more common & occurs at an earlier age in American blacks than in whites, Asian and others.
- **Genes.** Much effort is focused on finding Prost ca **genes**, but no definitive data are available. Overexpression of two ETS family transcription factors (which are also involved in Ewing sarcoma) were implicate in the pathogenesis of **Prost ca**.
- **Inherited mutations** of the BRCA1 or BRCA2 genes, which are linked to an increased risk of breast and ovarian cancers in some families, can also **increase prostate cancer risk in men (especially mutations in BRCA2**).
- **Men with Lynch syndrome (also known as hereditary non-polyposis colorectal cancer, or HNPCC),** a condition caused by inherited gene changes, have an increased risk for a number of cancers, including prostate cancer

Environmental influences is suggested by the

- (1) ↑ frequency of **Pca** in certain **industrial settings**&
- (2) significant **geographic** differences in the incidence of the **Pca,**
- **Males is immigrating** from low-risk to high-risk areas maintain a lower risk of **P ca**; the **risk is intermediate** in subsequent generations, in keeping with an environmental influence on **Pca** development.

- **Among environmental influences, a diet high in animal fat has been suggested as a risk factor.**

- Many prostate cancers are detected on the basis of elevated plasmatic levels of **prostate-specific antigen (PSA > 4 ng/mL),** **glycoprotein normally expressed by prostate tissue**.
- However, because men without cancer have also been found with elevated PSA, **a tissue biopsy** is the standard of care to confirm cancer's presence.
- **GROSSLY, 70% to 80% P ca arise in the prostate peripheral zone**& hence may be palpable as irregular hard nodules by PR examination, & because of this peripheral location, early **Pca is less likely to cause urethral obstruction than is NH.**
- Early **Prost ca** typically appears as hard, ill-defined subcapsular masses, C/S appear **firm, gray-white to yellow** lesions that infiltrate the adjacent gland .

- Locally advanced ca often **infiltrate** the (1) periurethral zones of the prostate,(2) seminal vesicles & (3) may invade bladder wall.

- **Denonvilliers fascia**, the connective tissue layer separating the lower genitourinary structures from the rectum, usually prevents growth of the **P ca** posteriorly resulting in the **infrequent Prost ca invasion of the rectum.**
- **Metastases** to regional pelvic LNs may occur early.

- Microscopically: most **Prost ca** are **adenocarcinomas** exhibiting variable degrees of differentiation.

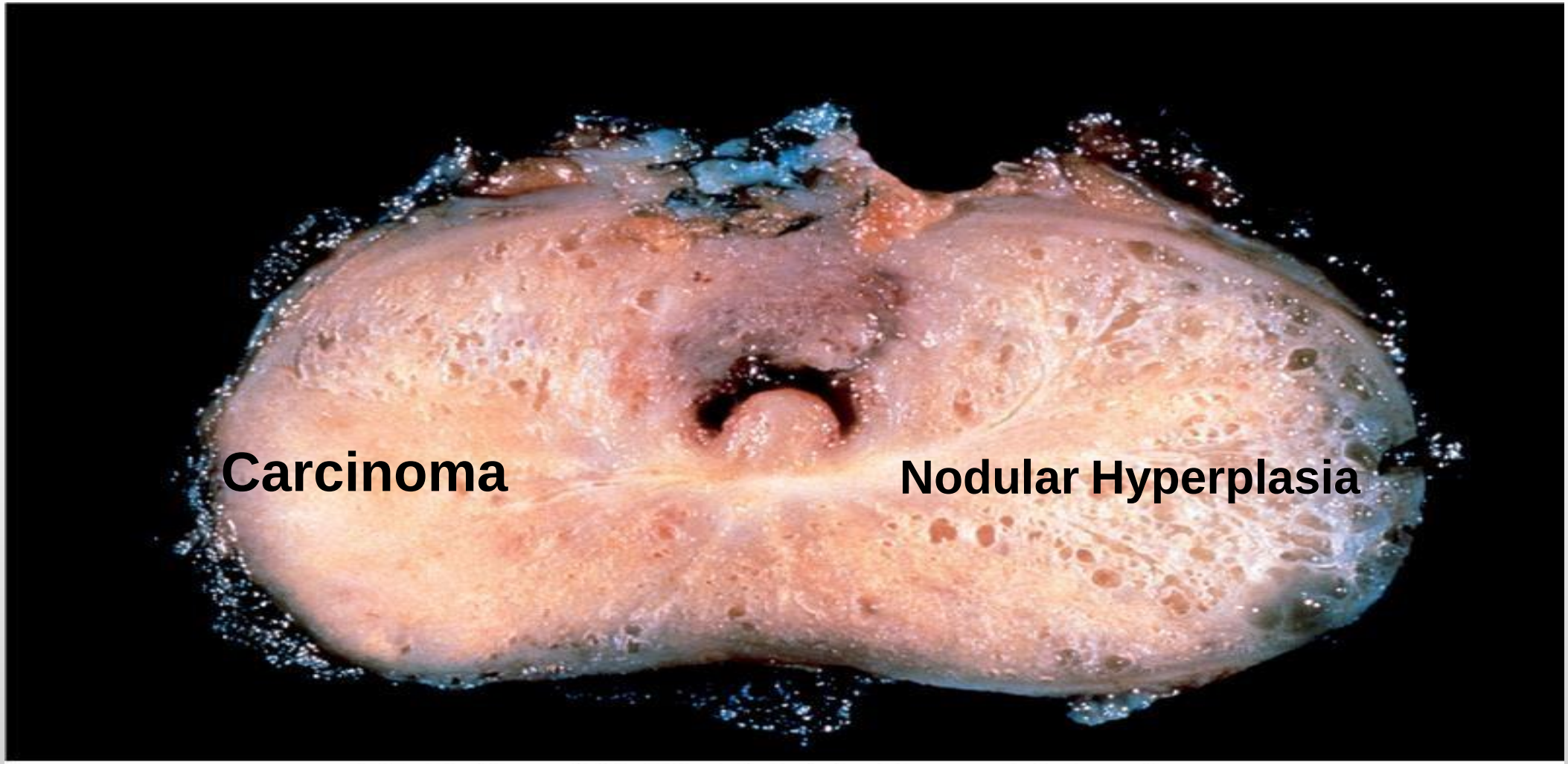
- The **well differentiated Prost ca** composed of small glands that infiltrate the adjacent stroma in an irregular, haphazard fashion.

- In contrast to normal & hyperplastic prostate:

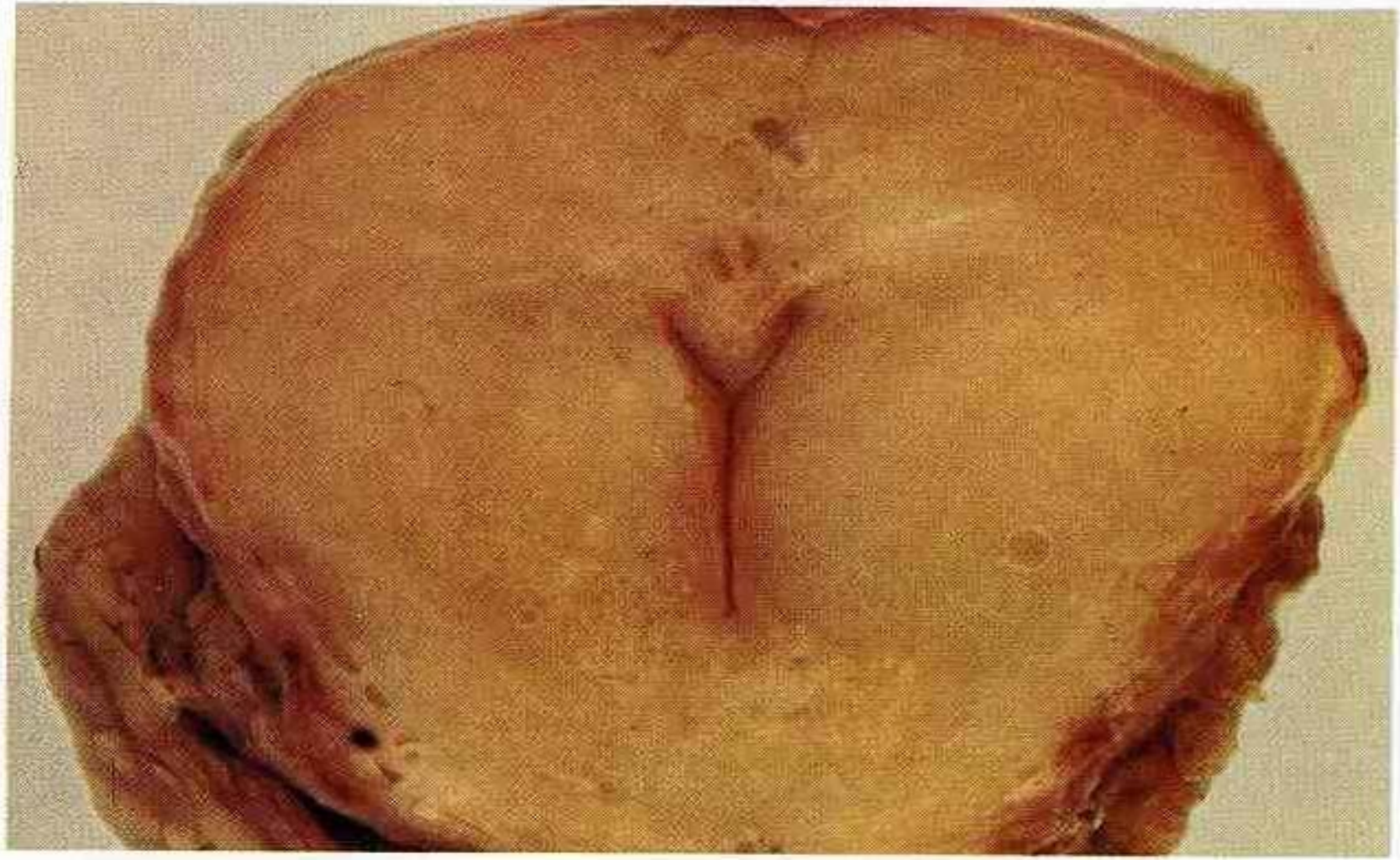
(1) Due to scant stroma, the glands in **Prost ca** lie back to back& appear to dissect sharply though the stroma,
(2) in **Prost ca ,** the glands are lined by a **single layer** of cuboidal cells with **absence of the basal cell layer** seen in normal or NH glands
(3) cell nuclei show **conspicuous nucleoli**.

- With increase degrees of anaplasia, irregular, ragged glandular structures, papillary or cribriform epithelium & in extreme cases, sheets of poorly differentiated cells are present.

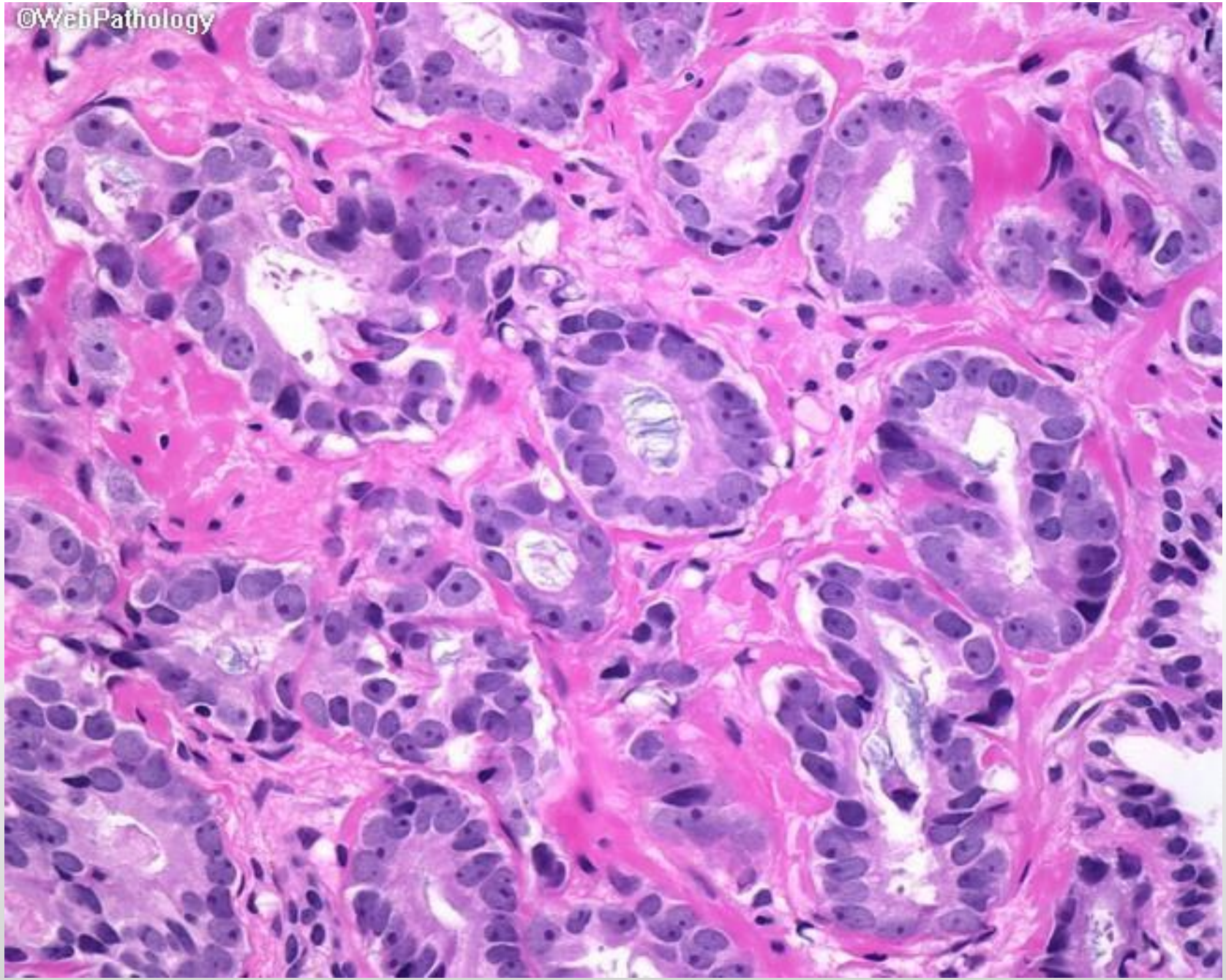
Prostatic adenocarcinoma. Carcinomatous tissue is seen in the lower left as...Subscapular solid whiter cancer in contrast to the Spongy benign peripheral zone on the other side



Adenocarcinoma: prostate. Diffusely enlarged malignant prostate. Note: (1) absence of nodularity, & (2) yellow-orange color, with yellowish areas of necrosis. Remember: Prostatic carcinoma is hard in consistency on P/R exam.



11.10 Adenocarcinoma: prostate



- This focus of prostate cancer has all the essential histologic features - small crowded glands lined by a single layer of cells, nuclear enlargement and hyperchromasia, prominent nucleoli, and intraluminal blue mucin. A benign gland is partially visible at the lower right side of the image. Contrast its nuclear size to those of adjacent malignant glands.

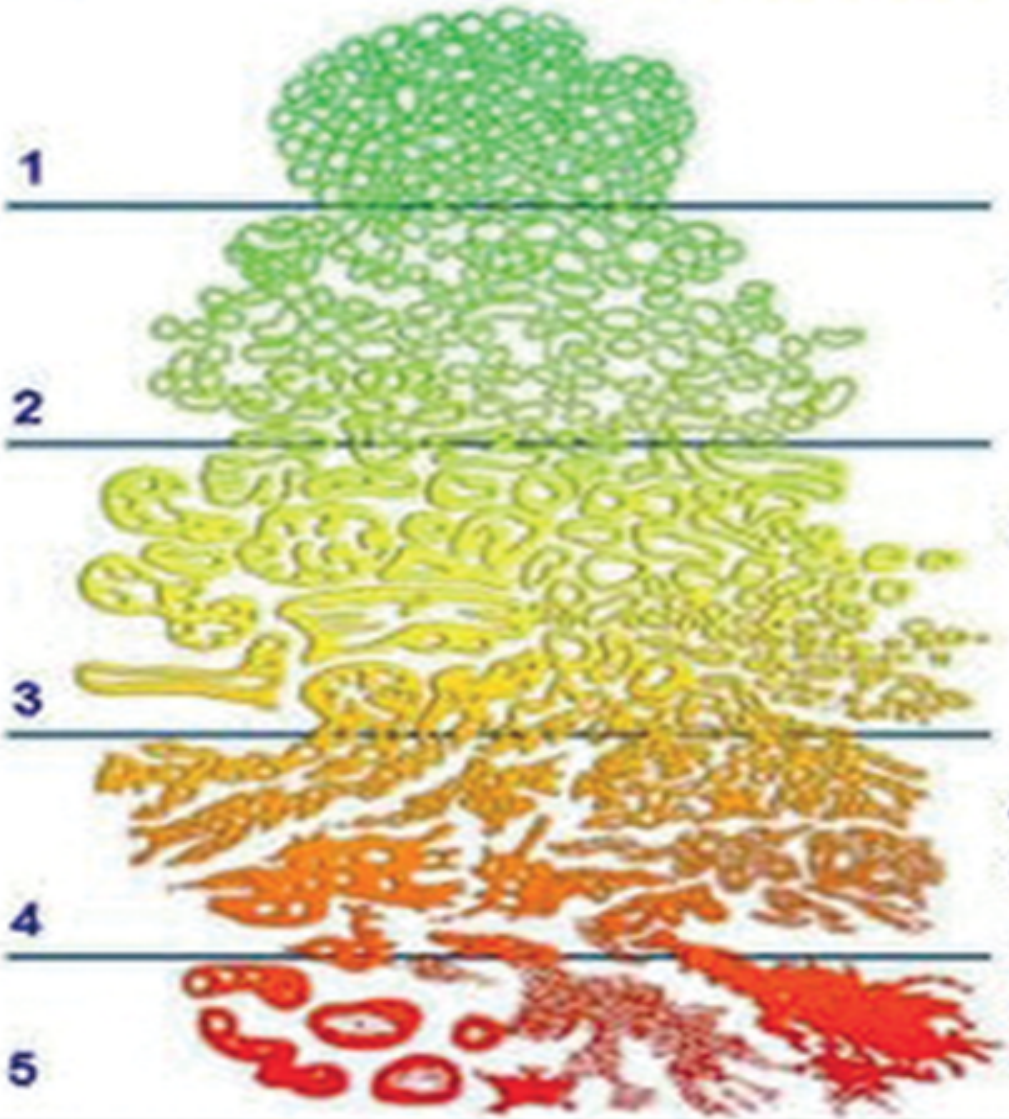
- Because of its frequent coexistence with infiltrating Pca, **PIN** has been suggested as a probable precursor to P ca.

PIN (prostatic intraepithelial neoplasia)has been subdivided into high- & low-grade patterns, depending on the degree of atypia.

- Importantly, **high-grade PIN** shares molecular changes with invasive Pca, supporting the argument that **PIN** is an intermediate between normal & frankly malignant P tissue.

- **The commonly used method for P ca histologic grading is the Gleason system(1 to 5 degrees),based on the degree of glandular architecture & differentiation + nuclear anaplasia + mitotic activity.**

Gleason's Pattern Scale



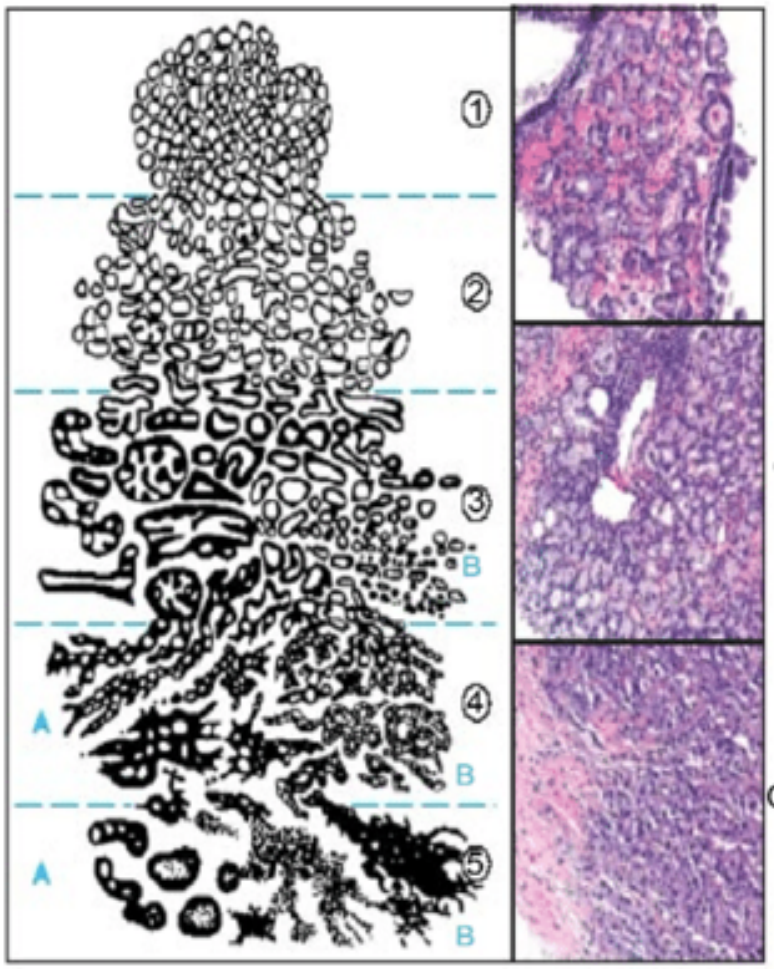
1. Small, uniform glands.
2. More space (stroma) between glands.
3. Distinctly infiltration of cells from glands at margins.
4. Irregular masses of neoplastic cells with few glands.
5. Lack of or occasional glands, sheets of cells.

Well differentiated

Moderately differentiated

Poorly differentiated
Anaplastic

Using this system, the grades of the most prevalent and second most prevalent patterns (if at least 5% of the total), are added together to yield the overall Gleason score. For example, if the most prevalent pattern/grade is 2, and the second most prevalent grade is 1, then the Gleason score is 2+1=3.



(a)

Grade 3

Grade 4

Grade 5

TRANDITIONAL GLEASON SCORE	NEW GRADING SYSTEM GROUP 1
GLEASON 3+3=6 Only individual discrete well-formed glands	GRADE 1
GLEASON 3+4=7 Predominantly well-formed glands with a lesser component of poorly-formed/ fused/cribriform glands	GRADE 2
GLEASON 4+3=7 Predominantly poorly-formed/ fused/cribriform glands with a lesser component of well-formed glands	GRADE 3
GLEASON 4+4=8 Only poorly-formed/fused/ cribriform glands or -Predominantly well-formed glands with a lesser component lacking or -Predominantly lacking glands with a lesser component of well-formed glands	GRADE 4
GLEASON 9-10 Lacks gland formation (or with necrosis) with or without poorly-formed/fused/cribriform gland	GRADE 5

(b)

❑ Clinically, **Prost ca** is often clinically:

(1) silent ,particularly during their early stages.

- **10%** of localized Prost ca are discovered unexpectedly, during histologic examination of P tissue removed for NH, while in autopsy studies, the incidence approaches **30%** in men between 30 and 40y.

- As most Prost ca begin in the peripheral regions of the prostate, they may be discovered during routine PR exam.

(2)Extensive **disease** may produce **"prostatism**“, i.e., local discomfort & evidence of lower **UT obstruction,** & with hard, fixed prostate on PR examination.

(3) **Regrettably,** an uncommon mode of presentation is evidence of **metastases**.

- Bone metastases, particularly to the axial skeleton, are common & may cause either **osteolytic** or, more commonly, **osteoblastic** (presence of which in an older male is strongly suggestive of advanced P ca) lesions.

- The pathologic distinction between high-grade prostate adenocarcinoma (PAC) involving the urinary bladder and high-grade urothelial carcinoma (UC) infiltrating the prostate can be difficult. However, making this distinction is clinically important because of the different treatment modalities for these two entities.
- Prostatic and urothelial markers, including **PSA, NKX3.1, p63, thrombomodulin, GATA3 and High molecular weight cytokeratin** are very useful for differentiating PAC from UC.
- The optimal combination of prostatic and urothelial markers could improve the ability to differentiate PAC from UC pathologically.

- Prostate-specific antigen (PSA) and prostate acid phosphatase (PAP) have been known to assist in verifying the prostatic lineage in cases of metastatic carcinoma of unknown origin . However, in poorly differentiated carcinomas, the sensitivities of PSA and PAP decrease.
- PSA is a proteolytic enzyme produced by both normal & neoplastic prostatic epithelium. Assay of serum levels of prostate-specific antigen(PSA) has gained widespread use in the diagnosis of early P ca.
- Traditionally, a serum PSA level of 4.0 ng/L has been used as the upper normallimit.

- PSA diagnostic value is enhanced considerably, however, when it is used in conjunction with other procedures, such as **(1) PR examination, (2) transrectal sonography, & (3) needle biopsy.**

- In contrast to its limitations as a diagnostic screening test, serum PSA concentration is of great value **in monitoring** patients after treatment for P ca, **with rising levels after ablative therapy indicative of recurrence and/or the development of metastases**

Table 18-3 TNM Staging of Prostatic Adenocarcinoma:

T1-Clinically **Inapparent** Lesion By Palpation/Imaging Studies.

T1a -Involvement of ≤5% of resected tissue

T1b -Involvement of >5% of resected tissue

T1c -**Ca present on needle biopsy**(following elevated PSA)

T2-Palpable Or Visible Cancer Confined To Prostate

T2a -Involvement of ≤50% of one lobe

T2b -Involvement of >50% of one lobe, but unilateral

T2c -Involvement of both lobes

T3-Local Extraprostatic Extension

T3a-Extracapsular extension

T3b-Seminal vesical invasion

T4-Invasion of Contiguous Organs And/Or Supporting Structures Including Bladder Neck, Rectum, External Sphincter, Levator Muscles, Or Pelvic Floor

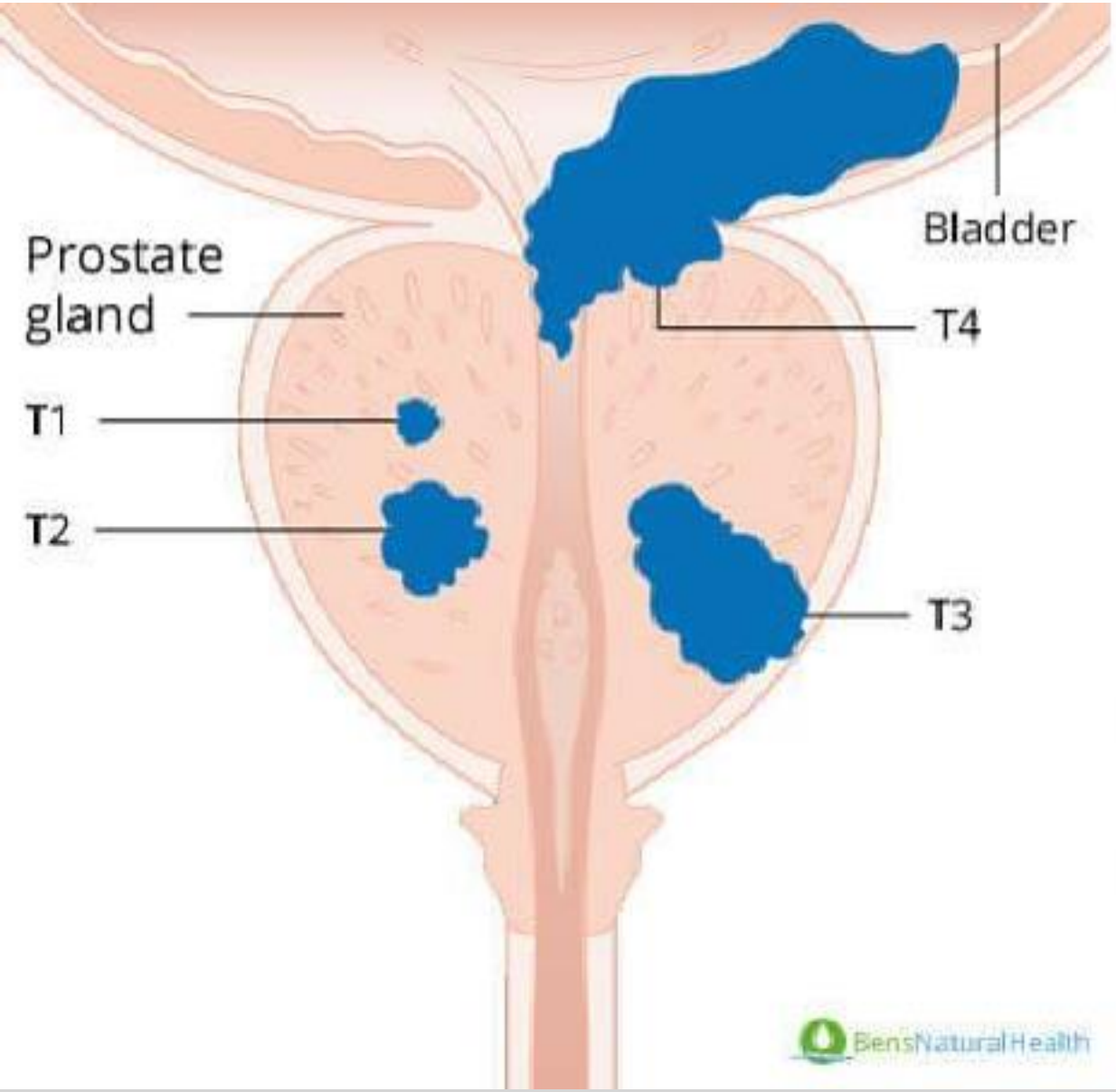
Status of Regional Lymph Nodes (N)

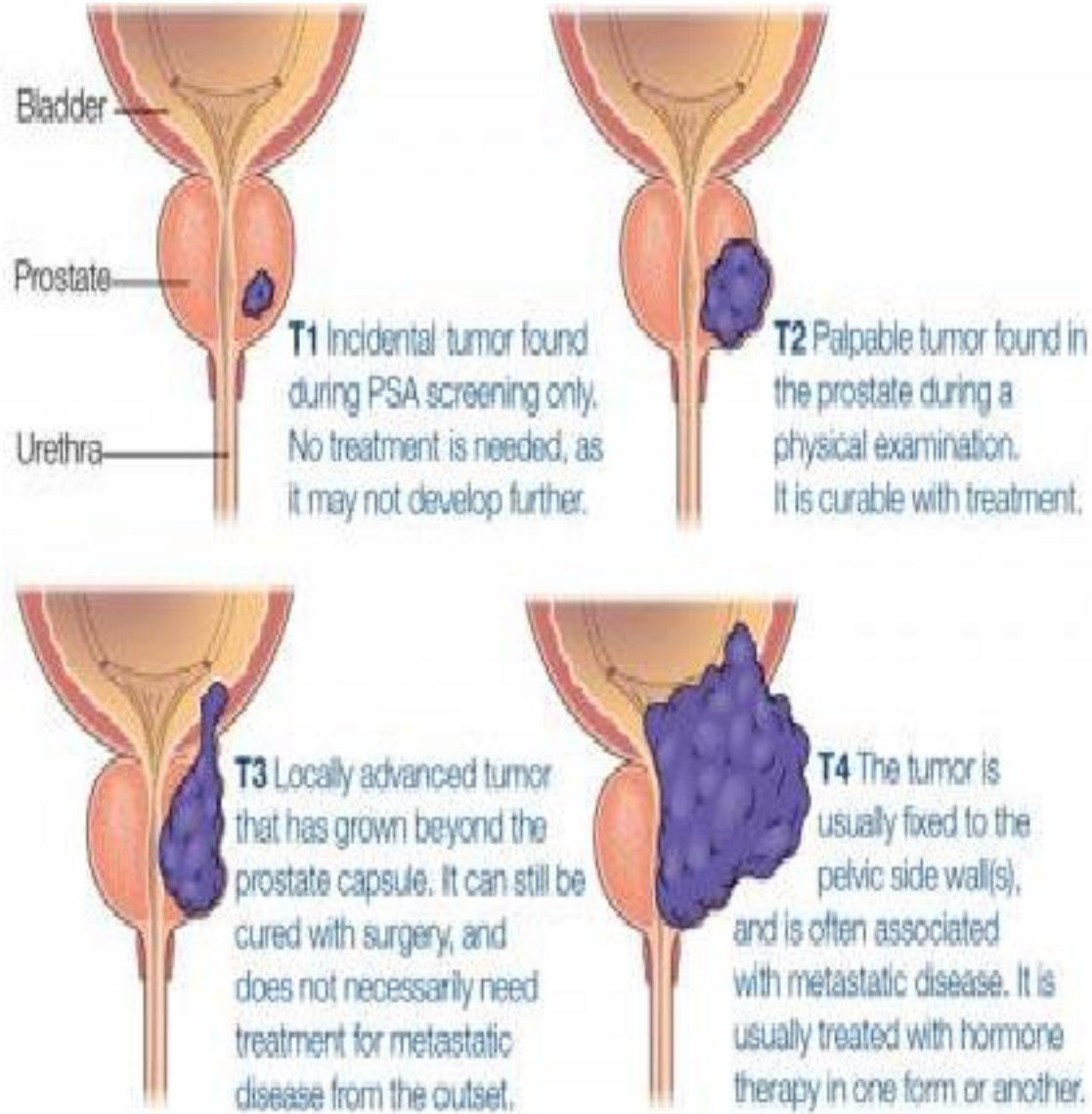
N0 -No Regional LN Metastases N1
-Metastasis In Regional LN

Distant Metastases (M)
M0 -No Distant Metastases
M1 -Distant metastases present

- Anatomic staging of **Pca** (by clinical examination, surgical exploration, radiographic imaging techniques) &, in some systems, & the histologic **grade** of the T & levels of T markers has an important role in the evaluation & treatment of Pca & correlate well with prognosis.

Prostatic cancer stages





- Prostatic ca is treated with various combinations of **surgery, radiation therapy, & hormonal** manipulations.
- Localized disease is usually treated with surgery, external-beam, or internal radioactive seeds radiation therapy
- Hormonal therapy has a central role in the treatment of advanced ca. Specifically, most **Pca are androgen sensitive** & are inhibited to some degree by androgen ablation, & therefore surgical or pharmacologic **castration, estrogens**, & androgen receptor-blocking agents have all been used to control the growth of disseminated Prost ca.
- Prognosis: 90% of patients with stage T1 or T2 lesions survive 10 years or longer. The outlook for patients with disseminated disease remains poor.