Diseases of Male Genital Tract

Penile Diseases

Testicular Diseases

Prostatic Diseases

Penile Diseases

- Congenital Anomalies
- Inflammation
- Tumors
  - Benign Tumors
  - Premalignant lesion(carcinoma in situ)
  - Malignant Tumors

•WHO histological classification of tumours of the penis

Malignant epithelial tumours of the penis

- Squamous cell carcinoma 8070/3[1]
- Basaloid carcinoma 8083/3
- Warty (condylomatous) carcinoma 8051/3
- Verrucous carcinoma 8051/3
- Papillary carcinoma, NOS 8050/3

- Sarcomatous carcinoma 8074/3
- Mixed carcinomas
- Adenosquamous carcinoma 8560/3
- Merkel cell carcinoma 8247/3
- Small cell carcinoma of neuroendocrine type 8041/3
- Sebaceous carcinoma 8410/3
- Clear cell carcinoma 8310/3
- Basal cell carcinoma 8090/3

Precursor lesions

- Intraepithelial neoplasia grade III Bowen disease 8081/2
- Erythroplasia of Queyrat 8080/2
- Paget disease 8542/3
- **Melanocytic tumours**
- Melanocytic nevi 8720/0
- Melanoma 8720/3
- **Mesenchymal tumours**
- **Haematopoietic tumours**
- **Secondary tumours**

Benign Tumors

1-Condyloma Acuminatum-

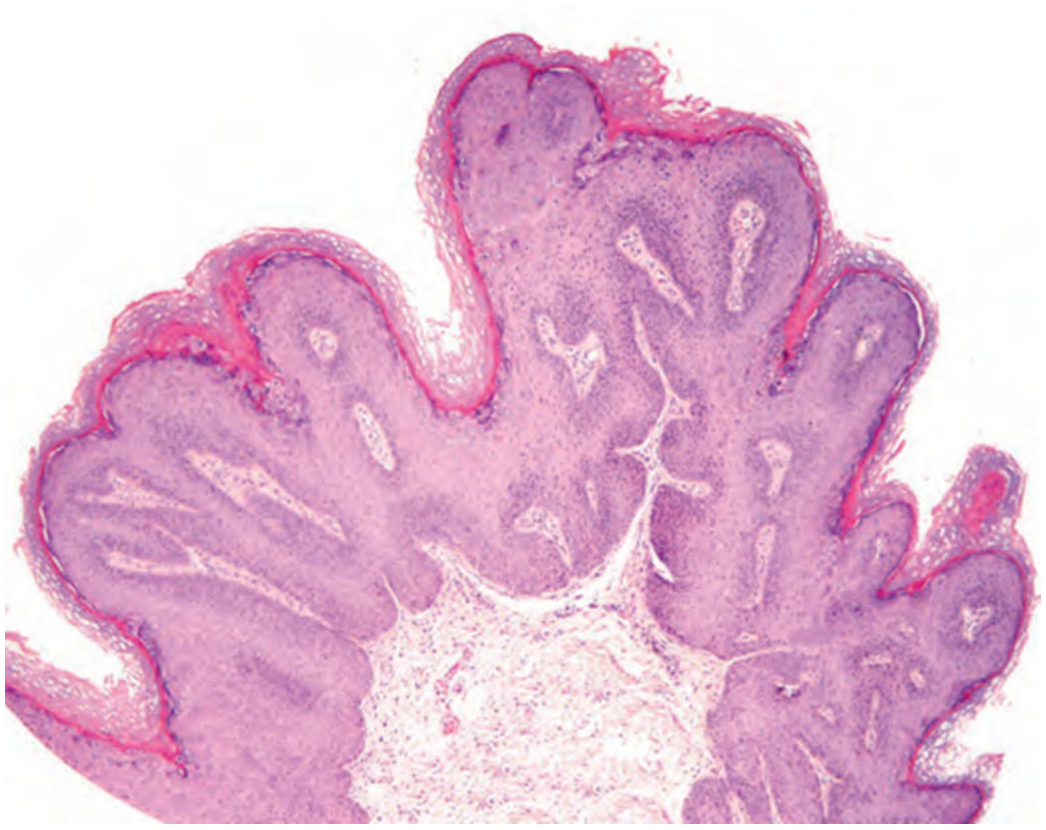
- Wart
- STD
- HPV

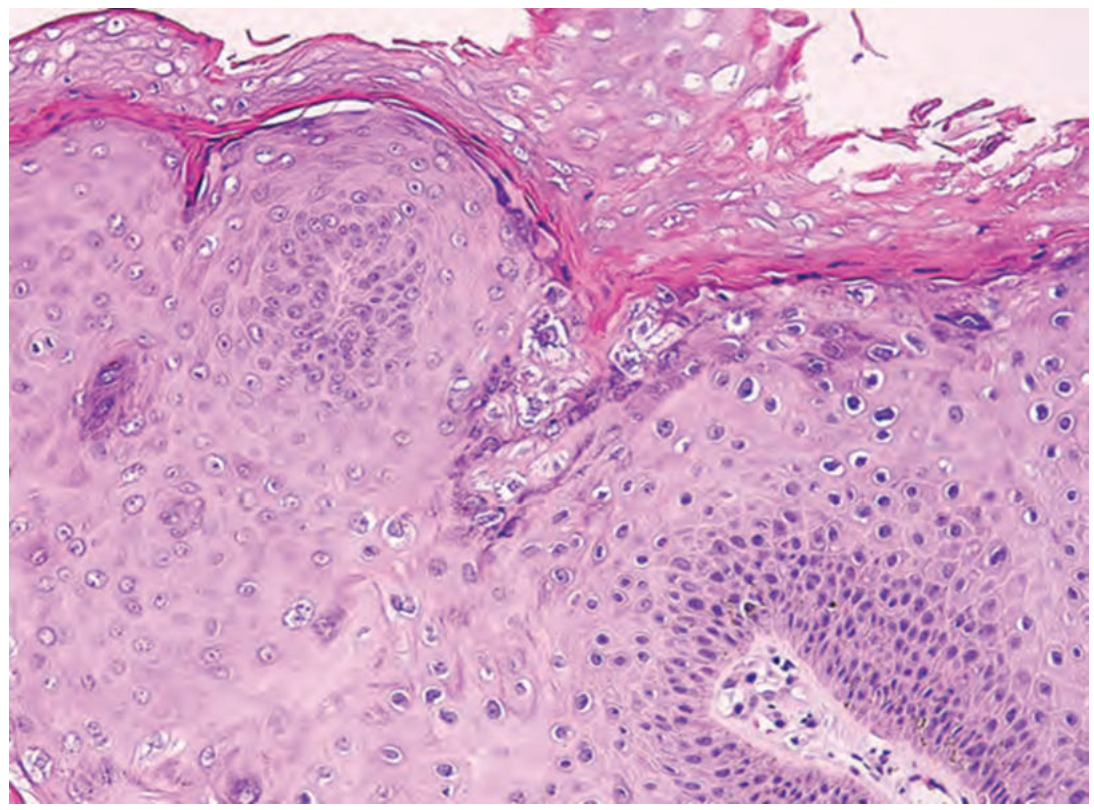
Morphology-

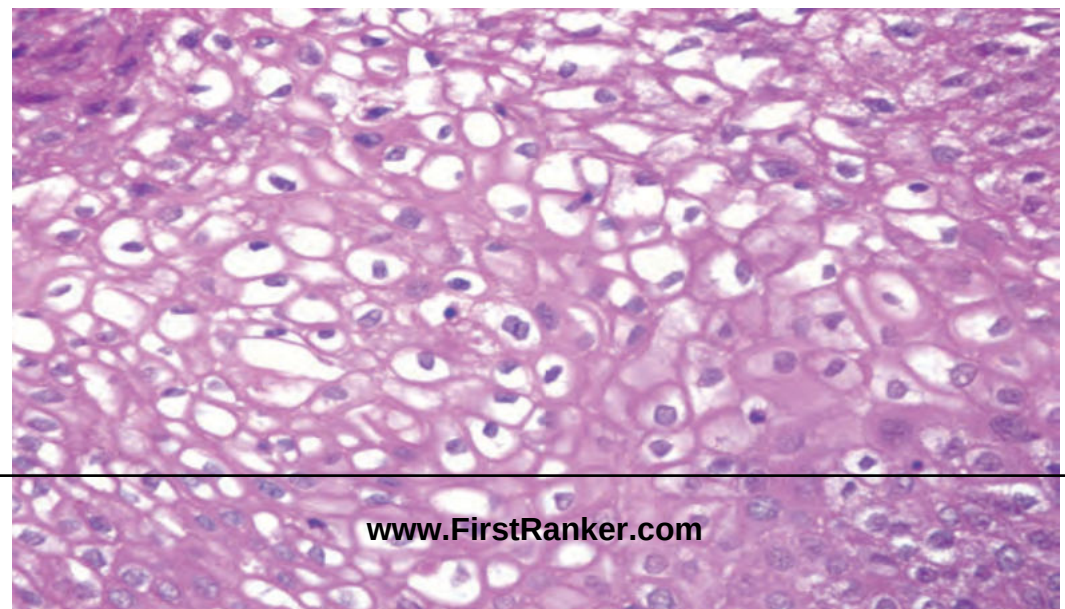
- coronal sulcus and inner surface of the prepuce
- single or multiple sessile or pedunculated, red papillary excrescences

Histologically-

- Acanthosis
- koilocytosis







2-Peyronie Disease-(Idiopathic Fibrous Induration)

- fibromatosis
- fibrous bands involving the **corpus cavernosum** of the penis
- Microscopically, dense fibrosis is associated with sparse, nonspecific, chronic inflammatory infiltration

Precursor lesions-

- Intraepithelial neoplasia Grade III

❑Clinical Variant

➢Bowenoid papulosis

➢Bowen disease

➢Erythroplasia of Queyrat

- Paget disease

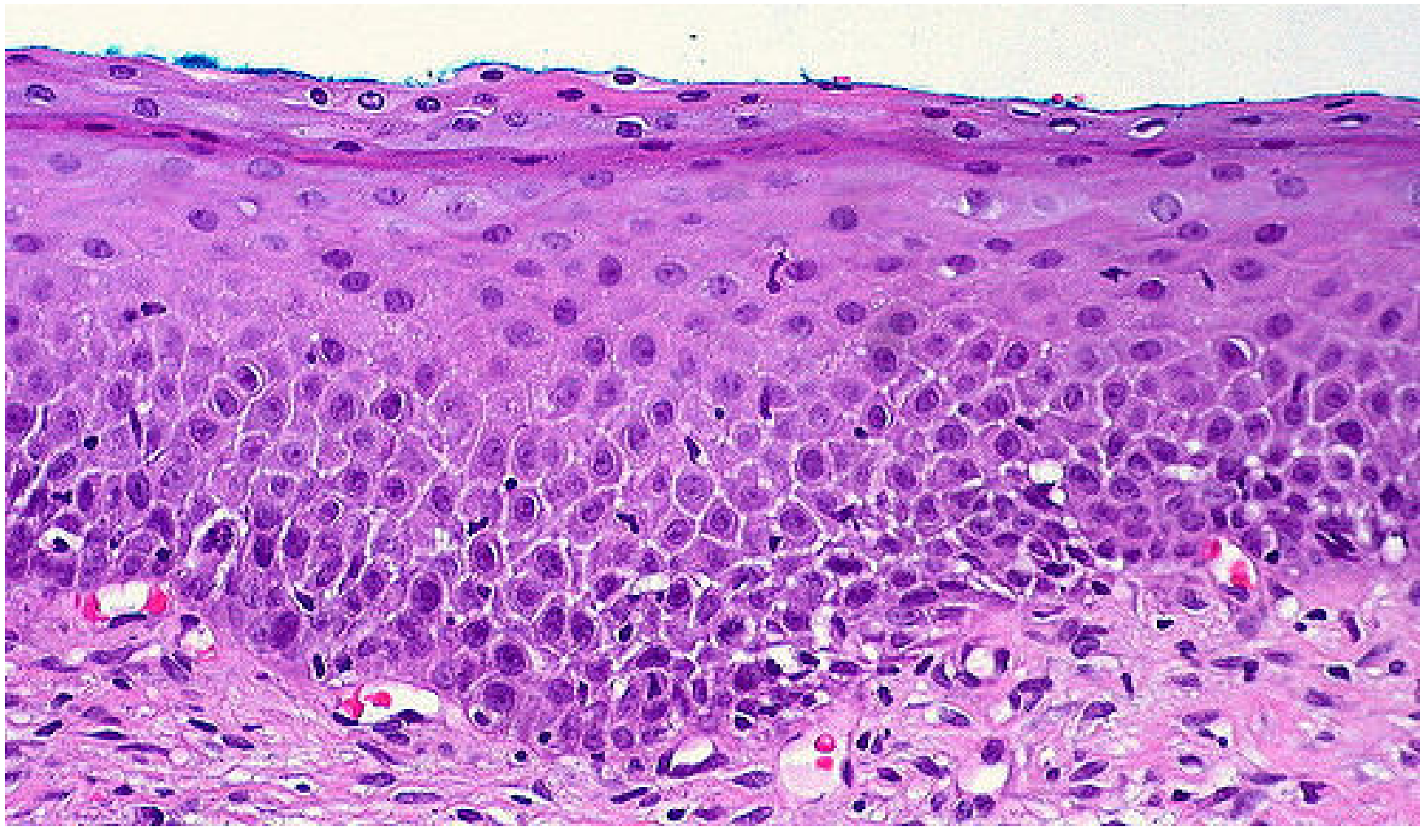
Bowenoid papulosis –

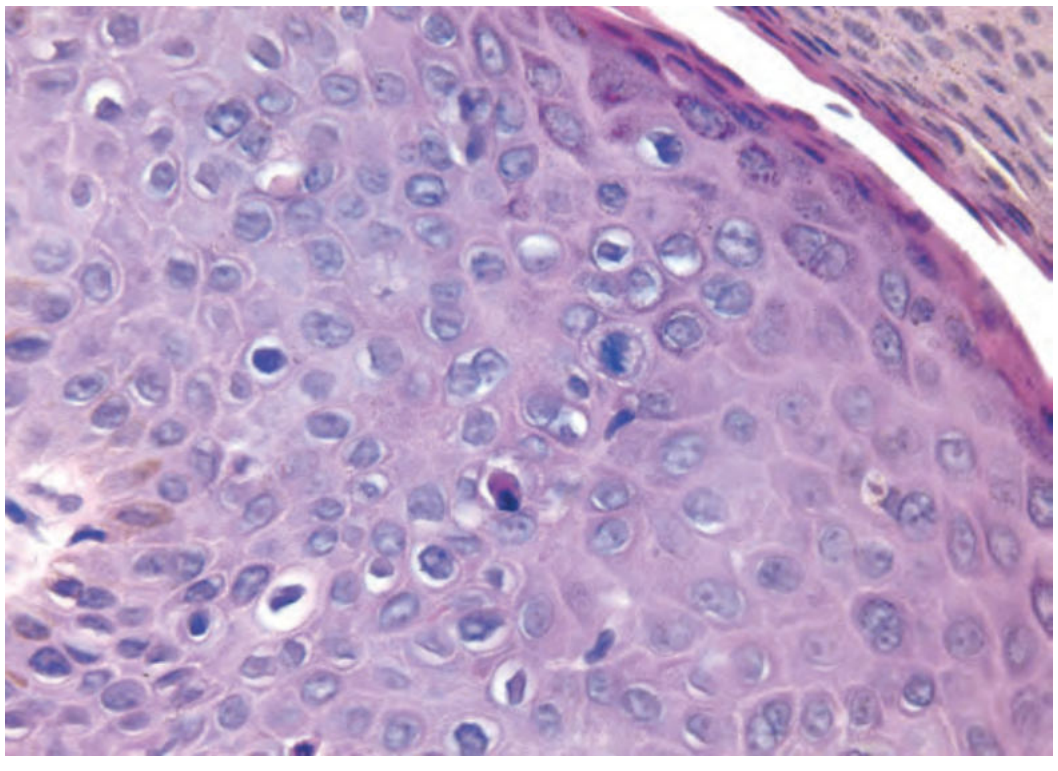
- younger age
- multiple reddish brown papular lesions
- histologically indistinguishable from Bowen disease
- HPV type 16

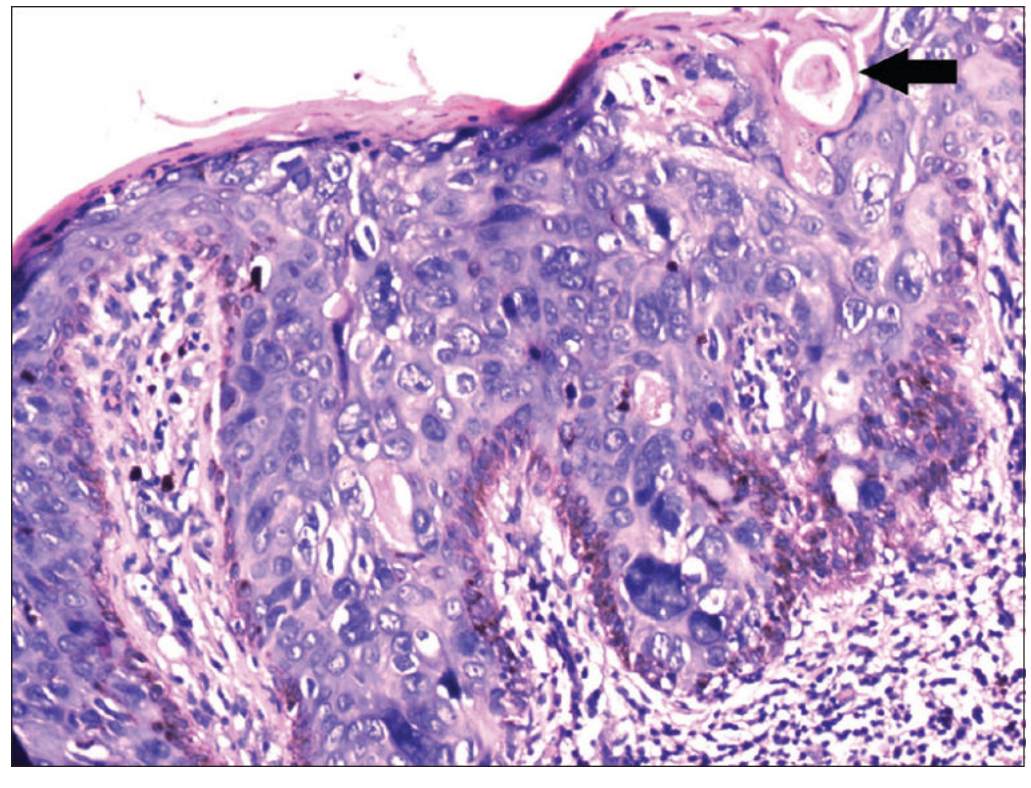
Bowen disease-

- >35Yr
- shaft of the penis and the scrotum
- solitary, thickened, gray-white, opaque plaque
- turn in to 10% scc (5-33% WHO)

Normal Skin histology







Invasive Carcinoma-

squamous cell carcinomas

Etiology-

- phimosis
- chronic inflammatory conditions, especially lichen sclerosus
- smoking
- ultraviolet irradiation
- history of warts, or condylomas

Clinical features

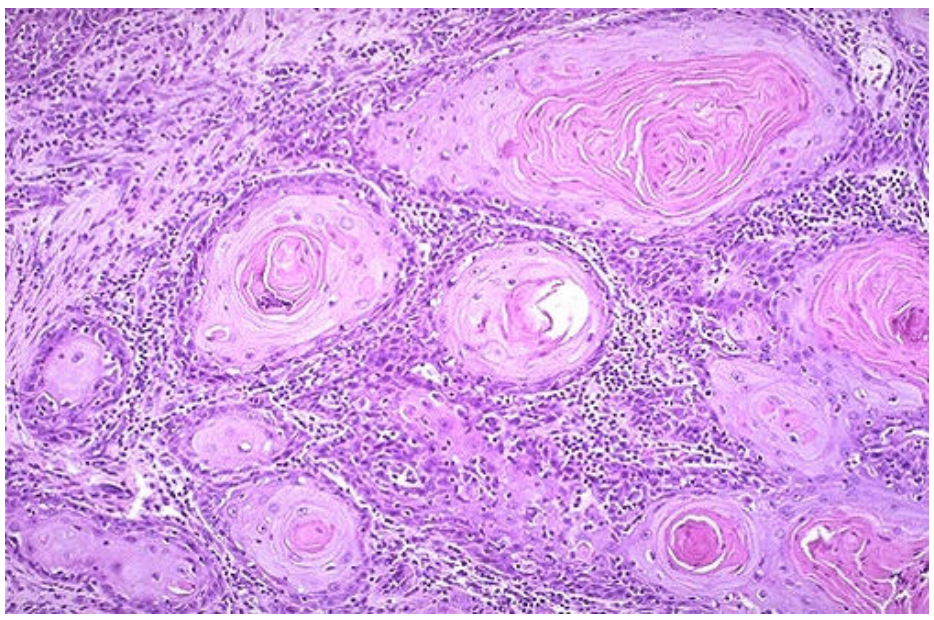
- 40 -60 years
- glans or inner surface of the prepuce

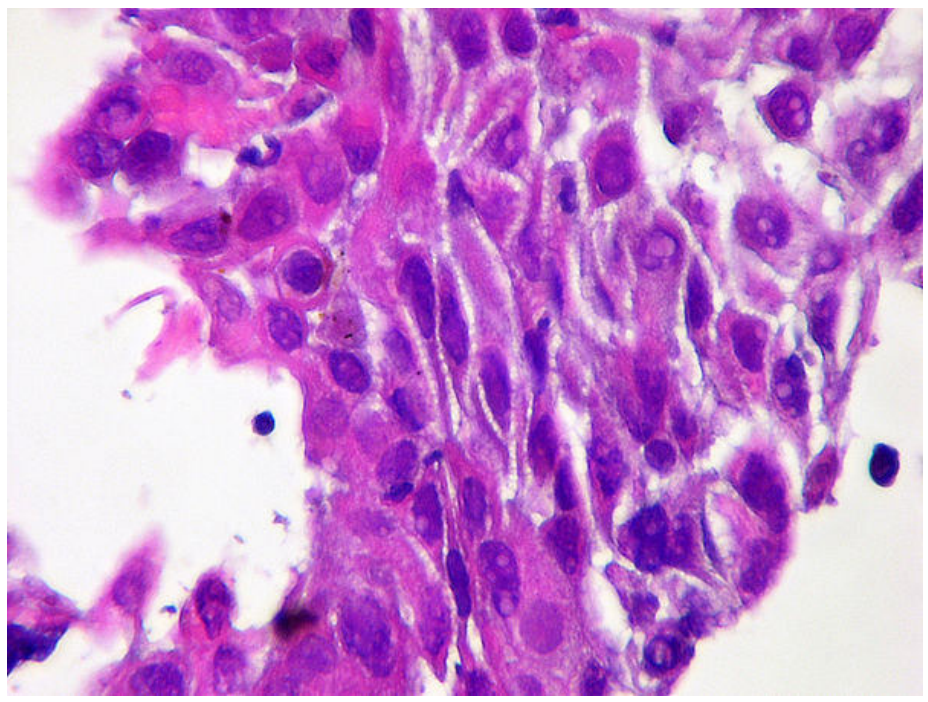
MORPHOLOGY-

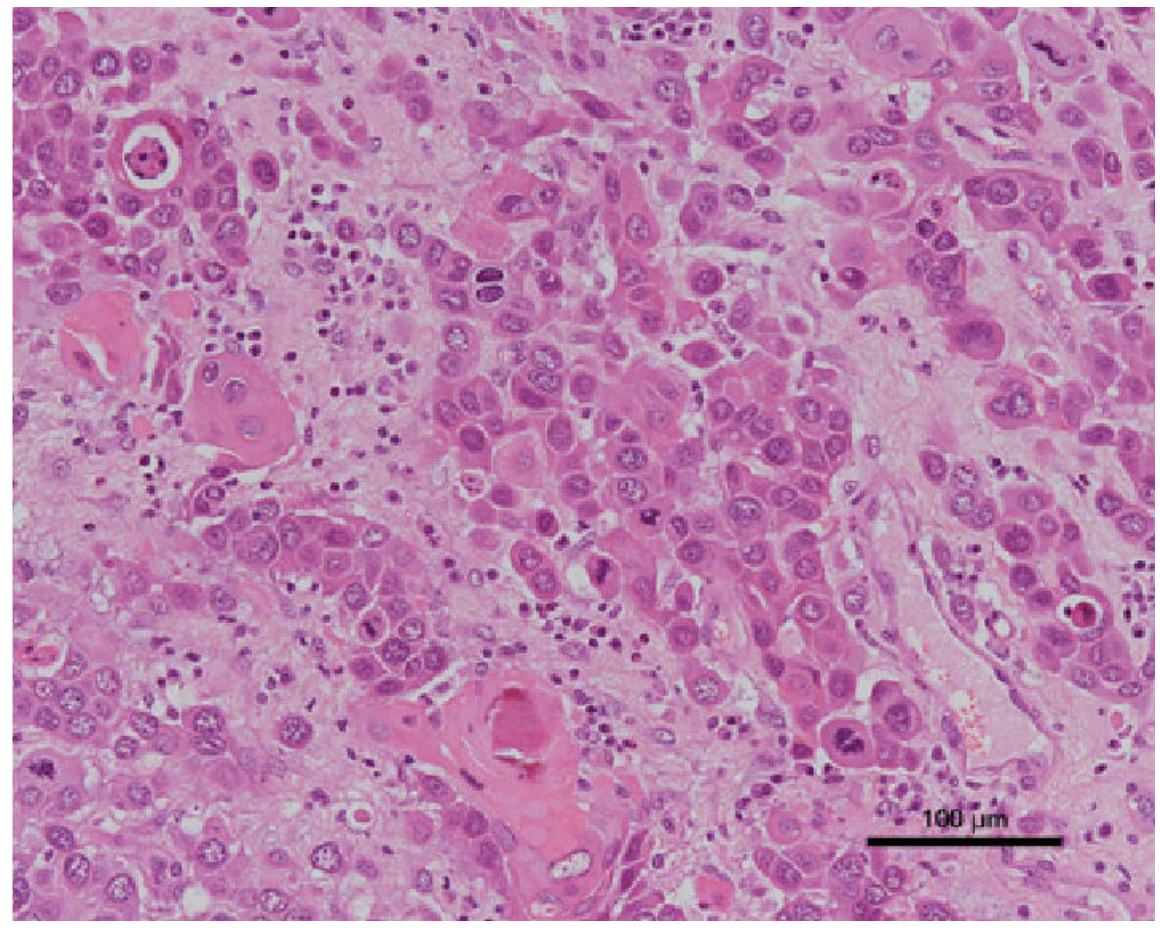
- papillary
- flat
- Ulcerated
- Exophytic

Histopathology-

- spectrum of differentiation from well to poorly differentiated.
- Superficial –WD
- Deep-PD





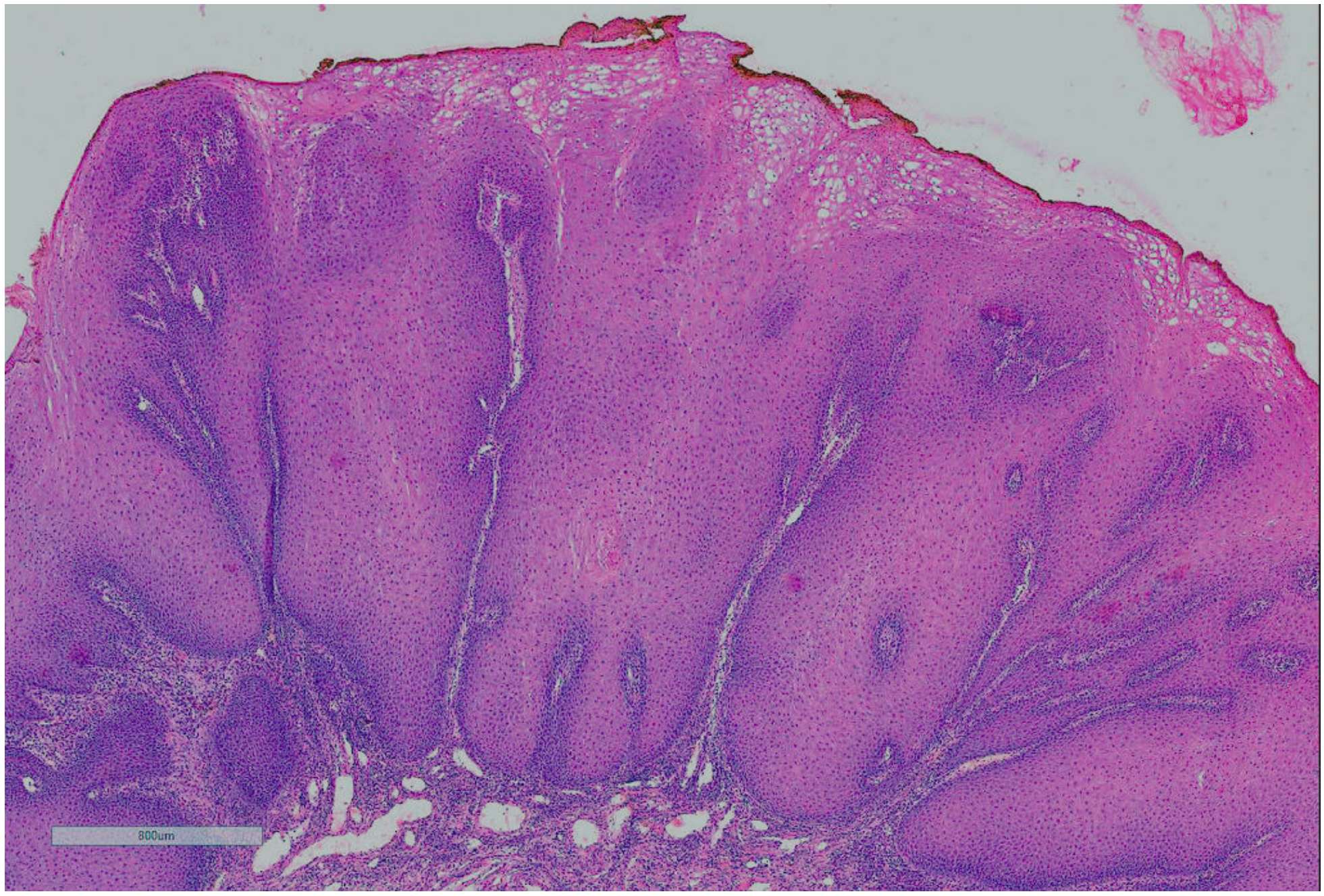


Verrucous carcinoma-

- variant of squamous cell carcinoma
- exophytic well-differentiated
- locally invasive, but rarely metastasize

Other variants

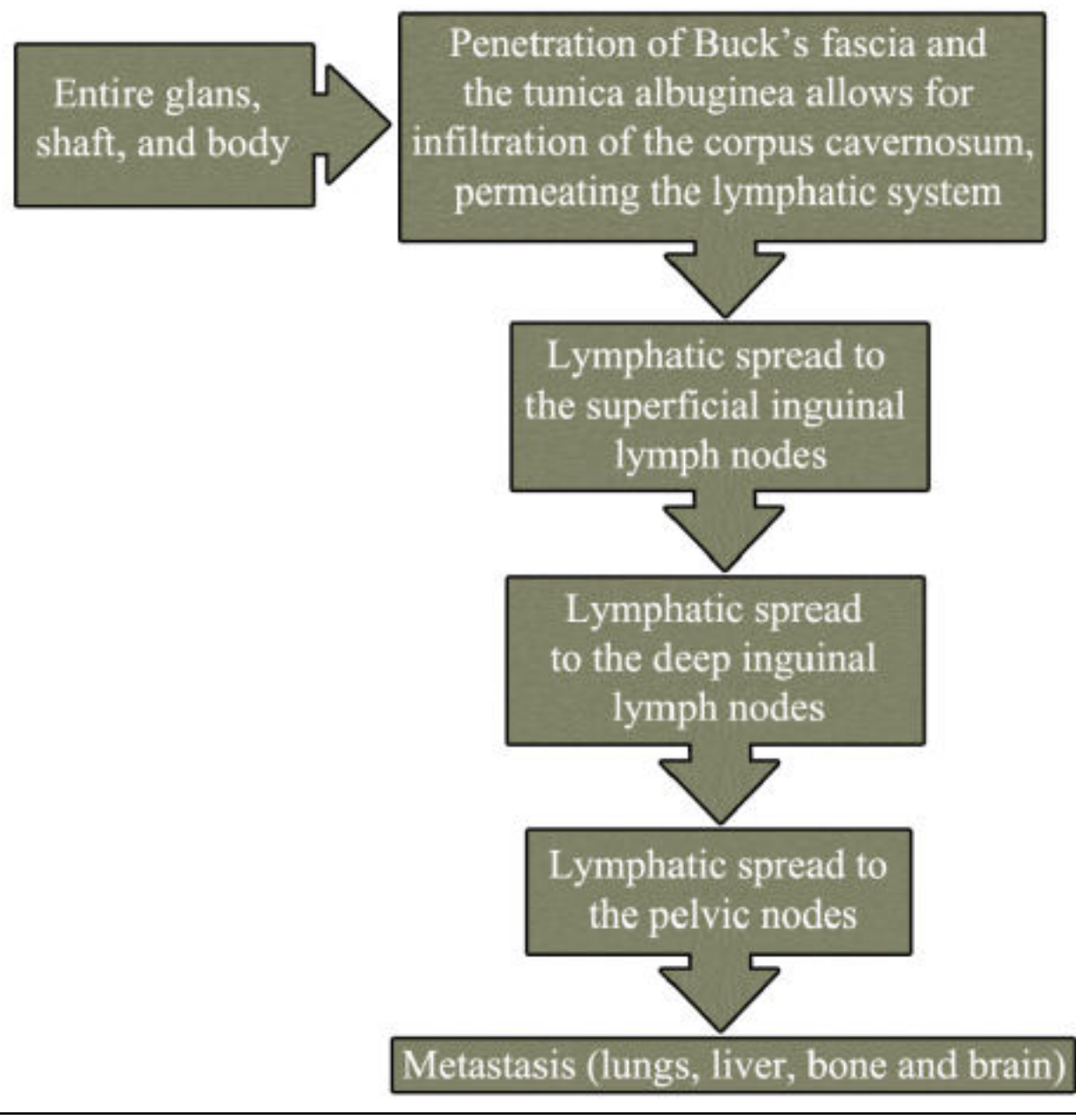
- basaloid, warty, and papillary variants

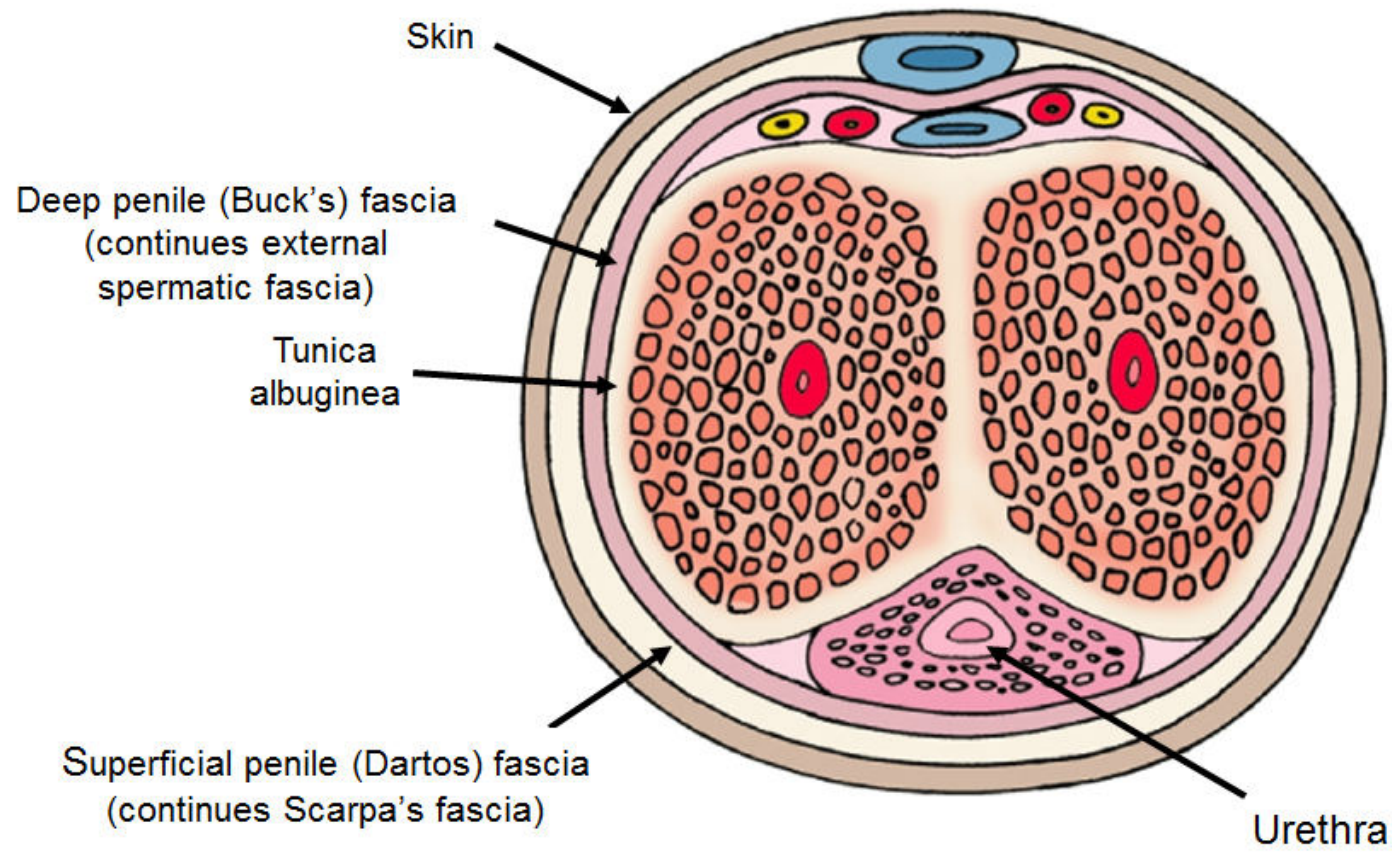


- acanthosis and hyperkeratosis
- into the underlying stroma with a broad based, pushing border
- No koilocytotic changes
- Not HPV related
- D/D Condyloma acuminatum

Tumour spread-

- superficial inguinal lymph node
- deep groin and pelvic nodes





Three most important pathological factors to predict final outcome are

- histological grade
- depth of invasion
- vascular invasion

Diseases of Prostate

- Inflammation
- Benign Enlargement
- Tumors

❑ Inflammation

- ➢Acute bacterial prostatitis
- ➢Chronic bacterial prostatitis
- ➢Chronic abacterial prostatitis
- ➢Granulomatous prostatitis

1. Acute bacterial prostatitis

Etiology-

- bacteria ,E. coli,
- from the urethra
- Diagnosis-culture

MORPHOLOGY-

Gross- enlarged, swollen and tense

Cut section- abscesses and foci of necrosis

M/E-

- Necrosis
- Or as diffuse edema
- Congestion

➢biopsy is **contraindicated**

2-Chronic Prostatitis-

➢Chronic bacterial prostatitis-

- consequence of recurrent UTI
- E coli
- 10-12 wbc/hpf

➢Chronic abacterial prostatitis-

- more common
- No h/o Reccurent UTI
- Wbc in prostatic secretion
- culture of urine and prostatic secretions is always negative
- Chlamydia trachomatis and Ureaplasma urealyticum

MORPHOLOGY-

- ***Grossly,*** enlarged, fibrosed and shrunken
- Histologically-lymphocytes, plasma cells, macrophages and neutrophils within the prostatic tissue

3-Granulomatous Prostatitis-

- variety of chronic prostatitis

➢Etiology-

- Tubercular
- Fungal
- autoimmune origin

➢MORPHOLOGY-

- Grossly-firm to hard
- Histology-macrophages, lymphocytes, plasma cells and some multinucleate giant cells

❑Benign Prostatic Hyperplasia or Nodular Hyperplasia-

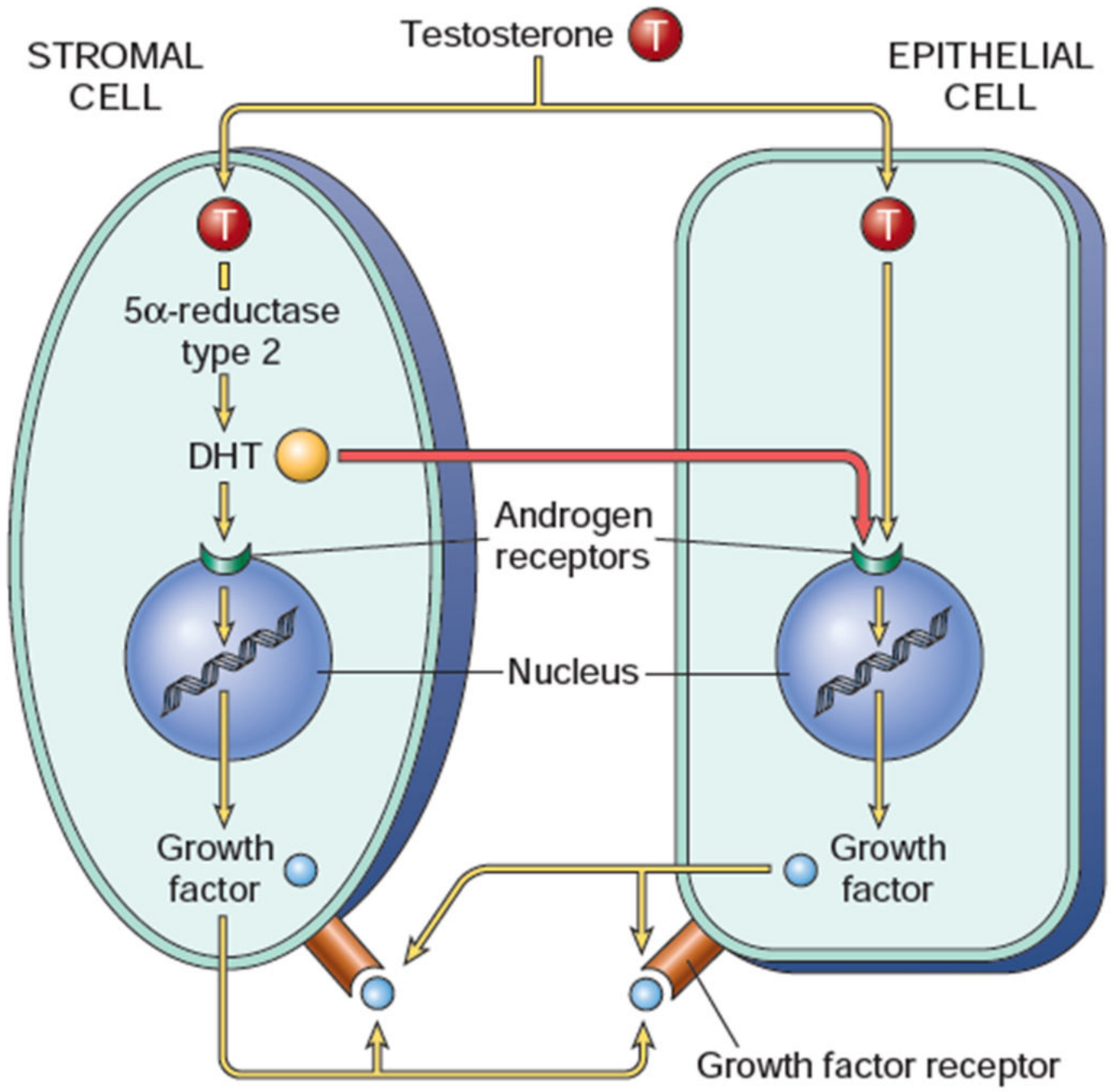
- most common benign prostatic disease
- Incidence increases >50yrs
- 70% >60yrs

ETIOLOGY-

- endocrinologic, racial, inflammation and arteriosclerosis
- advancing age,--androgen--→oestrogen-→periurethral inner prostat→sensitive to estrogen oestrogen--

↓

Nod hyprplasia



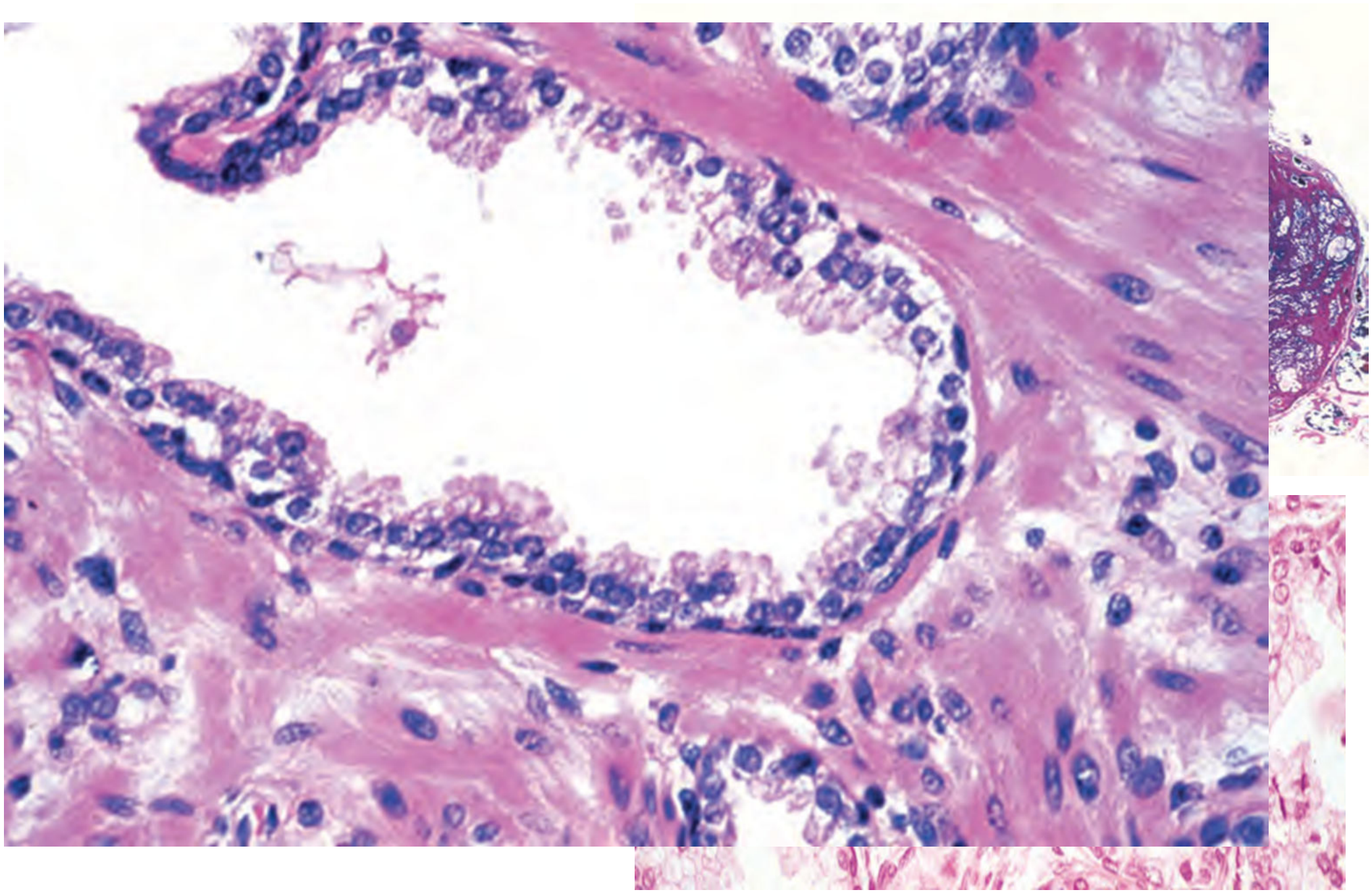
- Stromal cell produce type 2 5α-reductase enzyme
- epithelial cells do not express type 2 5α-reductase
- DHT-induced growth factors--→ increasing the proliferation of stromal cells and decreasing the death of epithelial cells

- MORPHOLOGY-
- Gross- nodular, smooth and firm and weighs 2-4 times its normal weight

Cut surface-

➢pale gray and tough-fibromuscular stroma-EARLY

➢yellow-pink and soft- gland-LATER



Microscopy- hyperplasia of all three tissue elements in varying proportions—

- glandular
- fibrous
- Muscular

called as fibromyoadenomatous nodules- well developed satge

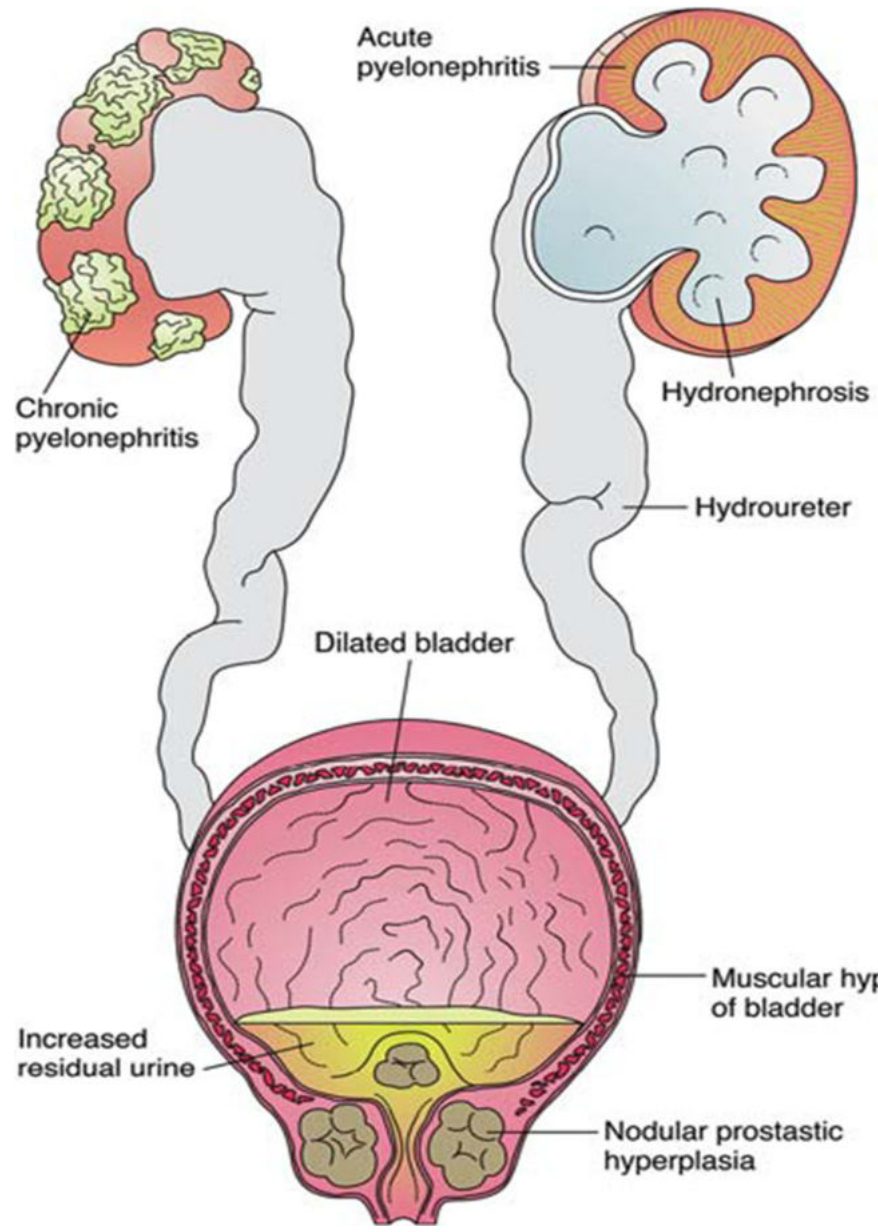
Variable histological features-

- lymphocytic aggregates
- small areas of infarction
- corpora amylacea
- foci of squamous metaplasia

CLINICAL FEATURES-

- frequency, nocturia
- difficulty in micturition
- pain
- haematuria

Complications of NPH



CARCINOMA OF PROSTATE

- men older than age 50 years
- ETIOLOGY-
  - ➢Endocrinologic factors

➢Racial and geographic influences-

- uncommon in Japanese and Chinese, while the prevalence is high in Americans

➢Environmental influences-

- high dietary fat, and exposure to polycyclic aromatic hydrocarbons

➢Nodular hyperplasia

➢Heredity-

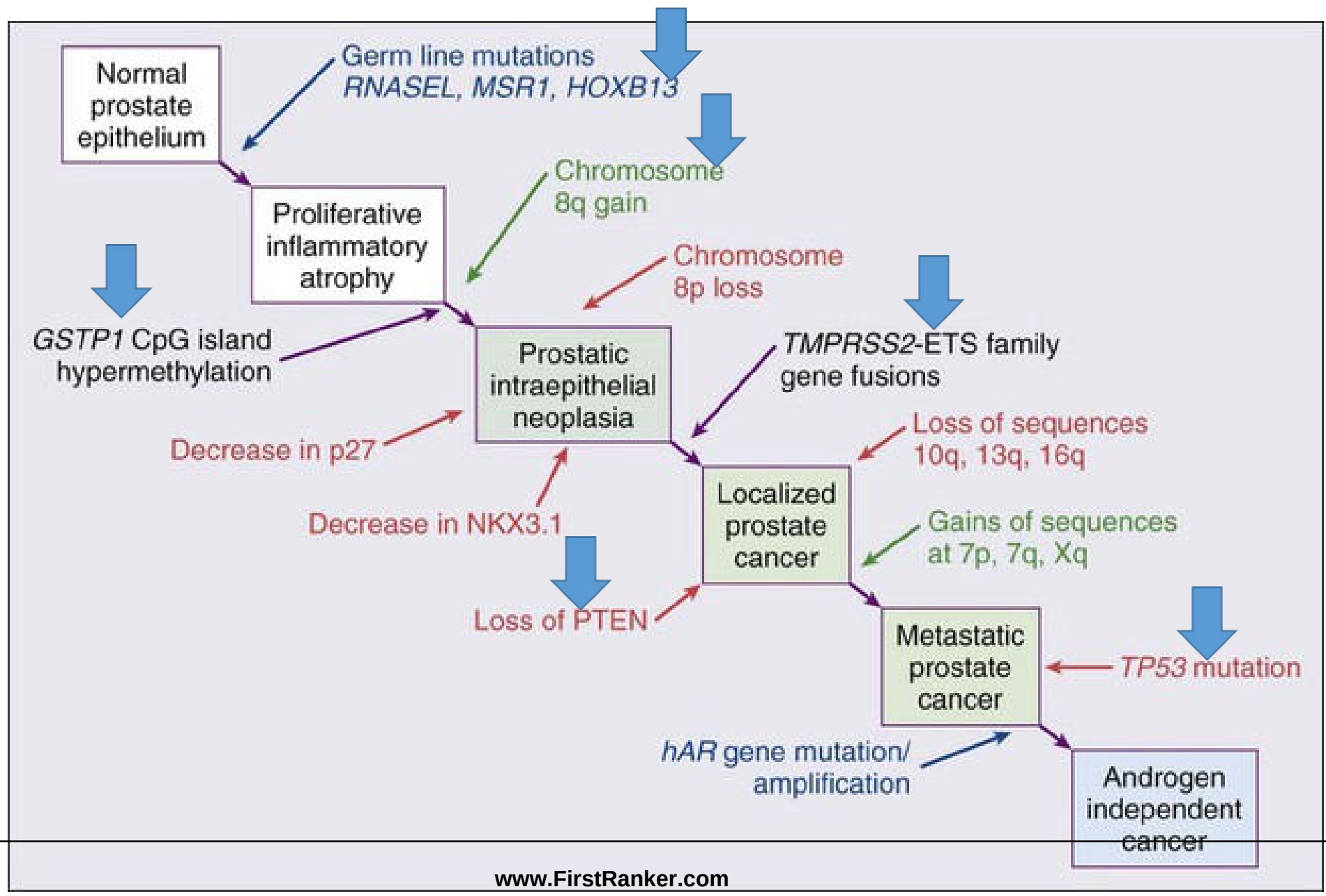
➢2-fold higher frequency in first-degree relatives

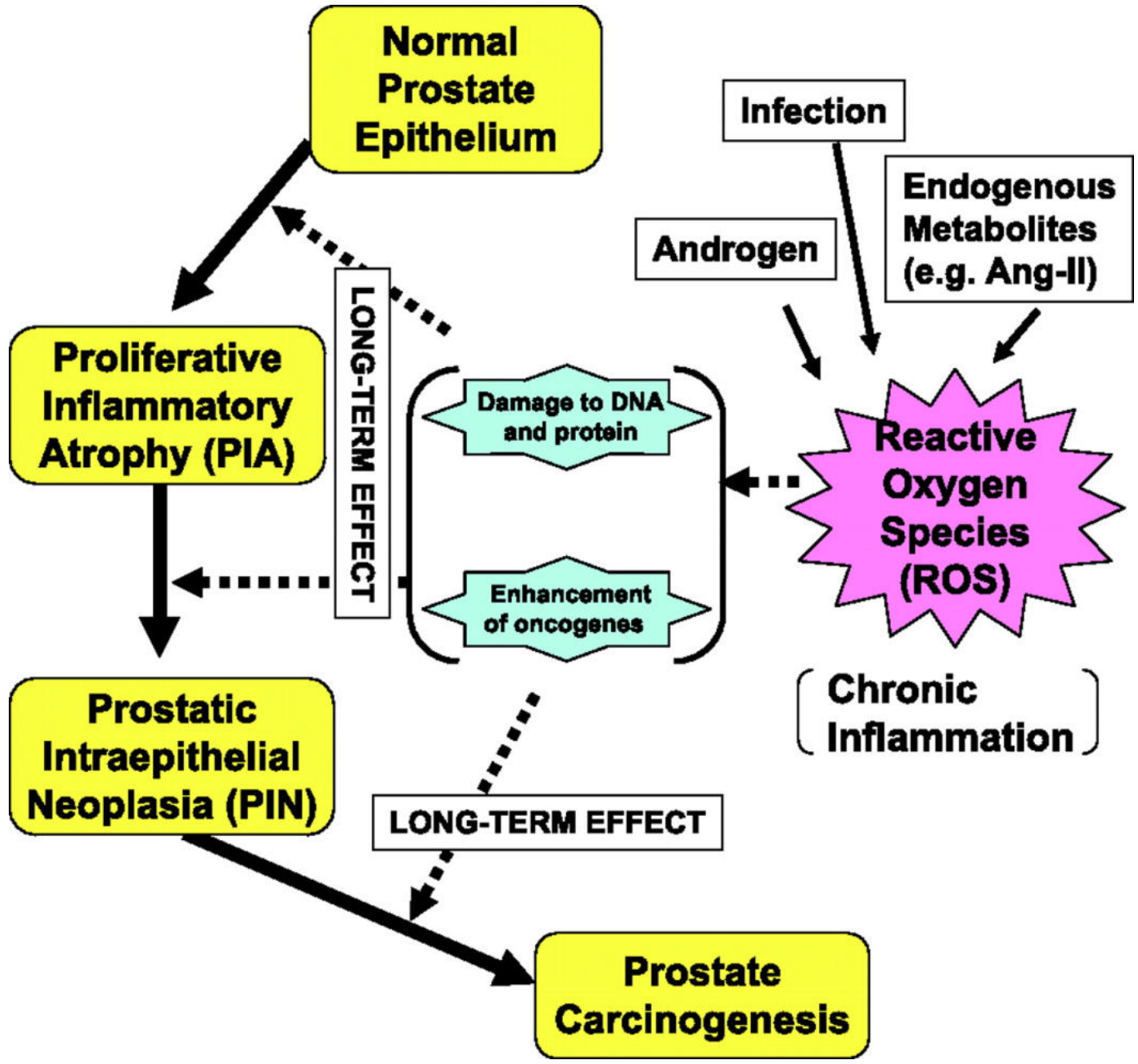
Molecular Pathogeneis

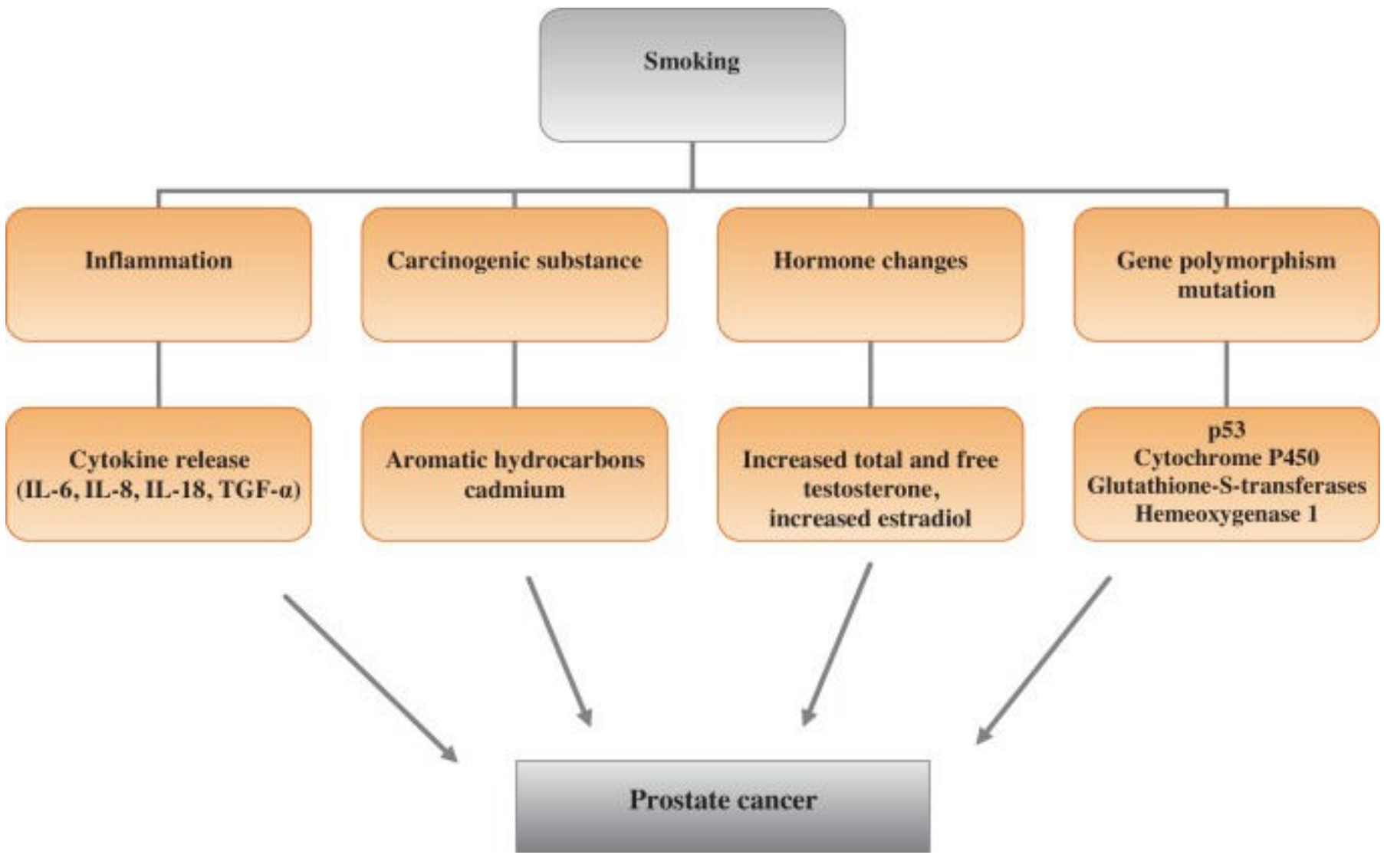
- Most common-**TPRSS2-ETS** fusion genes and mutations or deletions that activate the **PI3K/AKT** signalling pathway

Others

- PTEN
- BRCA2
- HOXB13
- 8q24 amplification
- Loss of P53, in last stage
- Glutathione S-transferase P1 gene,hypermethylation
- Epigenetic modification –RB,CDKN2A







MORPHOLOGIC FEATURES.

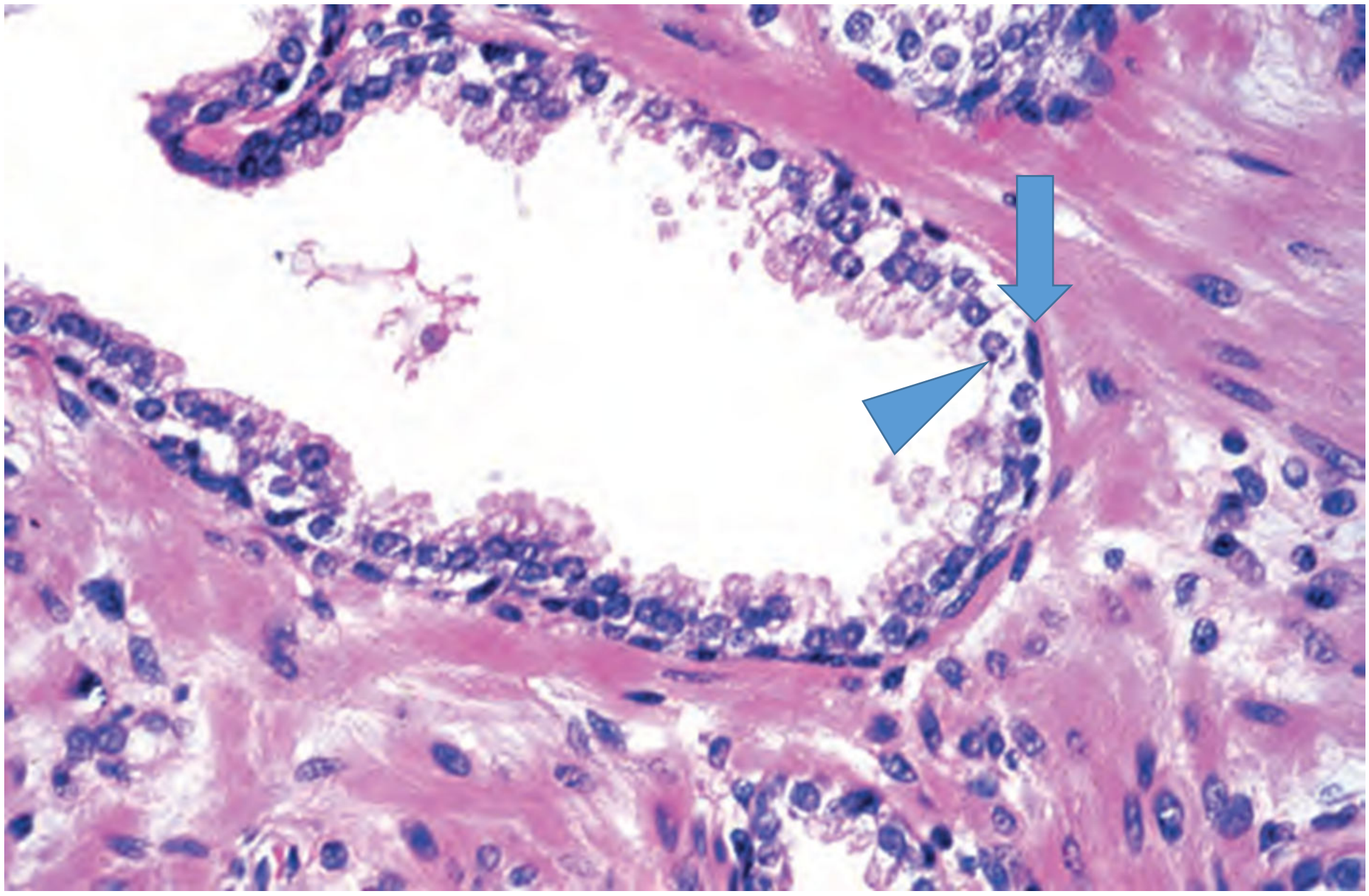
- Grossly, enlarged, normal in size or smaller than normal
- Cut section- gritty and firm,homogeneous and contains irregular yellowish areas

Microscopically-

- Adenocarcinoma ,96%
- transitional cell carcinoma
- squamous cell carcinoma
- undifferentiated carcinoma

Histologic characteristics-

- Architectural disturbance-closely packed in back-to-back arrangement without intervening stroma
- Gland pattern
- Stroma- scant , tumour cells may penetrate and replace the fibromuscular stroma



High-grade prostatic intraepithelial neoplasia (PIN)

- **Gleason's microscopic grading system-** based on two features:

i) Degree of glandular differentiation

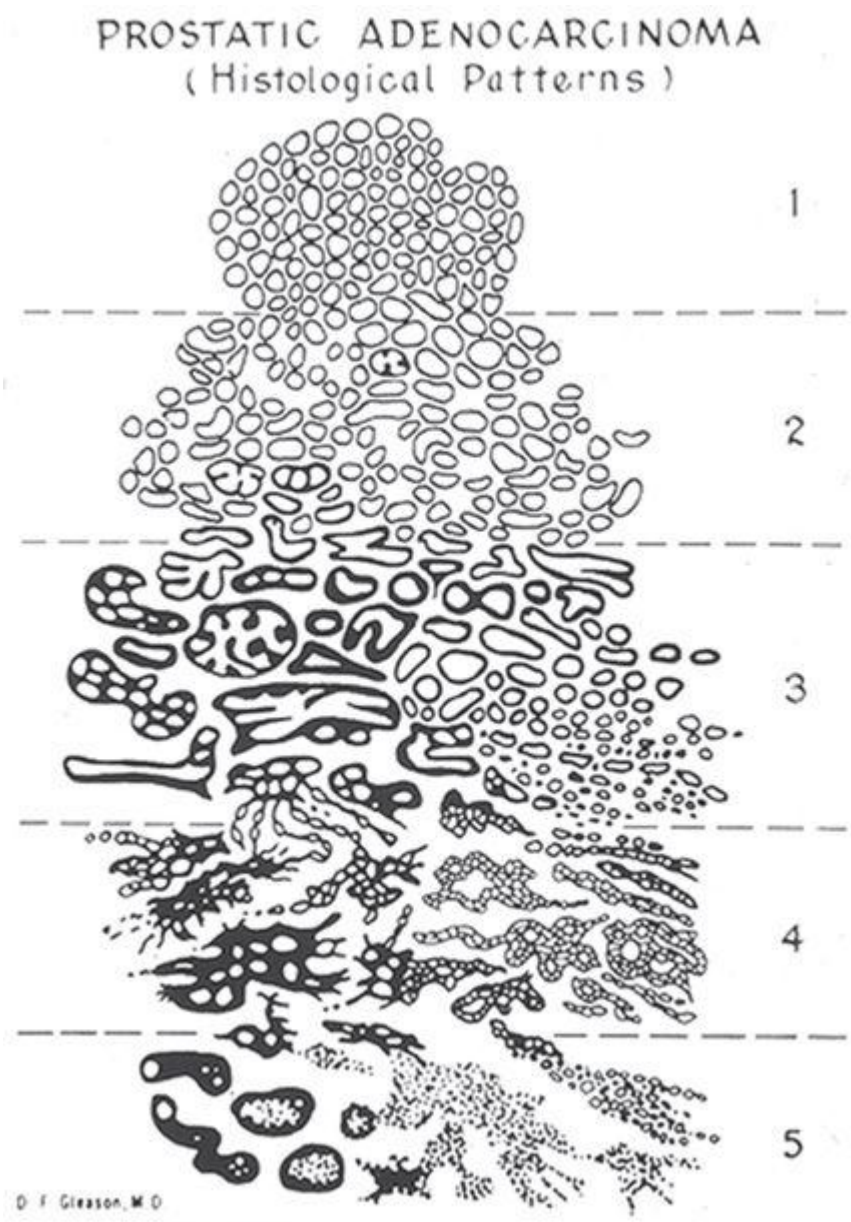
ii) Growth pattern of the tumour in relation to the stroma

These features are assessed by low-power examination

- Only one pattern- double the number
- Two pattern- predominant p+ secondary p
- Three pattern- pred p+ higher pattern

  3 (70%)+4(20%)+5(10%)→3+5=8

- 2 (1 + 1)- well-differentiated
- 10 (5 + 5)-and the least-differentiated tumors



1 closely packed uniform glands

2 loosely packed slightly variable glands

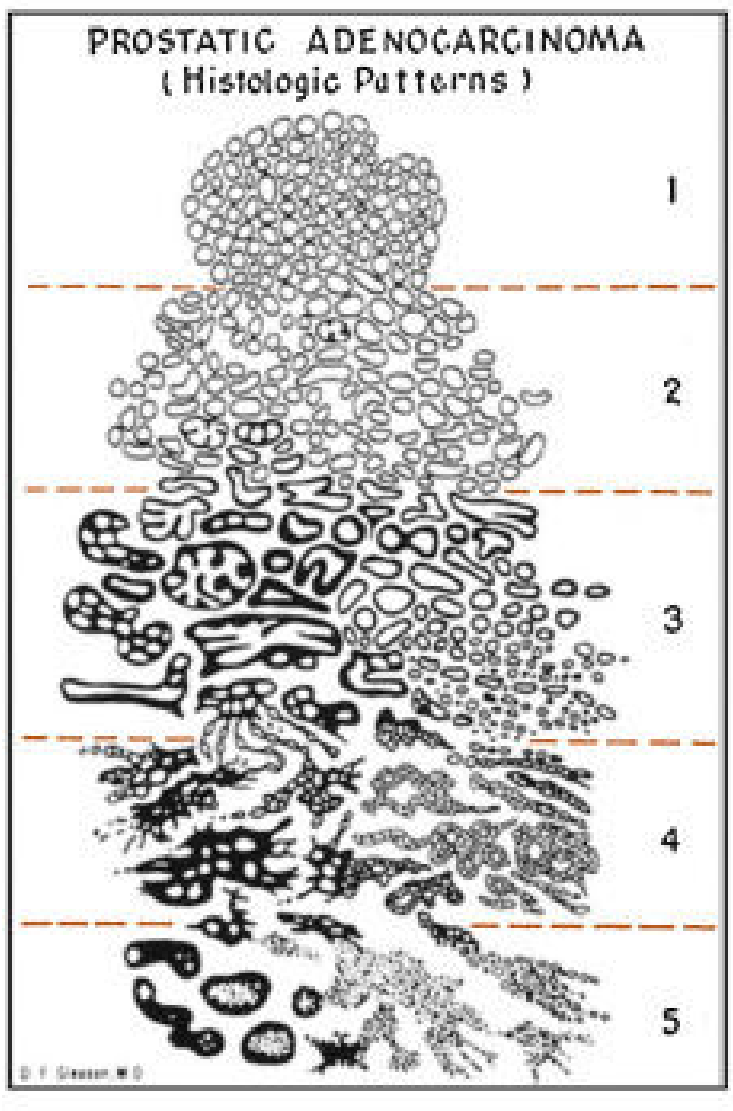
3 Single glands of variable size and density, with an infiltrative pattern

4 Ragged infiltration with poorly formed glands or sheets and cords of fused glands

5 Single cells,Solid sheet,comedonecrosis

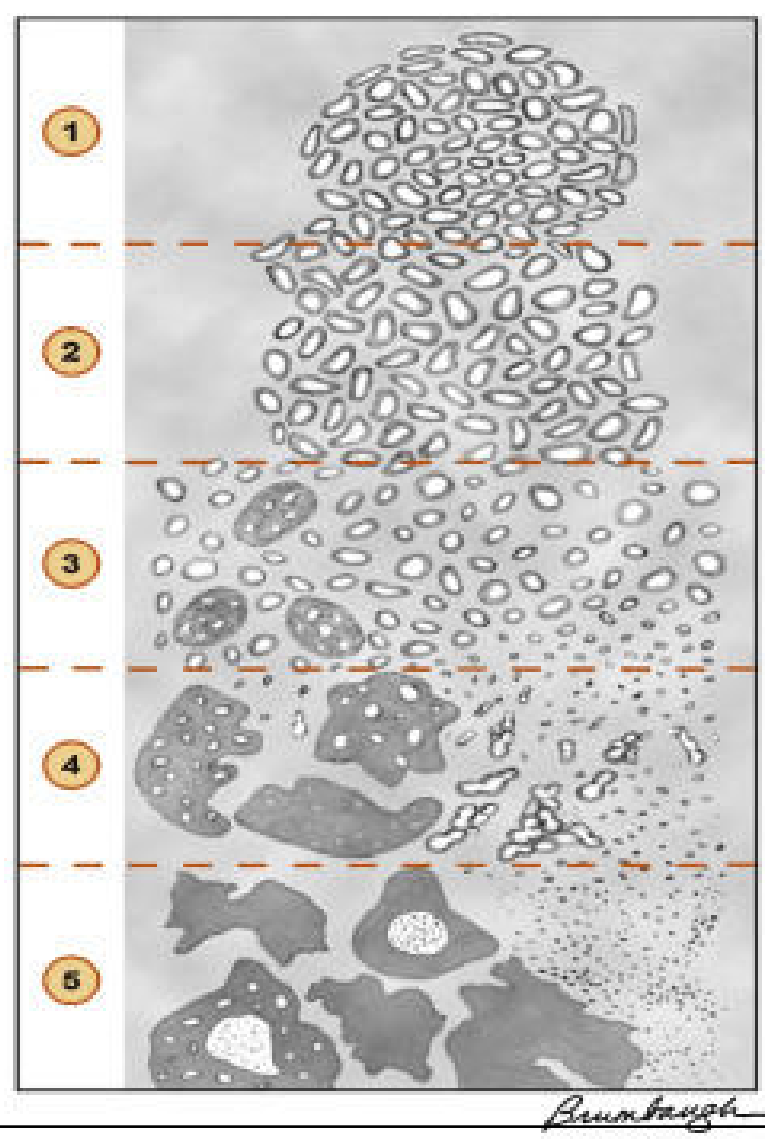
FIGURE 9.1 Original Gleason grading diagram.

Original Gleason



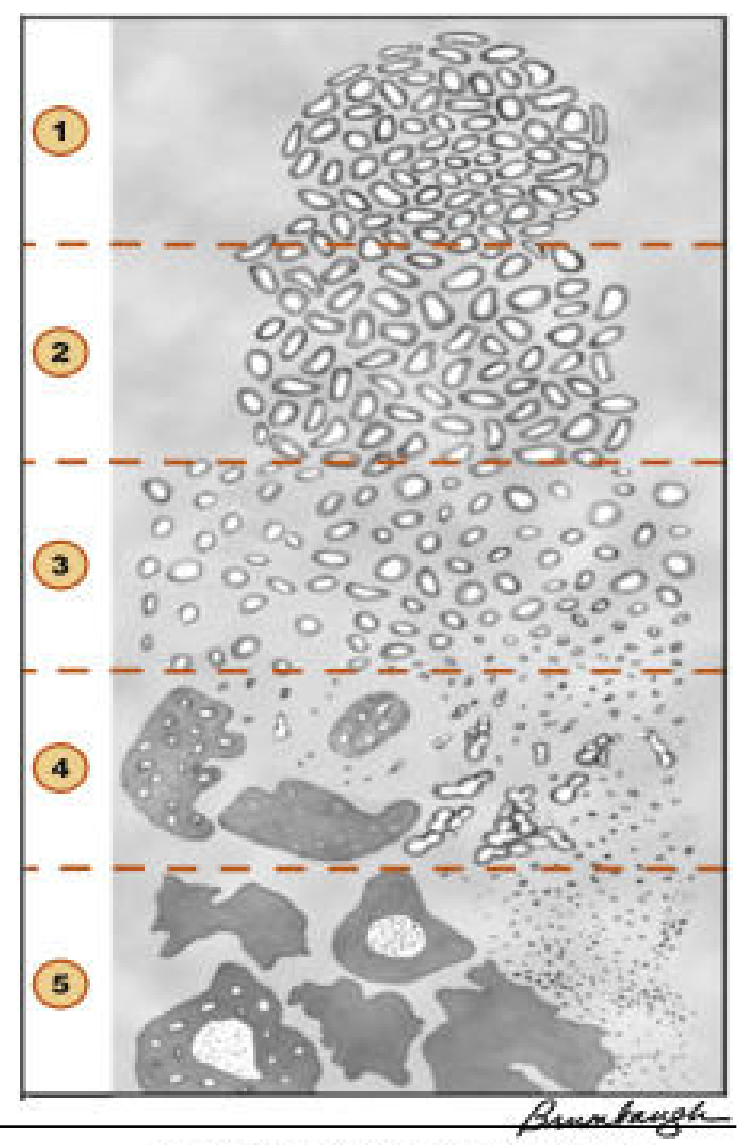
Hum Pathol 23;273-79, 1992

ISUP 2005 Gleason



Am J Surg Pathol 29:1228-42, 2005

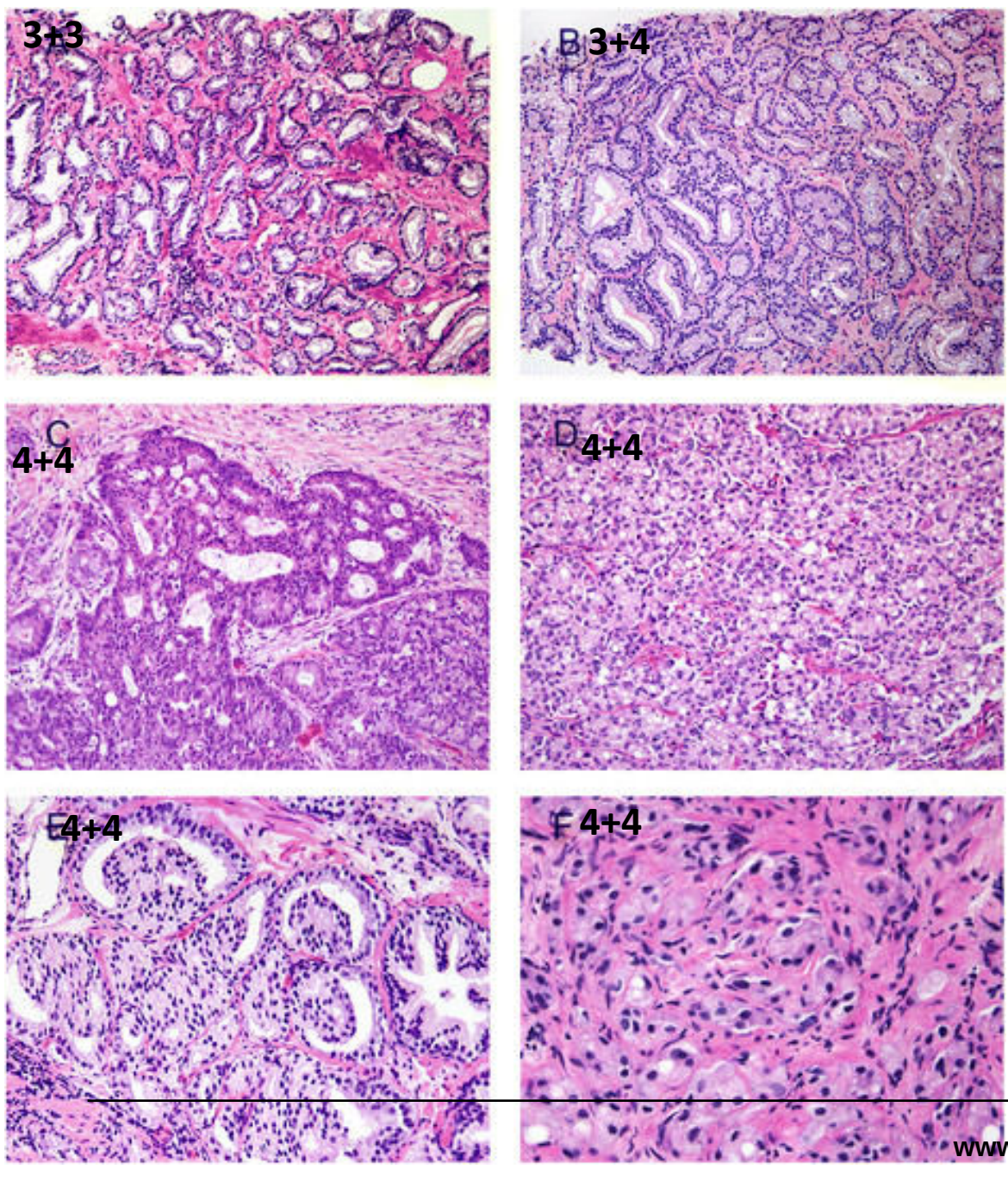
Gleason with proposed refinements and modifications to ISUP 2005



J Urol 183;433-40, 2010

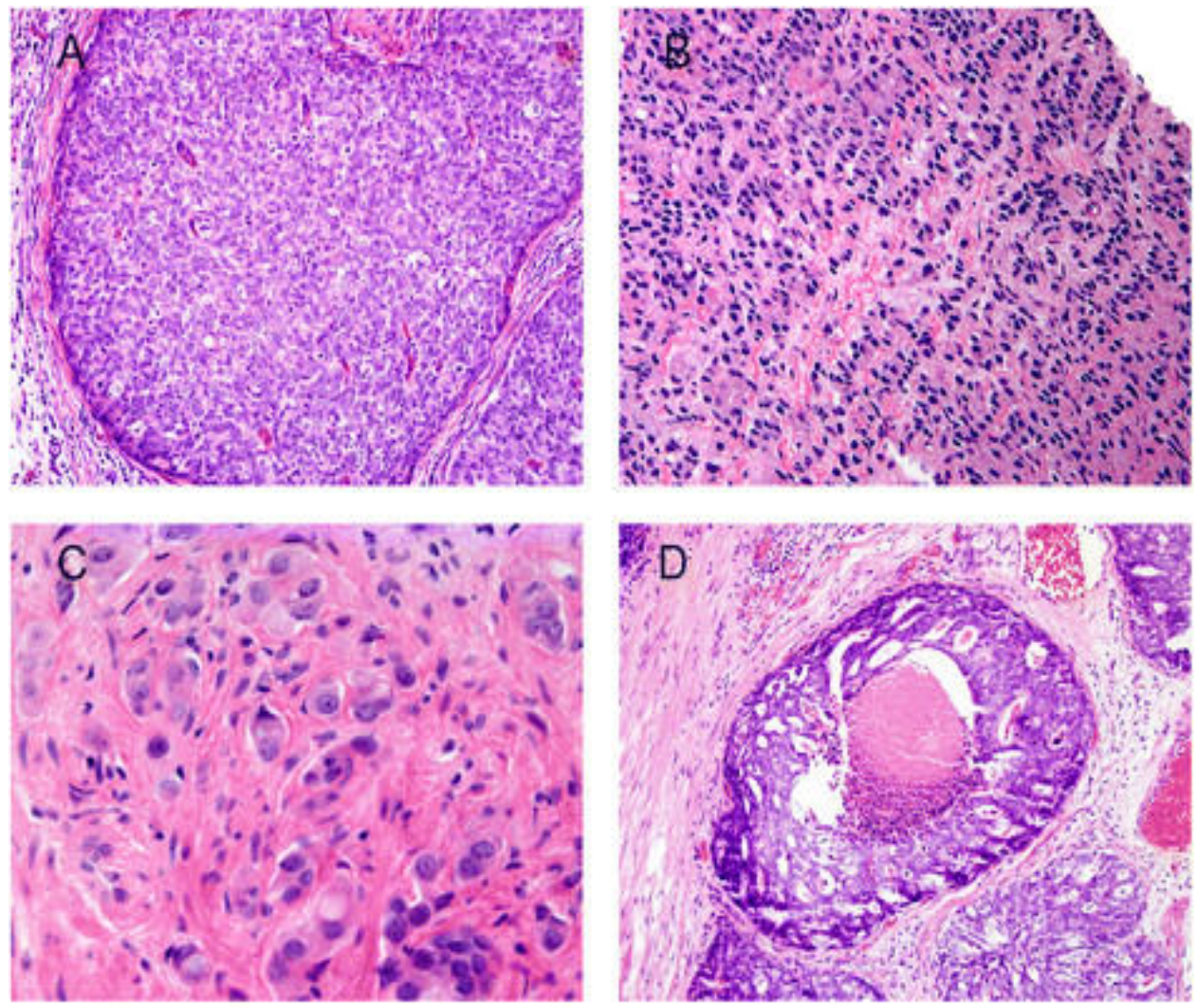
Table S1 The new WHO grade group system of prostate cancer

Grade group	Gleason score and pattern
1	Grade 6 (3+3)
2	Grade 7 (3+4)
3	Grade 7 (4+3)
4	Grade 8 (4+4, 3+5, or 5+3)
5	Grade 9 or 10 (4+5, 5+4, or 5+5)



STAGE	DESCRIPTION
1	Single, separate, uniform glands in closely packed masses with a definite, usually rounded, edge limiting the area of tumor
2	Single, separate, slightly less uniform glands, loosely packed (separated by small amounts of stroma), with less sharp edge
3a	Single, separate, much more variable glands; may be closely packed but usually irregularly separated; ragged, poorly defined edge
3b	Like 3a, but very small glands or tiny cell clusters
3c	Sharply and smoothly circumscribed rounded masses of papillary or loose cribriform tumor ('papillary intraductal tumor')
4a	Raggedly outlined, raggedly infiltrating, fused glandular tumor
4b	Like 4a, with large pale cells ('hypernephroid')
5a	Sharply circumscribed, rounded masses of almost solid cribriform tumor, usually with central necrosis ('comedocarcinoma')
5b	Ragged masses of anaplastic carcinoma with only enough gland formation or vacuoles to identify it as adenocarcinoma

GS-5+5



Biomarkers of prostate cancer

1-PSA

- PSA density
- PSA velocity
- age-specific reference ranges
- ratio of free and bound PSA (free psa low in cancer)

2-PCA3

3-combination of urinary PCA3 with screening of urine for TMPRSS2-ERG fusion DNA>psa alone

Testis

Must know

1-Classification of testicular tumor

2-Tumor markers in diagnosis

3-Morphology of

a) Seminoma
b) Embryonal carcinoma
c) Yolk sac tumor

4-Cryptorchidism

Testicular lesion

- Congenital Anomalies
- Regressive Changes
- Inflammation (*Nonspecific , Specific Inflammations, Granulomatous (Autoimmune) Orchitis)*
- Vascular Disorders(torsion)
- Spermatic Cord and Paratesticular Tumors
- Testicular Tumors

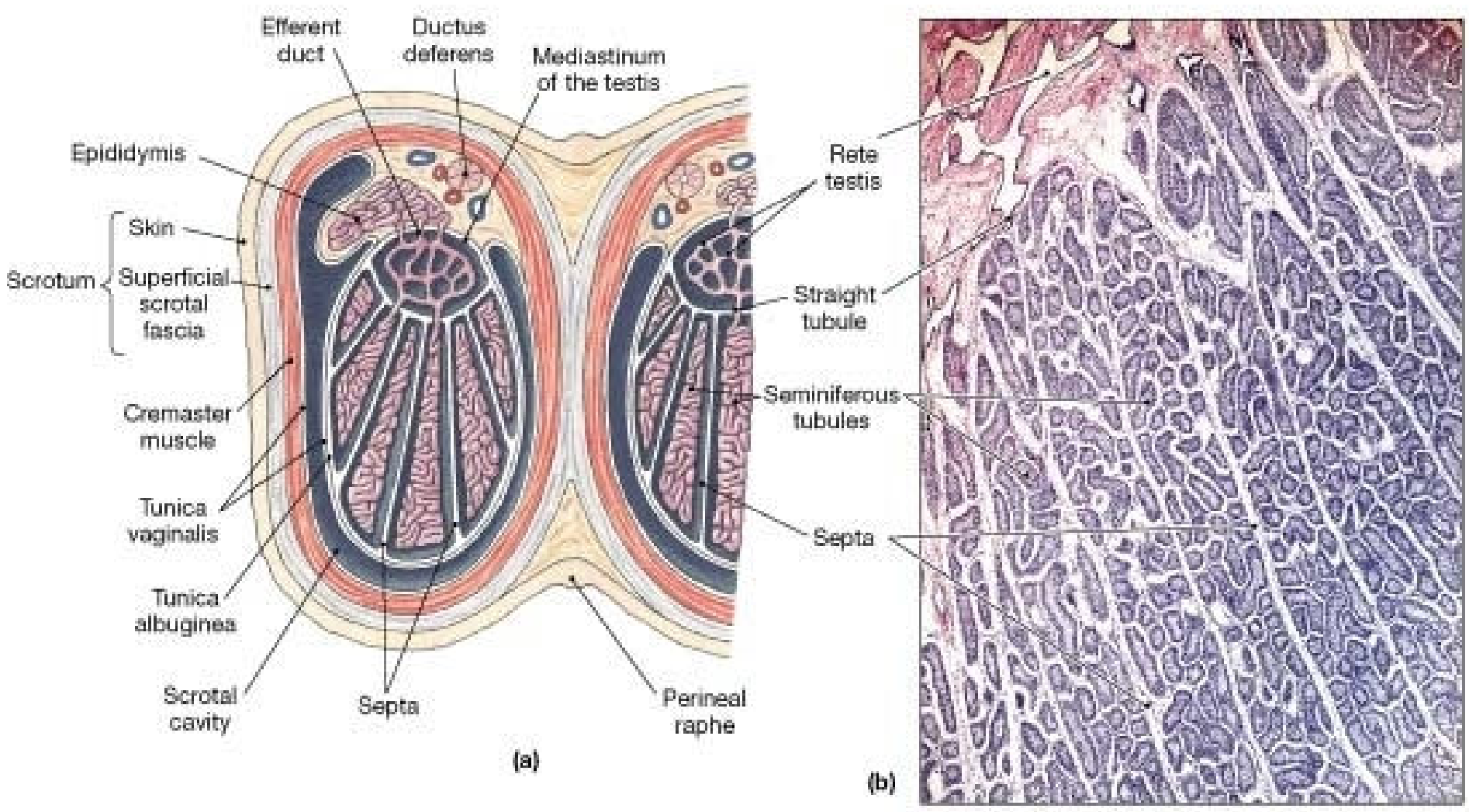


FIGURE 28-4 Structure of the Testes. **(a)** Diagrammatic sketch (frontal section) and anatomical relationships of the testes. **(b)** Micrograph of a section through a testis. (LM × 26)

INFLAMMATIONS-

- Inflammation of the testis is termed as orchitis and of epididymis is called as epididymitis; the latter being more common

1-Non-specific Epididymitis and Orchitis-

- may be acute or chronic
- common routes of spread are via the **vas deferens, or lymphatic and haematogenous routes**
- caused by urethritis, cystitis, prostatitis and seminal vesiculitis
- common infecting organisms in *Neisseria gonorrhoeae* and *Chlamydia trachomatis*

Grossly,

- **acute stage-** firm, tense, swollen and congested

  may be multiple abscesses, especially in gonorrhoeal infection

- **chronic stage-** variable degree of atrophy and fibrosis

Histologically,

- ***acute-*** congestion, oedema and diffuse infiltration by neutrophils, or formation of neutrophilic abscesses

- **Chronic-** focal or diffuse chronic inflammation, disappearance of seminiferous tubules, fibrous scarring and destruction of interstitial Leydig cells

2-Granulomatous (Autoimmune) Orchitis -

Non-tuberculous granulomatous orchitis-

- unilateral, painless testicular enlargement
- may resemble a **testicular tumour** clinically
- autoimmune basis is suspected

Gross- enlarged

- Cut section of the testicle is greyish-white to tan-brown
- ***Histologically,*** granulomatous reaction(non caseating) is present diffusely throughout the testis and is confined to the seminiferous tubules
- Peritubular fibrosis
- interstitial lymphocytes and plasma cells

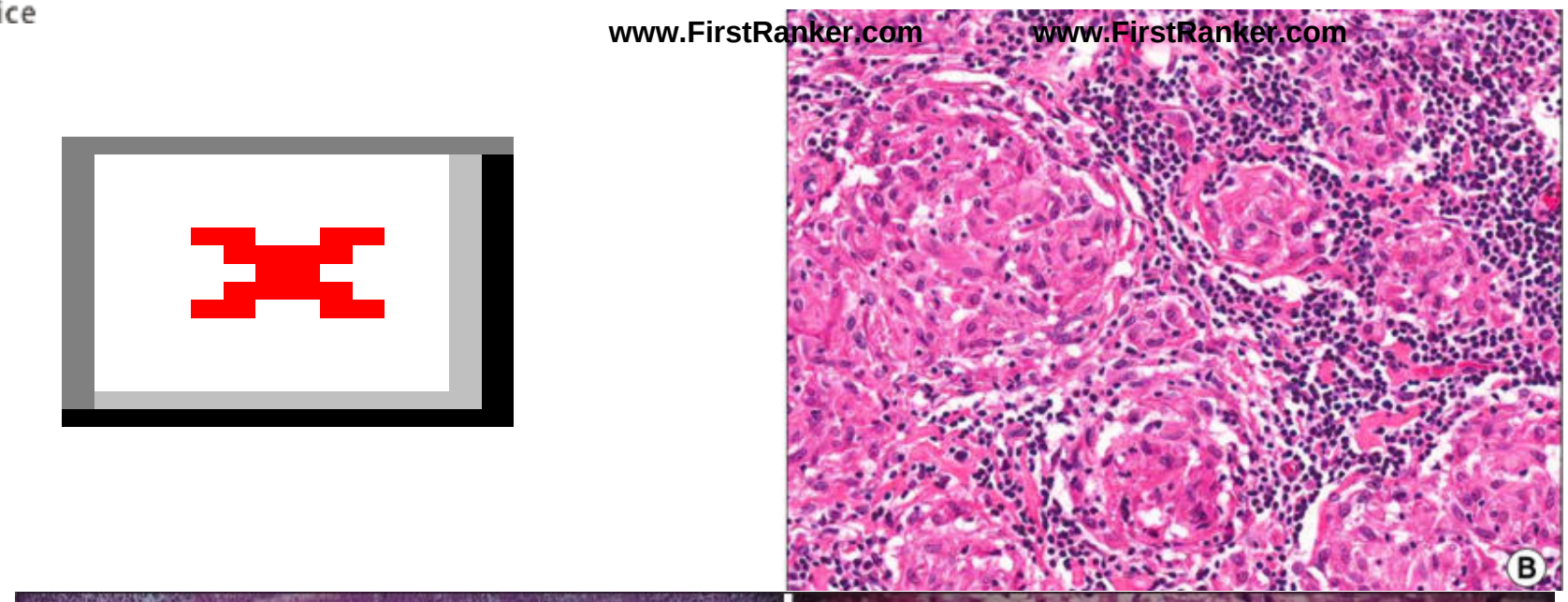
3-Tuberculous Epididymo-orchitis-

- invariably begins in the epididymis and spreads to the testis

- May spread via -tuberculous seminal vesiculitis, prostatitis and renal tuberculosis
- haematogenous spread- from tuberculosis of the lungs

Grossly, discrete, yellowish, caseous necrotic areas

- ***Microscopically,*** numerous tubercles which may coalesce to form large caseous mass
- Characteristics of typical tubercles such as epithelioid cells, peripheral mantle of lymphocytes, occasional multinucleate giant cells and central areas of **caseation necrosis** are seen
- AFB positive



4-Spermatic Granuloma(epididymitis nodosa)

- inflammatory lesions due to invasion of **spermatozoa into the stroma**

MORPHOLOGIC FEATURES-

Grossly,

- a small nodule, 3 mm to 3 cm in diameter in head of epididymis

- firm, white to yellowish-brown

- ***Histologically,***
- **Characteristically, the centre of spermatic granuloma contains spermatozoa and necrotic debris+epethelioid cell granuloma**

Vascular disorder

Torsion of Testis

- usually followed by sudden muscular effort or physical trauma
- Twisting of the spermatic cord
- sudden cessation of venous drainage and arterial supply
- Trauma may occure in either in a fully-descended testis or in an **undescended testis**

1-Neonatal torsion-

- occurs either in utero or shortly after birth

- It **lacks any associated anatomic defect in testis**

2-“Adult” torsion-

- is typically seen in **adolescence** and presents with the sudden onset of testicular pain

- Viable- manually untwisted within approximately 6 hours of the onset of torsion

MORPHOLOGIC FEATURES-

duration and severity of vascular occlusion

- may be coagulative necrosis of the testis and epididymis
- may be haemorrhagic infarction

Spermatic Cord and Paratesticular Tumors

1-Lipomas

- common lesions involving the **proximal spermatic cord**, identified at the time of inguinal hernia repair
- represent retroperitoneal adipose tissue that has been pulled into the inguinal canal along with the hernia sac, rather than a true neoplasm

2-Adenomatoid tumor-

- **most common** benign paratesticular tumor
- upper pole of the epididymis

- grossly , well circumscribed small nodules
- Microscopically- Proliferation of glandular structures, irregularly lined by cuboidal to flattened epithelial cell

- Treatmet- local excision

Malignant tumor

- rhabdomyosarcomas -children
- liposarcomas- adults

CLASSIFICATION OF TESTICULAR TUMOR

- most useful **classification of tumors** is **histogenetic**
- Named according to from which tissue they arise and of which they consist

Table 21-5 Pathologic Classification of Common Testicular Tumors

Germ Cell Tumors
Seminomatous tumors
Seminoma
Spermatocytic seminoma
Nonseminomatous tumors
Embryonal carcinoma
Yolk sac (endodermal sinus) tumor
Choriocarcinoma
Teratoma
Sex Cord-Stromal Tumors
Leydig cell tumor
Sertoli cell tumor

WHO histological classification of testis tumours

- **Germ cell tumours**
- Tumours of one histological type (pure forms)
- Tumours of more than one histological type (mixed forms)
- **Sex cord/gonadal stromal tumours Pure forms**
- **Miscellaneous tumours of the testis**
- **Haematopoietic tumours**
- Tumours of collecting ducts and rete
- Tumours of paratesticular structures
- Mesenchymal tumours of the spermatic cord and testicular adnexae
- Secondary tumours of the testis

TNM classification of germ cell tumours of the testis

Testicular cancer is staged using the TNM system created by the American Joint Committee on Cancer (AJCC)

It's based on 4 key pieces of information:

- **T** refers to how much the main (primary) **tumor** has spread to tissues next to the testicle
- **N** describes how much the cancer has spread to regional (nearby) **lymph nodes**
- **M** indicates whether the cancer has **metastasized** (spread to distant lymph nodes or other organs of the body)
- **S** indicates the serum (blood) levels of tumor markers that are made by some testicular cancers

- **Letters or numbers appear after** T, N, M, and S to provide more details about each piece of information.
- The numbers 0 through 4 indicate **increasing severity**
- The letters “IS” after the T stand **for in situ,** which means the tumor is contained in **one place** and has not yet penetrated to a deeper layer of tissue.
- The letter X after T, N, M, or S means “**cannot be assessed**” because the information is not known

TNM classification of germ cell tumours of the testis

pTNM pathological classification

- pTx –Primary tumour **cannot be assessed**
- pT0 **No evidence** of primary tumour pTis Intratubular germ cell neoplasia (**carcinoma in situ)**
- pT1 Tumour **limited to testis and epididymis without** vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis
- pT2 Tumour pT1+v/L + **involvement of tunica vaginalis**
- pT3 Tumour invades **spermatic cord** with or without vascular/lymphatic invasion
- pT4 Tumour invades **scrotum** with or without vascular/lymphatic invasion

pN – Regional lymph nodes

- pNX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- pN1 <**2 cm or** </=**5 or fewer positive nodes**
- pN2 **2 to 5 cm in greatest dimension**; or **more than 5 nodes positive**, none more than 5 cm; or evidence of extranodal extension of tumour
- pN3 Metastasis with a lymph node mass **more than 5 cm** in greatest dimension

S – Serum tumour markers

- SX Serum marker studies not available or not performed
- S0 Serum marker study levels within normal limits
- LDH, hCG (mIU/ml) ,AFP (ng/ml)

Cryptorchidism

- Cryptorchidism is a complete or partial failure of the intra-abdominal testes to descend into the scrotal sac

associated with

- testicular dysfunction
- an increased risk of testicular cancer

- **In 70% of cases, the undescended testis lies in the inguinal ring**
- in 25% in the abdomen

ETIOLOGY. exact etiology is **not known** in majority of cases

1. Mechanical factors-

- short spermatic cord
- narrow inguinal canal
- adhesions to the peritoneum
- problems with development of the gubernaculum
- a patent processus vaginalis, or impaired intra-abdominal pressure have also been hypothesized to contribute to cryptorchidism

2. Genetic factors-

- up to 23% of cases
- Mutations in **insulin-like factor 3** and its receptor, **LGR8**, have been demonstrated in a small number of cases
- trisomy 13

3. **Hormonal factor-** rarely associated

- deficient androgenic secretions
- mullerian inhibiting substance
- insulin-like 3 hormone

4. **Neuromuscular**- abnormalities of the **genitofemoral nerve's calcitonin gene-related peptide**

Miscellaneous-

- Maternal alcohol consumption
- analgesic consumption
- smoking
- Gestational diabetes

MORPHOLOGIC FEATURES. Cryptorchidism is unilateral in 80% cases

Grossly, small in size, firm and fibrotic

Histology-

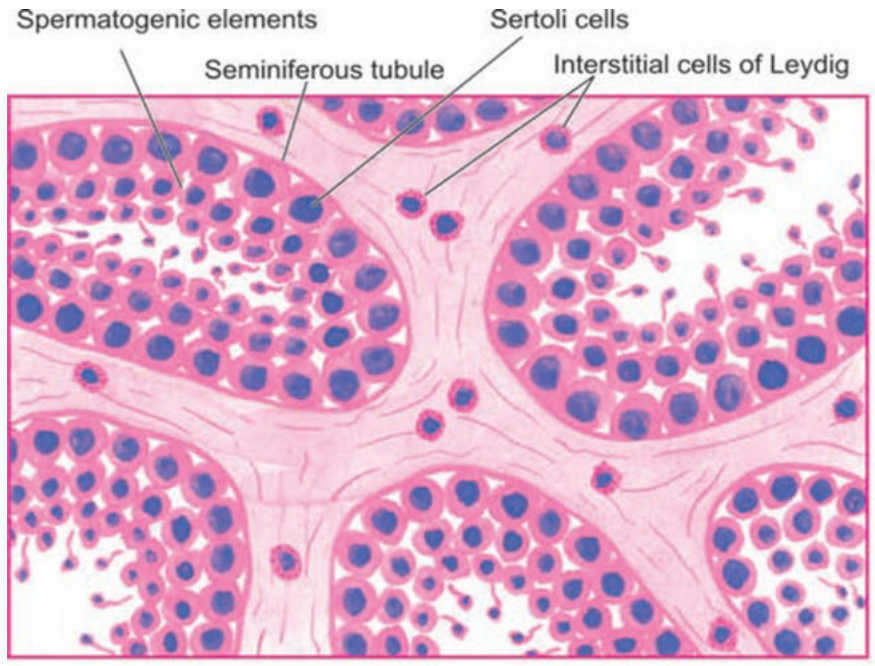
1-Seminiferous tubules

- tubular basement membrane is **thickened**
- **hyalinised tubules** with **a few Sertoli** cells
- foci of **spermatogenesis** are discernible in 10% of cases

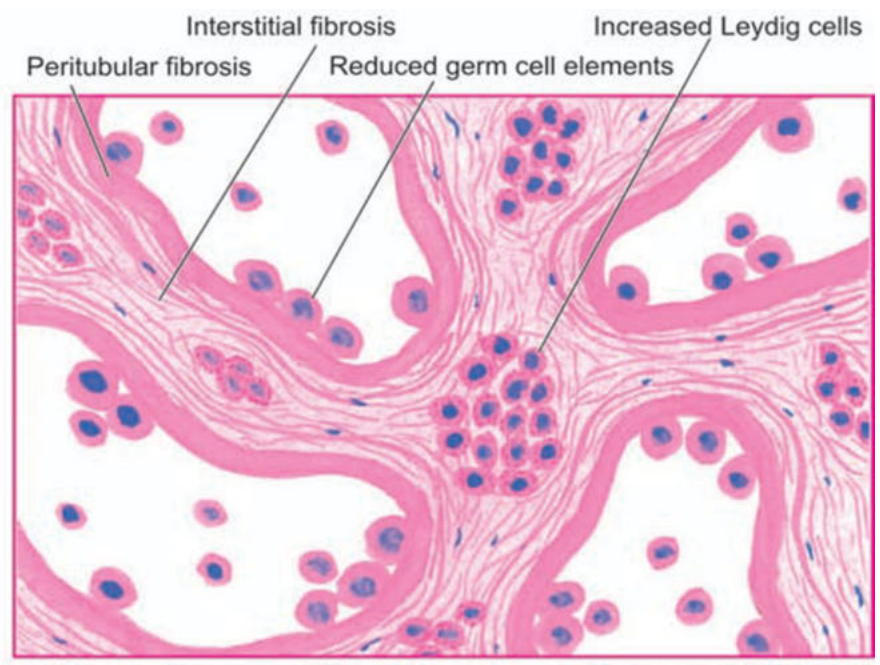
2. *Interstitial stroma:* usually increase in the

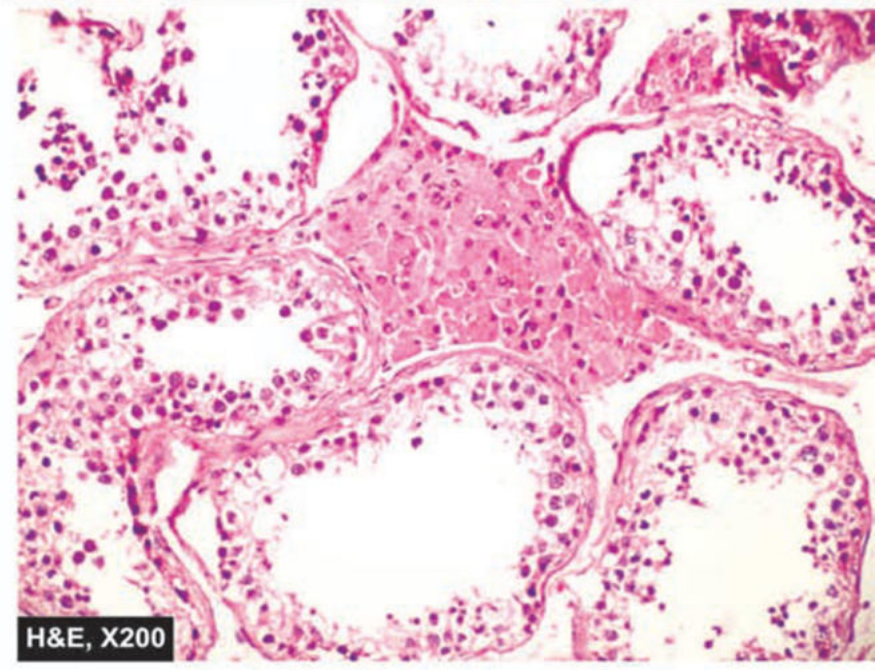
➢**interstitial fibrovascular stroma**

➢ **Leydig cells**,

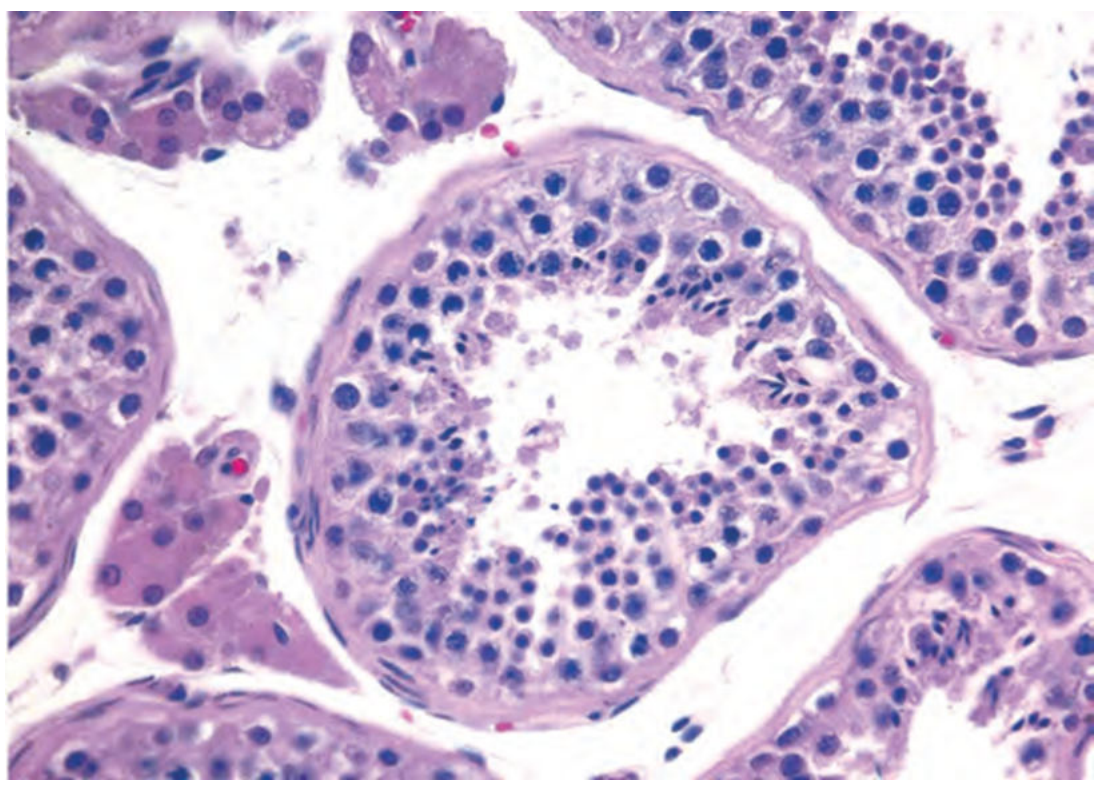


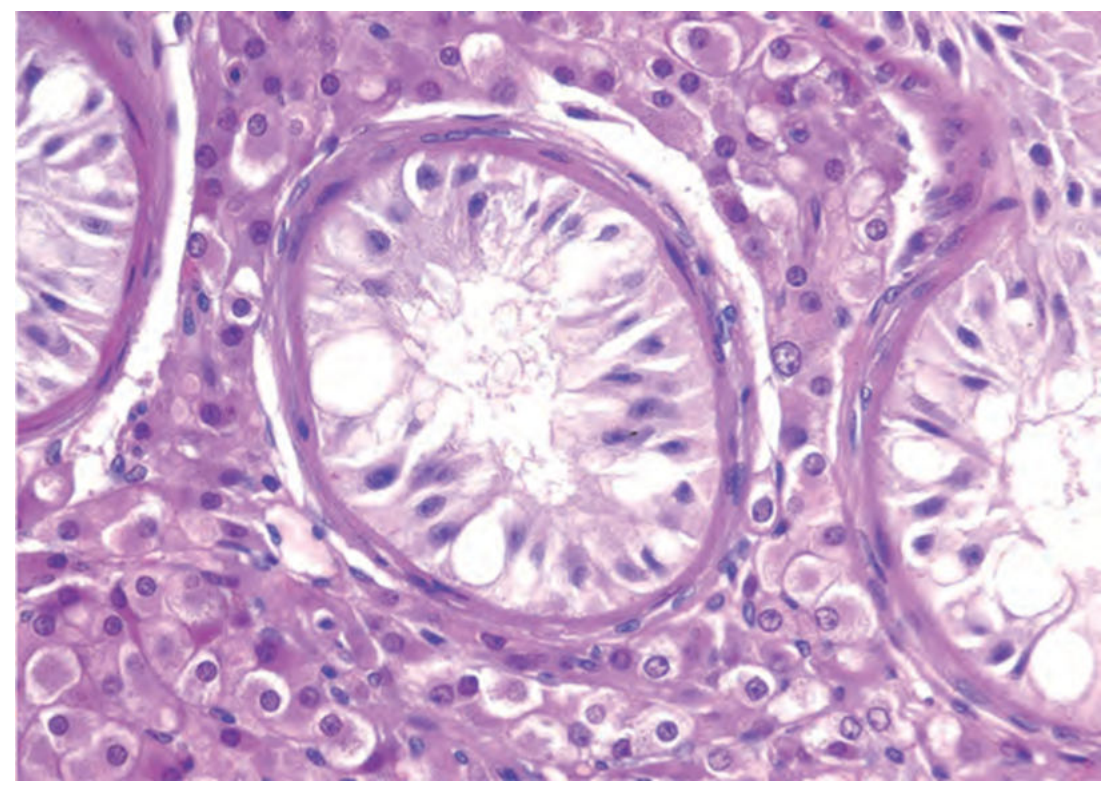
A, NORMAL TESTIS





B, CRYPTORCHID TESTIS





- **CLINICAL FEATURES.** asymptomatic and is discovered only on physical examination

1. Sterility-infertility. Bilateral cryptorchidism is associated with sterility while unilateral disease may result in infertility

2. Inguinal hernia. A concomitant inguinal hernia is frequently present along with cryptorchidism

3-Malignancy. Cryptorchid testis is at 30-50 times increased risk of developing testicular malignancy

- most commonly seminoma and embryonal carcinoma, than a normally descended testis
- risk of malignancy is greater in intraabdominal testis than in testis in the inguinal canal

- current recommendations are for correction at **6 to 12 months** of age
- carcinoma arises from foci of **intratubular germ cell neoplasia** within the atrophic tubules
- Orchiopexy reduces the risk of sterility and cancer

Tumour marker

Tumour markers- Germ cell tumours of the testis secrete polypeptide hormones and certain enzymes which can be detected in the blood

There are two principal serum tumour markers

- alpha fetoprotein (**AFP**) and
- beta subunit of human chorionic gonadotropin (**shCG**)

- In addition, carcinoembryonic antigen (**CEA**), human placental lactogen **(HPL),** placental alkaline phosphatase, testosterone, oestrogen and luteinising hormone may also be elevated

AFP-

- synthesized by **fetal yolk sac** and also the **liver and intestine**
- elevated in **50-70% of testicular germ cell tumours**
- Markedly elevated in yolk sac tumor
- **a serum half life of 4.5 days**
- However, elevated serum AFP levels are **also found in liver cell carcinoma**

hCG-

- secreted by **placental trophoblastic cells**
- elevated in **non-seminomatous germ cell tumours of the testis** (e.g. in **choriocarcinoma**, yolk sac tumour and embryonal carcinoma)
- elevated in 50% of patients with germ cell tumours
- elevation in seminoma in 10-25% of cases

Lactate dehydrogenase (LDH)-

- may also be elevated
- direct relationship between LDH and tumour burden
- However, this test is nonspecific although its degree of elevation correlates with bulk of disease

Applications-

- **In the evaluation of testicular masses**
- **In the staging of testicular germ cell tumors**. For example, after orchiectomy, persistent elevation of HCG or AFP concentrations indicates stage II disease even if the lymph nodes appear of normal size by imaging studies
- **In assessing tumor burden**
- **In monitoring the respons to therapy**. After eradication of tumors there is a rapid fall in serum AFP and HCG. With serial measurements it is often possible to predict recurrence before the patients become symptomatic or develop any other clinical signs of relapse

TESTICULAR TUMOR

Testicular tumor

- Most germ cell tumours occur between the **ages of 20 and 50 years**
- **usual** germ cell tumours , yolk sac tumour and the better differentiated types of teratoma
- **older patients-**Spermatocytic seminoma and malignant lymphoma
- Before puberty, seminoma is extremely uncommon

ETIOLOGIC FACTORS

- **Cryptorchidism**
- **Other developmental disorders-** androgen insensitivity syndrome
- **Genetic factors-**high incidence in first-degree family members, twins
- **Other factors.** A few less common factors

➢ *Orchitis*

➢ *Trauma*

➢ *Carcinogens.* LSD, hormonal therapy for sterility, copper, zinc etc

Prenatal risk factors –

- consistent associations of testicular cancer with **low birth weight**

Exposures in adulthood

- Possible etiological clues, however, include a **low level of physical activity**

❑**PATHOGENESIS-**vast majority of these tumours originate from germ cells

1-Developmental disorders- contribute to the pathogenesis

2-Molecular genetic features-common molecular pathogenesis of all germ cell tumours:

- *Hyperdiploidy* is almost a constant feature
- isochromosome of short arm of chromosome 12
- *Telomerase activity* is present in all germ cell tumours of the testis
- Other mutations include *p53*, *cyclin E* and *FAS* gene

3-Intratubular germ cell neoplasia (ITGCN) or carcinoma insitu-

Most testicular germ cell tumors originate *from a precursor lesion called intratubular germ cell neoplasia (ITGCN)****exceptions*** to this rule are

- pediatric yolk sac tumors
- Teratomas
- adult spermatocytic seminoma

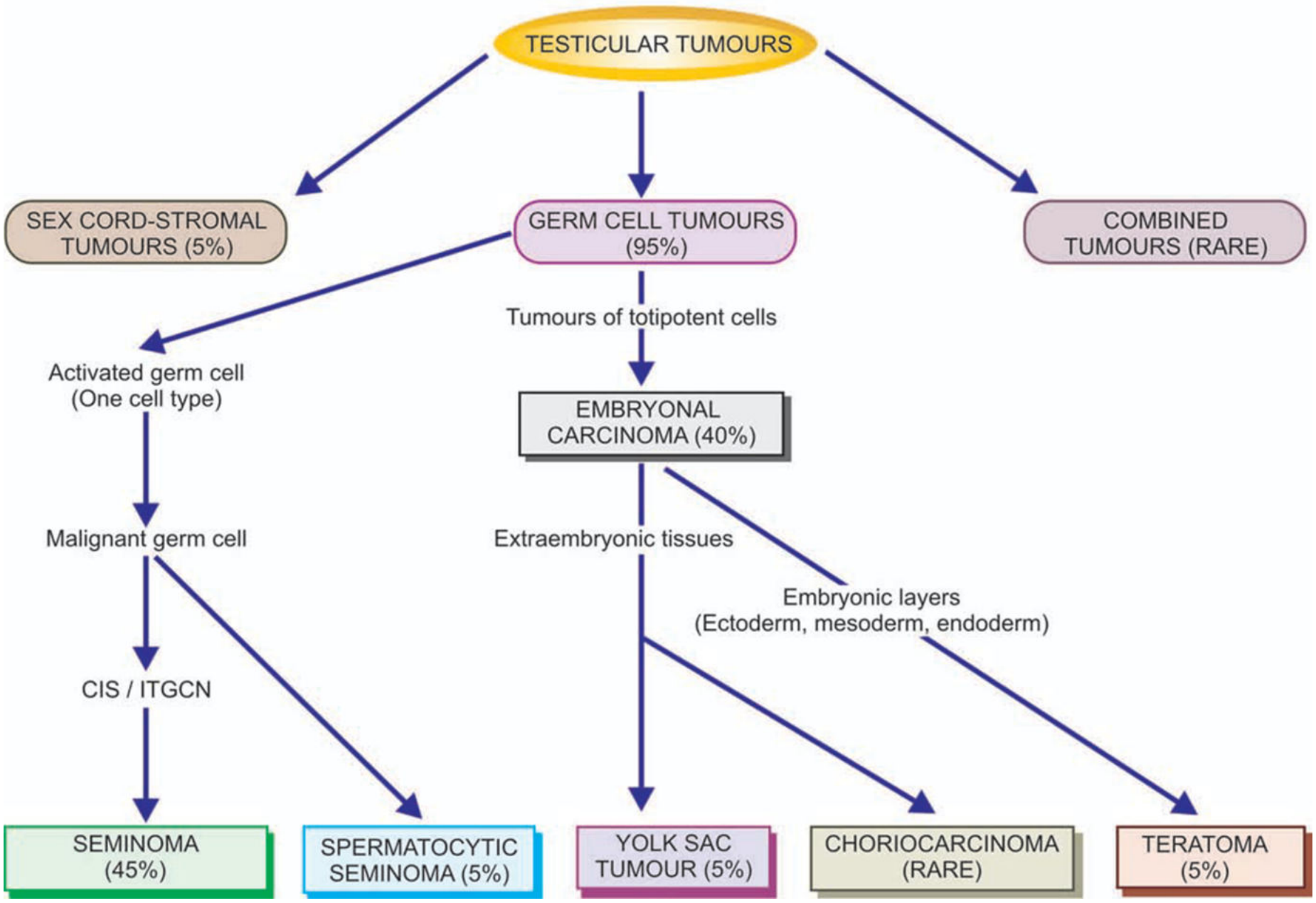
4-Three hit' process. Germ cells in seminiferous tubules undergo

a. ***first hit-****activate the cell*

b. ***second hit-*** *occure in CIS cell and further activate*

c. third hit- via some epigenetic phenomena cell become invasive

this sequential tumorigenesis explains the development of seminomatous tumours



CLINICAL FEATURES AND DIAGNOSIS

- gradual **gonadal enlargement** and a **dragging sensation** in the testis
- secondary symptoms such as pain, lymphadenopathy, and urinary obstruction (Metastatic involvement)

SPREAD-

- *Lymphatic spread*- retroperitoneal para-aortic lymph nodes, mediastinal lymph nodes and supraclavicular lymph nodes
- *Haematogenous spread* -lungs, liver, brain and bones

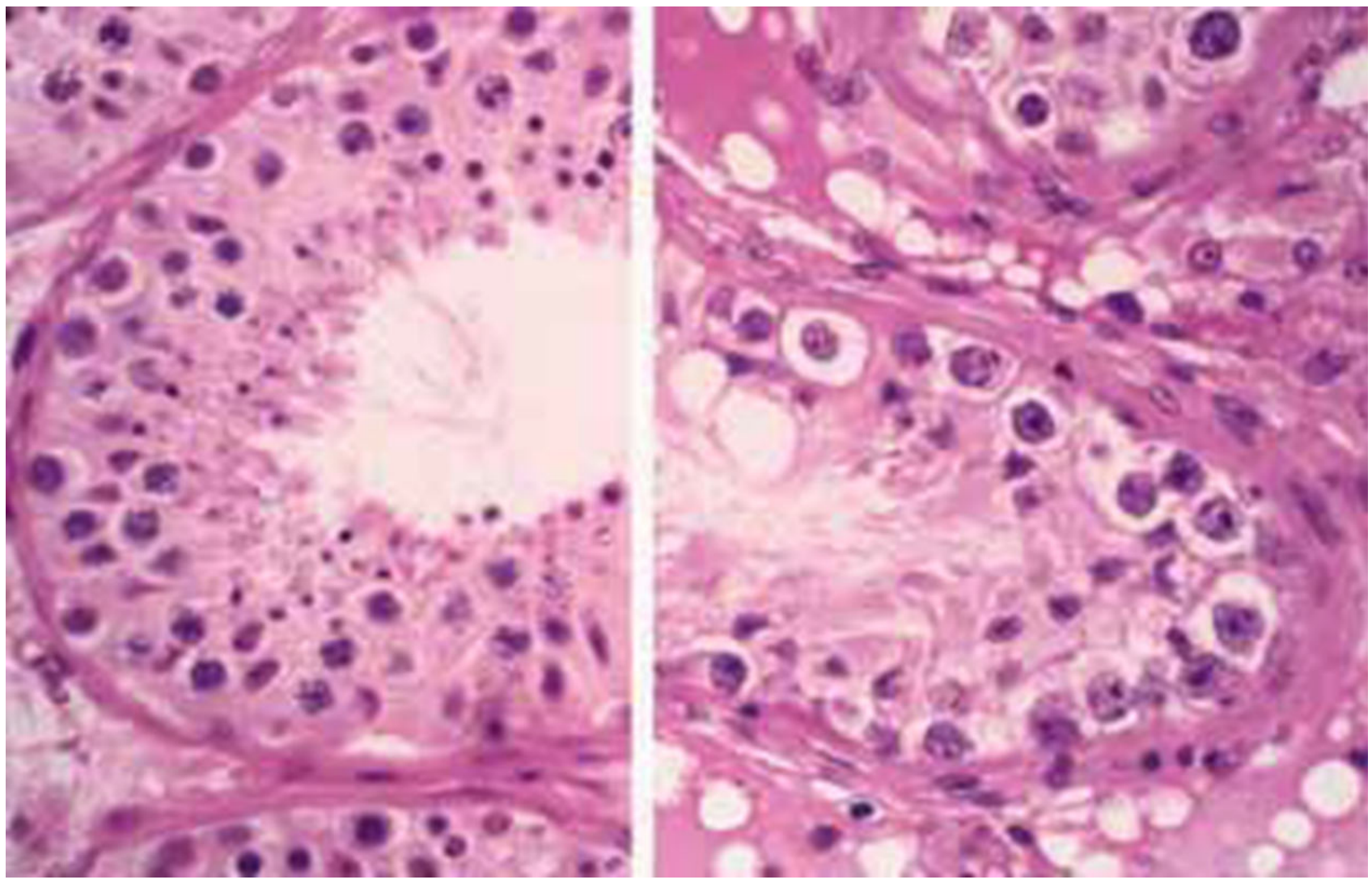
1-Intratubular germ cell neoplasia, unclassified type (IGCNU)

- *Also called* carcinoma *in situ* (CIS) stage of germ cell tumours
- preinvasive stage of germ cell tumours
- intratubular **seminoma** and intratubular **embryonal carcinoma** are common
- 2-4% of cryptorchidism pt show
- **Clinical features -** atrophic testis, infertility, maldescended testis, and intersex features

- **gross-** no grossly visible lesion
- **Histopathology** - Germ cells with abundant vacuolated cytoplasm, large, irregular nuclei and prominent nucleoli located within the seminiferous tubules
- restricted to the seminiferous tubules without evident invasion into the interstitium

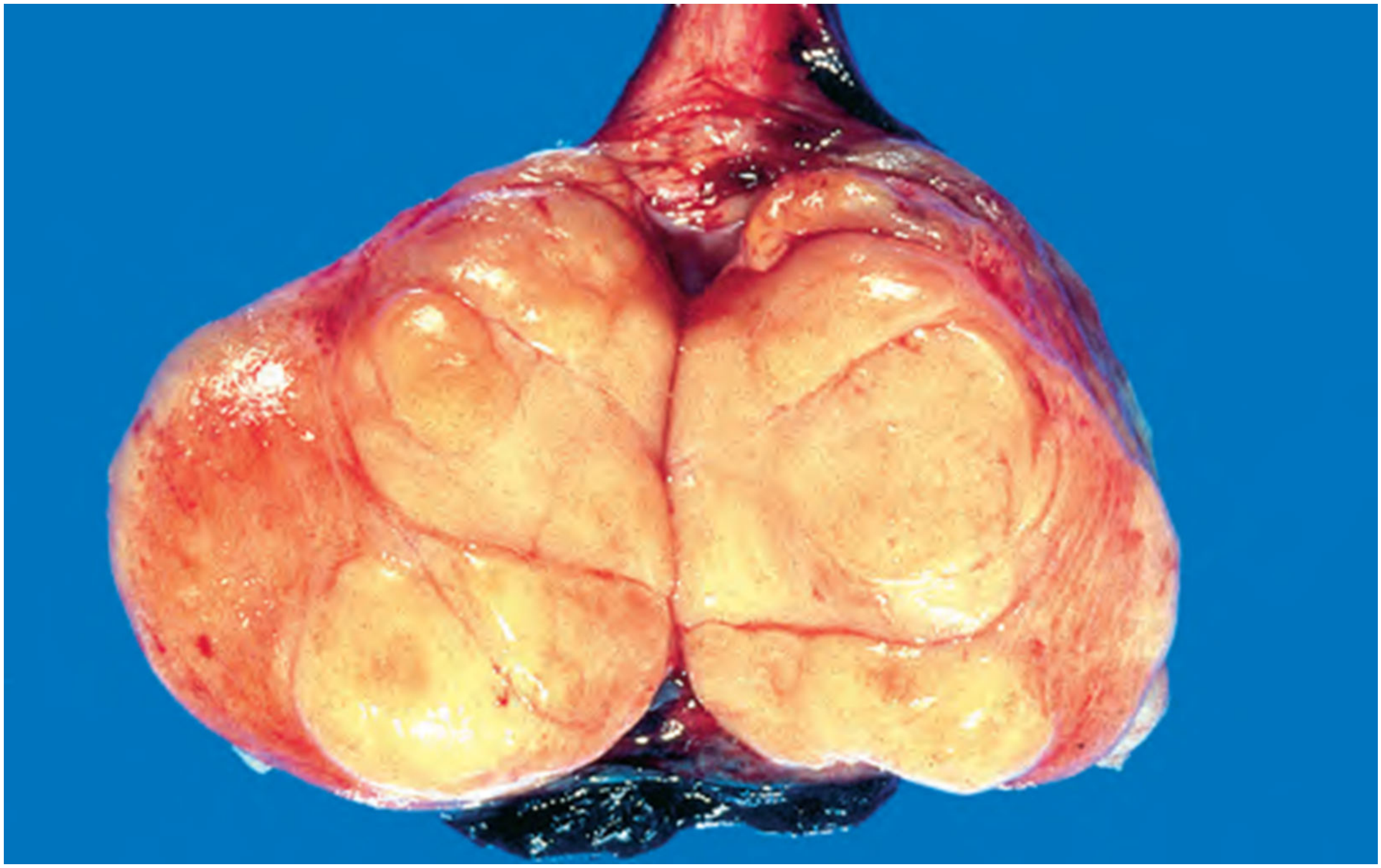
- *Immunoprofile-* PLAP can be demonstrated in 83-99% of intratubular germ cell neoplasia of the unclassified type (IGCNU) cases and is widely used for diagnosis

Comparison of morphological features of normal seminiferous tubules (left part) and intratubular germ cell neoplasia (IGCNU) in seminiferous tubules (right part).



Seminoma

- Seminomas are the **most common type of germ cell tumor**, making up about (50%)
- peak incidence is the **third decade**
- it is called ***dysgerminoma*** *in ovary*



MORPHOLOGY- cut surface has a homogeneous, graywhite, lobulated, usually devoid of hemorrhage or necrosis

Generally the tunica albuginea is not penetrated

but occasionally extension to the epididymis, spermatic cord, or scrotal sac occurs

Microscopy- typical seminoma is composed of sheets of uniform cells divided into poorly demarcated lobules by delicate fibrous septa containing a lymphocytic infiltrate

Tumor cell-

cell is large and round to polyhedral and has a distinct cell membrane; clear or watery-appearing cytoplasm; and a large, central nucleus with one or two prominent nucleoli

Stroma-

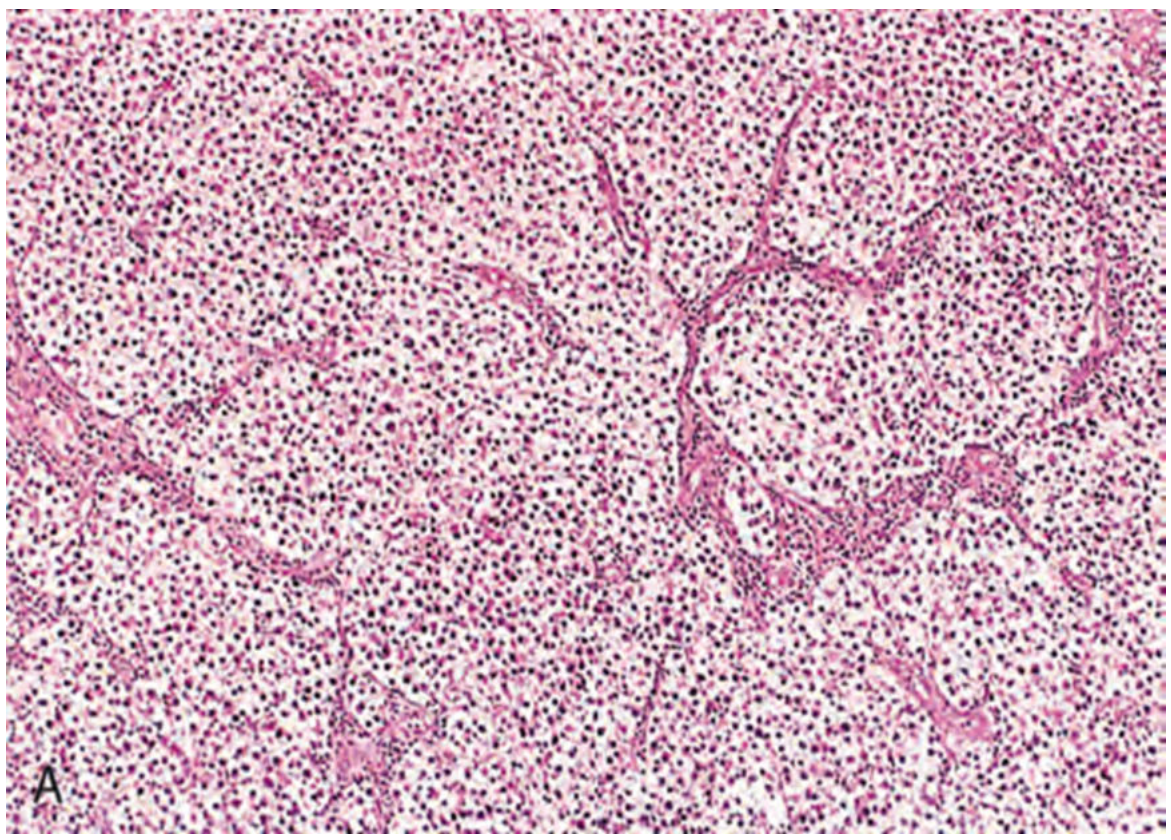
- delicate fibrous tissue which divides the tumour into lobules
- characteristic lymphocytic infiltration, indicative of immunologic response of the host to the tumour

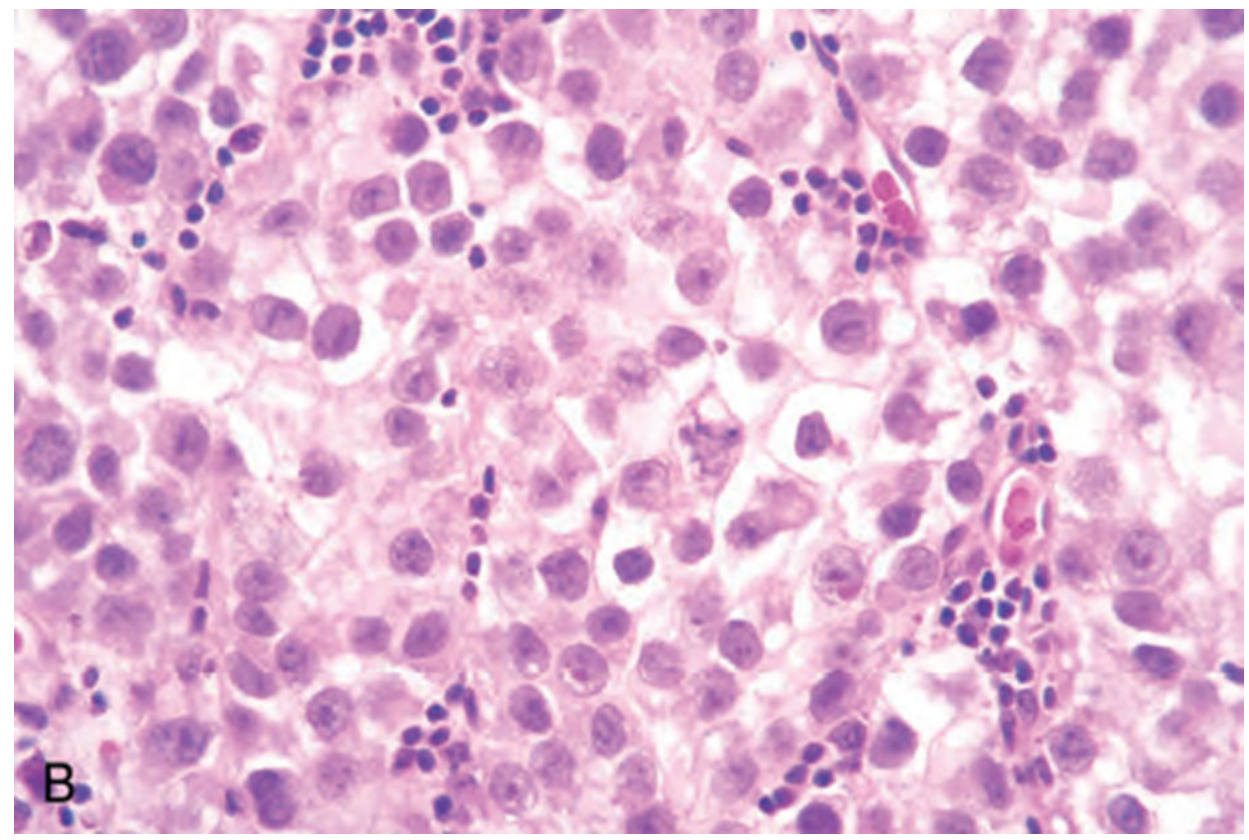
Variable features-

- tumor giant cells and greater mitotic activity
- 15% of seminomas contain syncytiotrophoblasts
- ill-defined granulomatous reaction (20%)

Special stain-Cytoplasm contains variable amount of glycogen that stains positively with **PAS reaction**

IHC- seminoma cells stain positively for KIT, (regardless of KIT mutational status), OCT4, and placental alkaline phosphatase (PLAP)





Prognosis-

- better than other germ cell tumours
- tumour is highly radiosensitive

Spermatocytic Seminoma-

- Spermatocytic seminoma is both clinically and morphologically a distinctive tumour from classic seminoma

- Incidence of about 5% of all germ cell tumours
- older patients
- generally in 6^{th} decade of life
- bilateral in 10% of patients

- ***Grossly,*** spermatocytic seminoma is homogeneous, larger, softer and more yellowish and gelatinous than the classic seminoma

- ***Histologically,*** the distinctive features are as under:

1. Tumour cells. lymphocyte-like to huge mononucleate or multinucleate giant cells. Majority of cells are, however, of **intermediate size.** Mitoses are often frequent.

2. Stroma. stroma lacks lymphocytic and granulomatous reaction seen in classic seminoma.

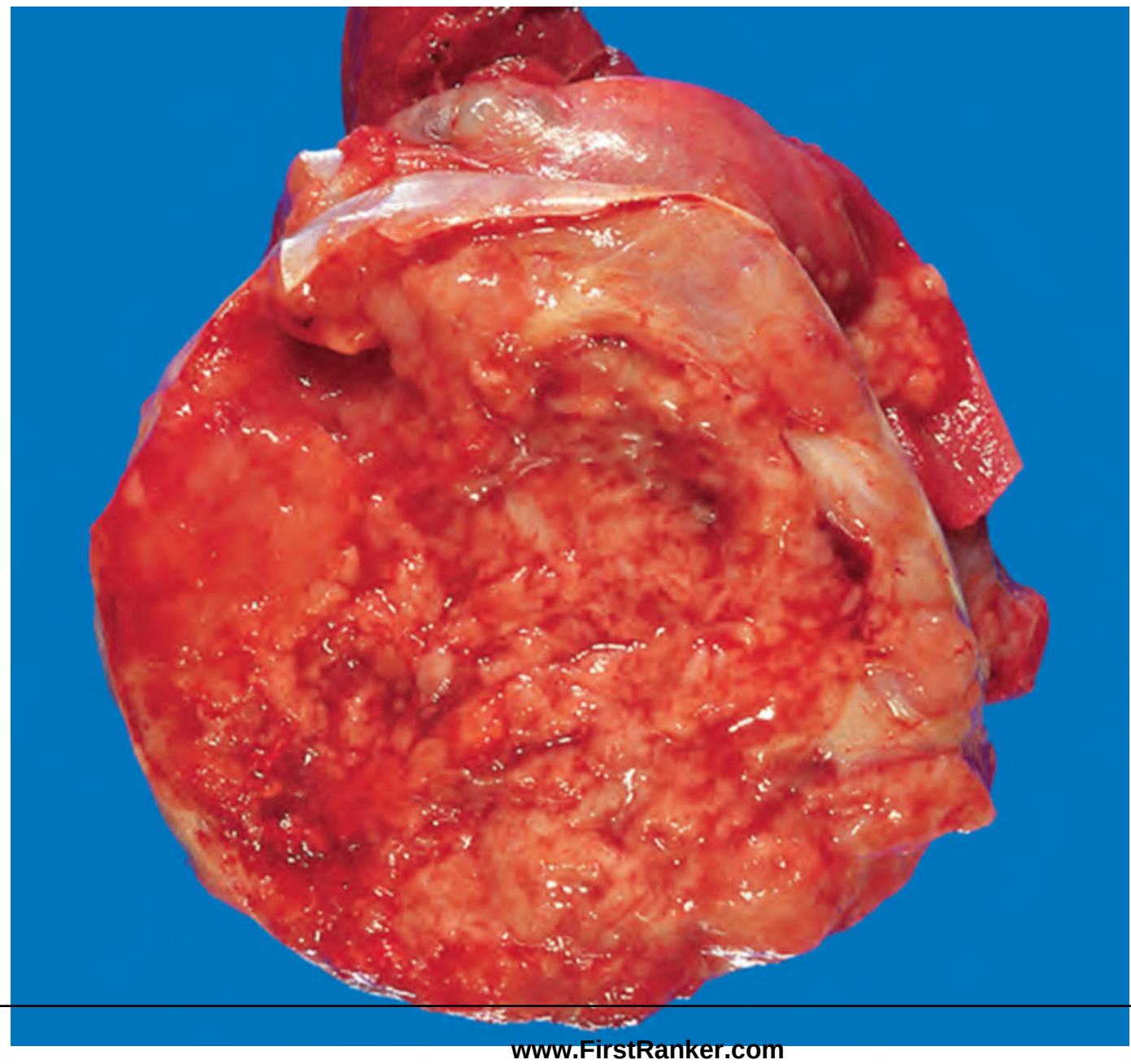
- *prognosis* of spermatocytic seminoma is excellent
- slow-growing and rarely metastasises
- tumour is radiosensitive

Embryonal Carcinoma-

- 30% of germ cell tumours more common
- 2nd to 3rd decades of life
- 90% cases are associated with elevation of AFP or hCG or both

Grossly,- a small tumour in the testis

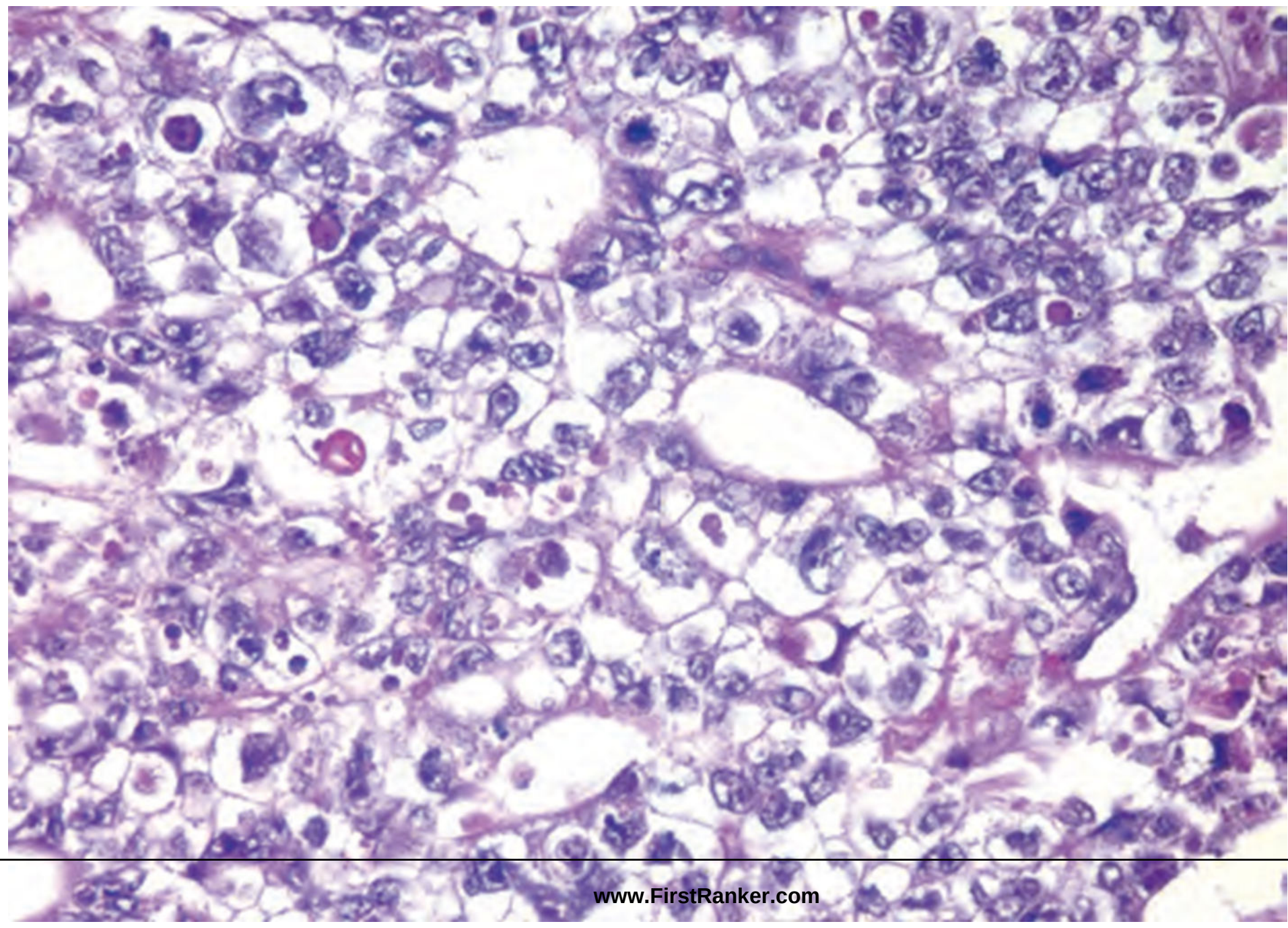
- **distorts the contour of the testis** as it frequently invades the tunica and the epididymis
- Cut surface- grey white, soft with areas of haemorrhages and necrosis



Microscopy-

1. tumour cells are arranged in a variety of *patterns*— glandular, tubular, papillary and solid

2.*tumour cells* are **highly anaplastic carcinomatous** cells having large size, amphophilic cytoplasm and prominent hyperchromatic nucleoli



Yolk Sac Tumour *(Synonyms: Endodermal Sinus Tumour, Orchioblastoma, Infantile Embryonal Carcinoma)*

- most common testicular tumour of **infants and young children upto the age of 4** year
- may be present as the major component in **40% of germ cell tumours**
- AFP levels are elevated in **100% cases** of yolk sac tumours

- ***Grossly,*** the tumour is generally soft, yellow-white, mucoid with areas of necrosis and haemorrhages

Microscopically, yolk sac tumour has the following features

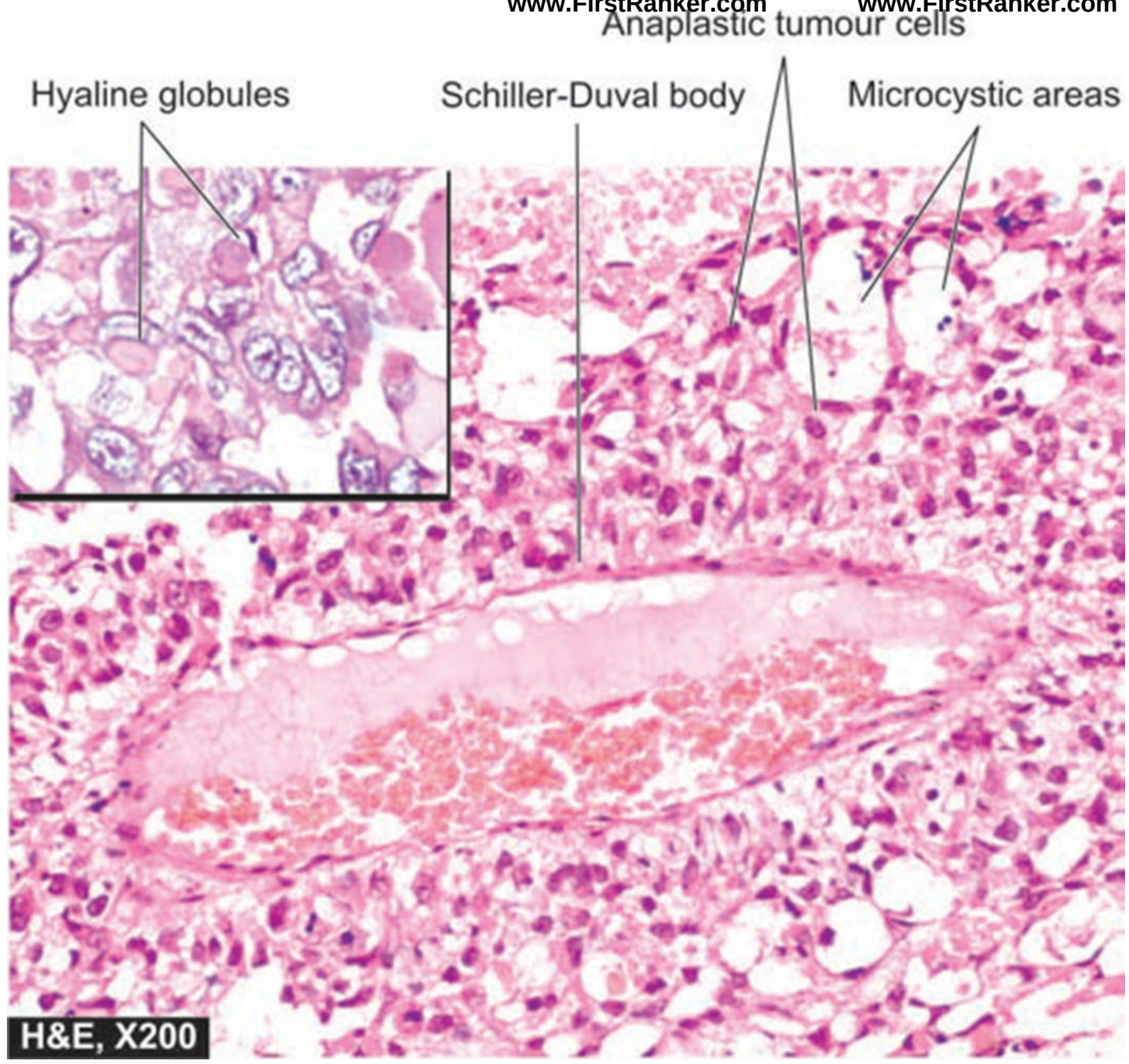
1. *patterns*—loose **reticular network, papillary, tubular and solid arrangement**

2. flattened to cuboid epithelial cells with clear vacuolated cytoplasm

3.A pathognomonic feature is **Schiller -Duvel body**

a central vessel surrounded by tumor cells in a cystic space often lined by flattened tumor cells

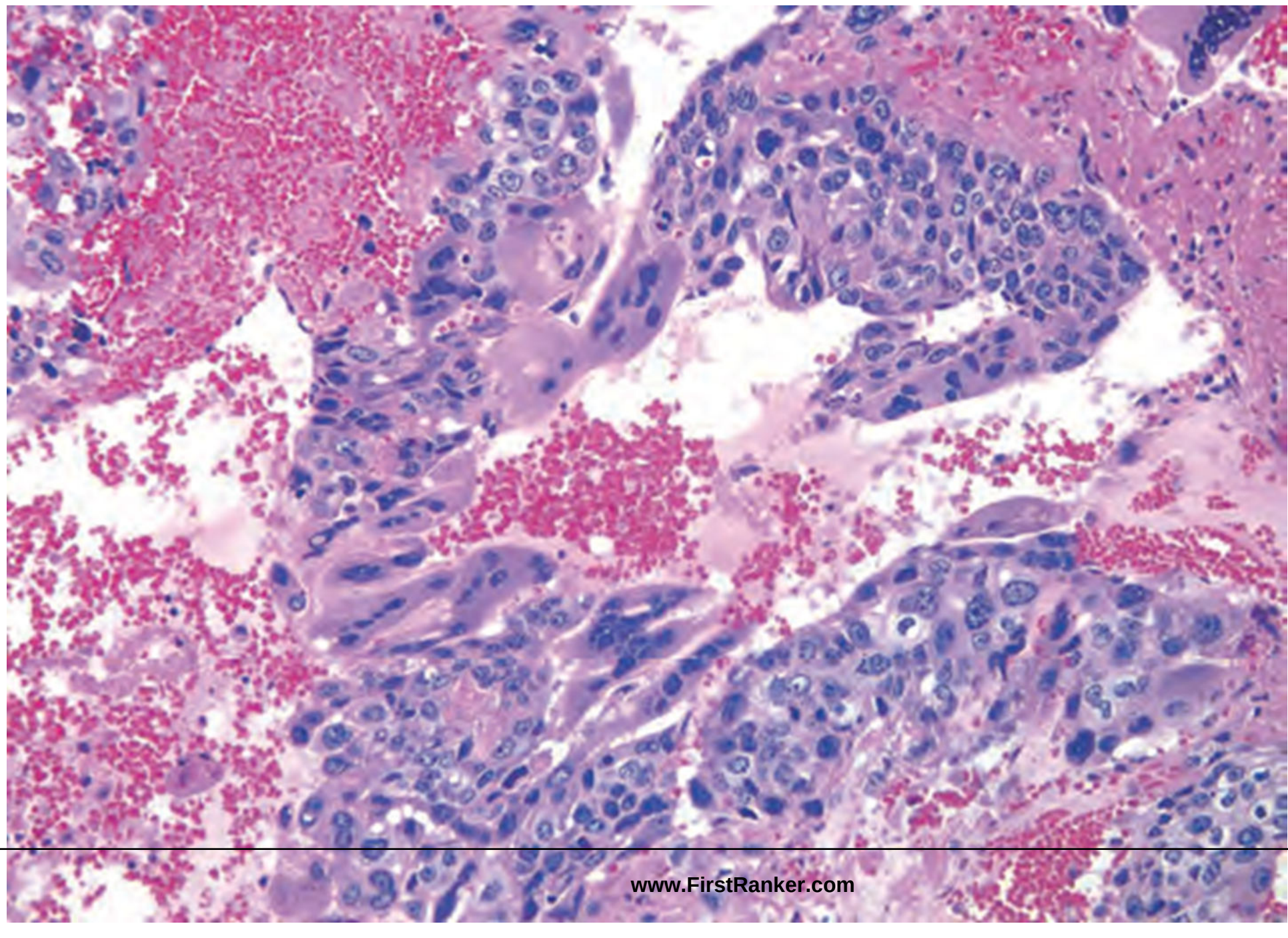
4. presence of both intracellular and extracellular PAS-positive *hyaline globules*



Choriocarcinoma

- highly malignant tumour composed of syncytiotrophoblast and cytotrophoblast
- 2nd decade of life
- serum and urinary levels of hCG are greatly elevated in 100% cases

- ***Grossly,*** the tumour is usually small and may appear as a **soft, haemorrhagic and necrotic mass**
- ***Microscopically,*** the characteristic feature is **syncytiotrophoblast and cytotrophoblast without formation of definite placental-type villi**



Teratoma-

- Teratomas are complex tumours composed of tissues derived from more than one of the **three germ cell layers**—endoderm, mesoderm and ectoderm
- more common in infants and children and constitute (40%)
- in adults they comprise 5% of all germ cell tumours

- Many structures are derived from the three embryonic germ layers during organogenesis

ECTODERM	MESODERM	ENDODERM
• Epidermis of skin and its derivatives (including sweat glands, hair follicles) • Epithelial lining of mouth and rectum • Sensory receptors in epidermis • Cornea and lens of eye • Nervous system • Adrenal medulla • Tooth enamel • Epithelium of pineal and pituitary glands	• Notochord • Skeletal system • Muscular system • Muscular layer of stomach, intestine, etc. • Excretory system • Circulatory and lymphatic systems • Reproductive system (except germ cells) • Dermis of skin • Lining of body cavity • Adrenal cortex	• Epithelial lining of digestive tract • Epithelial lining of respiratory system • Lining of urethra, urinary bladder, and reproductive system • Liver • Pancreas • Thymus • Thyroid and parathyroid glands

MORPHOLOGIC FEATURES. Testicular teratomas are classified into 3 types:

1. Mature (differentiated) teratoma
2. Immature teratoma
3. Teratoma with malignant transformation

Gross-

- large, grey-white masses enlarging testis

- *Cut surface* shows characteristic variegated appearance—grey-white solid areas, cystic and honey-combed areas, and foci of cartilage and bone

Microscopicy-

- three categories of teratomas show different appearances:

1-Mature (differentiated) teratoma. Well differentiated structures such as cartilage, smooth muscle, intestinal and respiratory epithelium, mucus glands, cysts lined by squamous and transitional epithelium, neural tissue, fat and bone

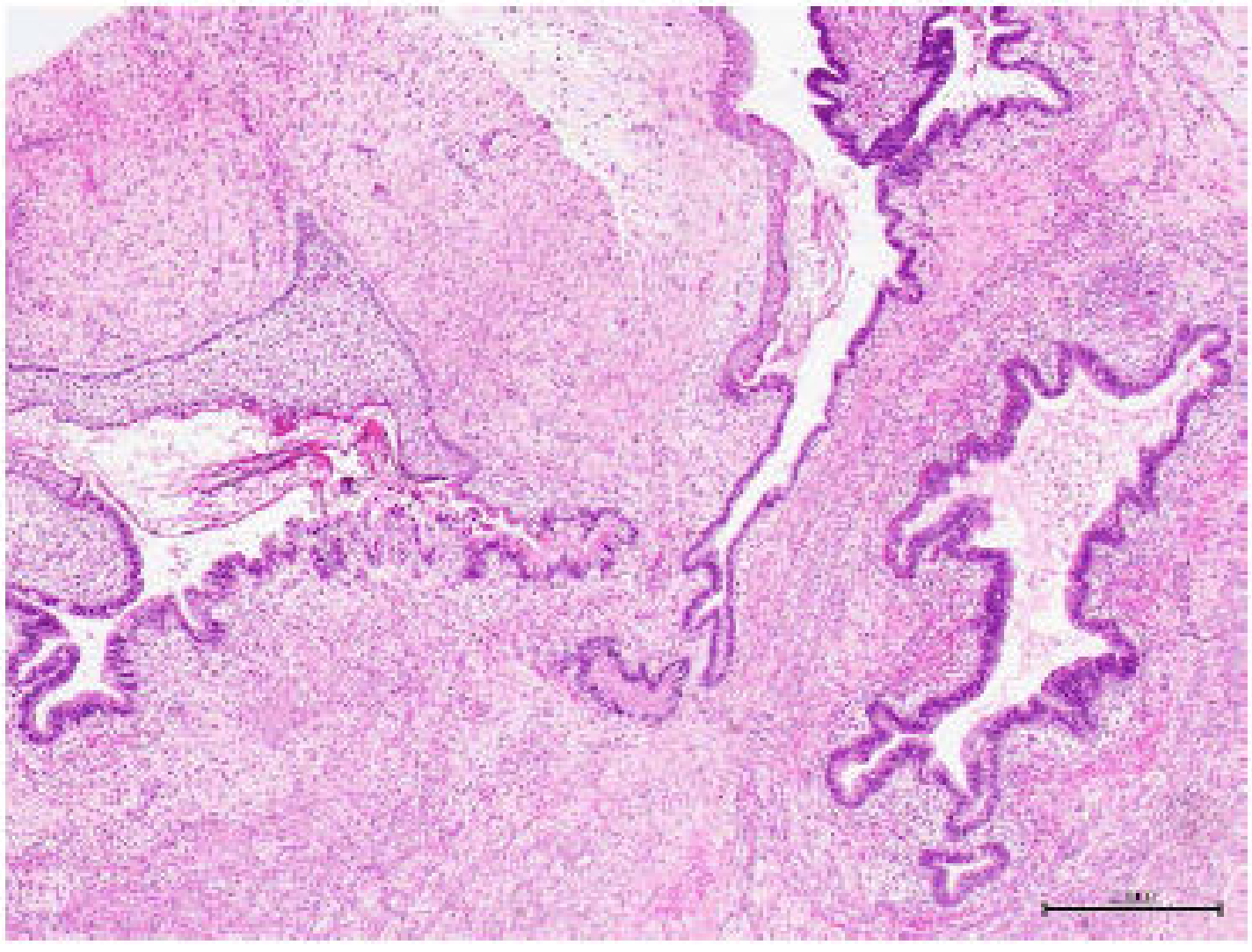
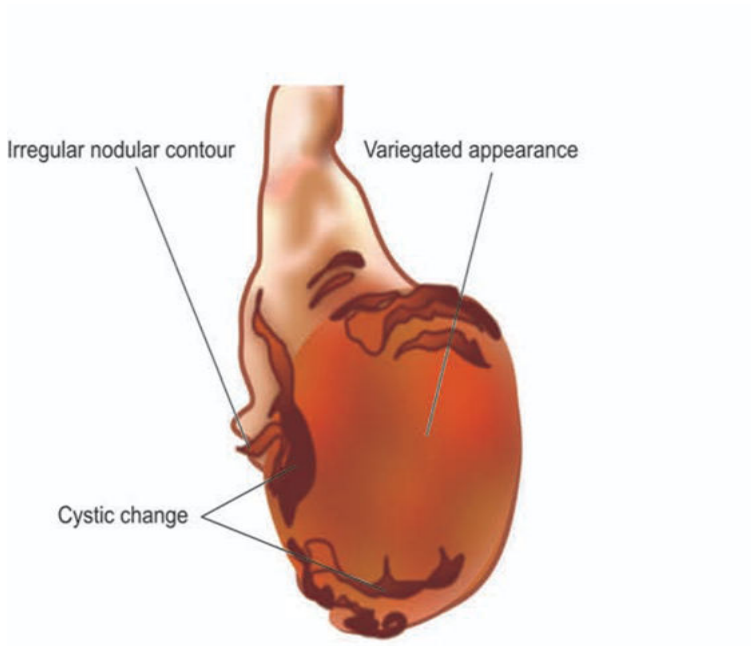
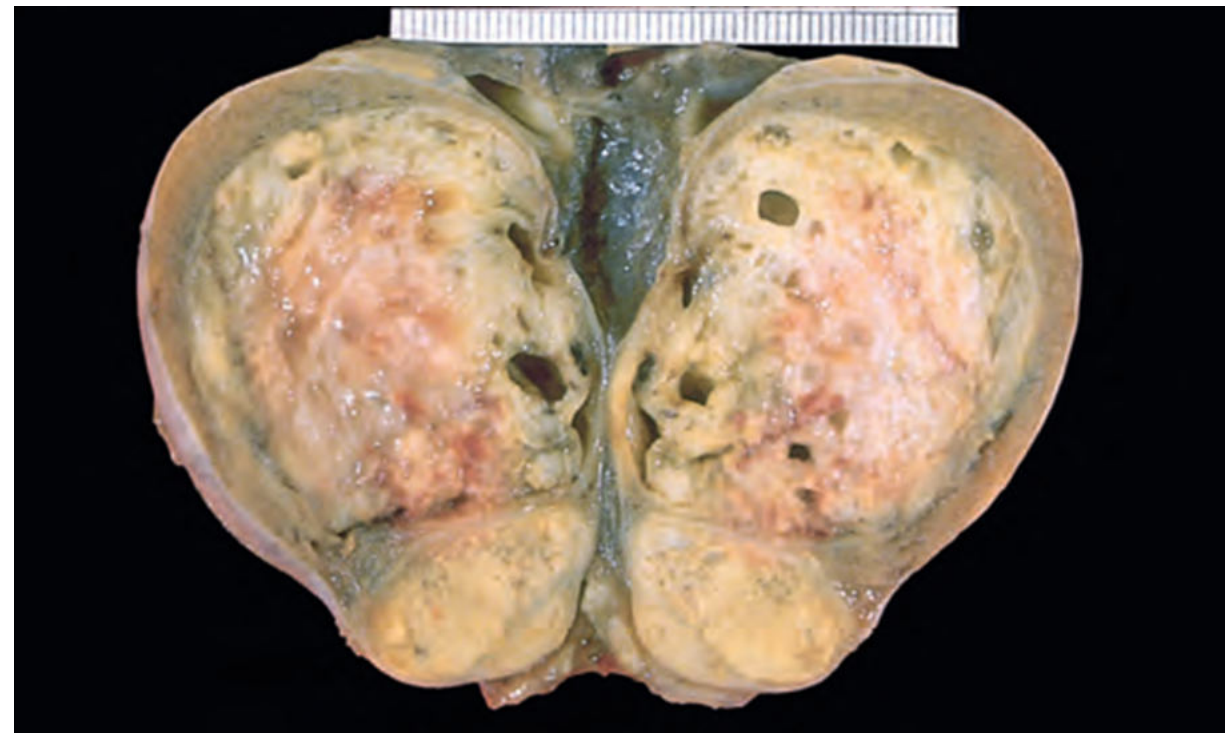


Figure 1: Mature teratoma (H&E, 40x) showing squamous epithelium (left upper) and enteric glandular epithelium (bottom right).

2-Immature teratoma.

- incompletely differentiated and **primitive or embryonic tissues**
- Mature+poorly-formed tissue (cartilage, mesenchyme, neural tissues, abortive eye, intestinal and respiratory tissue elements) etc
- **Mitoses are usually frequent**





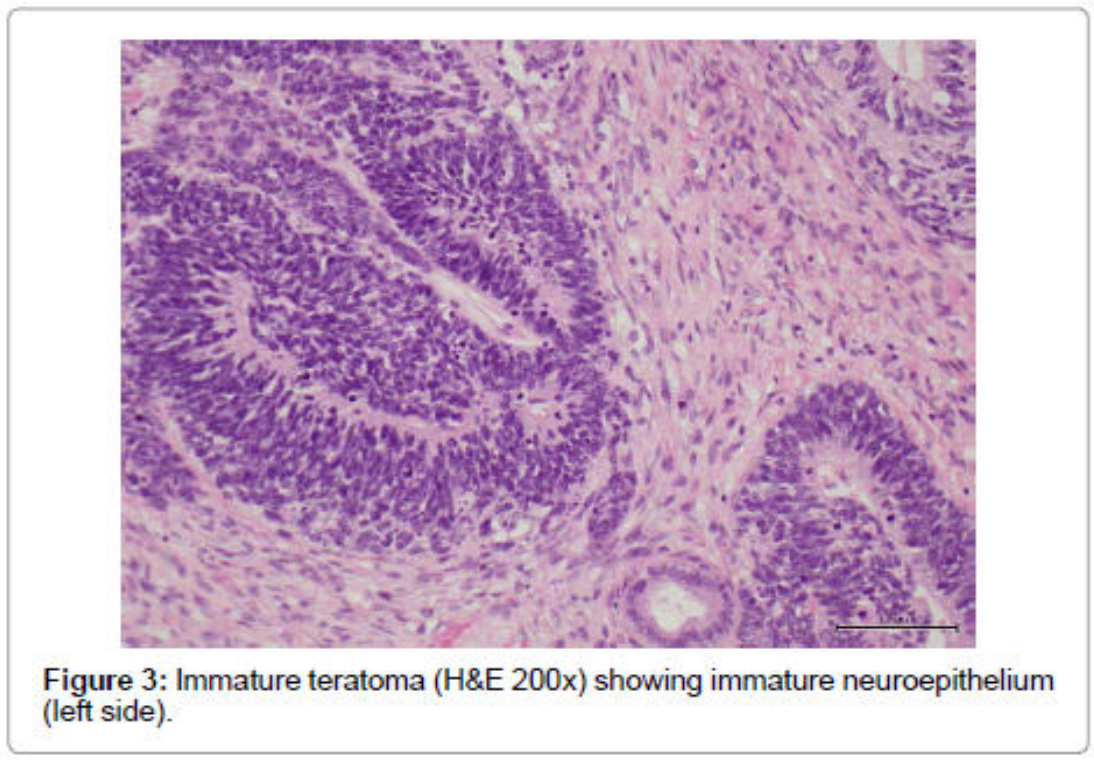
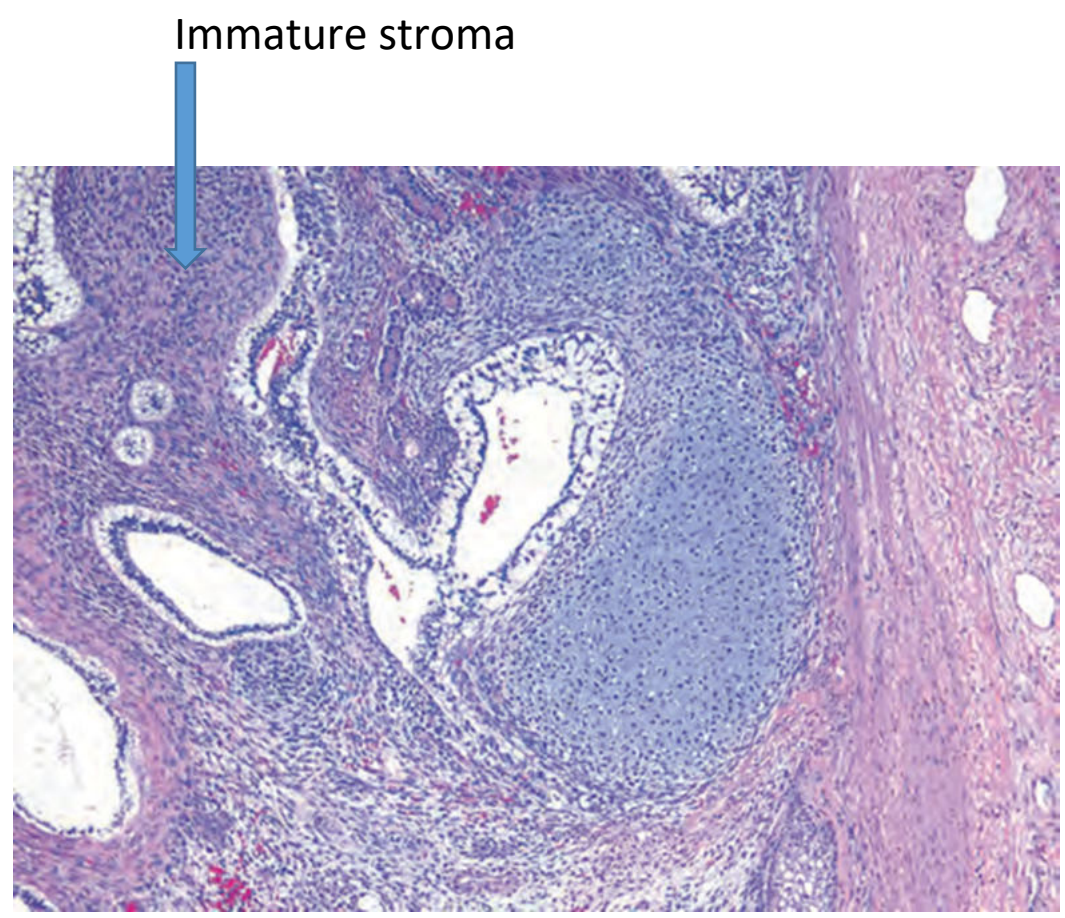


Figure 3: Immature teratoma (H&E 200x) showing immature neuroepithelium (left side).



3-Teratoma with malignant transformation-

- extremely rare form of teratoma
- one or more of the tissue elements show malignant transformation

➢squamous cell carcinoma

➢mucin-secreting adenocarcinoma,

➢sarcoma, or other cancers

- importance of recognizing a non–germ cell malignancy arising in a teratoma is that these secondary tumors are **chemoresistant**

Mixed Germ Cell Tumours

- About 60% of germ cell tumours have more than one of the above histologic types (except spermatocytic seminoma) and are called mixed germ cell tumours

most common combinations of mixed germ cell tumours are as under:

1. Teratoma, embryonal carcinoma, yolk sac tumour and syncytiotrophoblast
2. Embryonal carcinoma and teratoma (teratocarcinoma)
3. Seminoma and embryonal carcinoma

- **SEX CORD-STROMAL TUMOURS-**Tumours arising from specialised gonadal stroma

source of tumor-

- theca, granulosa and lutein cells in the female
- **Sertoli** and **interstitial Leydig cells** in the male

Must know

1-classification

2-Tumor markers in diagnosis

3-Morphology of

a) Seminoma
b) Embryonal carcinoma
c) Yolk sac tumor

4-Cryporchidism