Pathology of Male genital tract

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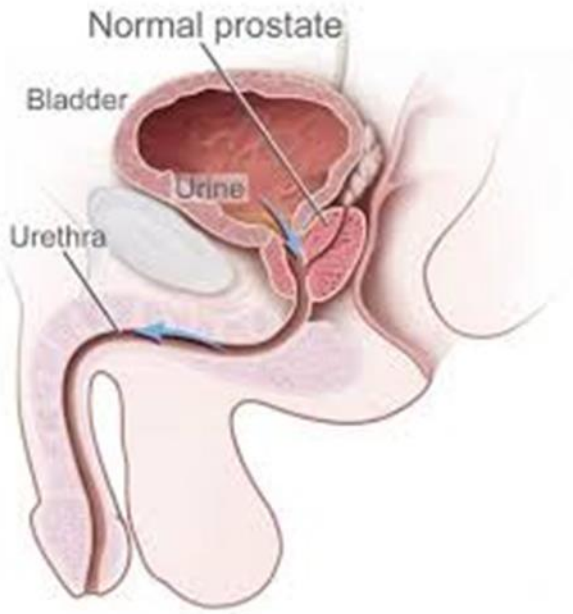
Objectives

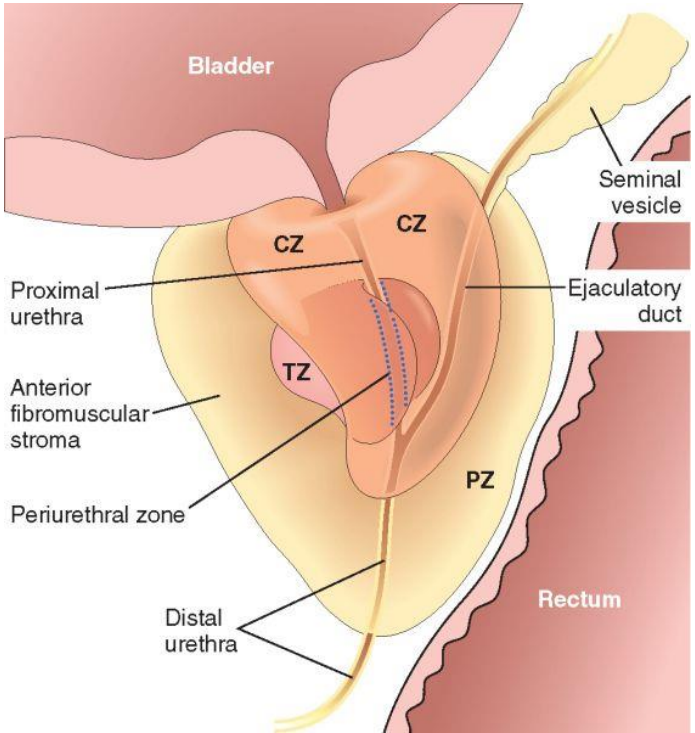
Should be able to

- Discuss different pathologies for prostatic enlargement
- Describe different pathologies that cause scrotal swelling
- Classify testicular tumours
- Describe morphology of common testicular tumours
- Discuss pathology of intraepithelial and invasive penile cancer

Normal prostate gland

- A retroperitoneal organ encircling the bladder neck
- Weighs about 20g
- Palpable on rectal examination
- Blood supply-internal iliac artery
- Prostatic veins drain into the prostatic venous plexus





Prostatic parenchyma is divided into 4 zones
- Peripheral
- Central,
- Transitional
- Anterior fibromuscular stroma

The types of proliferative lesions are different in each region

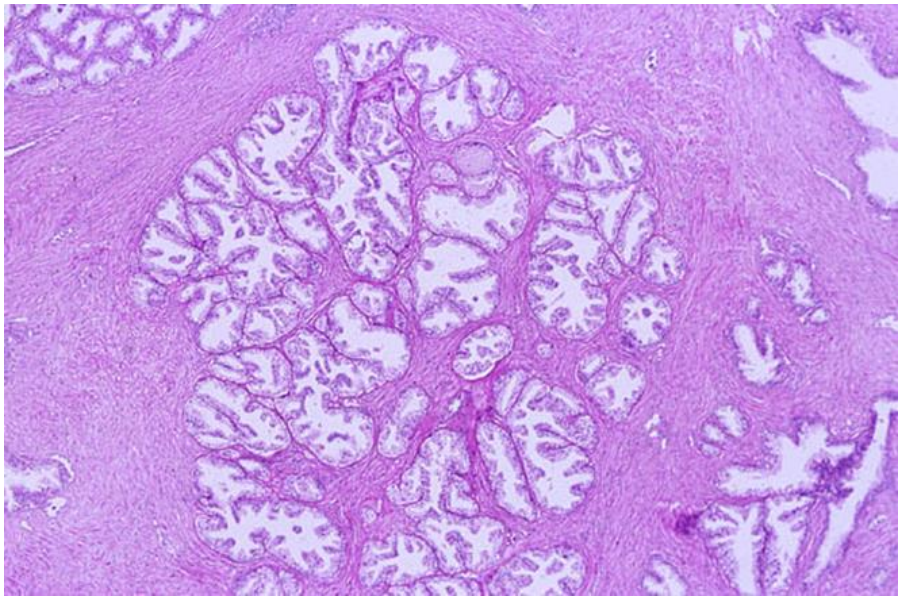
Eg: BNH- transitional zone

Carcinomas - peripheral zone

Microscopy- normal prostate gland

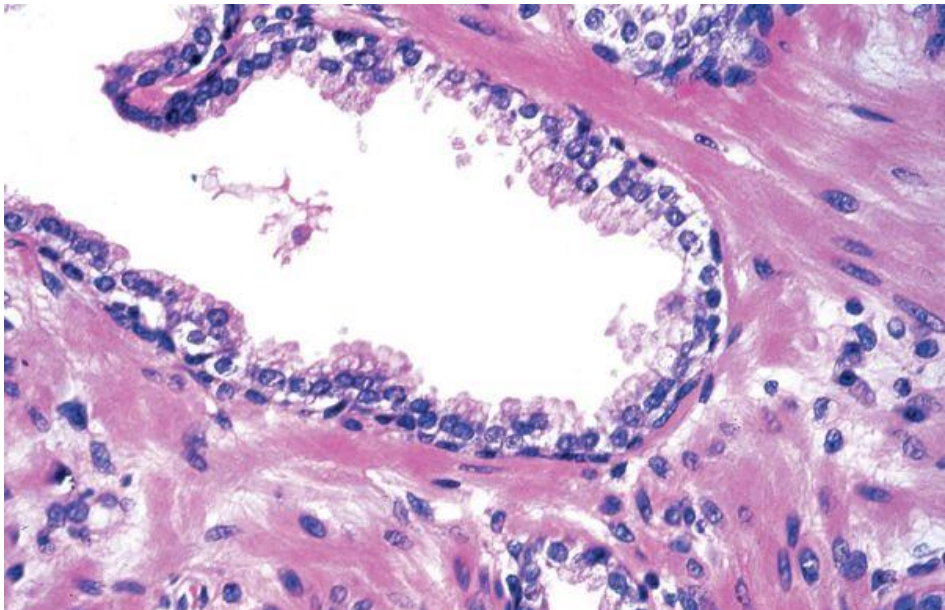
- Glands are arranged concentrically around urethra
- Inner periurethral group
- Submucosal group
- External group/ main prostatic glands

Microscopy- normal prostate gland



- Lobular arrangment of glandular acini
- Convoluted appearance with papillary infoldings

- Lined by cuboidal, pseudostratified columnar epithelium, lying on a myoepithelial layer
- Surrounded by a fibrous tissue stroma



Enlarged prostate gland

Main 3 pathologic processes affect the prostate gland

- Prostatitis
- Benign nodular hyperplasia (BNH)
- Prostatic carcinoma

Prostatitis

Acute suppurative prostatitis-

- secondary to ascending or descending infection

Chronic non specific prostatitis

- Folllowing recurrent episodes of acute prostatitis
- Lymphocyte and plasma cell infiltrate, acinar atrophy and stromal fibrosis

Granulomatous prostatitis

- Tuberculous prostatitis, non specific granulomatous prostatitis, instillation of BCG
- Can mimic malignancy
- Clinically due to hard enlargement of the gland
- Increased serum PSA level

Benign prostatic hyperplasia (BPH)/ Nodular Hyperplasia

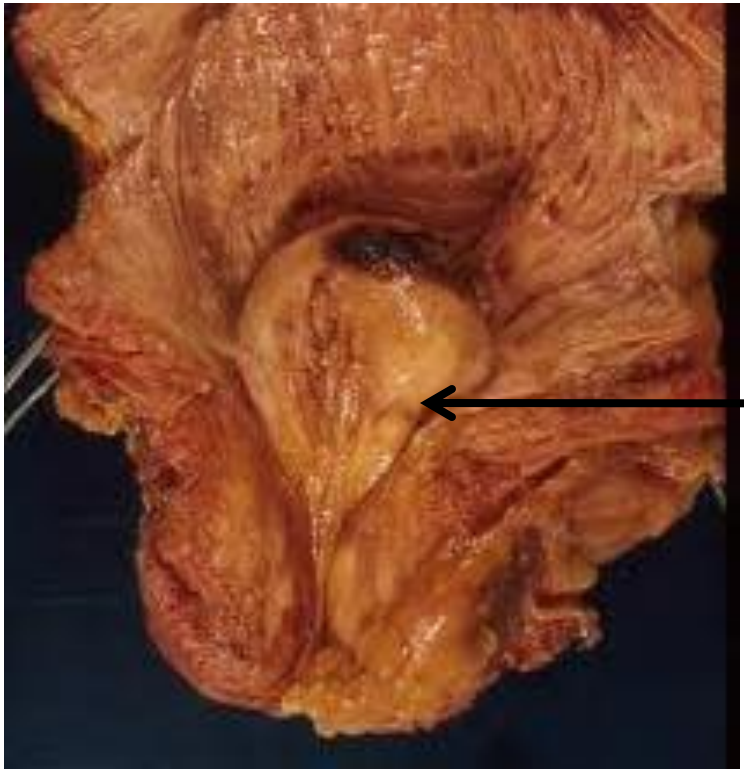
- A common non-neoplastic condition of prostate gland
- Commonly seen after 50 years of age
- Cause of BPH is unknown
- ? DHT-induced growth factors act by ↑ proliferation of stromal cells and ↓ death of epithelial cells.
- Mainly involves the periurethral glands
- Not a pre neoplastic condition

BPH Morphology

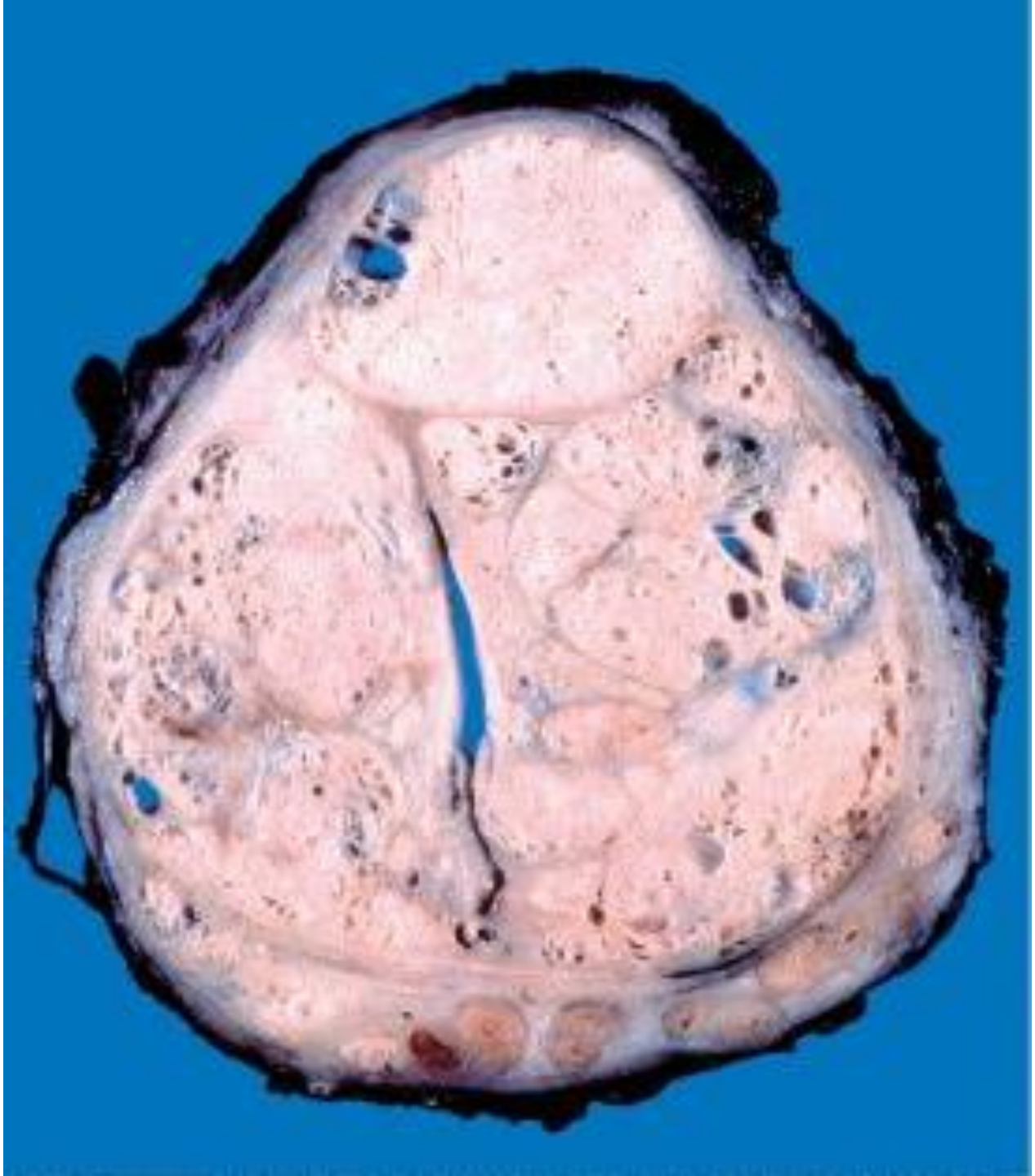
- Enlargement of the gland (60-100g)
- Originates in the periurethal region
- Mostly involves the TZ of lateral lobes
- Characterized by hyperplasia of both stromal and glandular components resulting in formation of discrete nodules
- Early nodules - stromal hyperplasia
- Later - glandular hyperplasia

Macroscopy of BPH

- The cut surface - multiple, circumscribed, solid nodules and cysts
- Nodules compress the prostatic urethra

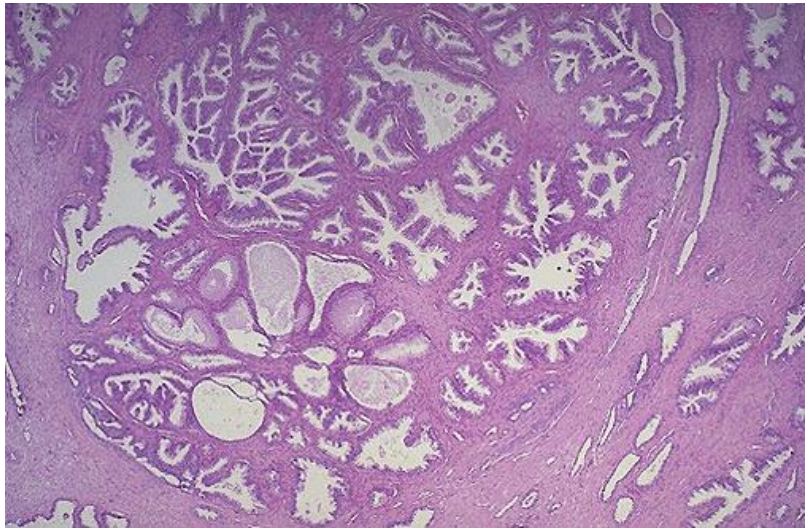


- Sometimes these nodule can protrude up into the bladder neck “Median Lobe”

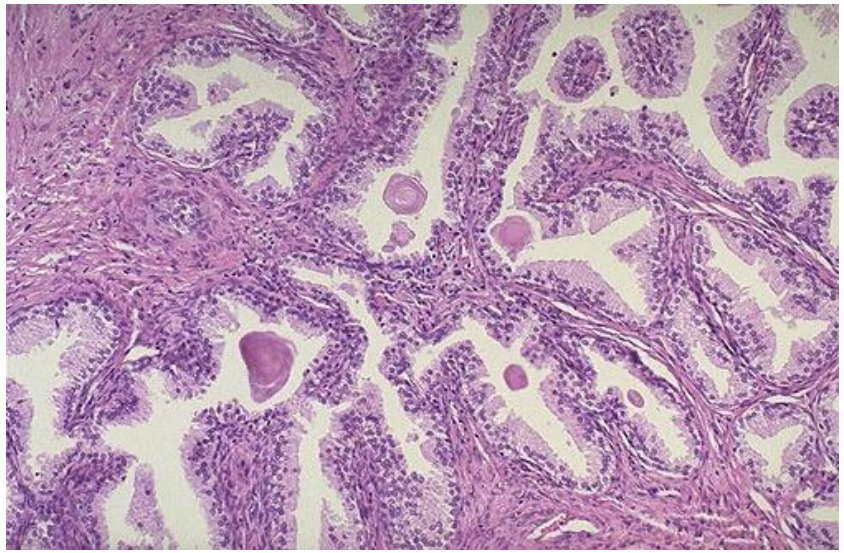


Microscopy of BPH

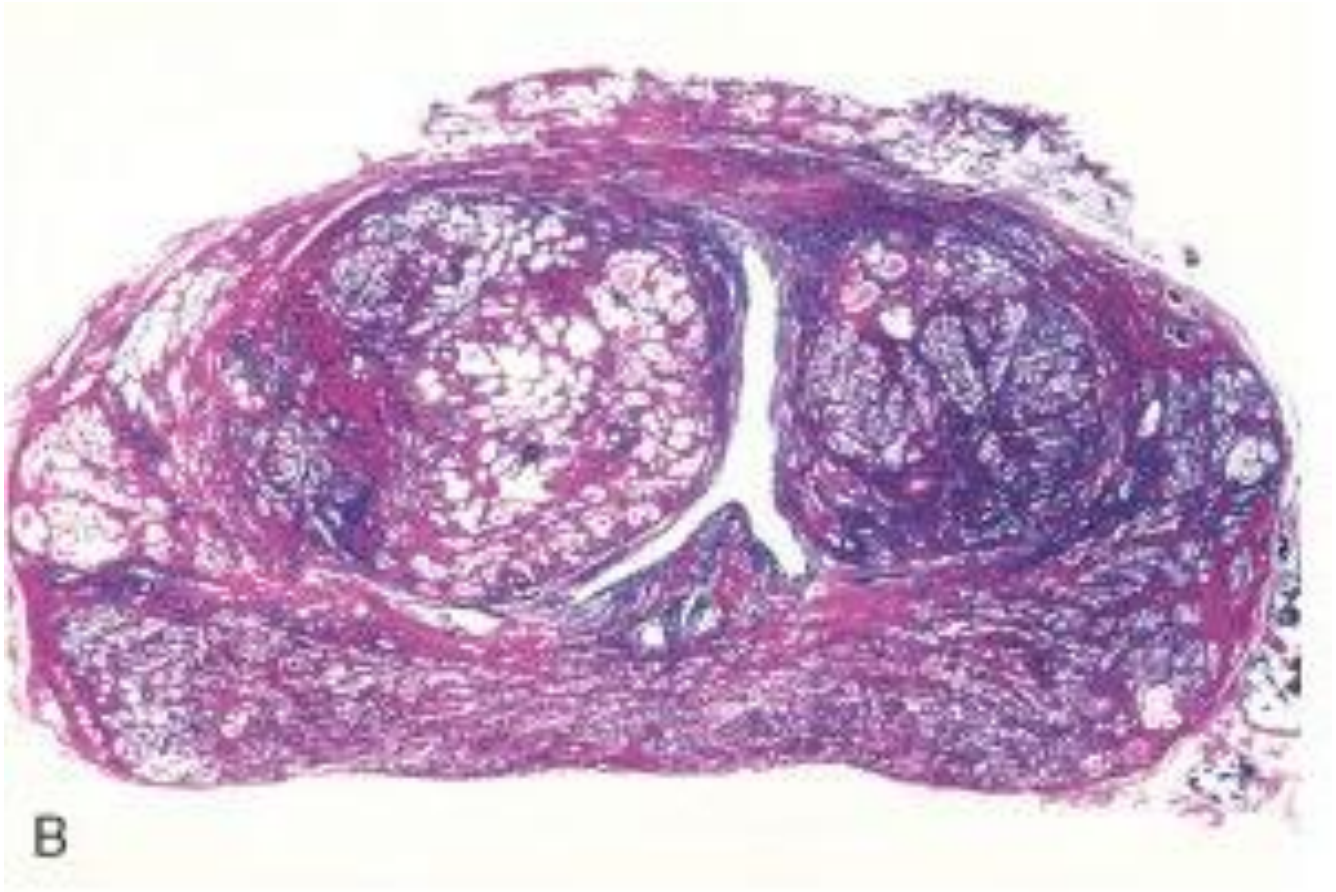
- Formation of nodules of purely stromal, fibromuscular to fibroepithelial



- A large hyperplastic nodule of glands
- Small to large cystically dilated glands lined by **two layers** of cells



- Glands are well-differentiated and still have some intervening stroma.
- Corpora amylacea within the glands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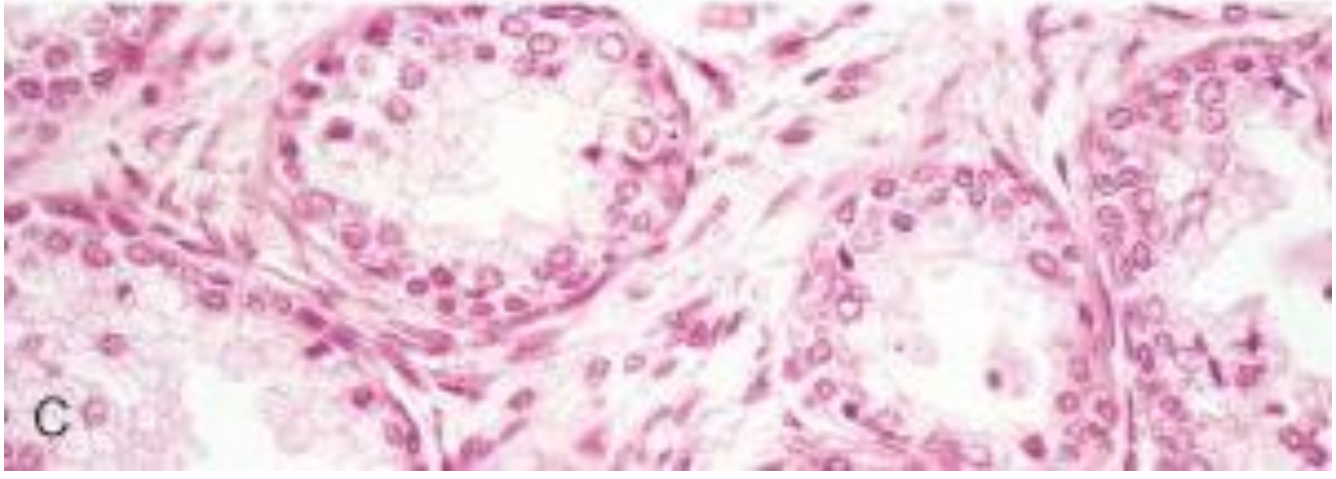
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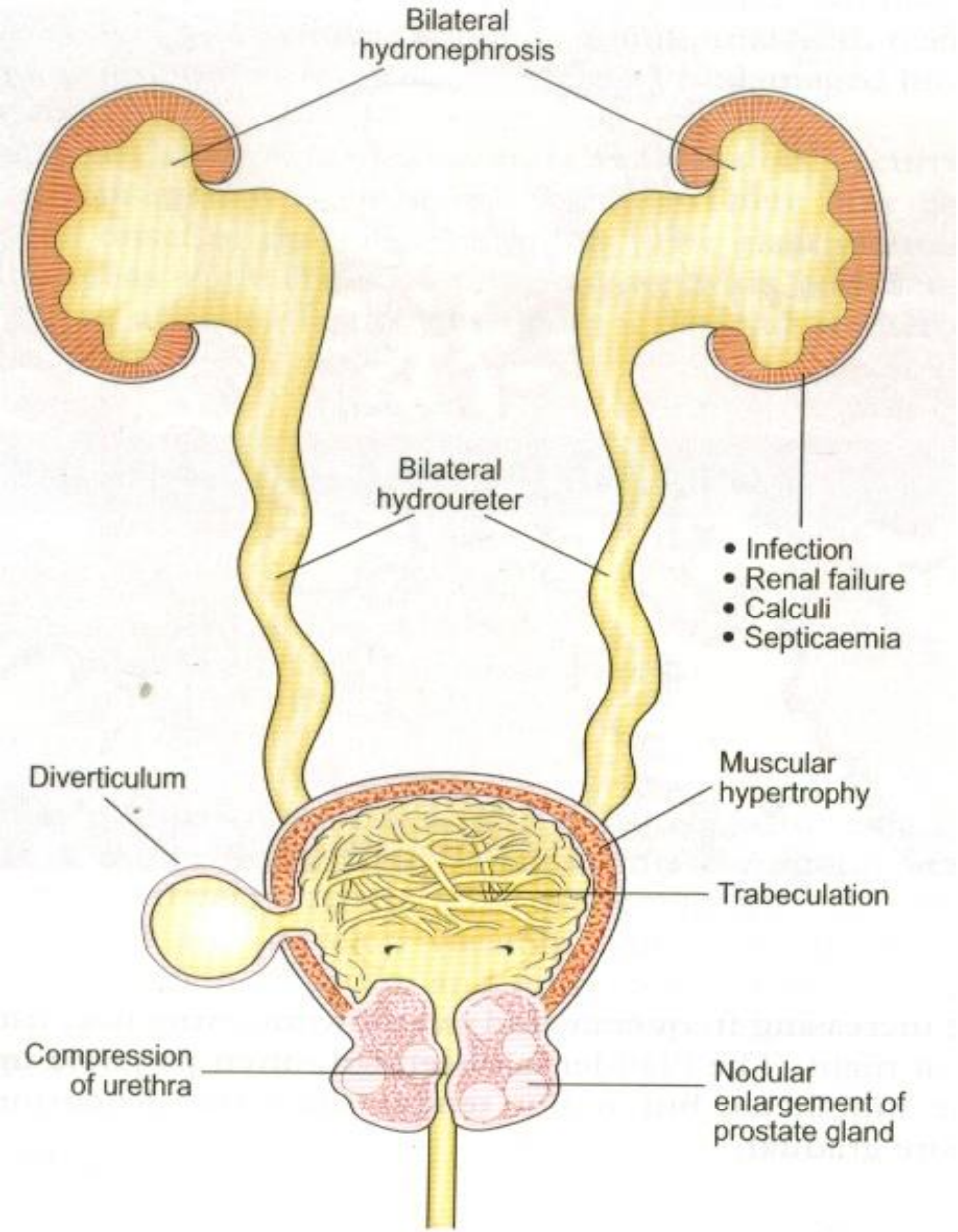
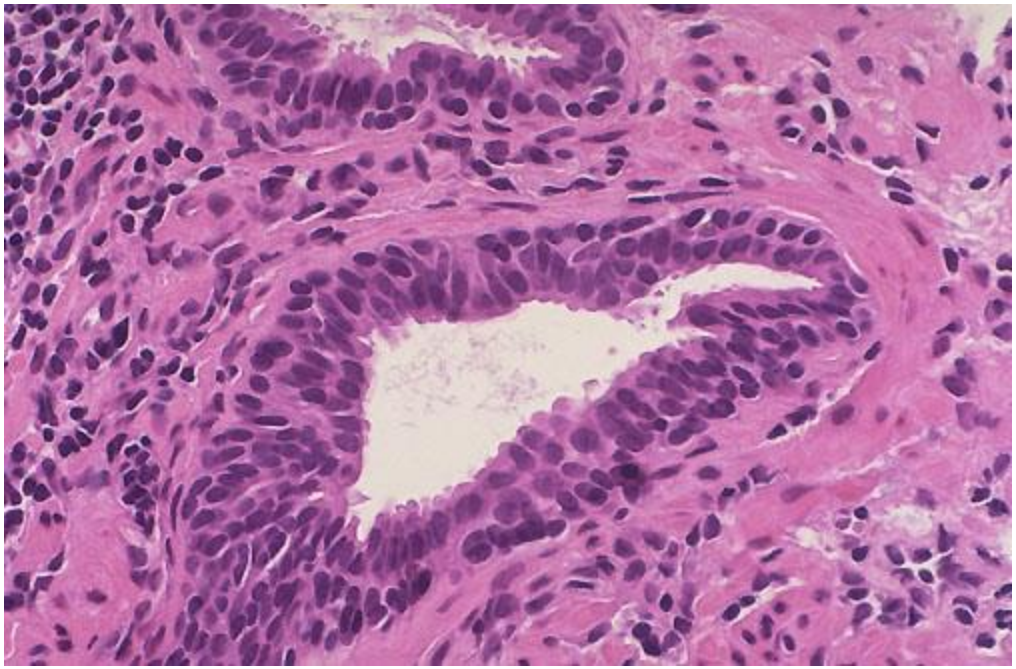
Complications of prostatic hyperplasia



Carcinoma of the prostate gland

- One of the commonest cancer seen in males
- A tumour of elderly
- Aetiology-unknown; probably hormone related
- A positive family history increases the risk
- BNH is not a pre neoplastic lesion but it is often found coincidental with carcinoma
- Involves the posterior subcapsular area of the gland
- Is preceded by prostatic intraepithelial neoplasia (PIN)

Prostatic Intraepithelial Neoplasia (PIN)

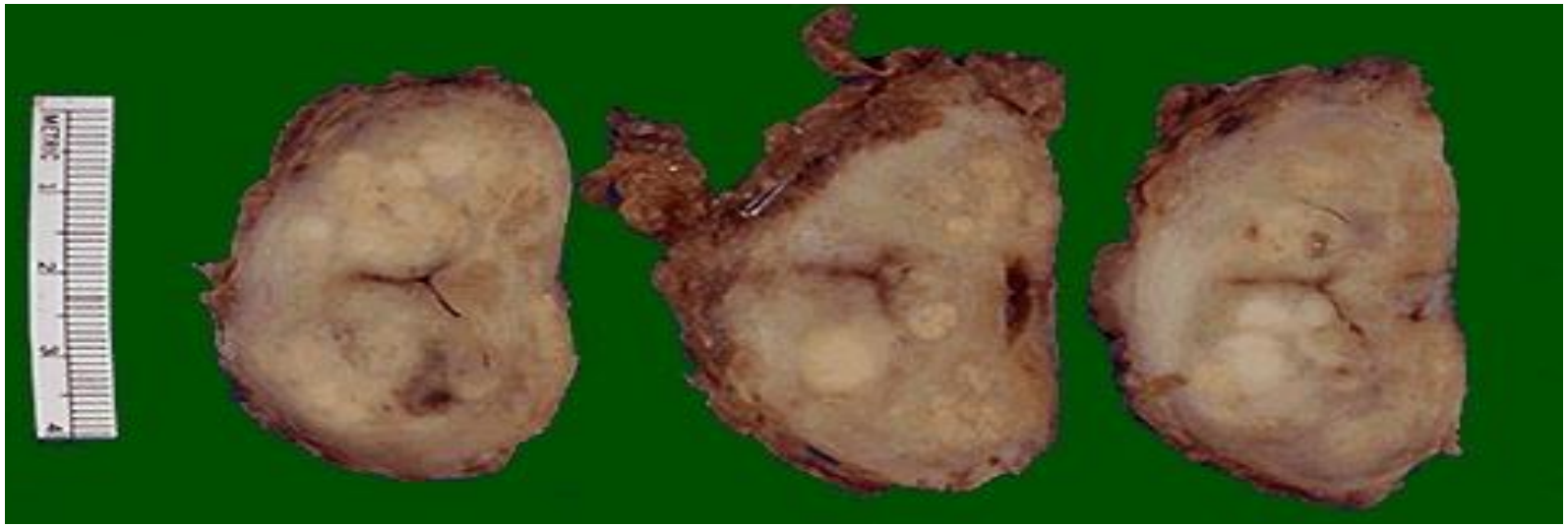


- Is a precancerous cellular proliferation
- Architecturally normal acini lined by cytologically atypical cells
- PIN could be low or high grade
- The finding of high grade PIN suggests that prostatic adenocarcinoma may also be present

Prostatic carcinoma-Clinicopathological types

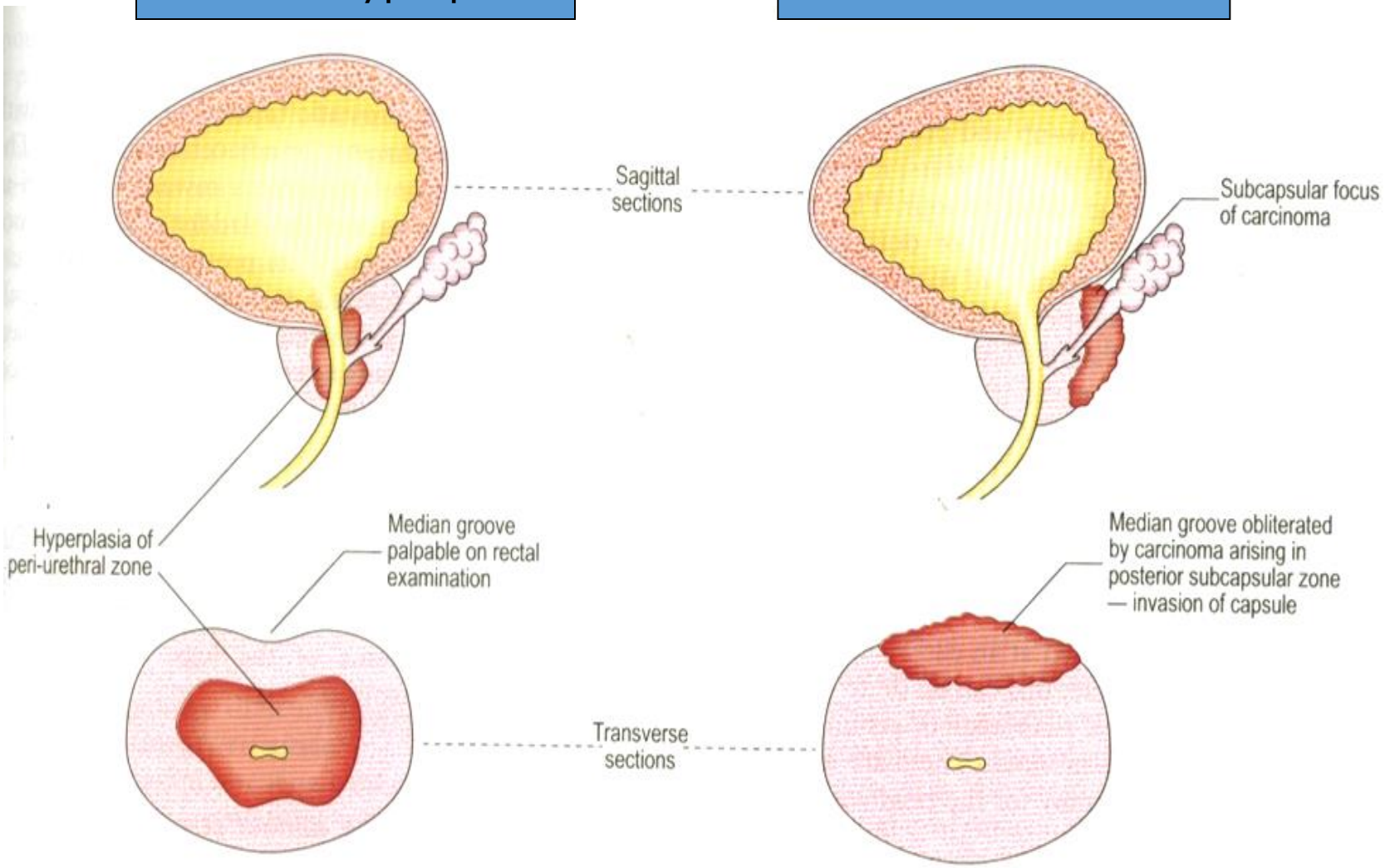
- **Clinical (symptomatic) carcinoma**
  - Important form
  - Arises in the posterior subcapsular area
  - Invades stroma and perineural spaces
  - Produces metastasis, mainly to bone
- "**Occult carcinoma**"
  - Sometimes small primary in prostate with widespread symptomatic metastasis-
- **Latent (Incidental carcinoma)**
  - Microscopic foci of cancer found incidentally on histological examination of prostates removed for BPH
  - Common , incidence is high in old age
  - Clinical significance ? read

Morphology -Prostatic carcinoma



- 70% -posterior subscapular location-palpable per rectum
- On slicing gritty and firm
- Easy to palpate than seen

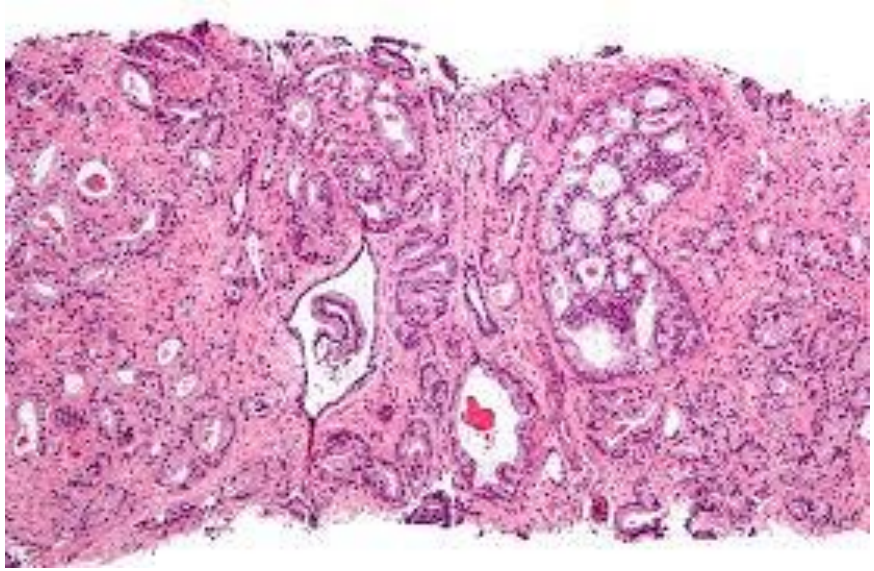
Prostatic hyperplasia versus carcinoma



Morphology -Prostatic carcinoma

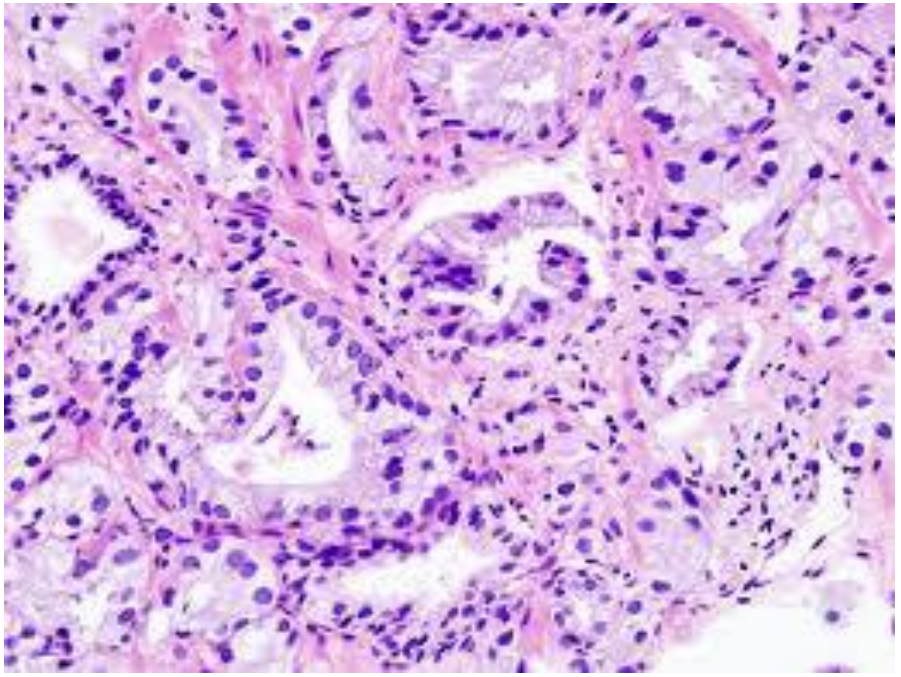
- An adenocarcinoma forming acini and tubules
- The neoplastic glands are typically smaller than normal glands, more crowded and lacks branching pattern.
- Lined by a **single layer** of cells
- Invasion of the stroma and the perineural space is seen
- Gleason's grading system which is based on architectural pattern of glands is used in determining prognosis

Microscopy of prostatic carcinoma

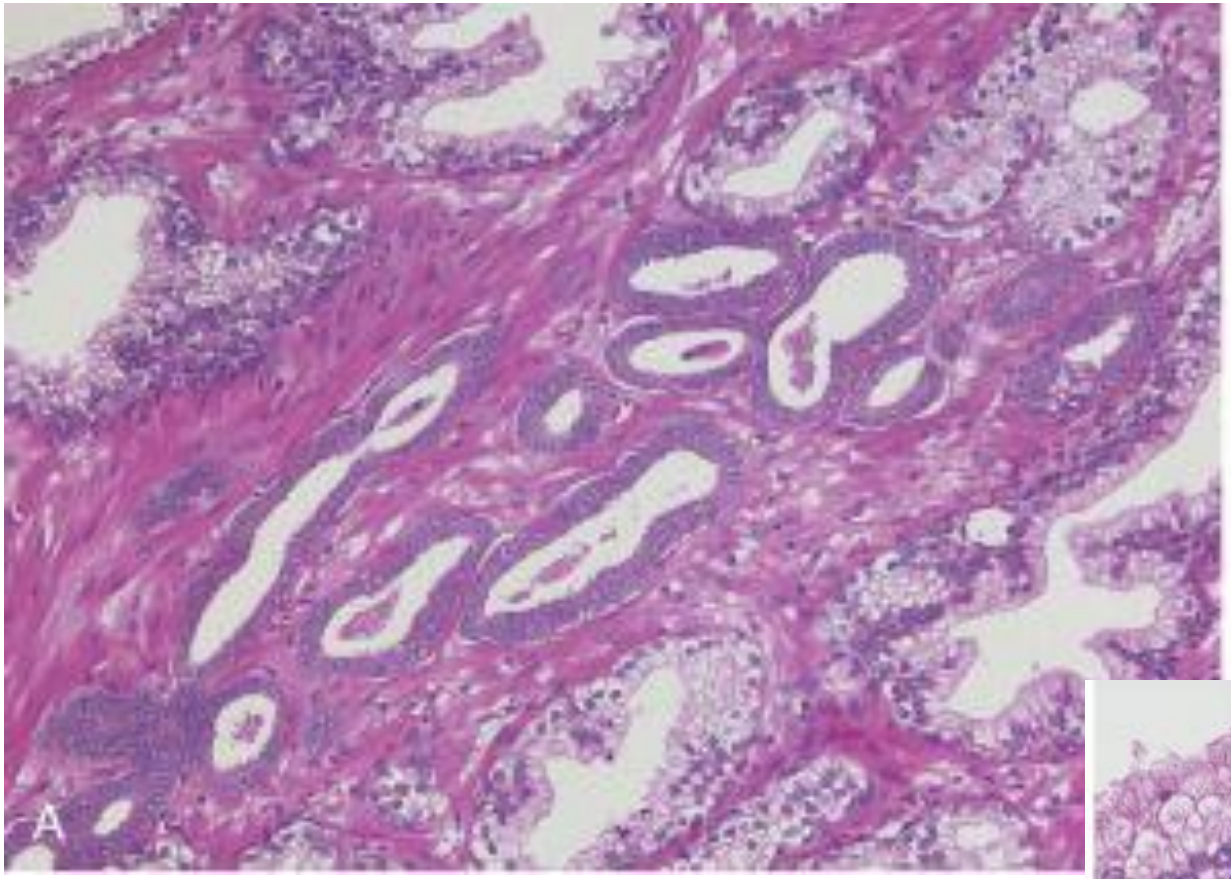


Small crowded glands

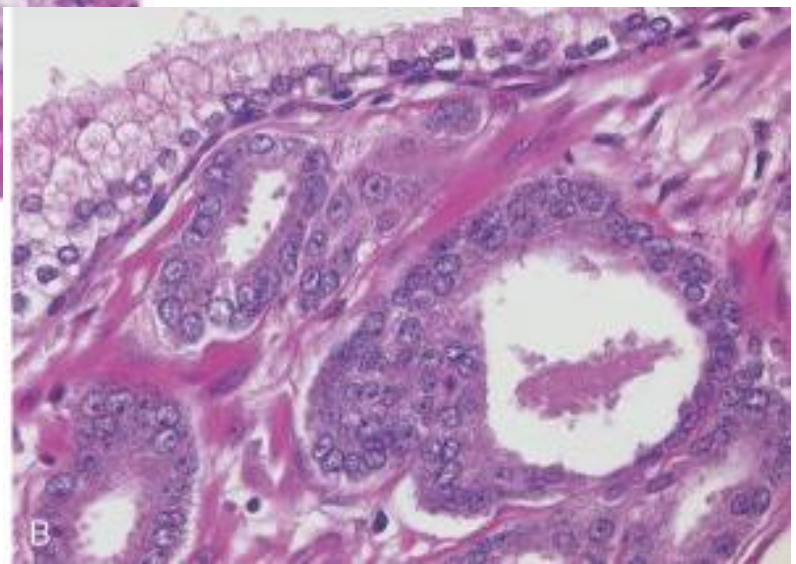
Lined by a single layer of cells



Microscopy of prostatic carcinoma



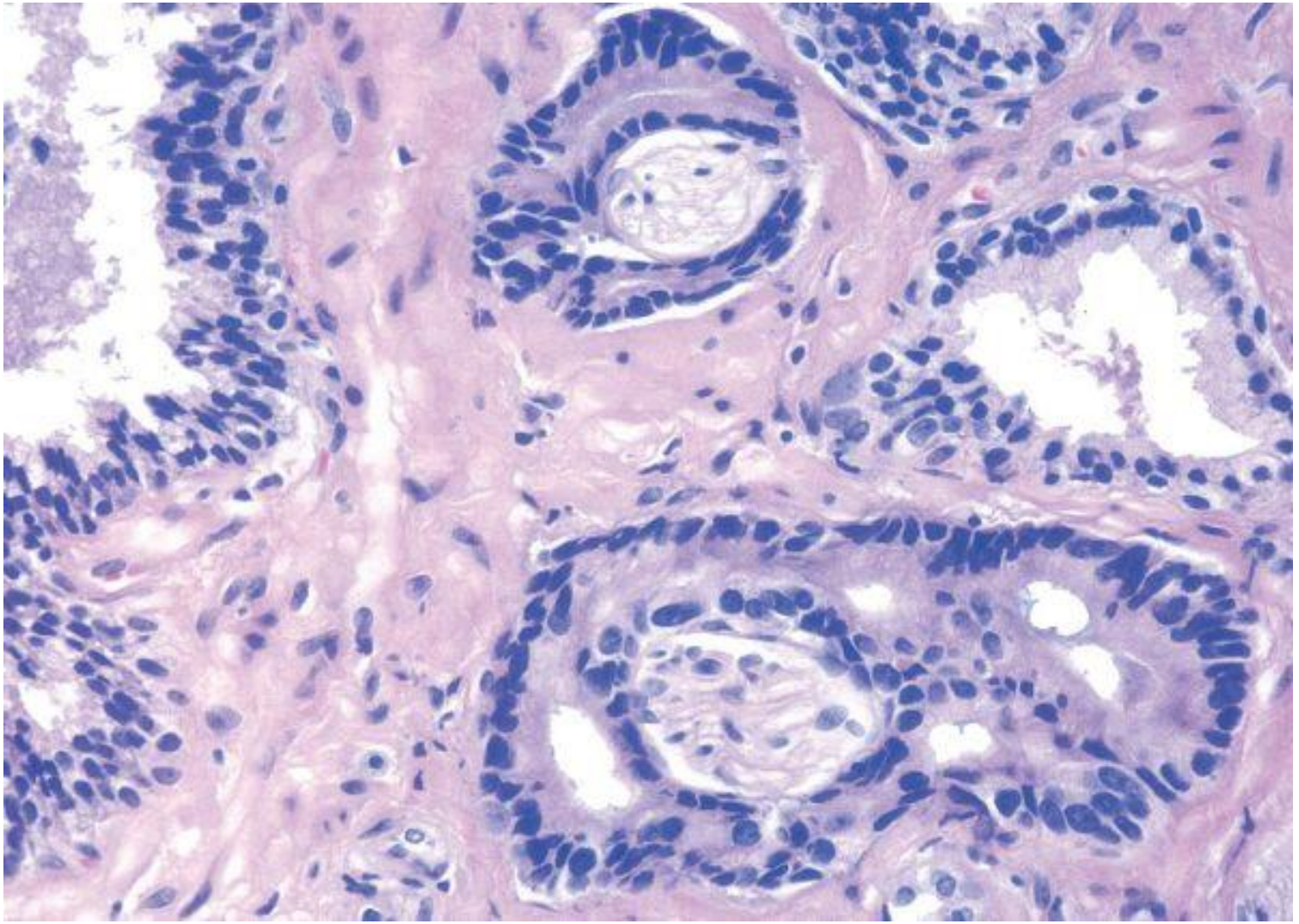
- Small focus of adenocarcinoma of the prostate
- Small glands crowded in between larger benign glands



• Small malignant glands with enlarged nuclei, prominent nucleoli, and dark cytoplasm

Carcinoma of the prostate gland- spread

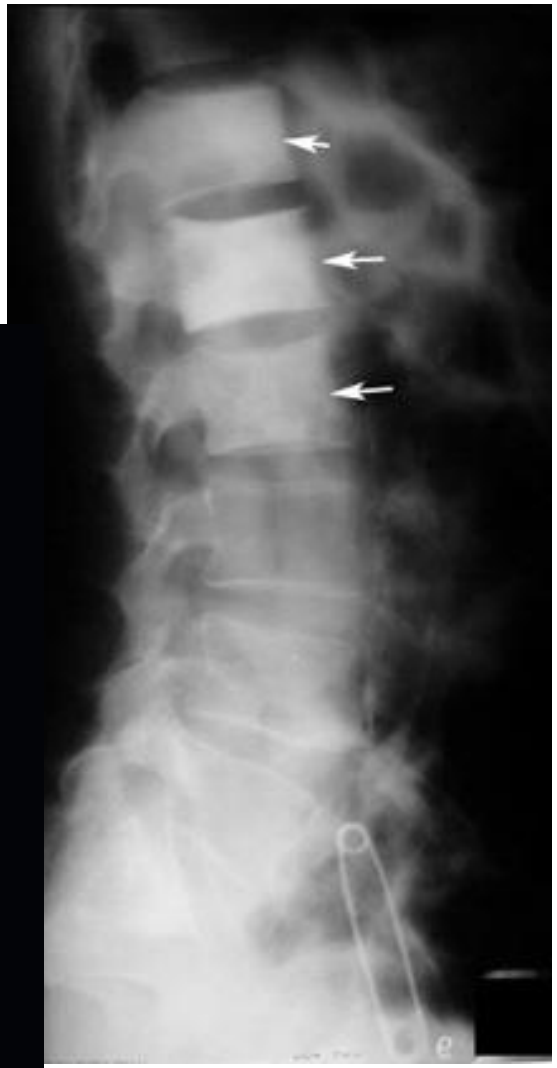
- Direct spread
  - stroma-capsule-urethra-bladder base – seminal vesicle
- Lymphatic spread
  -Sacral, iliac ,para aortic nodes
- Blood spread
  - Bone
  - Lung
  - Liver



Carcinoma of prostate showing perineural invasion by malignant glands.

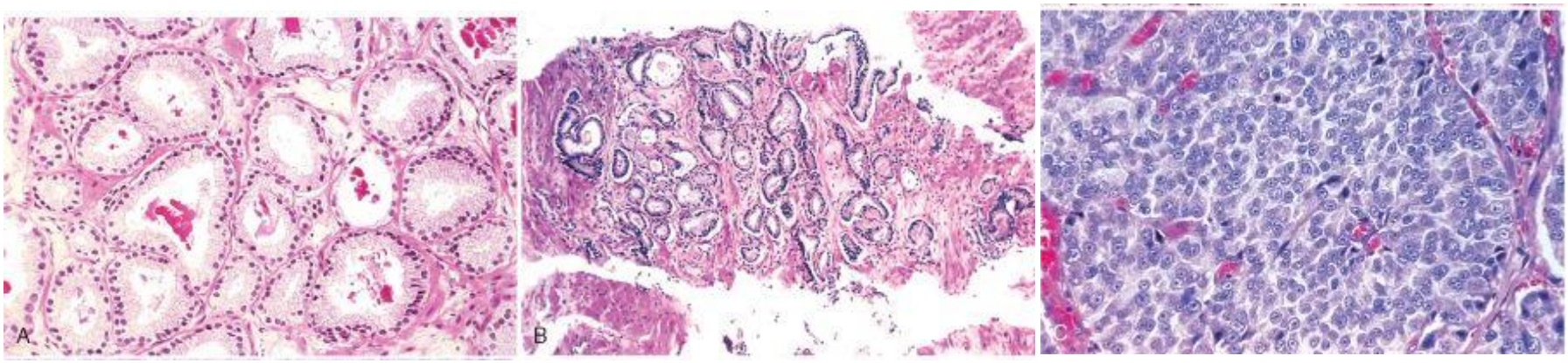
Bone metastasis in prostatic carcinoma

- Often gives osteoclerotic metastasis
- Sites-lumbar vertebrae and pelvis
- Increased alkaline phosphatase level



Grading and staging of prostatic carcinoma

- Most important prognostic factors
- Grading – based on glandular patterns of differentiation - Gleson grading 1-5



- Staging – TNM (read)

Penile tumours

- Tumours of the penis are, on the whole, uncommon.
- Most frequent are
  - Malignant -carcinoma
    - Carcinoma in-situ
    - Invasive carcinoma
  - Benign - Condyloma accuminatum

Condyloma accuminatum

- Benign sexually transmitted tumor
- Caused by human papillomavirus HPV type 6, and 11
- External genitalia or perineal areas
- Tend to recur but only rarely progress into in situ or invasive cancers

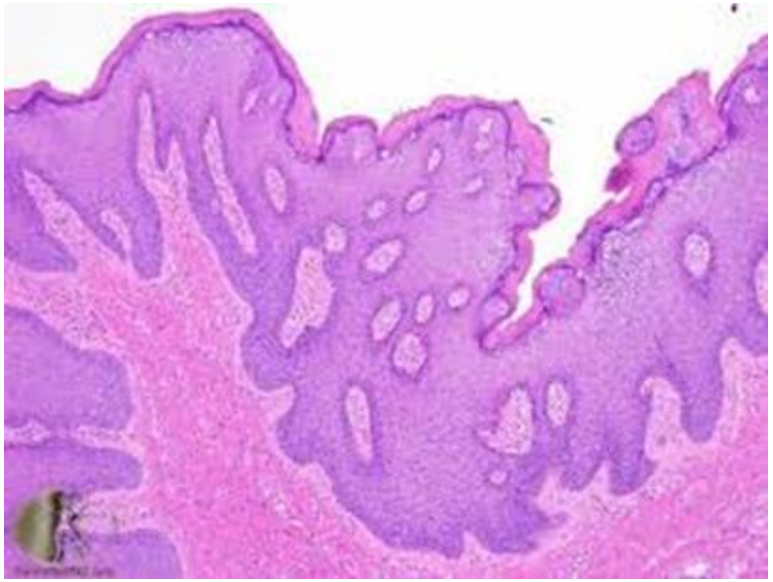
Macroscopy

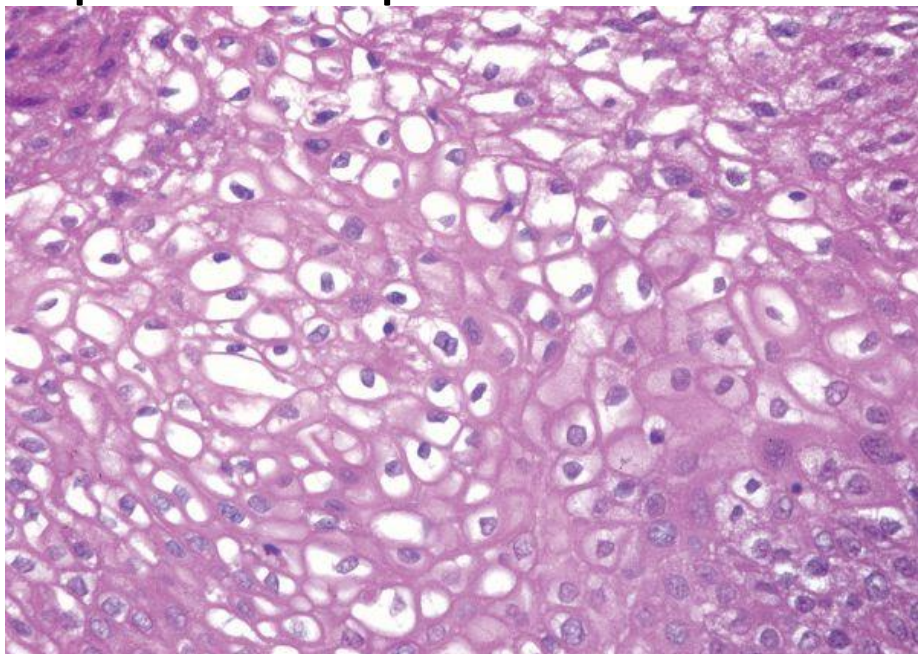
- Single /multiple
- Sessile/ pedunculated
- Red papillary excrescences

(1 mm to several mm)

Microscopy

- Epithelium covered branching, villous, papillary connective tissue stroma
- Superficial hyperkeratosis
- Acanthosis
- Orderly maturation of the epithelium preserved
- Koilocytosis

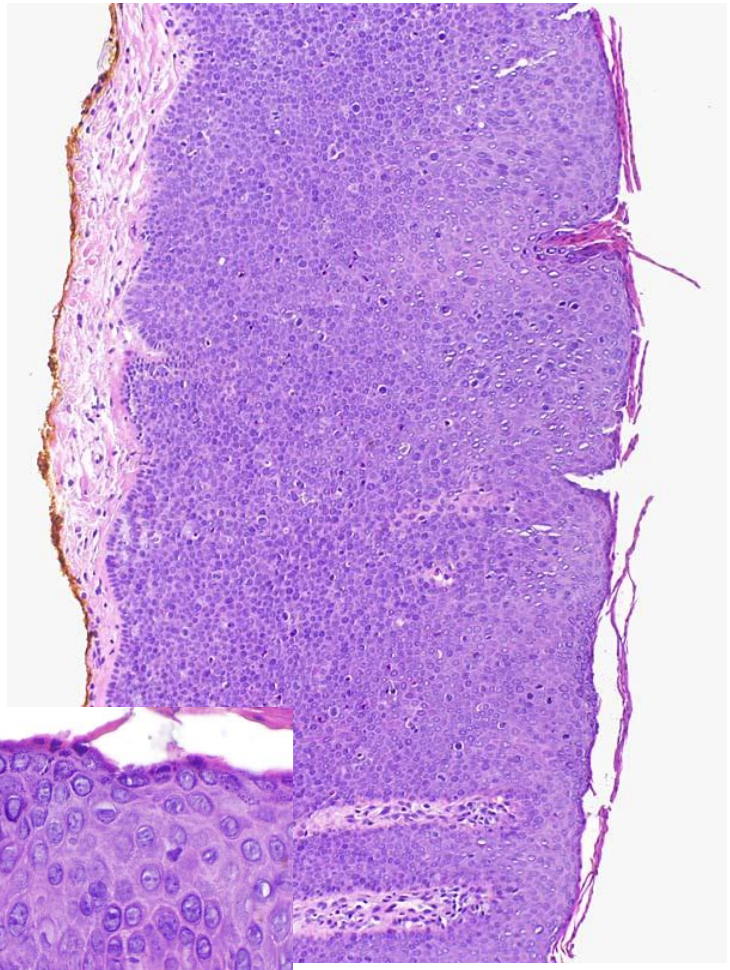


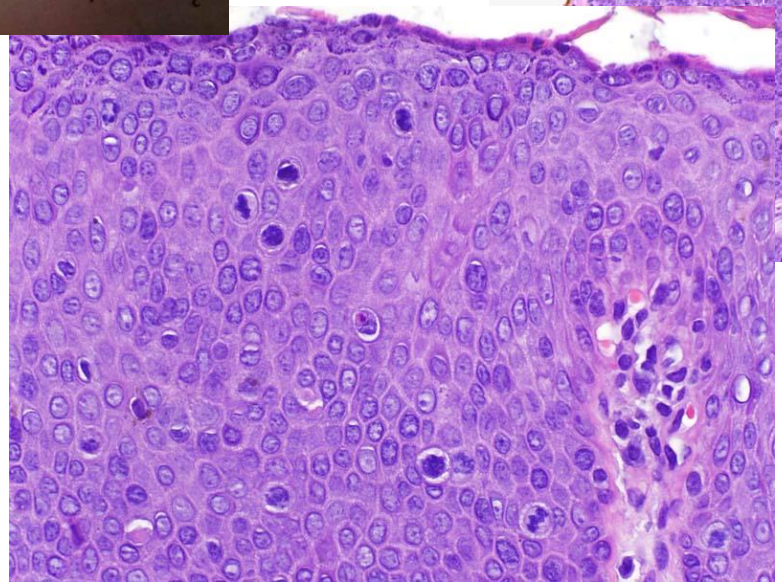


Carcinoma-in-situ

- Two distinct HPV (Type 16) related lesions
  - Bowen disease
  - Bowenoid papulosis
- Both show similar histological features
  - Epidermal proliferation with numerous mitoses
  - Atypical mitoses
  - Markedly dysplastic cells
  - Intact basement membrane

Carcinoma in-situ





Bowen disease

- Over the age of 35
- Solitary, thickened, gray white plaque on shaft of penis
- Single/multiple shiny red plaques on glans
- In 10% transform into invasive SCC

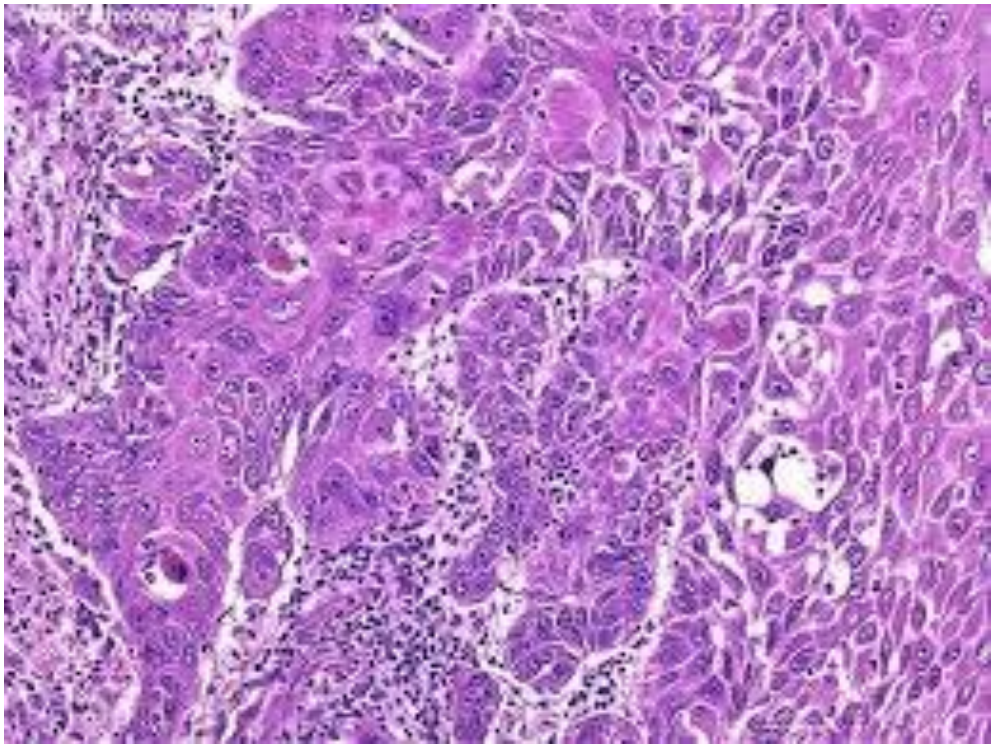
Bowenoid papulosis

- Sexually active adults
- Multiple reddish papules
- Never develops into invasive carcinoma

Invasive squamous cell carcinoma of penis

- Relatively common in Asian and African population
- Related to HPV (type 16)
- Extremely rare in circumcised males
- Macroscopically-
  - Glans penis or inner side of prepuce
  - Indurated nodule/plaque or ulcer
- Microscopically - well differentiated squamous cell carcinoma

Penile cancer



Scrotal swelling

- Painful
  - Orchitis (Epididymitis)

- Painless
  - Hydrocele
  - Haematocele
  - Varicocele
  - Tumours

Orchitis

- Due to infections in the UT → epididymis→ spermatic cord (vas deferens /lymphatics) →testis
- Uncommon in children, usually associated with a congenital genitourinary abnormality and infection with gram-negative rods
- In sexually active young men , the sexually transmitted pathogens C. trachomatis and Neisseria gonorrhoeae
- In older men common urinary tract pathogens, such as E. coli and Pseudomonas

Morphology

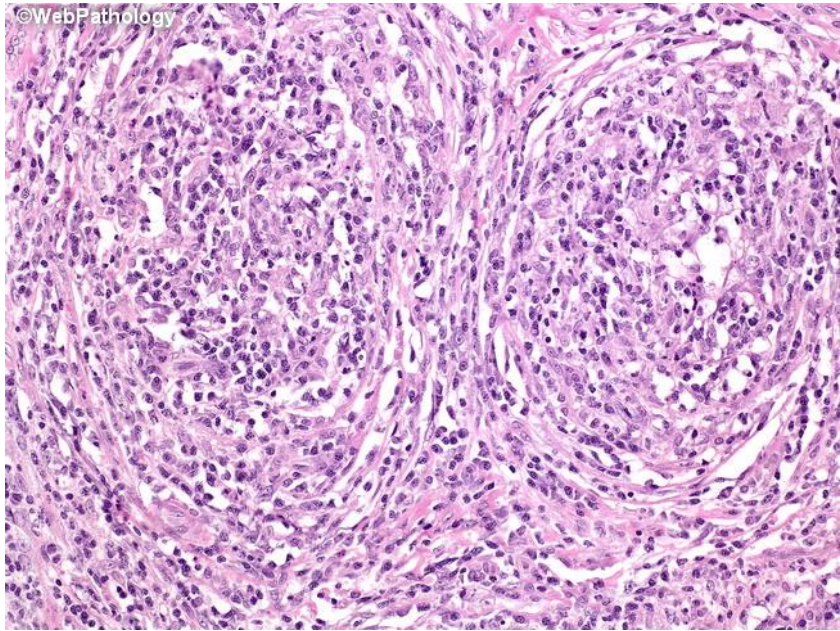
- Nonspecific acute inflammation limited to the interstitial connective tissue
- Extends to involve the tubules → progress to frank abscess formation

Granulomatous Orchitis

- Idiopathic ? Autoimmune
- Middle age males
- Tender testicular mass of sudden onset , fever +/- or insidious painless testicular mass mimicking a testicular tumor
- Histologically - granulomas restricted to spermatic tubules.

- Distinct granulomas are not present

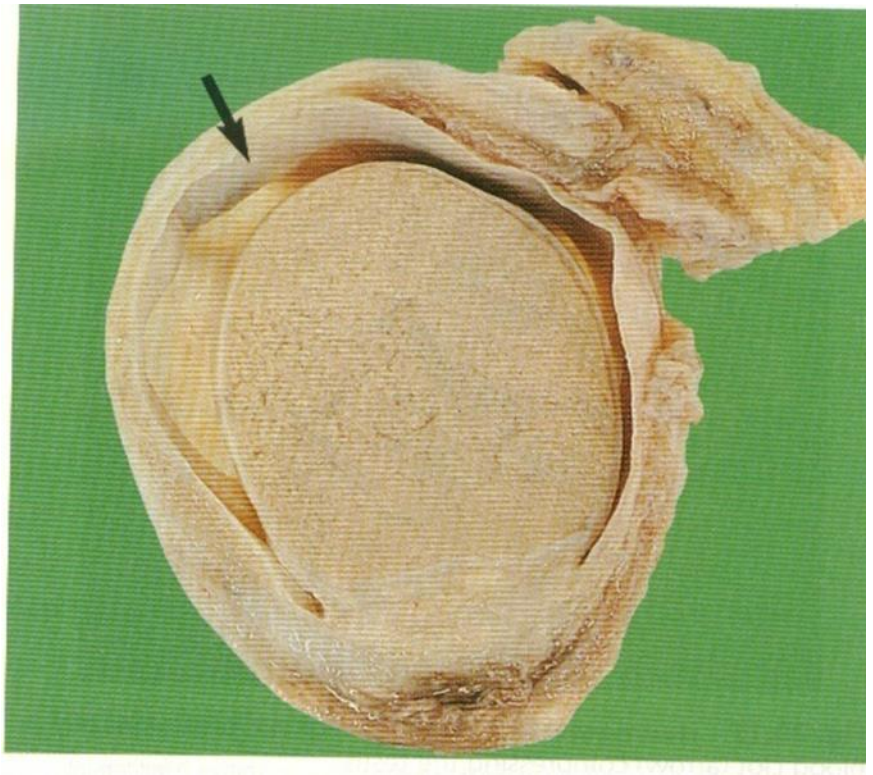
- Accumulation of epithelioid histiocytes, lymphocytes, plasma cells in the seminiferous tubules creates and appearance of granulomas



Hydrocele

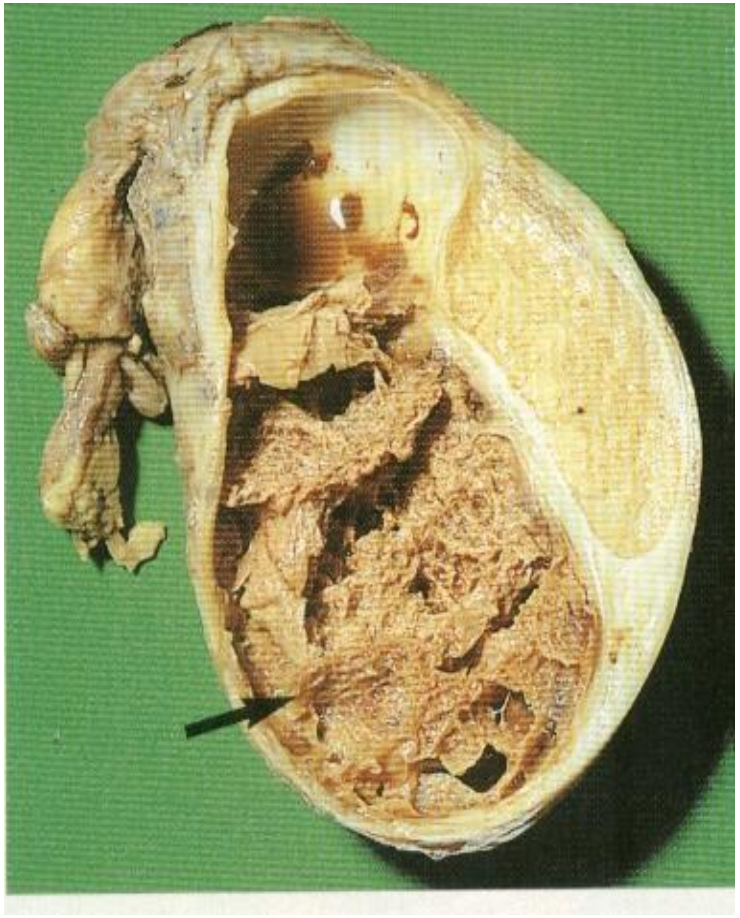
- The commonest cause for intrascrotal swelling
- Accumulation of serous fluid within the tunica vaginalis of the testis
- Congenital hydrocele - Appears in first few weeks of life
- Secondary hydrocele

- Inflammatory acute/ chronic



Haematocele

- A haemorrhage into tunica vaginalis



Testicular tumours

- A group of tumours that occurs predominantly in young males
- Majority (95%) derived of germ cells.
- Others are derived of sex cord-stromal cells, sertoli cells and interstitial cells
- Most germ cell tumours are highly aggressive with wide dissemination; but responds very well to current therapy
- Sex cord stromal tumours are generally benign

Testicular tumours-Aetiology

- Maldescended testis
- Testicular dysgenesis syndromes
- Increase in oestragenic substances in the environment
- Strong familial predisposition

Cryptorchidism

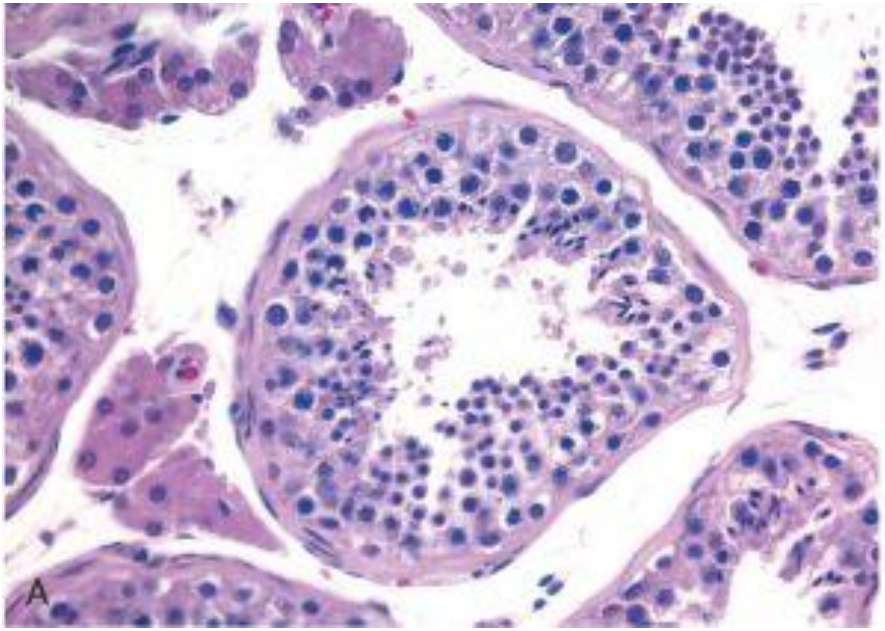
- Complete or incomplete failure of the intra-abdominal testes to descend into the scrotal sac
- Occurs as an isolated anomaly but may be accompanied by other malformations of the genitourinary tract, such as hypospadias
- Testicular descent occurs in two morphologically / hormonally distinct phase

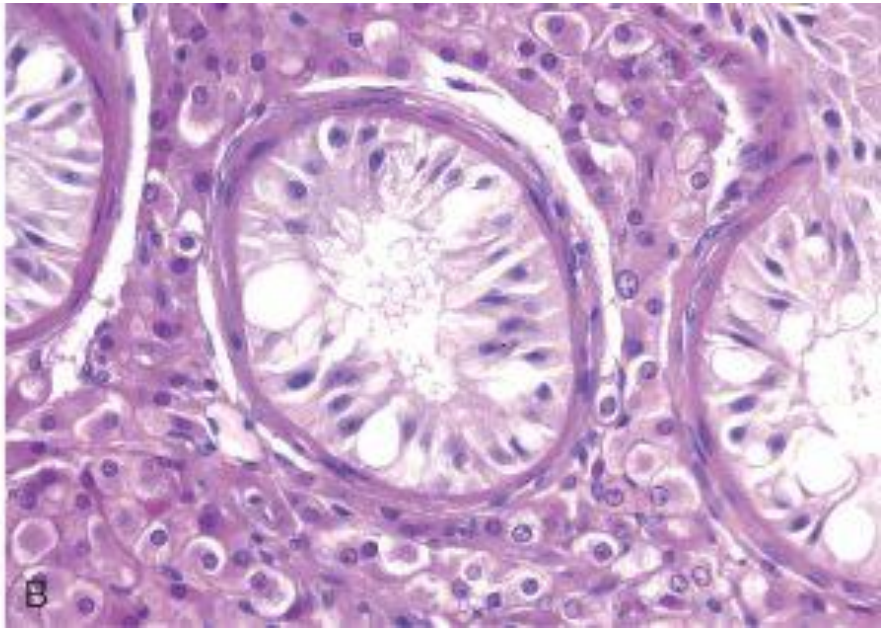
1. Trans-abdominal phase; testis comes to lie within the lower abdomen/ brim of the pelvis. Controlled by müllerian-inhibiting substance
2. Inguino- scrotal, phase; the testes descend through the inguinal canal into the scrotal sac, mediated by androgen-induced release of calcitonin gene–related peptide, from the genitofemoral nerve

- Arrested may occur anywhere along pathway of descent
- Defects in trans-abdominal descent are uncommon

Cryptorchidism - Morphology

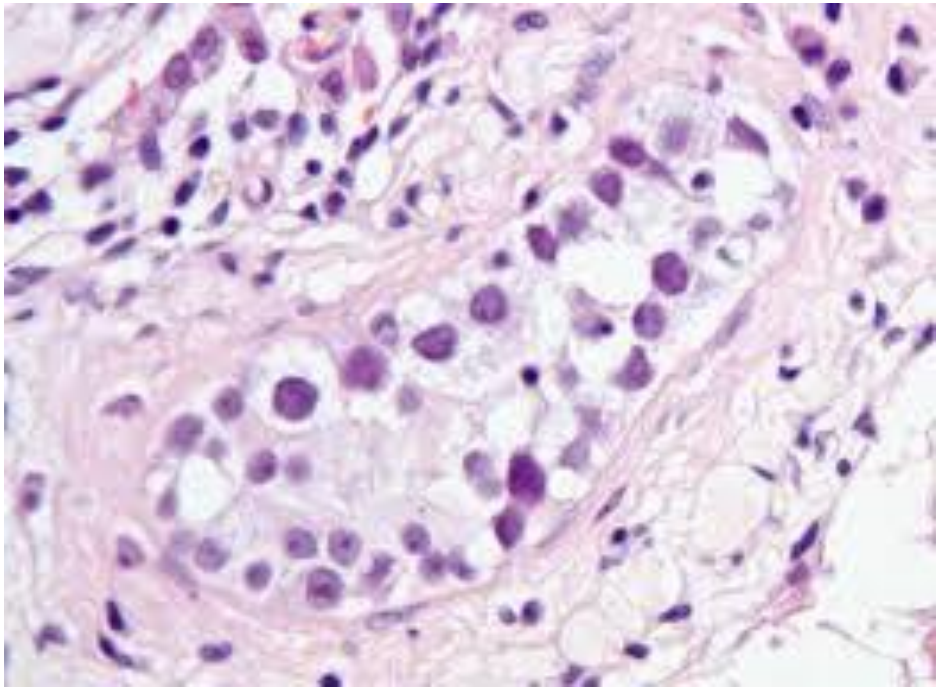
- Small in size and is firm in consistency
- Arrest in the development of germ cell
- Marked hyalinization and thickening of the basement membrane
- Tubules - dense cords of hyaline connective tissue outlined by prominent basement membranes
- Increase in interstitial stroma
- Leydig cell hyperplasia



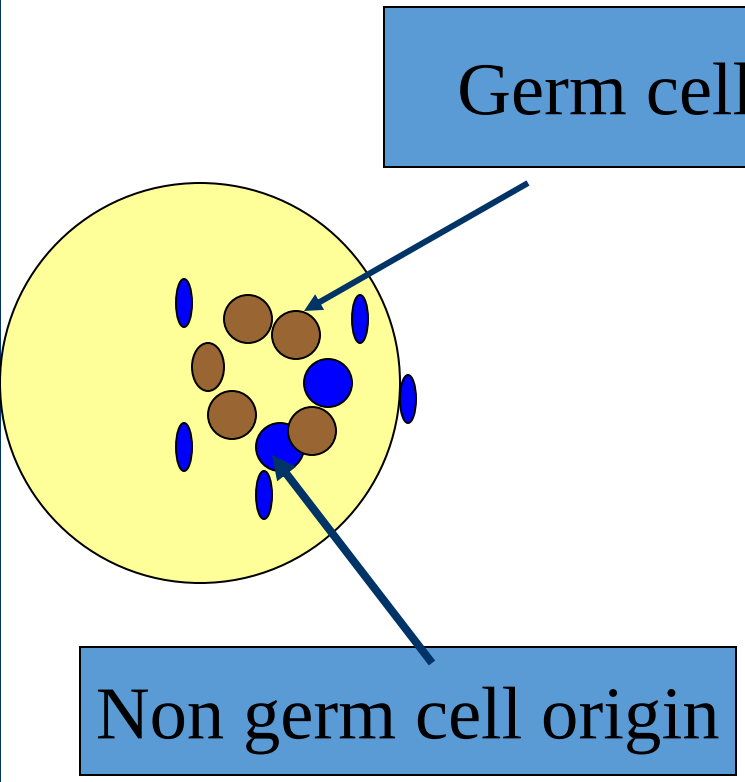


Germ cell neoplasia in-situ (ITGCN)

- Precursor lesion of testicular germ cell tumours
- Carcinoma-in-situ in seminiferous tubules
- Large and pleomorphic cells in tubules
- Also seen in cryptoorchid testis



Testicular tumours-classification



- **Seminoma**
- **Non seminomatous germ cell tumours (NSGCT)**
  - Teratoma
  - York sac tumour
  - Embryonal carcinoma
  - Choriocarcinoma

Mixed germ cell tumours

Sex cord stromal
- Leydig celltumour
- Sertoli cell tumour

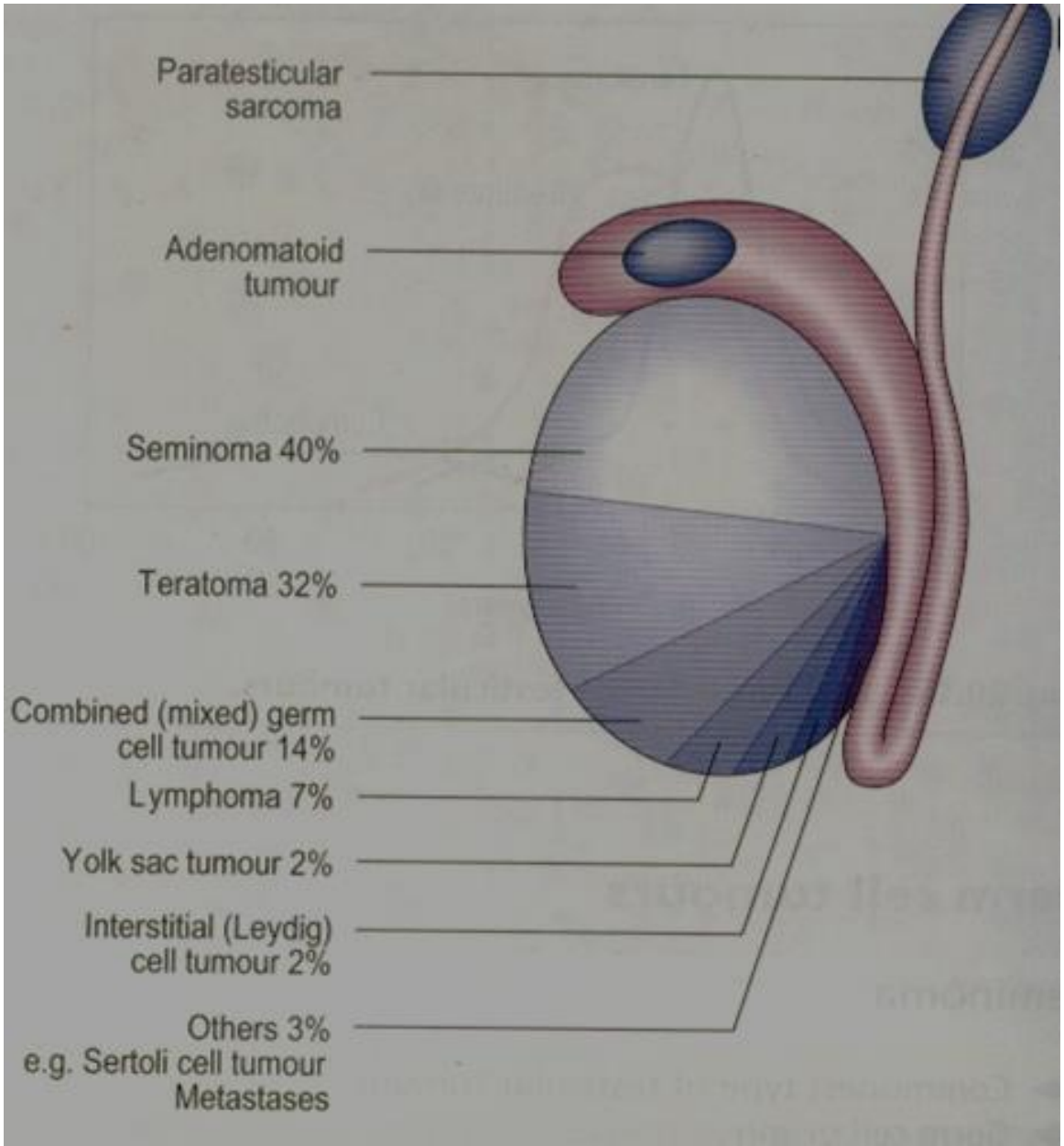
Lymphomas

sarcomas

Germ cell tumours-classification

- Different systems are being used by Americans and British
- Simply
  - Seminomas-tumour cells resemble primodial germ cells
  - Non seminomatous tumours- undifferentiated cells that differentiate into various lineages
    - Embryonic stem cell- Embryonal carcinoma
    - Extraembryonic- York sac tumour
    - Trphoblastic - Choriocarcinoma
    - Somatic- Teratoma
- Some tumours – admixture of seminomatous and non seminomatous components

Testicular tumours-classification



Testicular tumours-presenting features

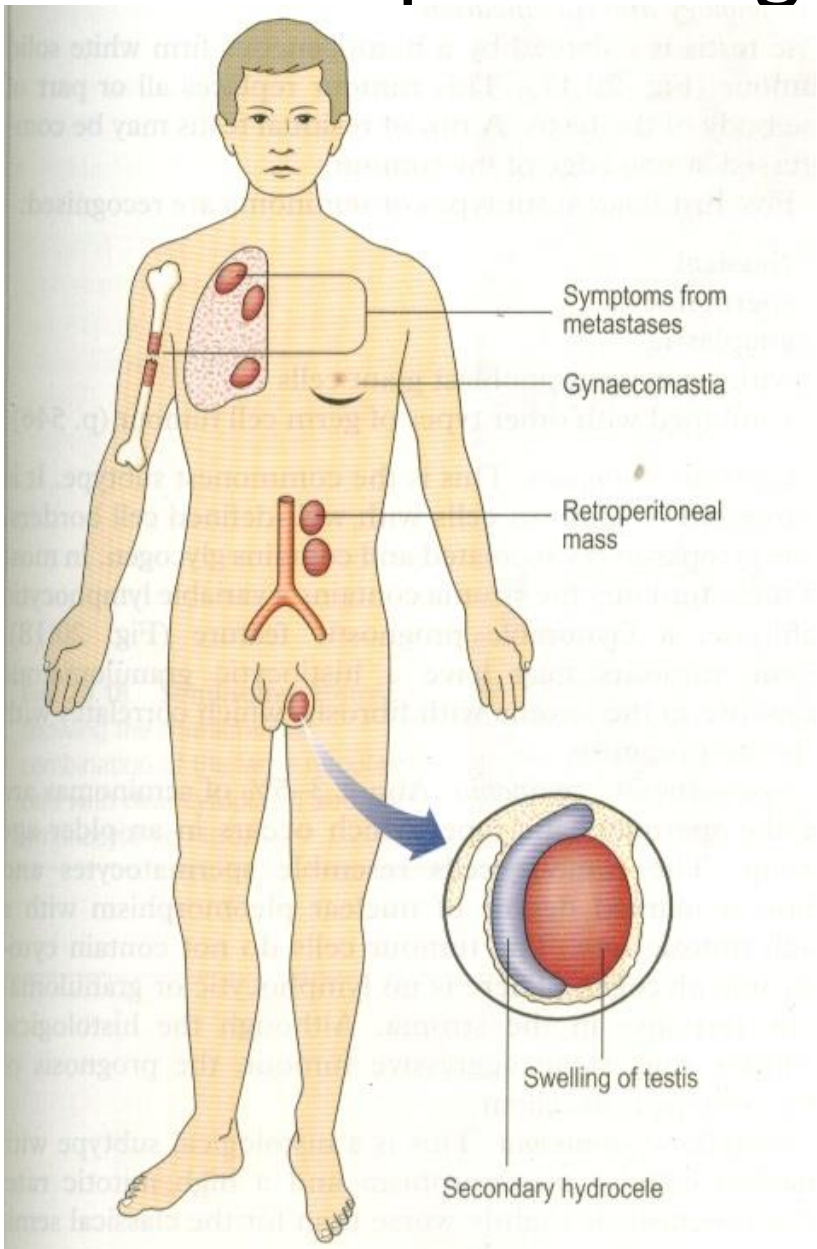


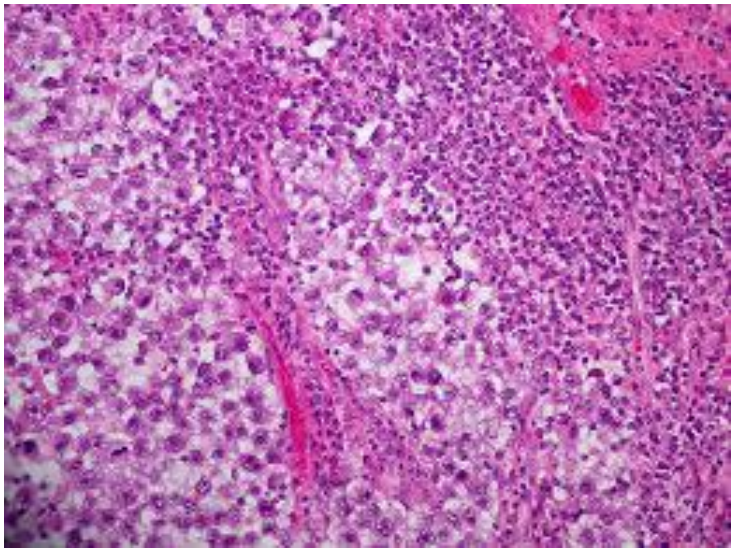
Fig. 20.14 Presenting features of testicular tumours.

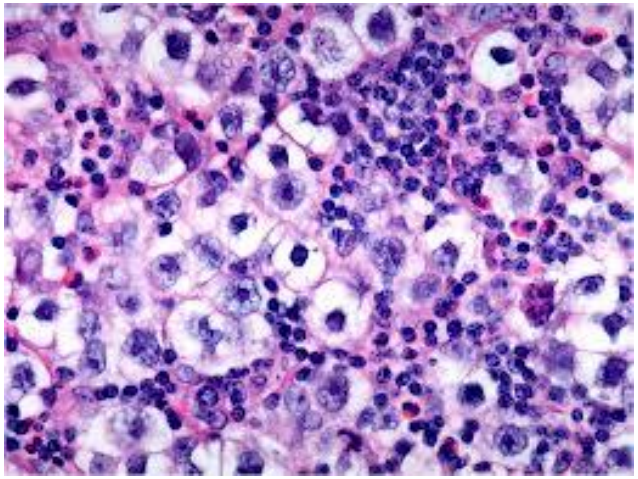
Seminoma

- The commonest type of testicular tumour
- Germ cell origin
- Peak incidence occurs in 30-50 years of age
- The testis is enlarged by homogenous firm whitish tumour
- Usually no haemorrhage or necrosis

Seminoma

- The tumour is composed of large cells with clear cytoplasm separated by lymphocyte rich stroma.





- Histologically identical to ovarian dysgerminoma (ref Ovarian tumours)
- Responds to radiotherapy well.

Teratoma

- A tumour representing differentiation of germ cells along somatic cell lines
- Can occur at any age; infancy-adult life
- Peak incidence is 20-30 years
- Tumour composed of tissue representing endoderm, mesoderm and ectoderm

Teratoma

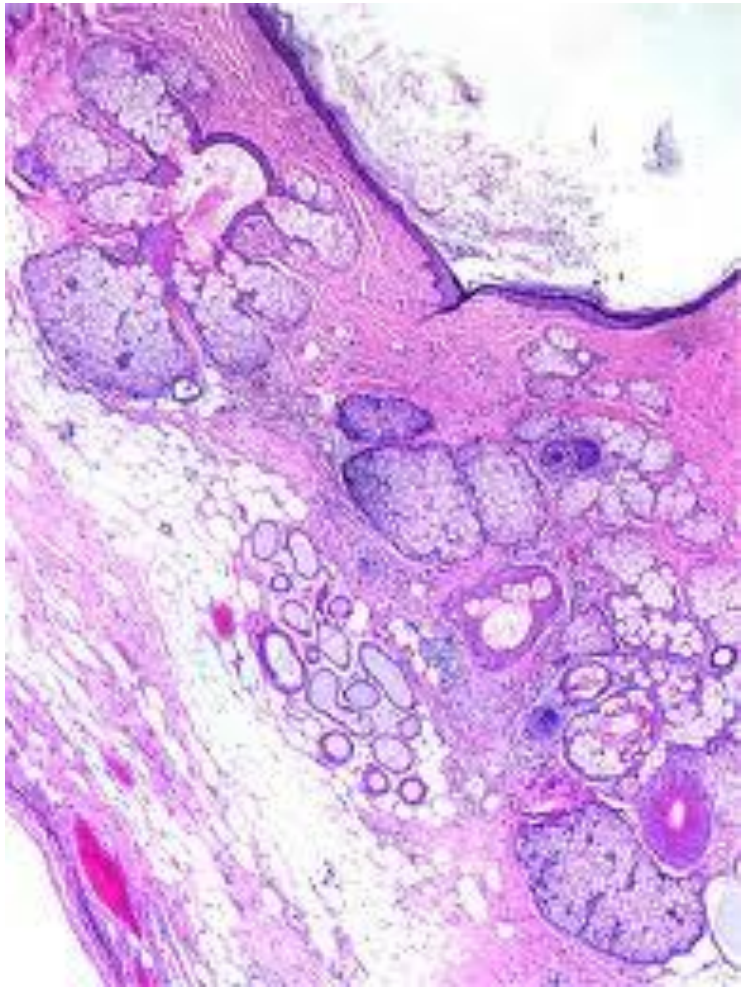
- In contrast to seminoma heterogenous appearance
- Solid tumour with cystic spaces
- Haemorrhage and necrosis

Microscopy- teratoma

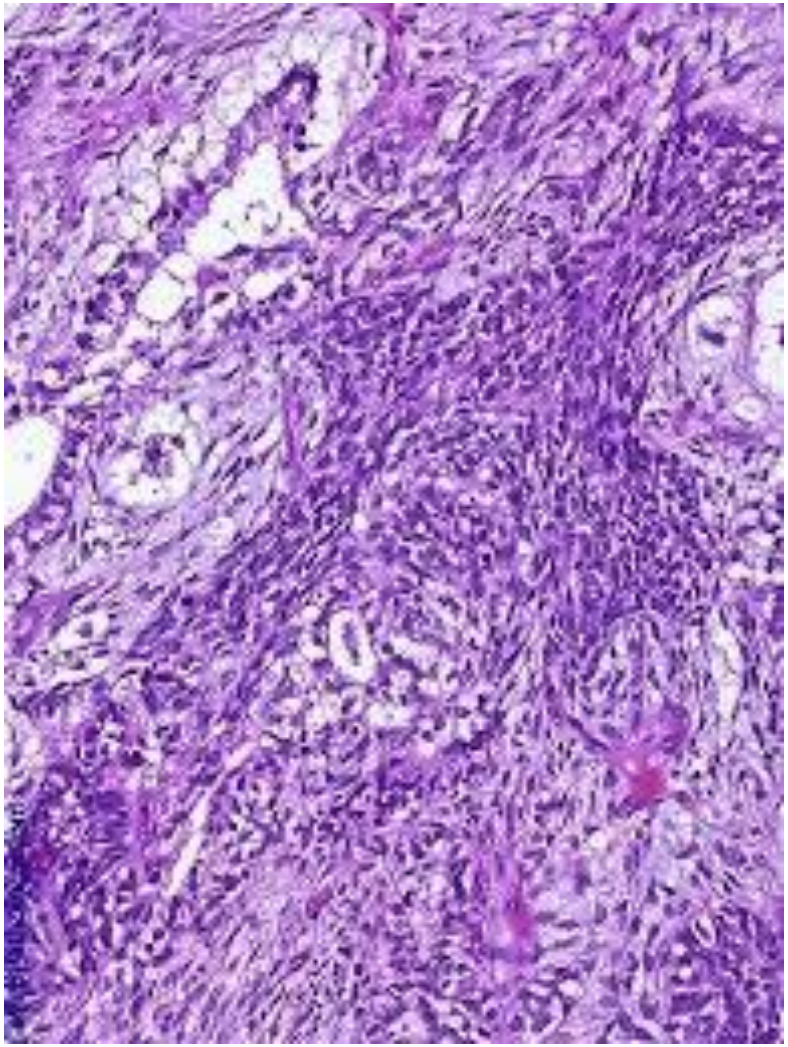
- Composed of heterogenous collections of differentiated or organoid structures
  - Neural tissue, muscle, cartilage, bone, squamous islands thyroid tissue , bronchial epithelium etc
- These elements may be
  - mature-resemble adult tissue
  - Immature-resemble fetal tissue
- Malignancy can arise in these non germ cell components
  - Squamous cell carcinoma
  - Mucinous adenocarcinoma

Teratoma

- Histologically three major variants
  - Mature teratoma-contain fully mature tissue of one or more germ cell layer
  - Immature teratoma - contain immature somatic elements reminiscent of those of developing fetal tissue
  - Teratoma with malignant transformation – development of frank malignancy in preexisting teratomatous component



Mature teratoma



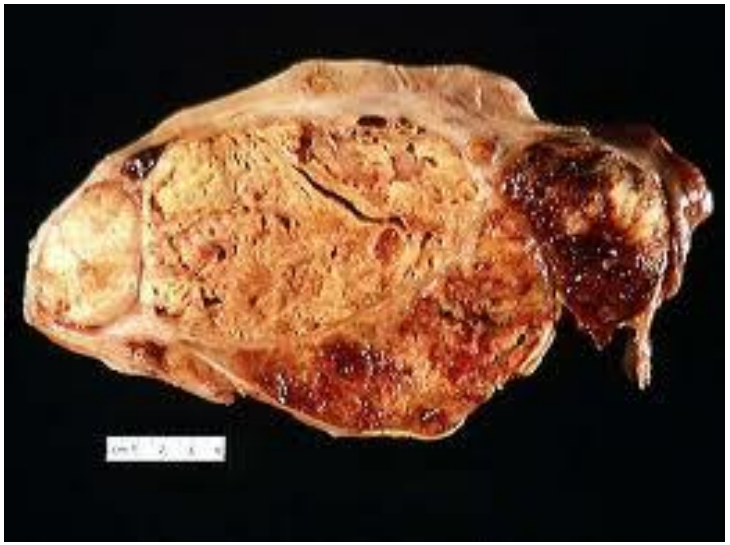
Immature teratoma

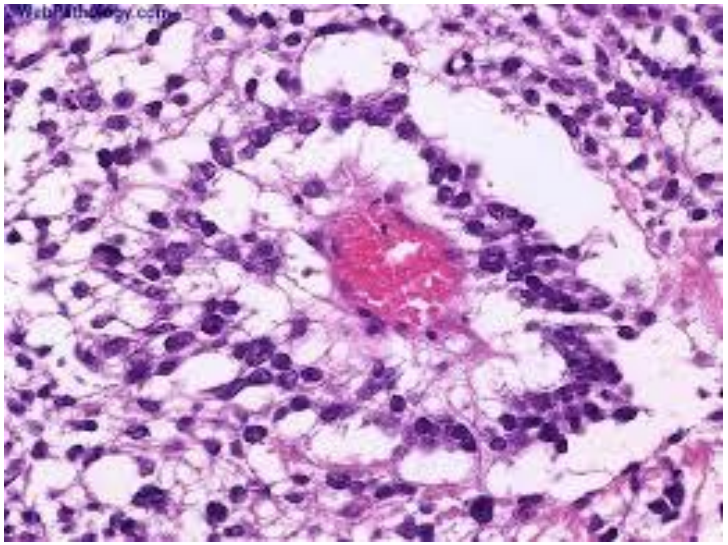
Teratomas

- Pure differentiated mature teratomas in prepubertal age is usually benign
- All testicular teratomas **in adults** are **regarded as malignant**

York sac tumour

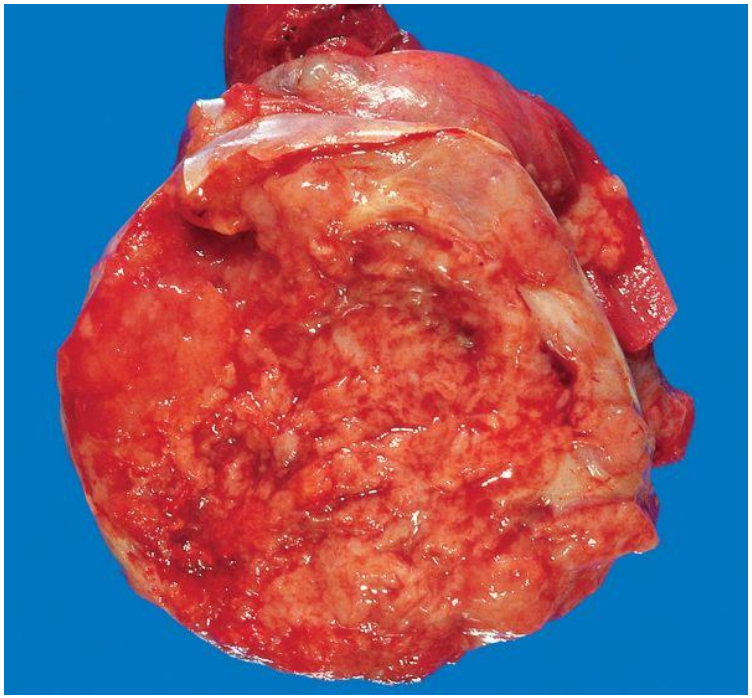
- Most common primary testicular tumour of children less than 3 years
- Good prognosis in this age group
- Alpha feto protein (AFP) levels are increased in almost all instances

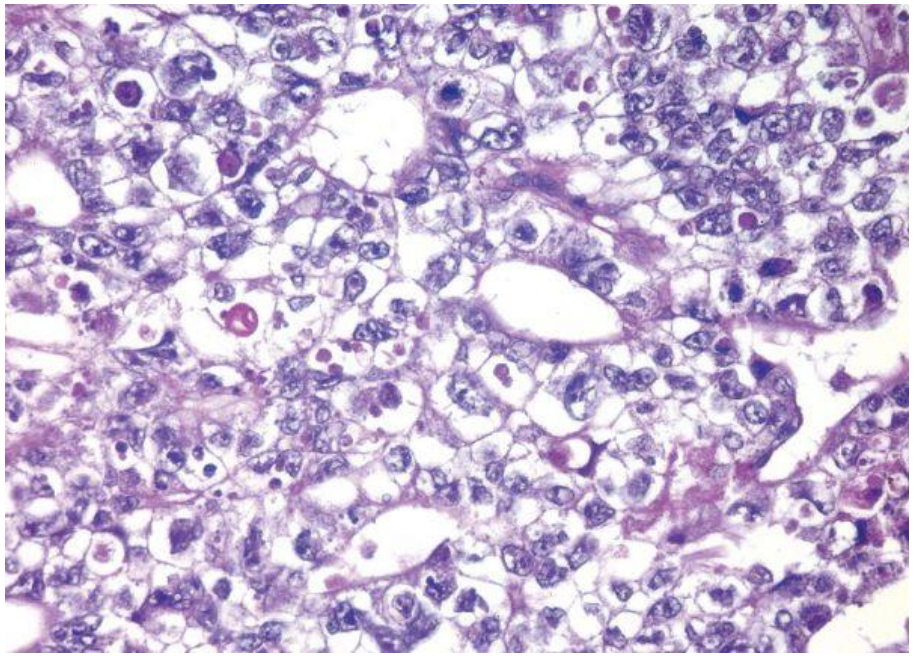




Embryonal Carcinoma

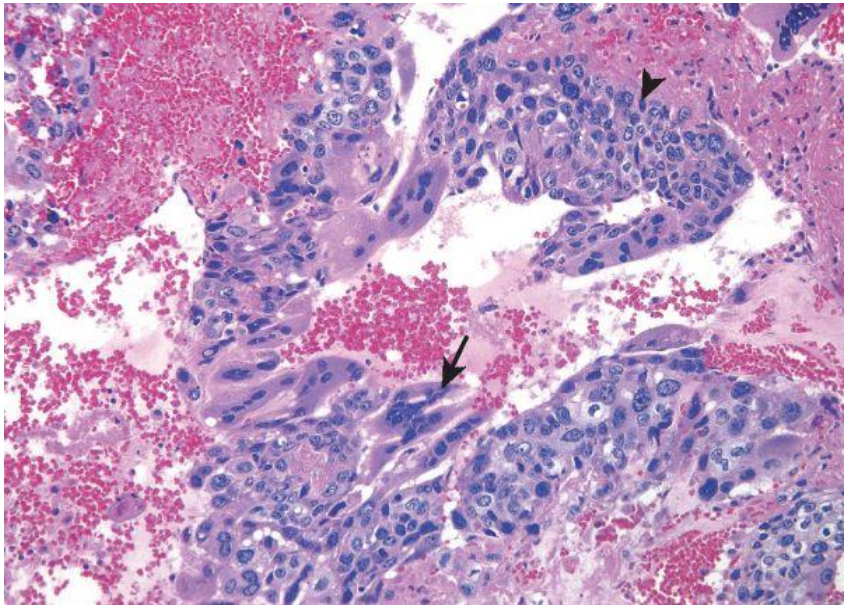
- Occur mostly in the 20- to 30-year age group
- More aggressive





Choriocarcinoma

- Highly malignant form of testicular tumor
- In its “pure” form choriocarcinoma is rare
- Hemorrhage and necrosis are extremely common
- Tumors contain two cell types syncytiotrophoblastic and cytotrophoblastic cells



Behaviour of germ cell tumours of testis

- Seminomas are confined to testis for a long duration
- NSGCT presents with advanced clinical disease
- NSGCT - haematogenous spread is frequent
- Seminomas are biologically more aggressive than NSGCT
- Seminomas are extremely radiosensitive
- NSGCT are less radiosensitive

Tumour markers in testicular tumours

- Certain tumour products appear in serum with some testicular tumours
- Important in
  - Assisting the diagnosis
  - Staging the disease
  - Assessing tumour burden
  - Monitoring the response to therapy
  - Early detection of tumour recurrence

Read further on tumour markers in testicular tumours

Tumour markers in testicular tumours

Tumour marker	Type of tumour
α feto protein (AFP)	York sac tumour
β hCG	. Choriocarcinoma . Other tumours with a trophoblastic component
PLAP	seminoma

These markers can be demonstrated in the tissue sections using immunohistochemical technique