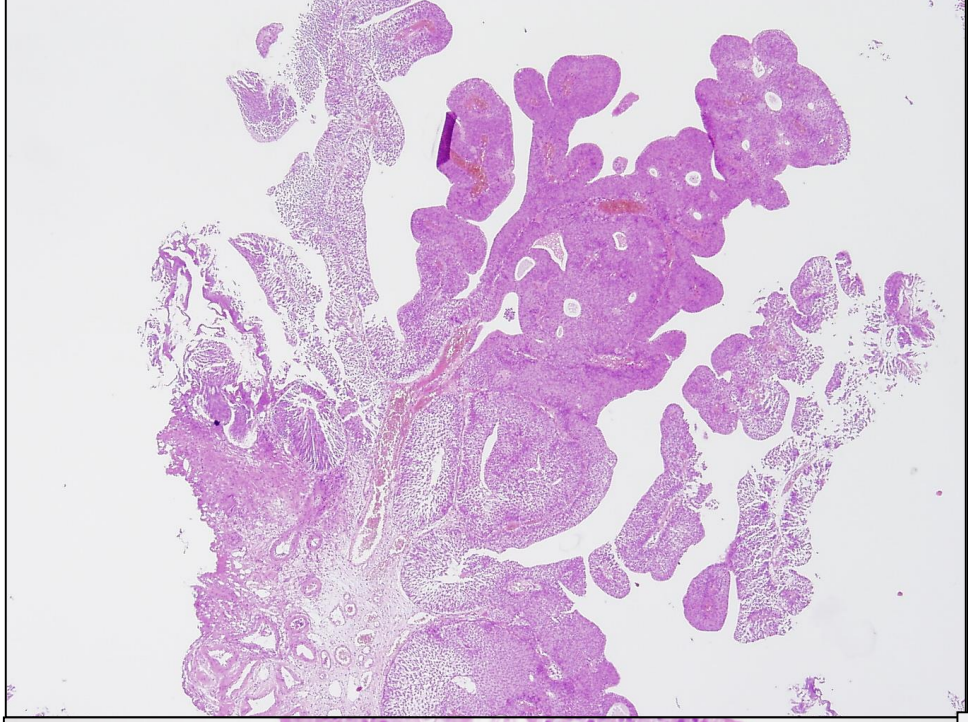
Pathology of the lower urinary tract and male genital system

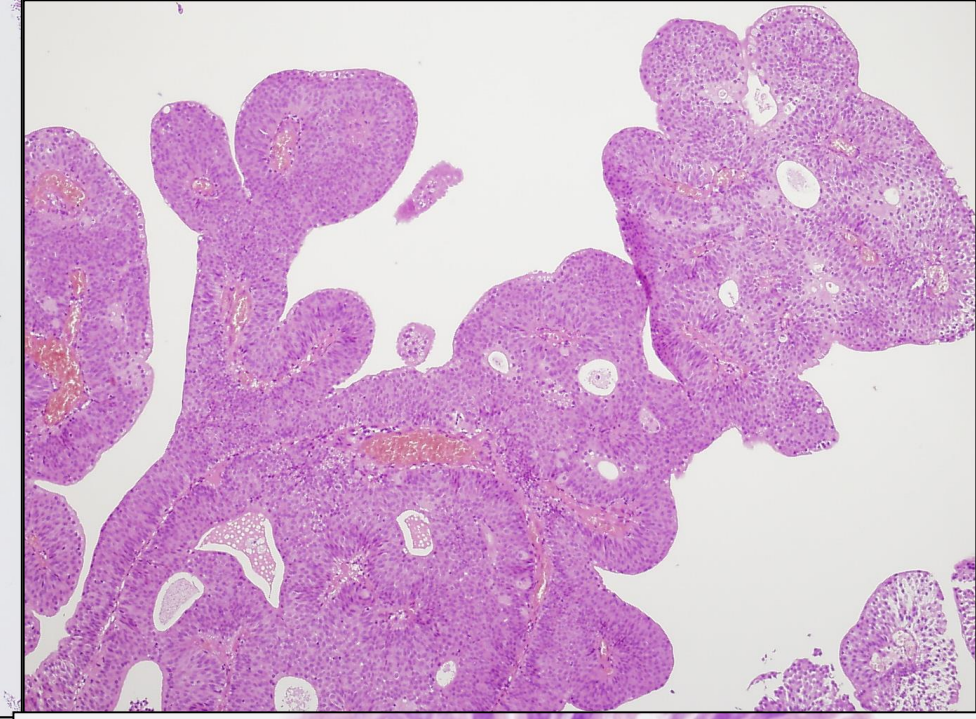
Neoplasms of the lower urinary tract

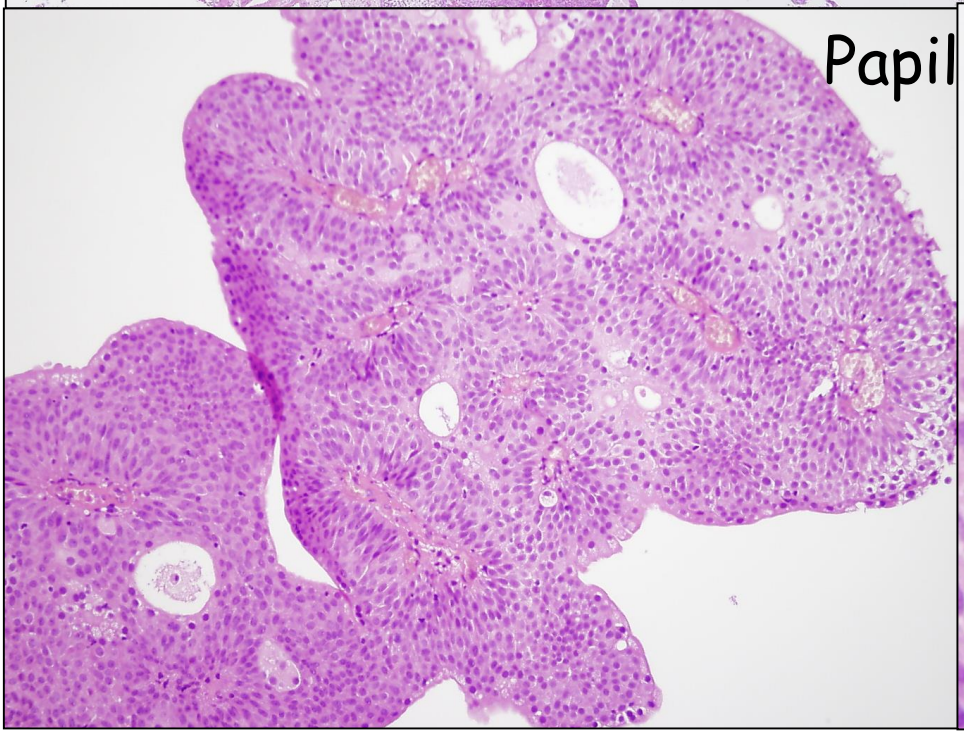
Incidence: Urinary bladder > upper urinary tract; male:female=3:1
Symptoms: **painless hematuria**, hydronephrosis → costovertebral angle tenderness (obstruction)

Etiology: **smoking**, arylamines (2-naphthylamine, benzidine), cyclophosphamide↪chronic cystitis, fast food diet, Thorotrast (radiocontrast agent)
Preventive: Increased fluid intake and vitamin A

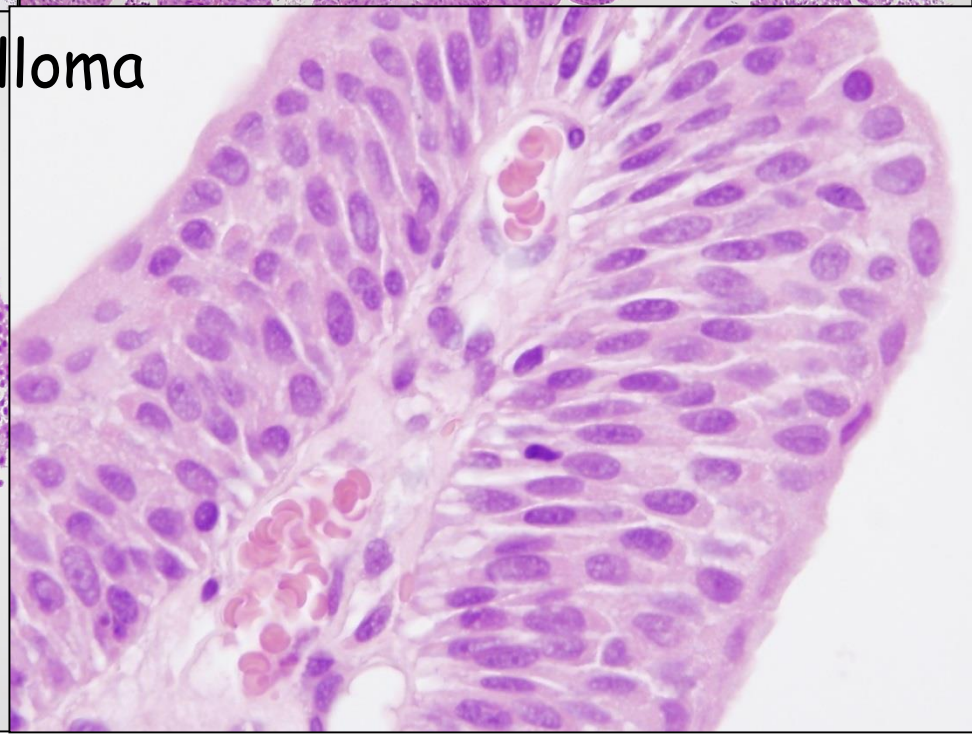
Histology: most often tumors are of urothelial origin
Prognosis depends on histologic Grade and T (level of infiltration)







Papilloma



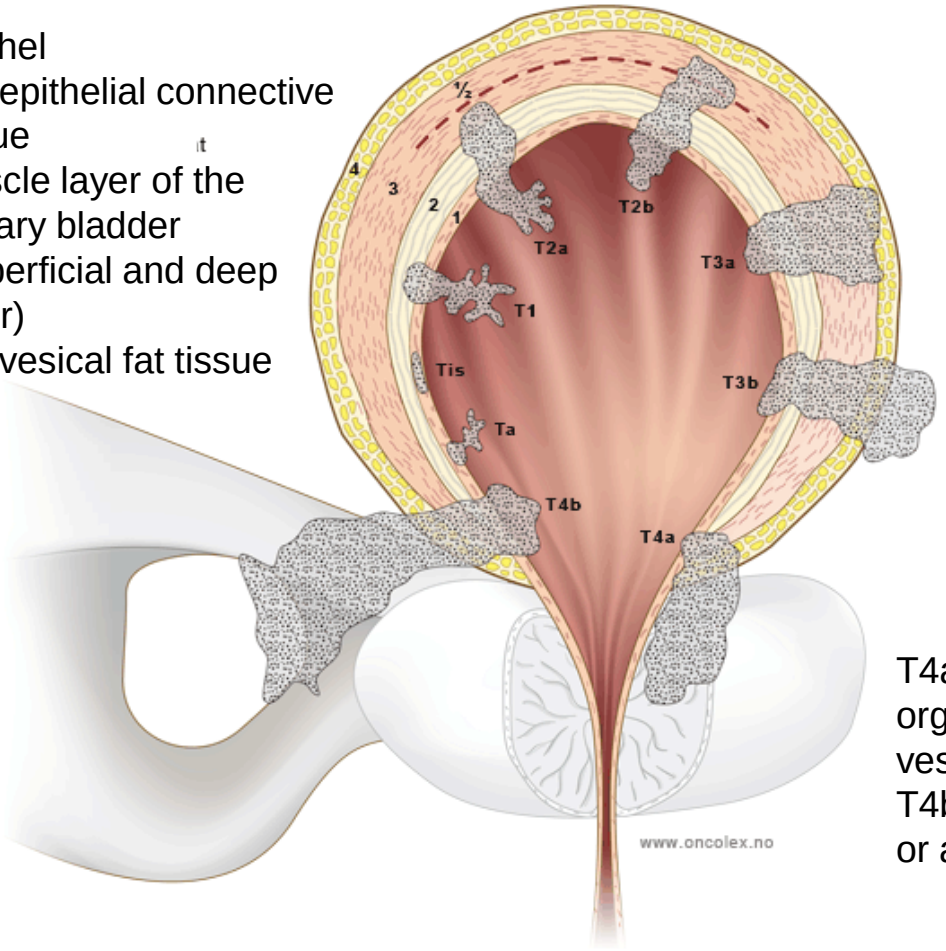
Urothelial neoplasms (Grade)

Morphological features	PUNLMP*	Low-grade	High-grade
Umbrella cells	Present	Usually present	Usually absent
Polarity	Fine	Mild – moderate disorder	Severe disorder
Cohesion	Cohesive	Cohesive	Dyscohesive
Nuclear polymorphism	Uniform	Round-oval	Marked
Nuclear polarization	Normal	Abnormal	Abnormal/absent
Hyperchromasia	Slight	Moderate	Moderate/marked
Stromal invasion	Rare	Not common	Usually present

*PUNLMP: papillary urothelial neoplasm of low malignant potential

Urothelial neoplasms (T)

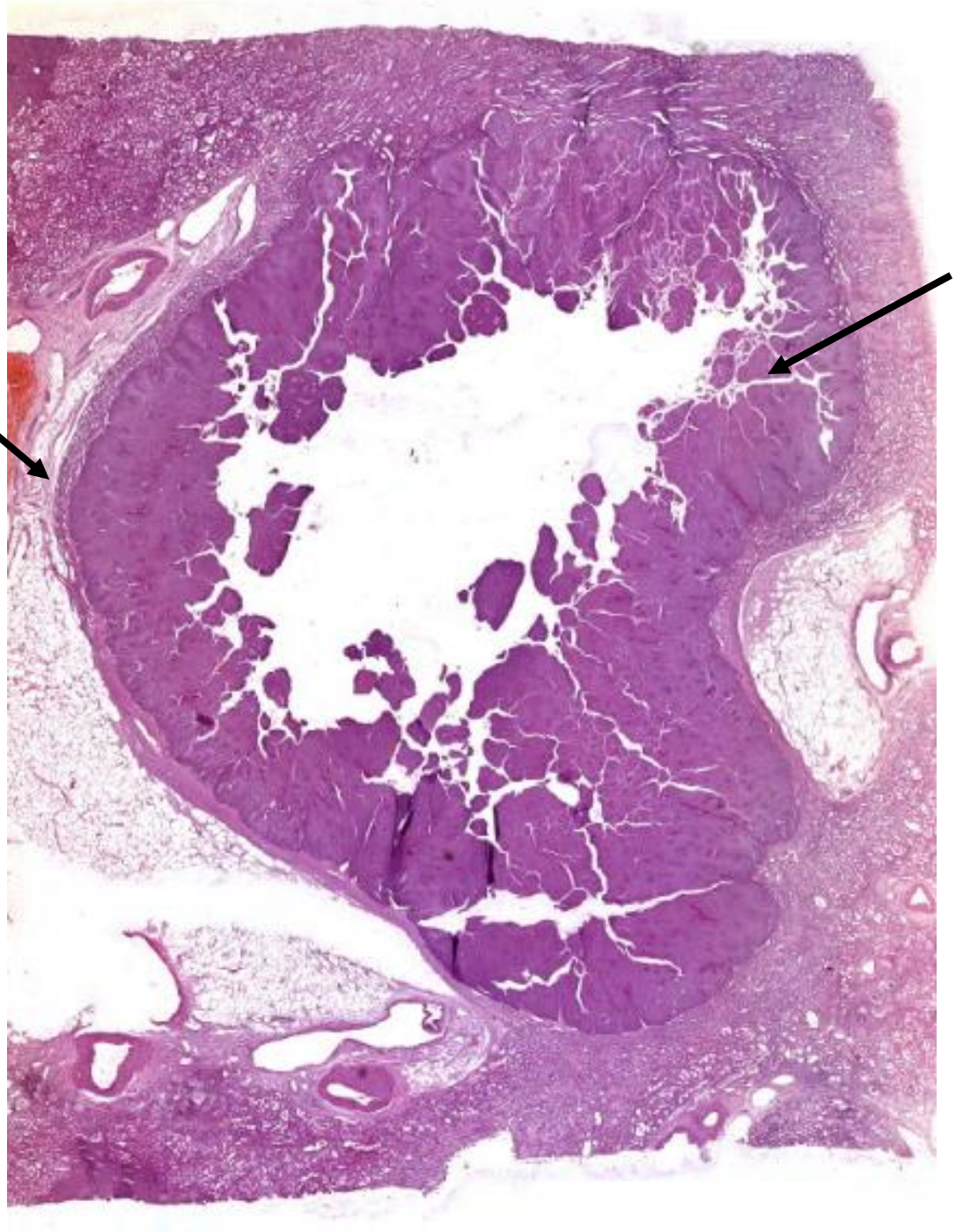
1. Epithel
2. Supepithelial connective tissue
3. Muscle layer of the urinary bladder (superficial and deep layer)
4. Perivesical fat tissue



T4a: tumor invasion of nearby organs(prostate, seminal vesicles / uterus, vagina
T4b: tumor invades pelvic wall or abdominal wall

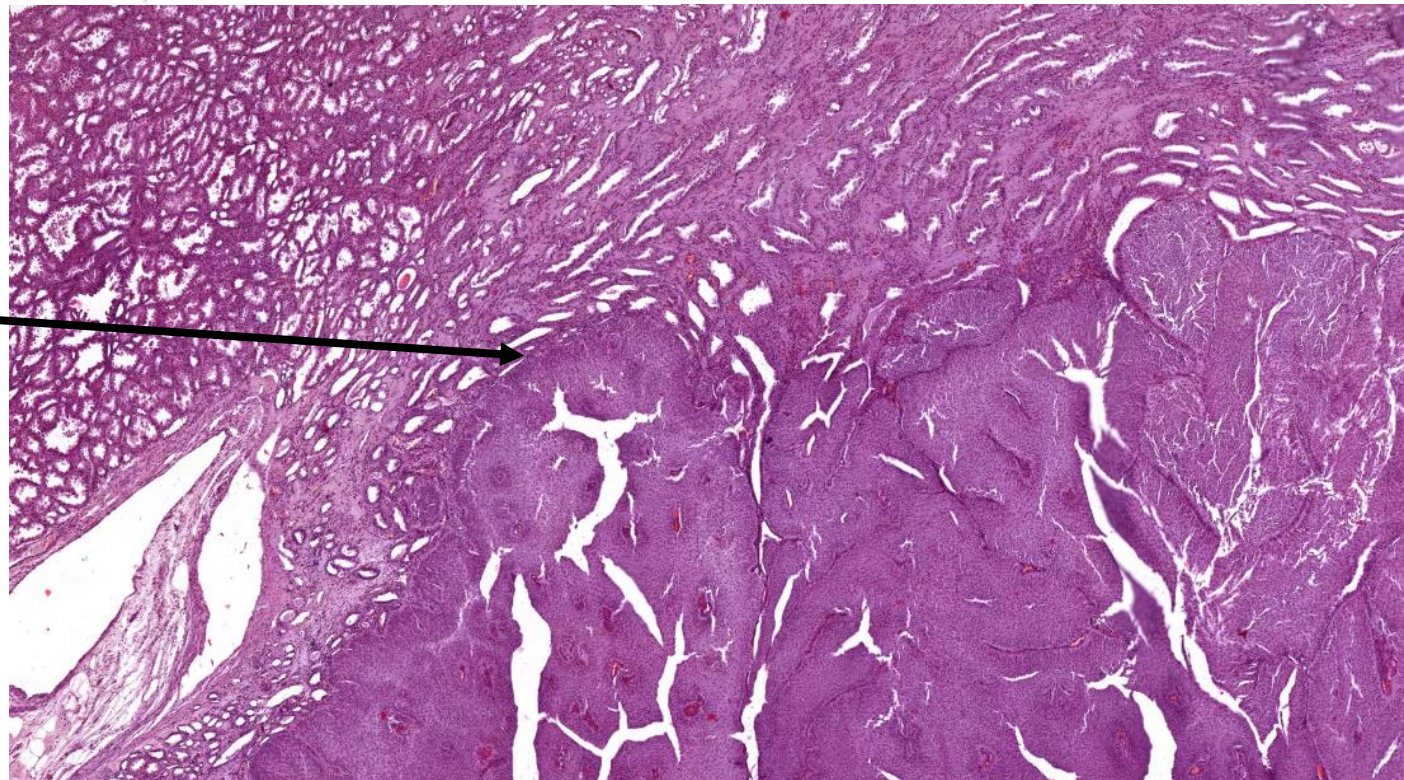
Urothelial carcinoma features

- Urothelial carcinoma (**papillary**/flat)
- Recurrent, multifocal lesions (metachronous)
- Diffuse carcinogenesis („field-cancerisation”)

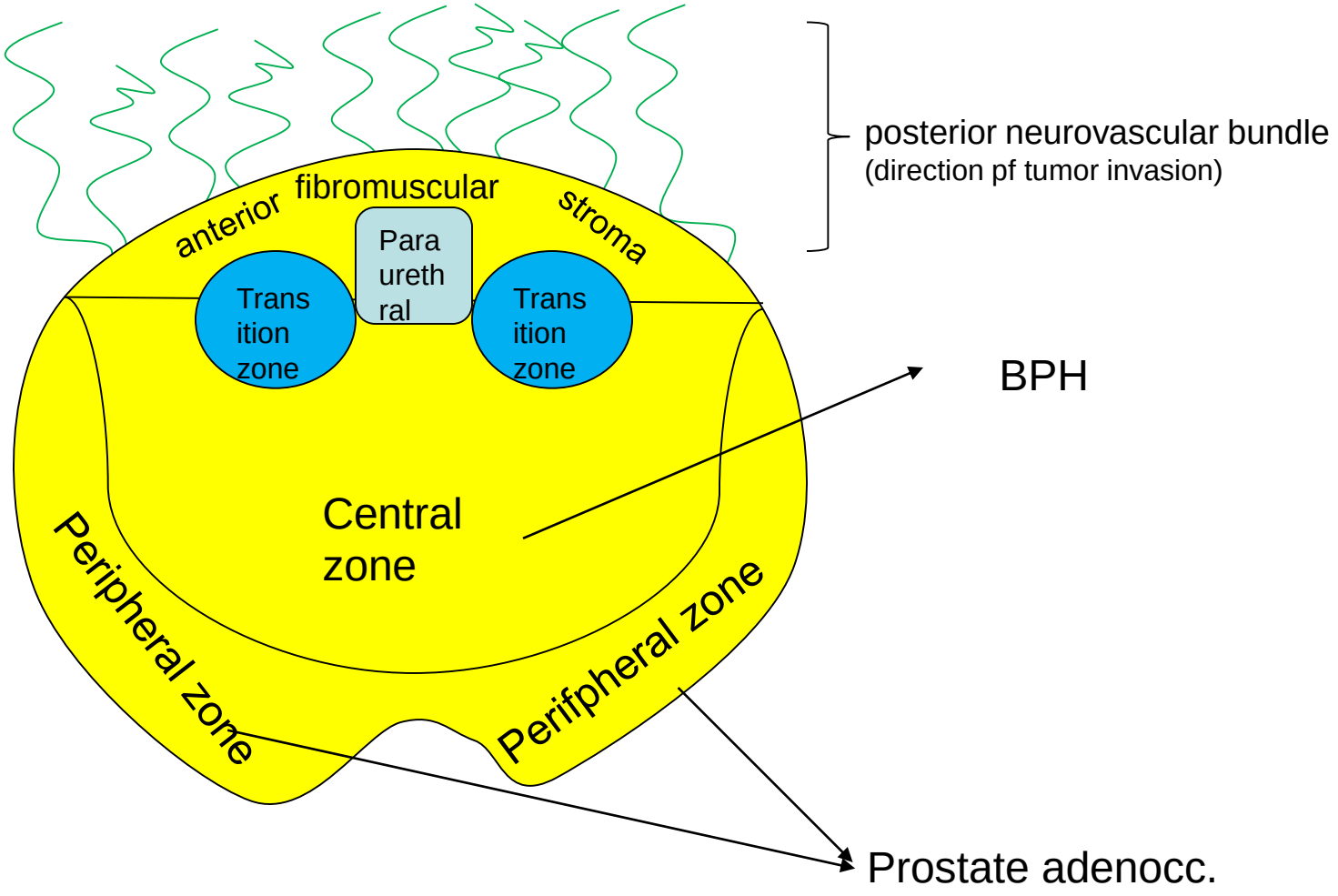

Pyelon
urothelial carcinoma

papillary tumor

Kidney parenchyma infiltration

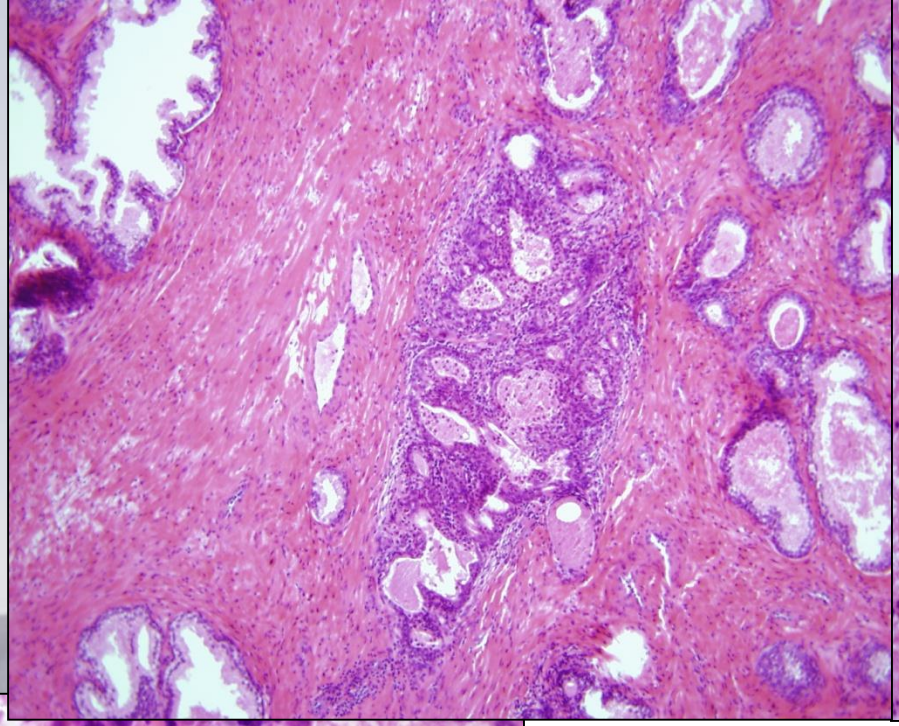


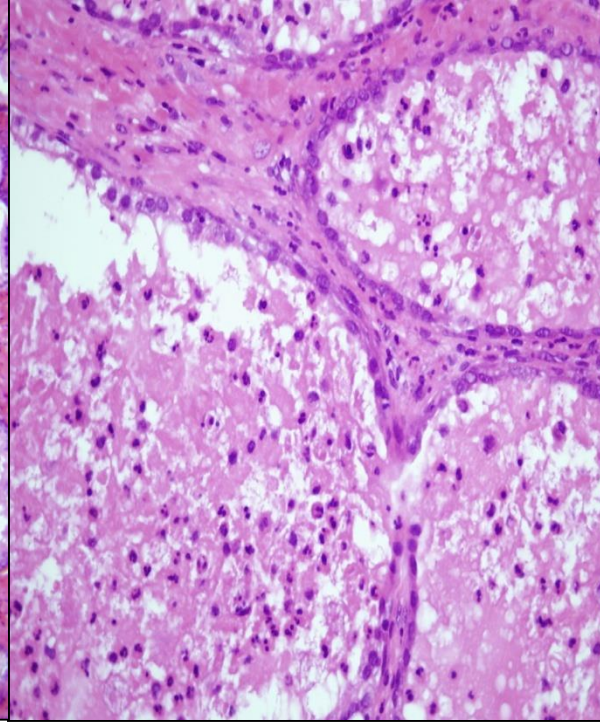
Prostate anatomy
(horizontal cut surface)

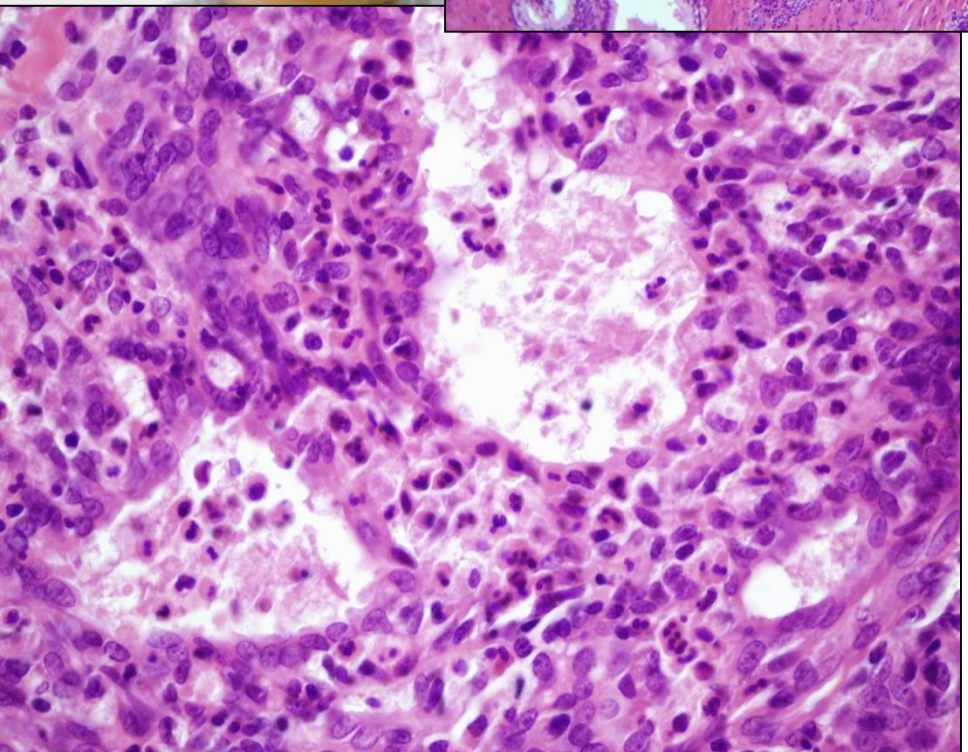


Prostatitis

- Occurs at least once during the lifetime of 50% percent of the male population
  - Acute
    - General inflammatory symptoms + dysuria, stranguria, lower abdominal pain, prostate tenderness during palpation, pyuria, microhematuria
  - Chronic
    - Lower abdominal and pelvic pain, nycturia, dysuria, urgent need to urinate, obstructive symptoms, erectile + ejaculatory dysfunction
    - Dg.: „three glass test” (1.→2.→prostate massage→3.)
  - Granulomatous
    - Retention of prostatic secretion and after TURP
    - Systemic inflammatory diseases (sarcoidosis, tuberculosis, Wegener-granulomatosis, fungal infections)

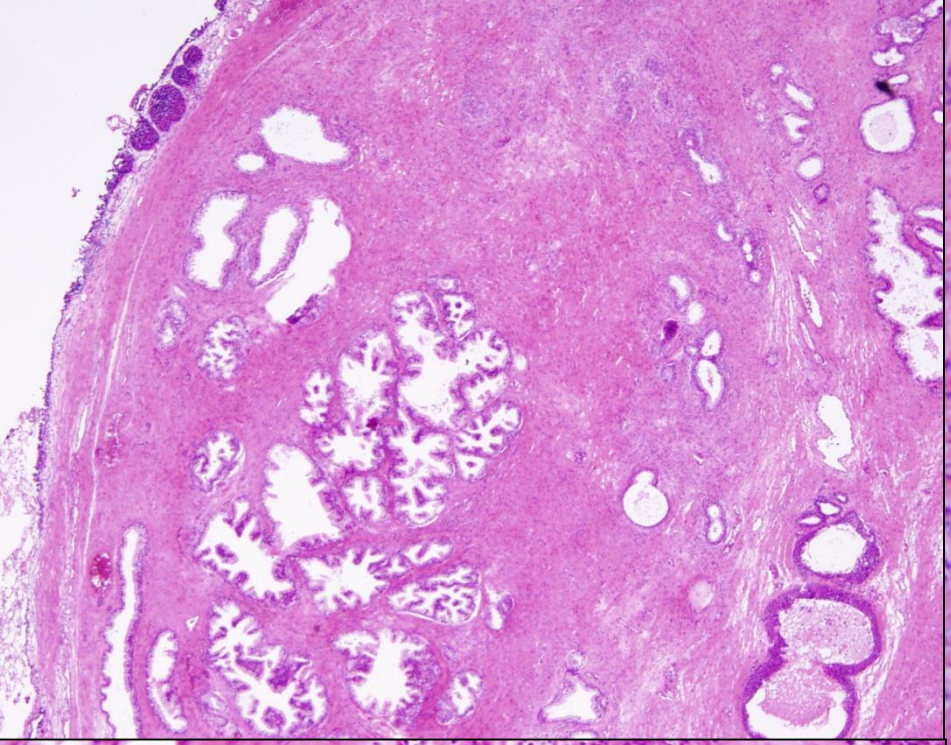


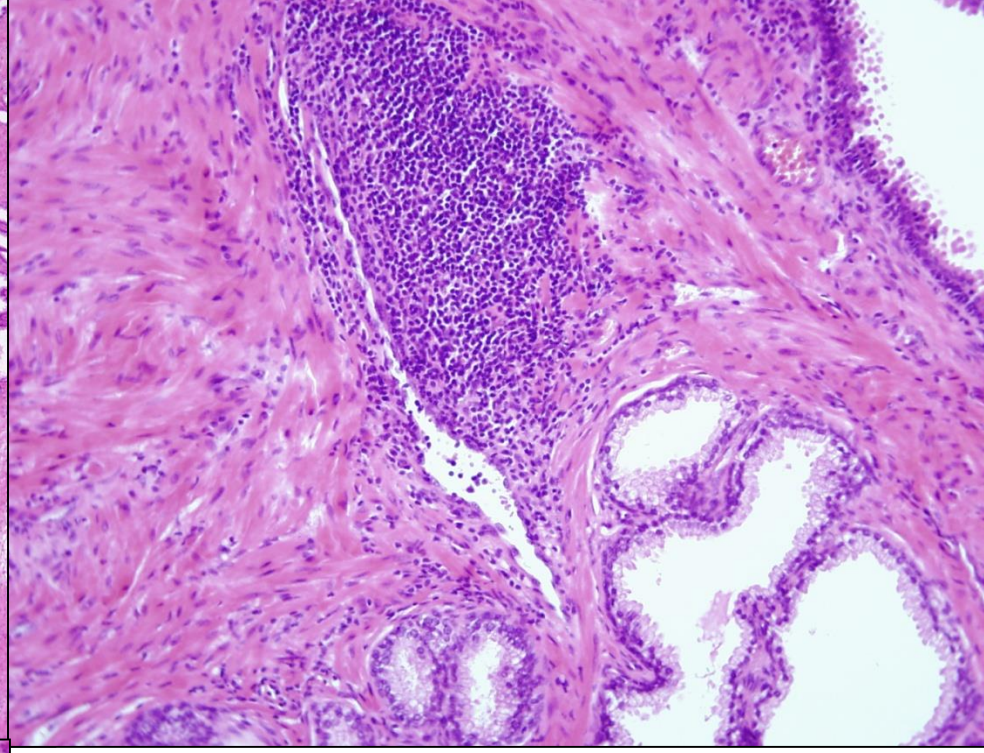


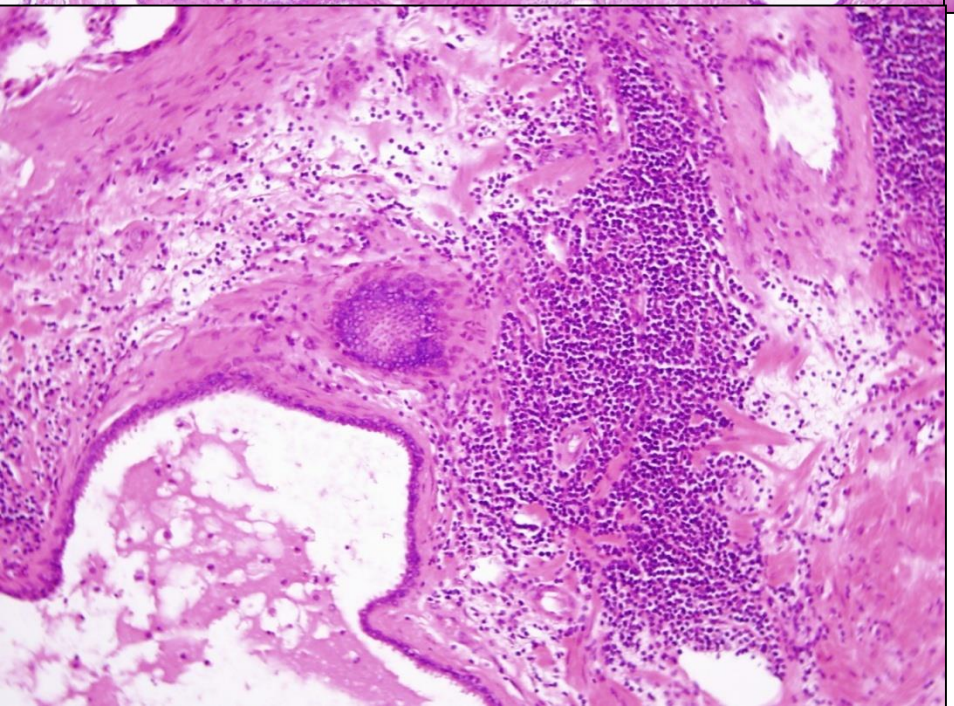


Acute prostatitis

Neutrophil granulocytes infiltrate the glandular epithelium→ destruction of epithelial lining → stromal infiltration, microabscesses





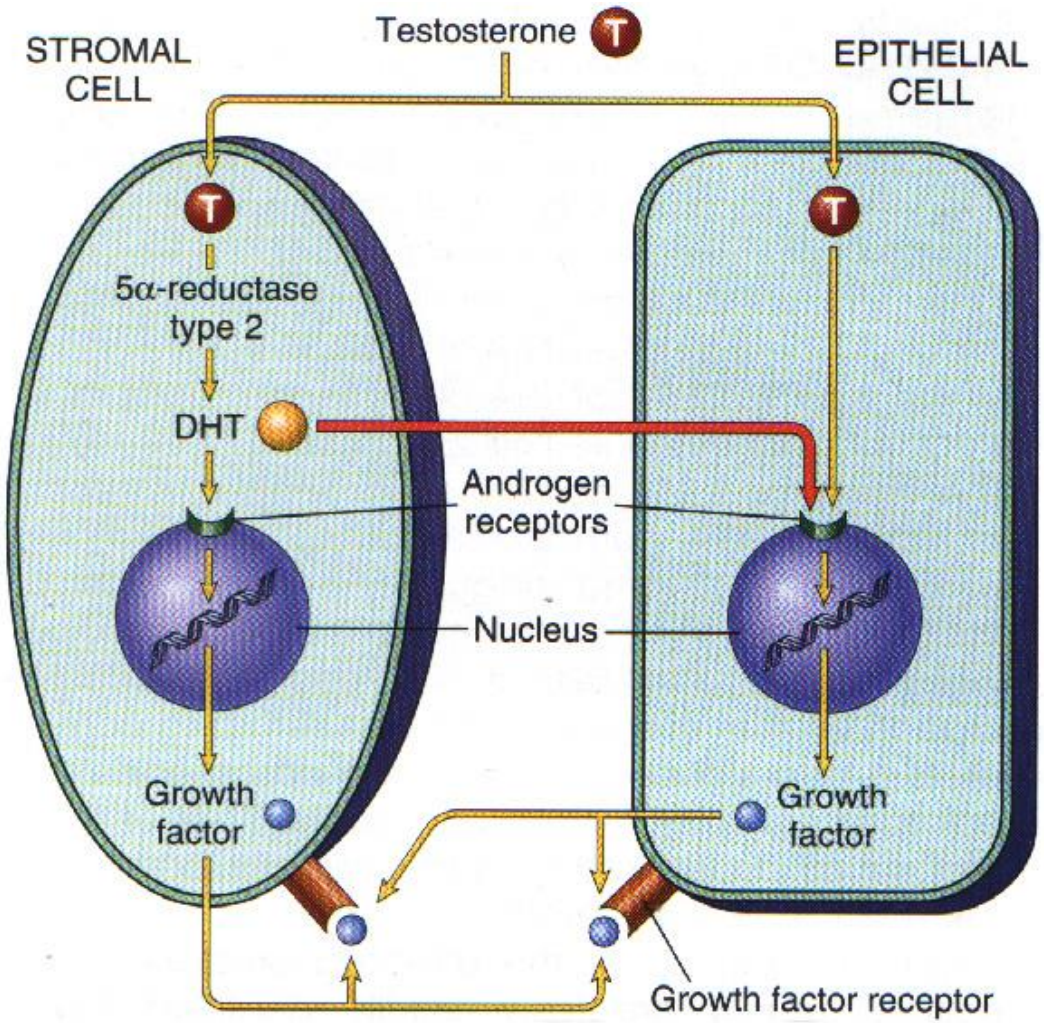


Chronic prostatitis

Non-specific appearance: lymphocyte infiltration + glandular destruction + acute inflammation

Prostate hyperplasia
Clinical features, diagnosis, therapy

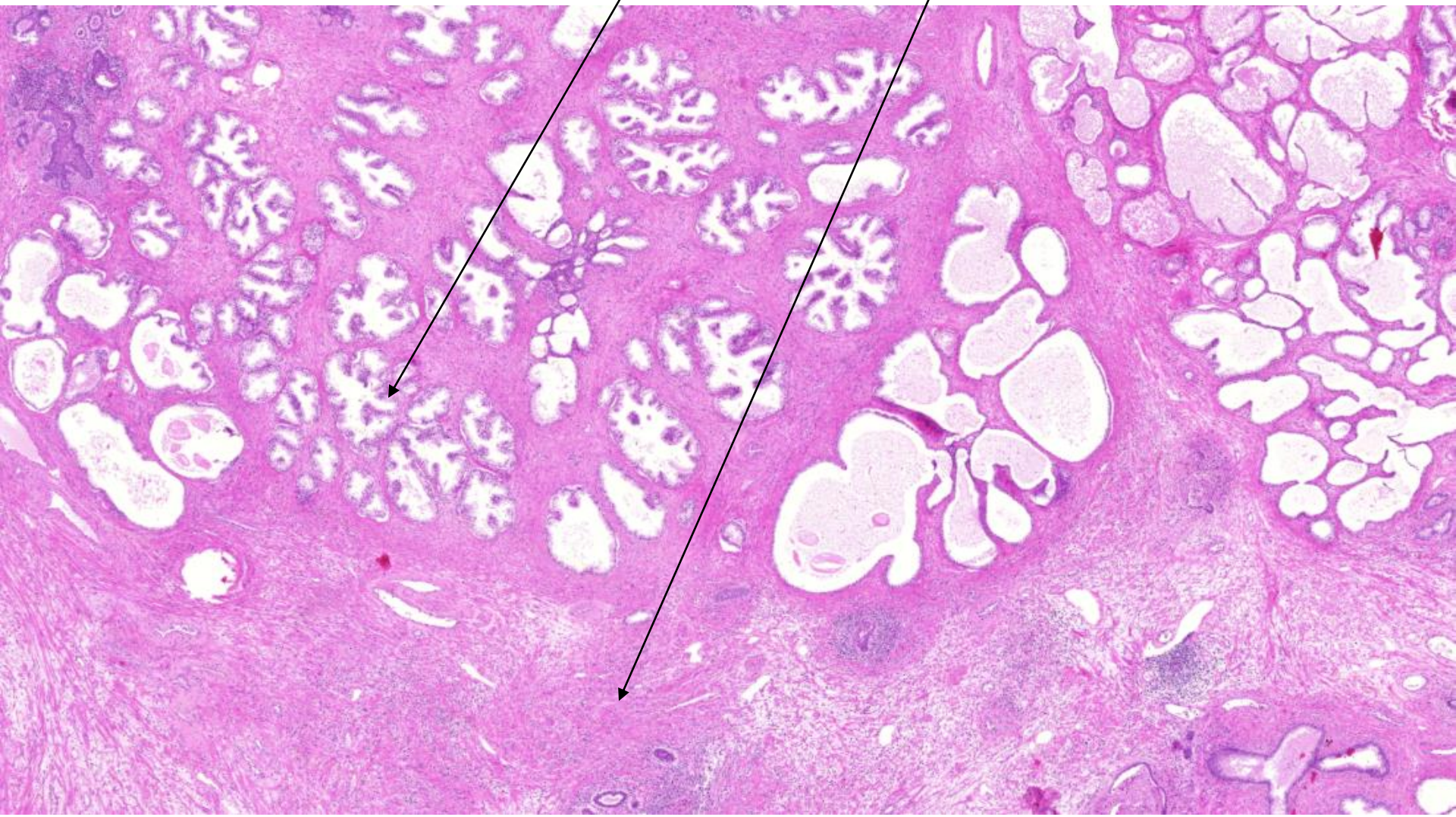
- Incidence increases >40 years
- Uretheral obstruction:
  - Weak urinary stream with interruptions, hesitation before beginning to urinate, terminal dribbling, dysuria
- Symptoms of irritation:
  - Nycturia, pollakiuria, alguria
- Rectal examination: symmetrical enlargement, „feels like an adenoma”
- Ultrasound, uroflow-examination + residual urine examination
- Th: alfa-blockers, 5-alfa-reductase inhibitors (>40g), TURP, adenomectomy (lasertherapy, hyperthermia)

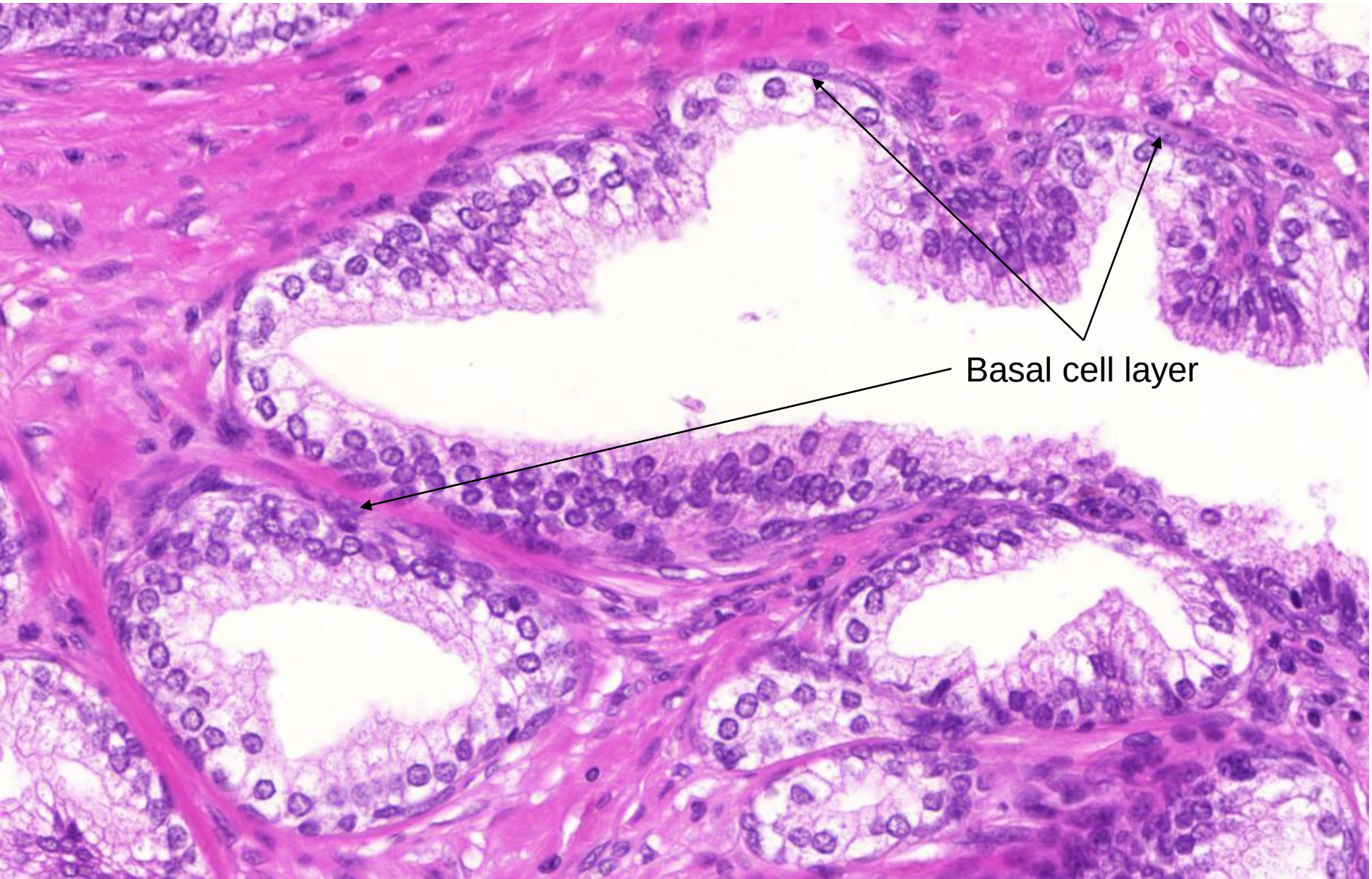

STROMAL CELL
Testosterone
EPITHELIAL CELL
T
T
T
5α-reductase type 2
DHT
Androgen receptors
Nucleus
Growth factor
Growth factor
Growth factor receptor

Hyperplasia histology

- Hyperplasia of epithelial and stromal components (hyperplasia adeno-myomatosa)
- Nodular structure (solid or cystic)
- The nodules cause obstruction of the urethra and the surrounding parenchyma
- Glands are lined by two layers of cells, **basal cell layer** and luminal columnar cells
- Corporae amylaceae are often present due to retention

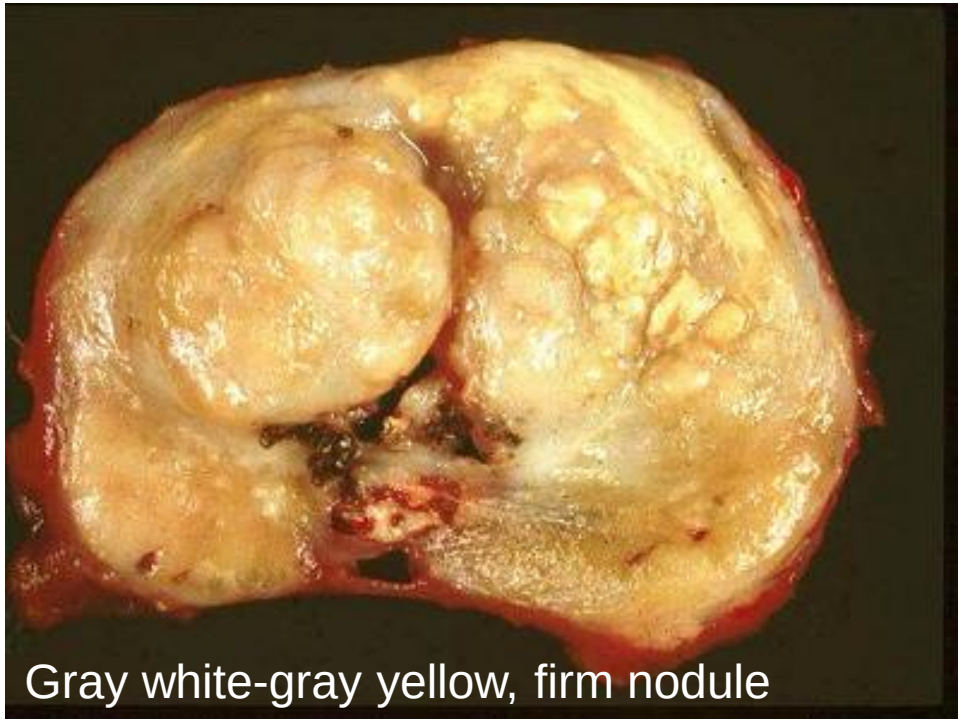
Hyperplasia of the epithelium and the stroma




Basal cell layer

Adenocarcinoma of the prostate

- Third most common tumor and cause of death among hungarian men; incidence is highest in men over age 65
- 70-80% arise peripherally → urinary symptoms are less common


Gray white-gray yellow, firm nodule

Metastasis: bone (can be both osteolithic and osteoplastic, Batson plexus), lung, liver, pleura, adrenal glands, distant lymph nodes, brain

- Clinically manifest: diagnosed
- Incidental: detected by chance during microscopic examination
- Latent: detected by chance during autopsy
- Occult:produces clinical evidence such as metastases or tumor markers, without the existence of the primary tumor being known

Diagnosis of prostate adenocarcinoma

- Rectal examination: firm nodule
- PSA (prostate specific antigen)
  - 4 ng/ml > normal
  - 4-10 ng/ml: grey zone
  - 10-25 ng/ml: concern of cancer (can be BPH)
  - 25 ng/ml < almost 100% definitive for carcinoma
- PCA3-test: prosztate massage→prostate acinar cells in urine→PCA3/PSA mRNS expression = PCA3 index
- **Transrectal mapping biopsy**

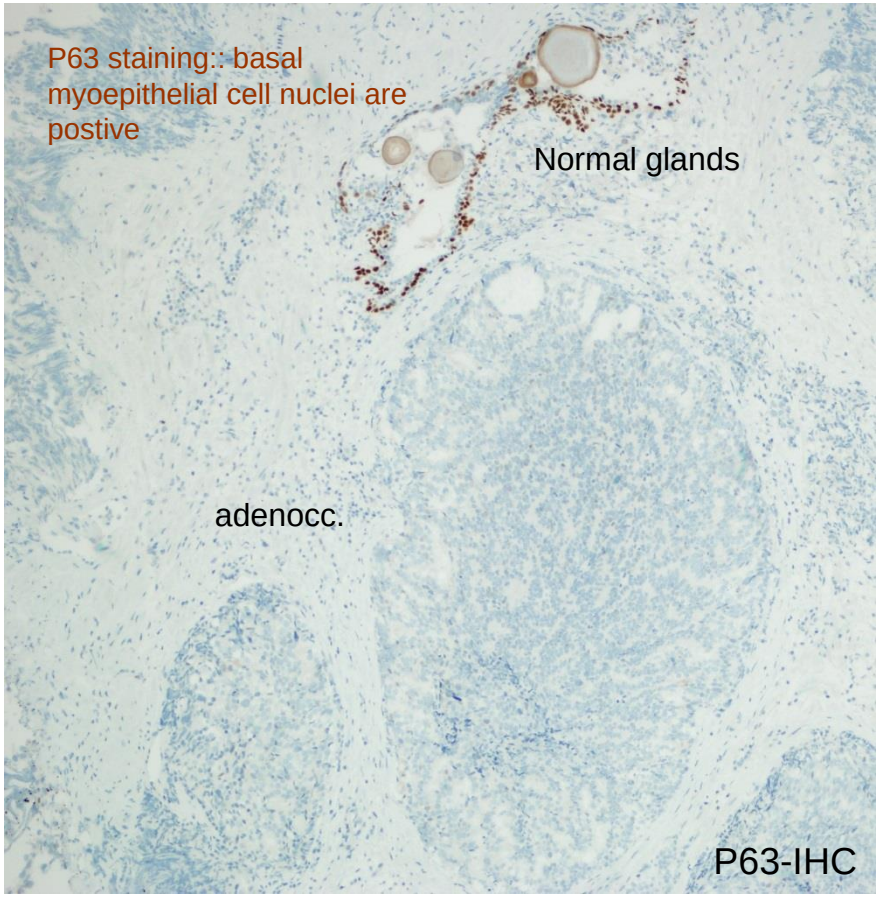
Mikroscopic features

Precancerous condition: PIN = prostate intraepithelial neoplasia

Prostate carcinoma:

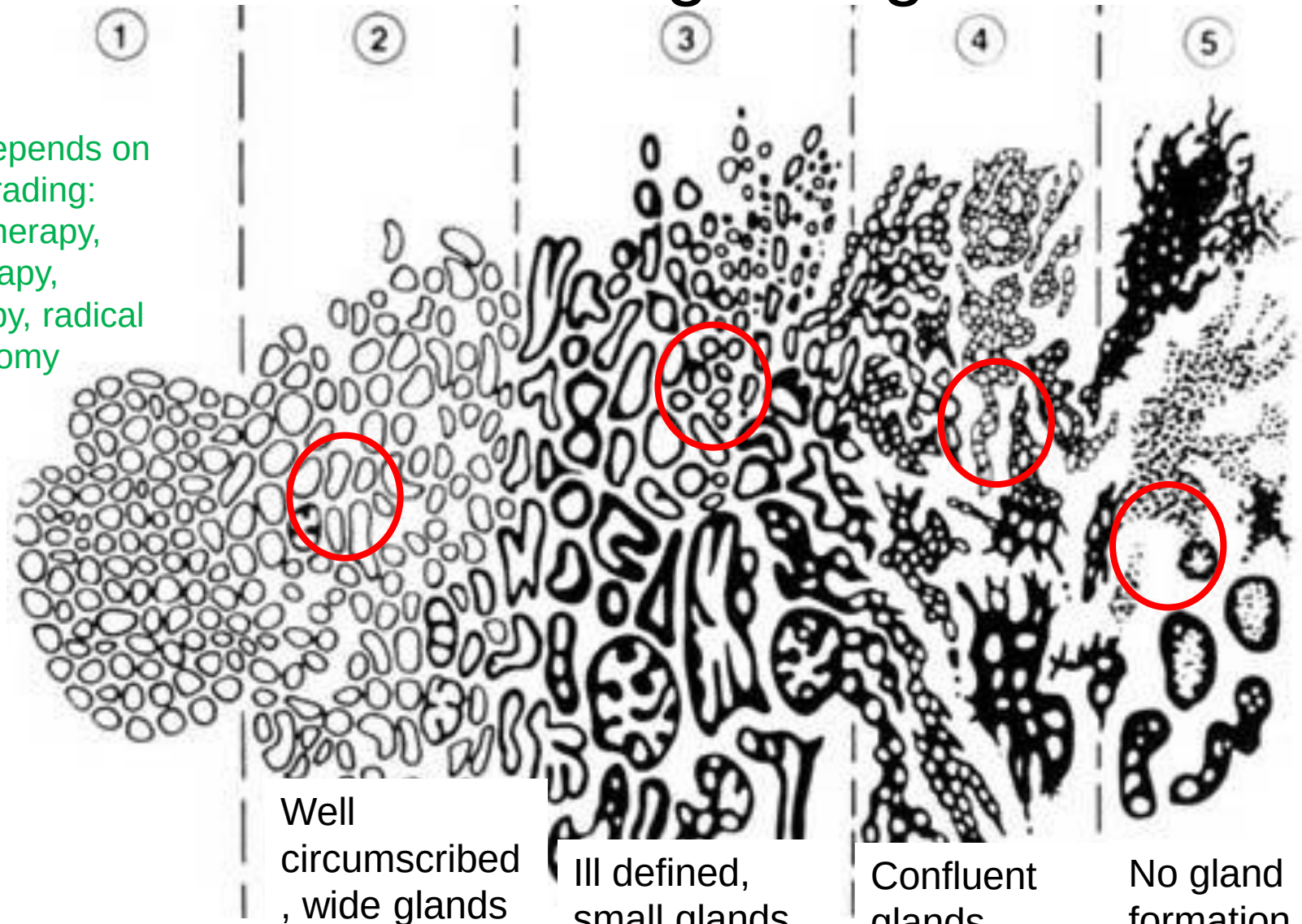
- back-to back, small glands (structural atypia!)
- prominent, eosinophilic nucleolus
- anlarged, hyperchrom nuclei

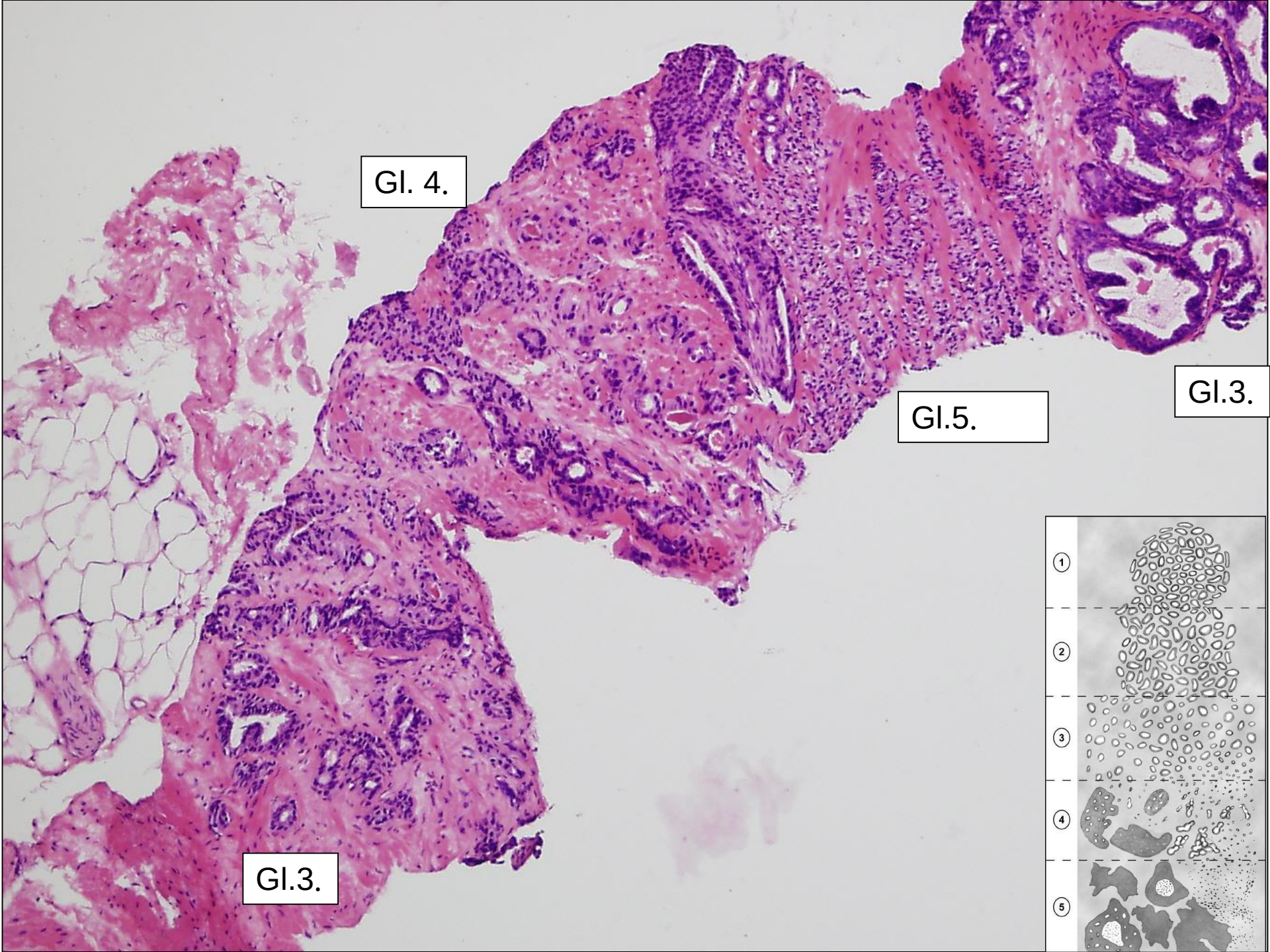
•basal cell layer is absent!

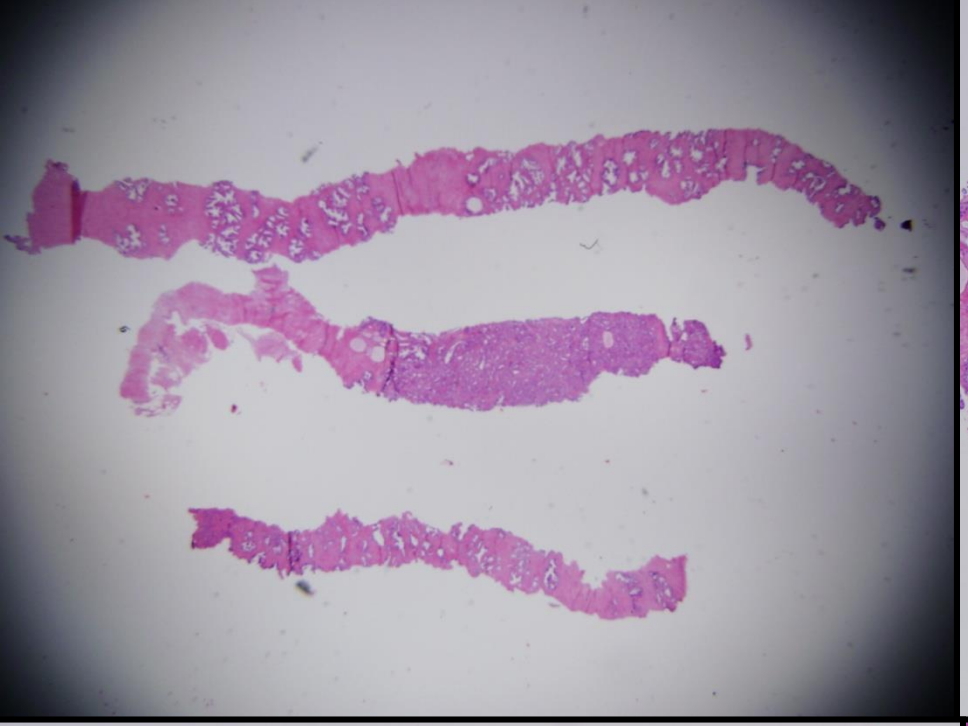


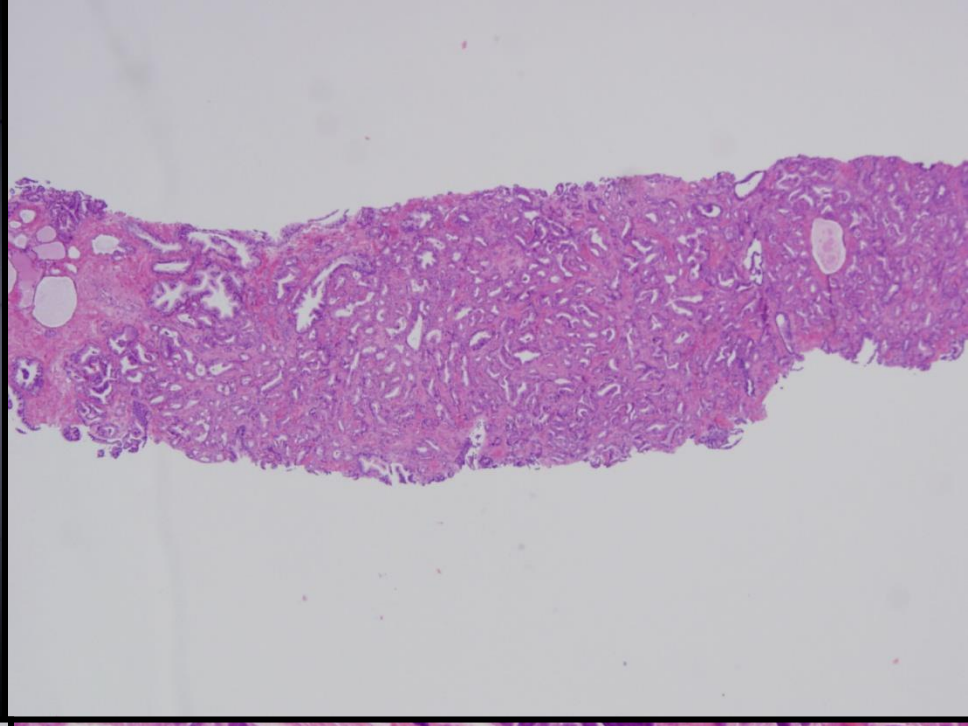
Gleason grading

Therapy depends on Gleason grading: hormone therapy, chemotherapy, radiotherapy, radical prostatecttomy



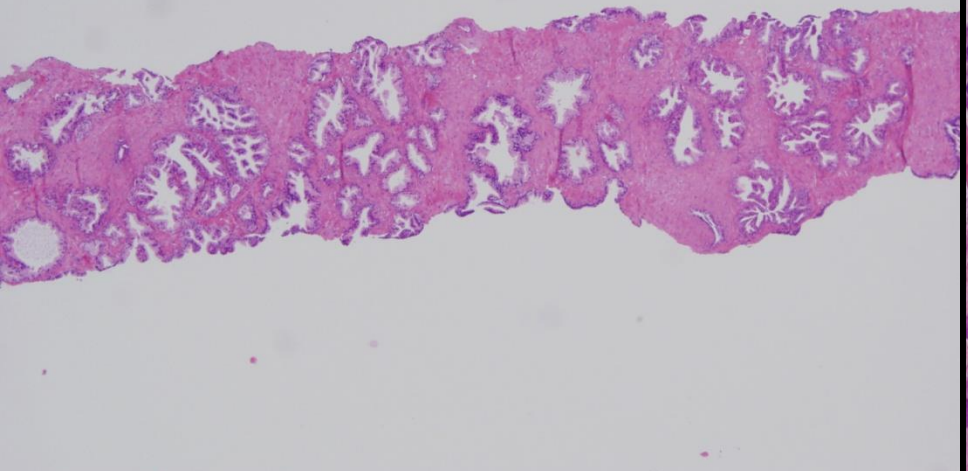

Gl. 4.
Gl.3.
Gl.5.
Gl.3.
1
2
3
4
5

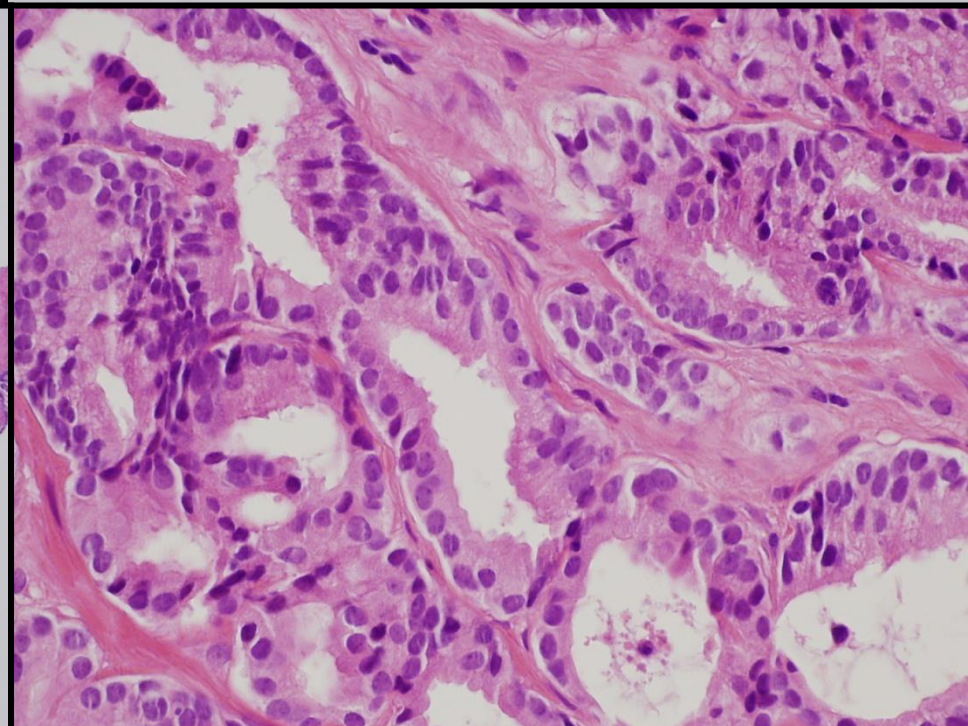




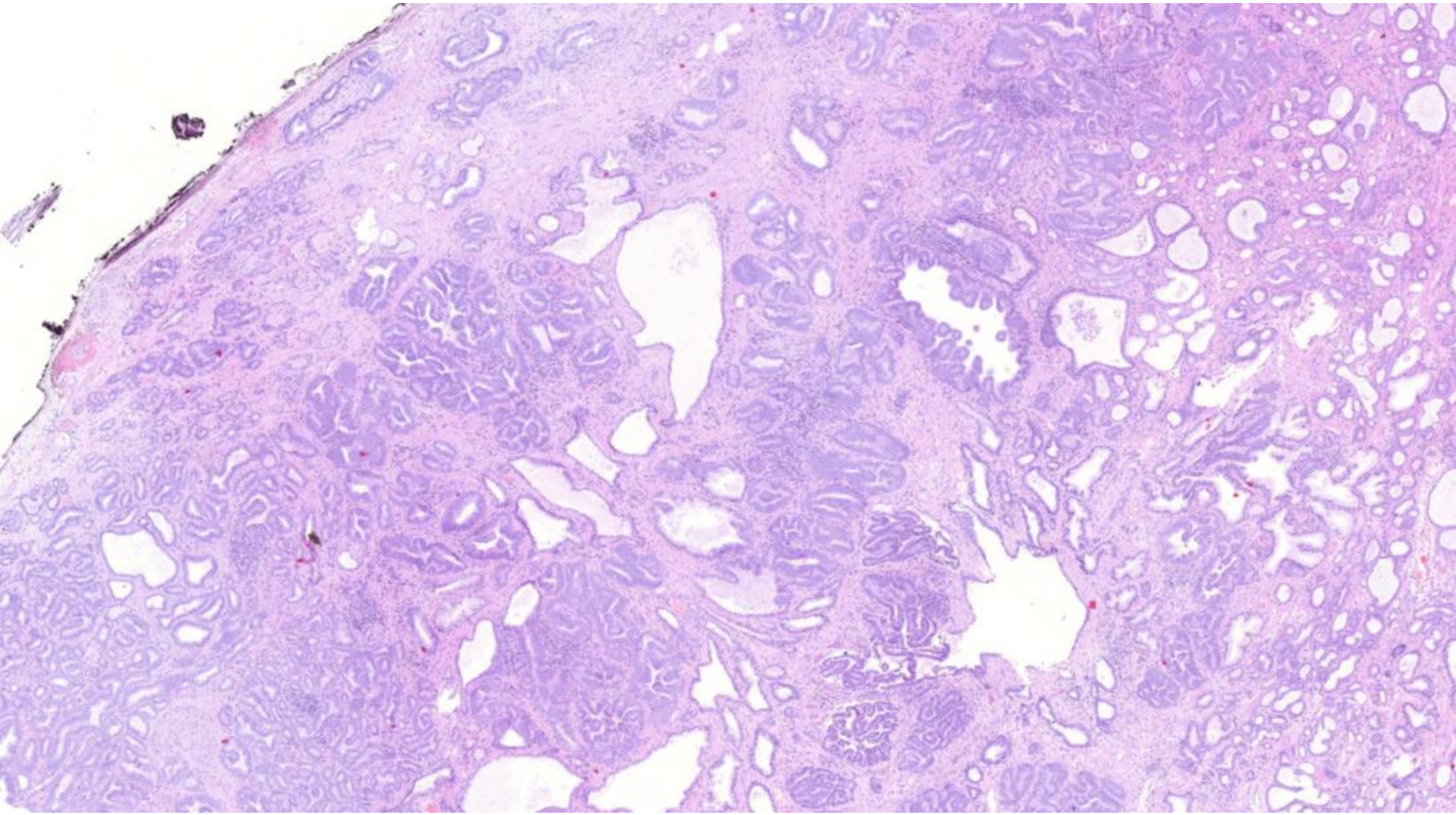
Dg.:adenocarcinoma,

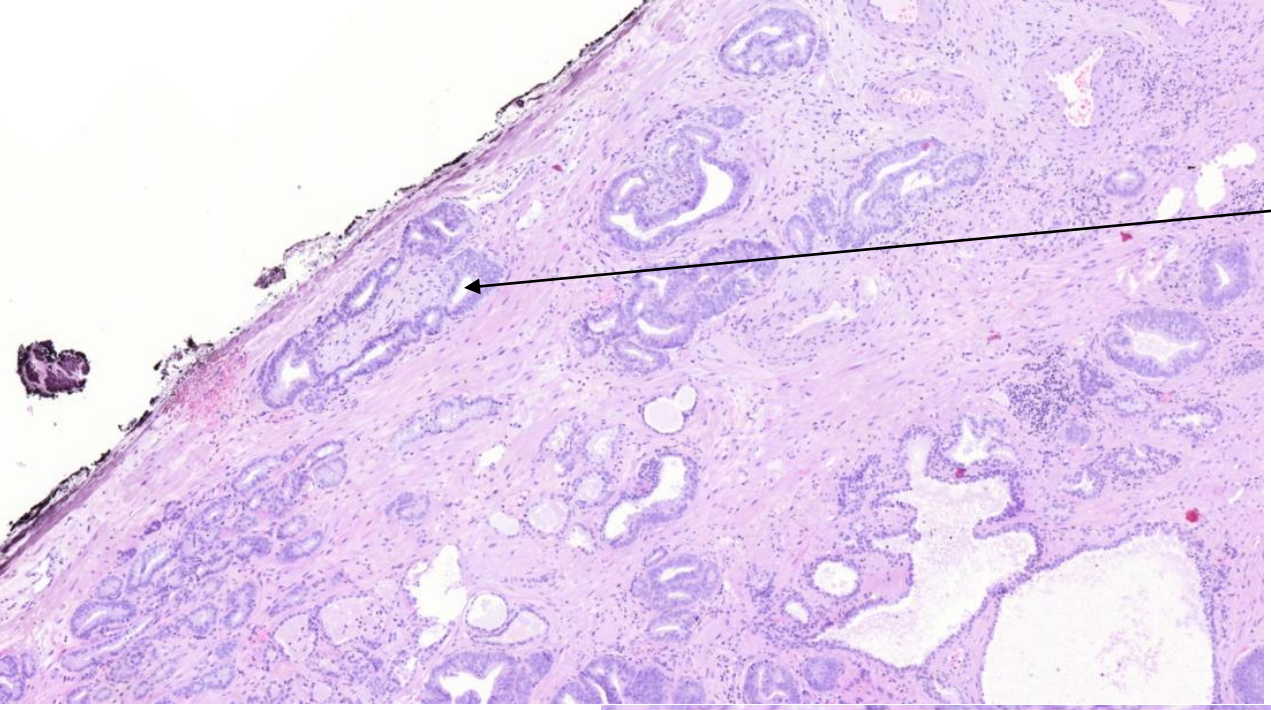
Gleason 3



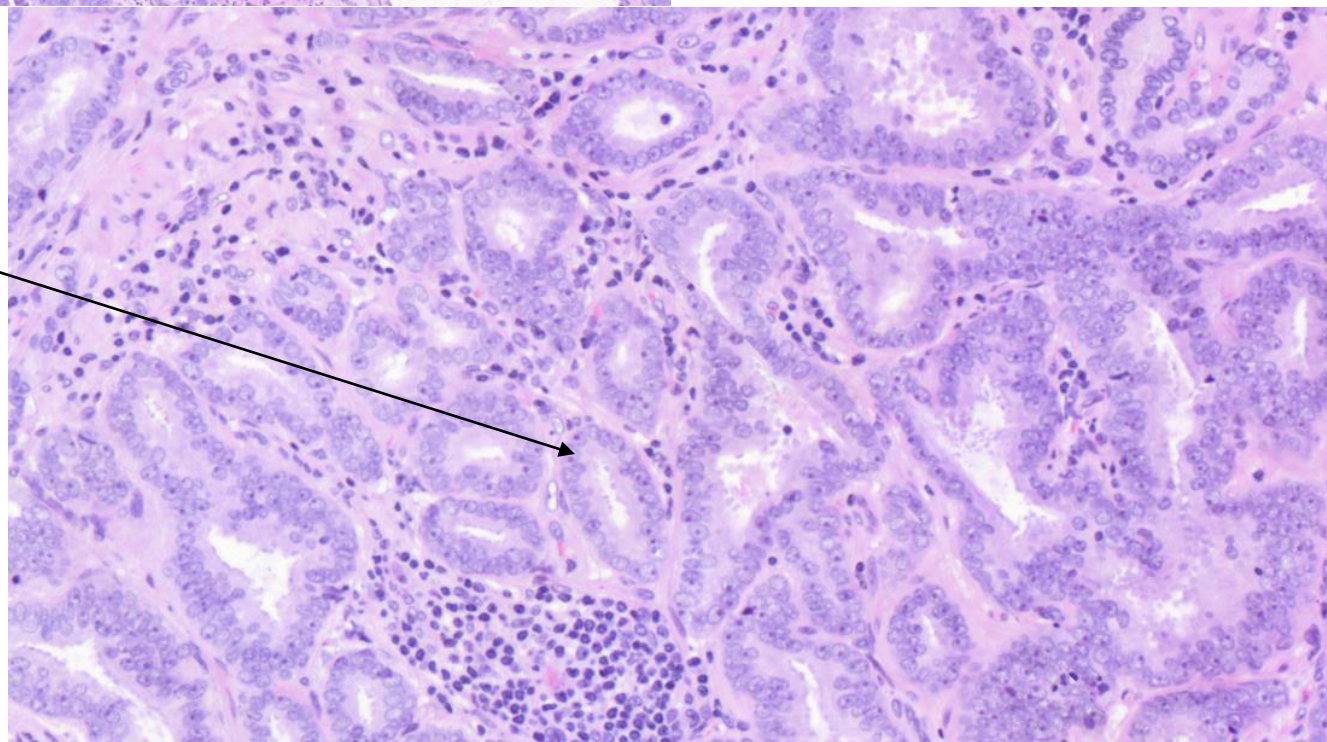


Prostate adenocarcinoma





Glands with small lumina
Tumorcells contain prominent nucleolus
NO basal cell layer



Testicular tumors

- Germ cell tumors
- Sex cord – gonadal stroma tumors (Sertoli / Leydig cell tumors)
- Other (gonadoblastoma, adenocarcinoma, hemangioma, testicular lymphoma)

Testicular tumors

- 95% malignant germ cell tumor, 60% mixed tumor
- 5% sex cord-gonadal stroma tumor (mostly benign, hormone secreting)
- Symptoms: slowly growing, painless mass, gynecomastia, early onset puberty
- Diagnosis: serum markers (AFP, β-HCG), UH
- Risk factors: cryptorchism, intersex disorders (testicular feminisation, Klienefelter syndrome), early onset puberty

WHO classification of tumours of the testis

Germ cell tumours derived from germ cell neoplasia in situ	
Non-invasive germ cell neoplasia	
Germ cell neoplasia in situ	9064/2
Specific forms of intratubular germ cell neoplasia	
Tumours of a single histological type (pure forms)	
Seminoma	9061/3
Seminoma with syncytiotrophoblast cells	
Non-seminomatous germ cell tumours	
Embryonal carcinoma	9070/3
Yolk sac tumour, postpubertal-type	9071/3
Trophoblastic tumours	
Choriocarcinoma	9100/3
Non-choriocarcinomatous trophoblastic tumours	
Placental site trophoblastic tumour	9104/1
Epithelioid trophoblastic tumour	9105/3
Cystic trophoblastic tumour	
Teratoma, postpubertal-type	9080/3
Teratoma with somatic-type malignancy	9084/3
Non-seminomatous germ cell tumours of more than one histological type	
Mixed germ cell tumours	9085/3
Germ cell tumours of unknown type	
Regressed germ cell tumours	9080/1
Germ cell tumours unrelated to germ cell neoplasia in situ	
Spermatocytic tumour	9063/3
Teratoma, prepubertal-type	9084/0
Dermoid cyst	
Epidermoid cyst	
Well-differentiated neuroendocrine tumour (monodermal teratoma)	8240/3
Mixed teratoma and yolk sac tumour, prepubertal-type	9085/3
Yolk sac tumour, prepubertal-type	9071/3
Sex cord–stromal tumours	
Pure tumours	
Leydig cell tumour	8650/1
Malignant Leydig cell tumour	8650/3
Sertoli cell tumour	8640/1
Malignant Sertoli cell tumour	8640/3
Large cell calcifying Sertoli cell tumour	8642/1
Intratubular large cell hyalinizing Sertoli cell neoplasia	8643/1*
Granulosa cell tumour	
Adult granulosa cell tumour	8620/1
Juvenile granulosa cell tumour	8622/1*
Tumours in the fibroma–thecoma group	8600/0
Mixed and unclassified sex cord–stromal tumours	
Mixed sex cord–stromal tumour	8592/1
Unclassified sex cord–stromal tumour	8591/1
Tumour containing both germ cell and sex cord–stromal elements	
Gonadoblastoma	9073/1
Miscellaneous tumours of the testis	
Ovarian epithelial–type tumours	
Serous cystadenoma	8441/0
Serous tumour of borderline malignancy	8442/1
Serous cystadenocarcinoma	8441/3
Mucinous cystadenoma	8470/0
Mucinous borderline tumour	8472/1
Mucinous cystadenocarcinoma	8470/3
Endometrioid adenocarcinoma	8380/3
Clear cell adenocarcinoma	8310/3
Brenner tumour	9000/0
Juvenile xanthogranuloma	
Haemangioma	9120/0
Haematolymphoid tumours	
Diffuse large B-cell lymphoma	9680/3
Follicular lymphoma, NOS	9690/3
Extranodal NK/T-cell lymphoma, nasal-type	9719/3
Plasmacytoma	9734/3
Myeloid sarcoma	9930/3
Rosai–Dorfman disease	
Tumours of collecting duct and rete testis	
Adenoma	8140/0
Adenocarcinoma	8140/3

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) [917A]. Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours. The classification is modified from the previous WHO classification [756A], taking into account changes in our understanding of these lesions.

*New code approved by the IARC/WHO Committee for ICD-O.

Classification of germ cell tumors

Germ cell neoplasia associated

- GCNIS (germ cell neoplasia in situ)
- Seminoma
- Non-seminomatosus germ cell tumors
  - Embryonal carcinoma
  - postpubertal yolk sac tumor
  - postpubertal teratoma
  - Teratoma with somatic type malignancy
  - Choriocarcinoma
  - Other trophoblast tumors
- Mixed tumors
- Regrediated tumors of testis

Non germ cell neoplasia associated

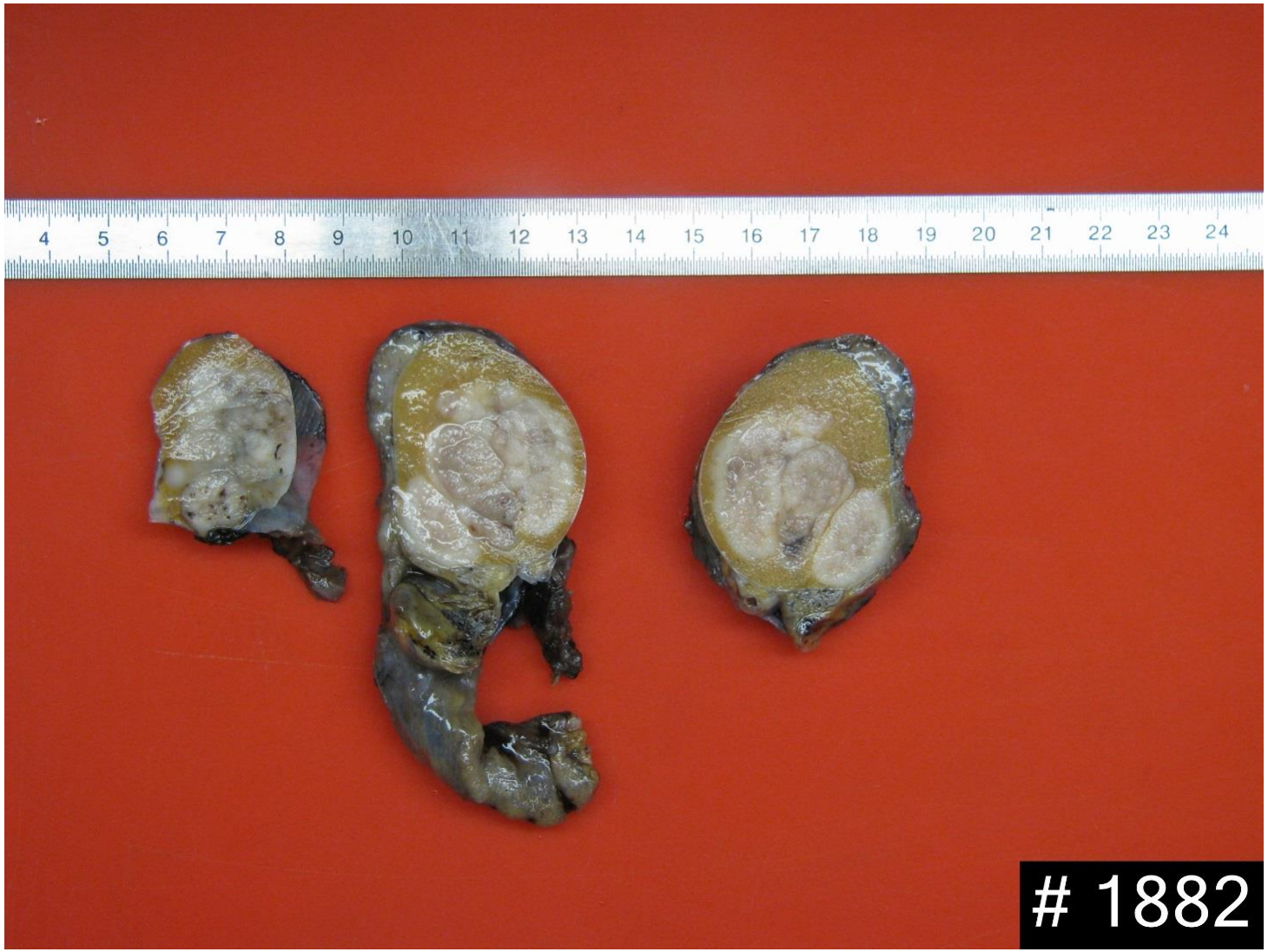
- Spermatocytic seminoma
- Prepubertal teratoma
  - Epidermoid cyst
  - Dermoid cyst
  - Well differentiated neuroendocrine tumor (monodermal teratoma)
- prepubertal yolk sac tumor
- mixed prepubertal teratoma and yolk sac tumor

Germ cell tumors incidence and tumor markers

- Seminoma: age 40+ (in some cases β-hCG, AFP never!)
- Embryonal cc.: age 20-30: AFP (90%)
- Yolk-sac (prepubertal): age 3 AFP (100%)
- Choriocarcinoma: age 20-30: β-hCG (100%)
- Teratoma: AFP, β-hCG
- Mixed tumors: age 15-30: AFP, β-hCG

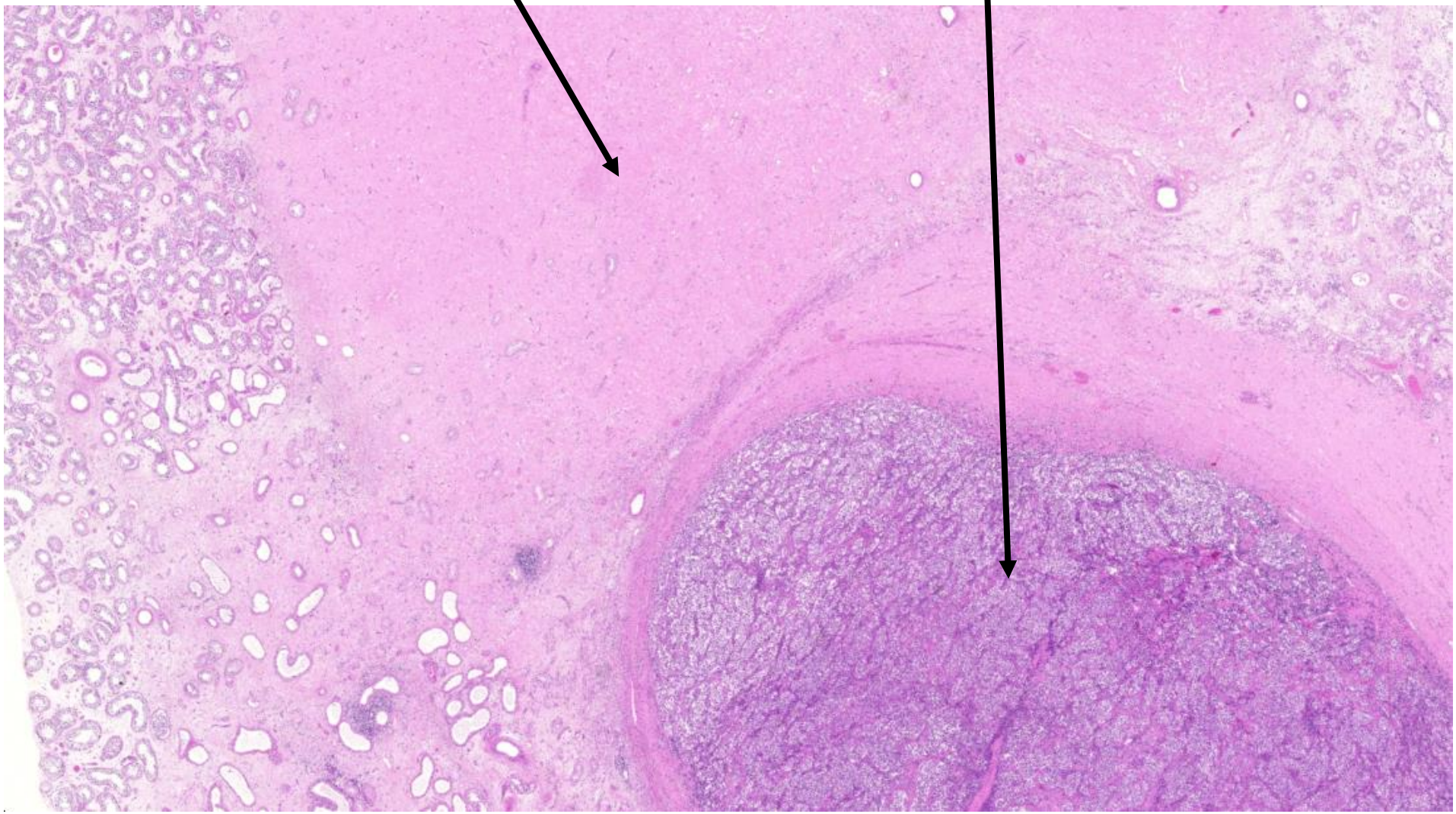
(LDH: non specific marker; serum level increases due to tissue destruction)

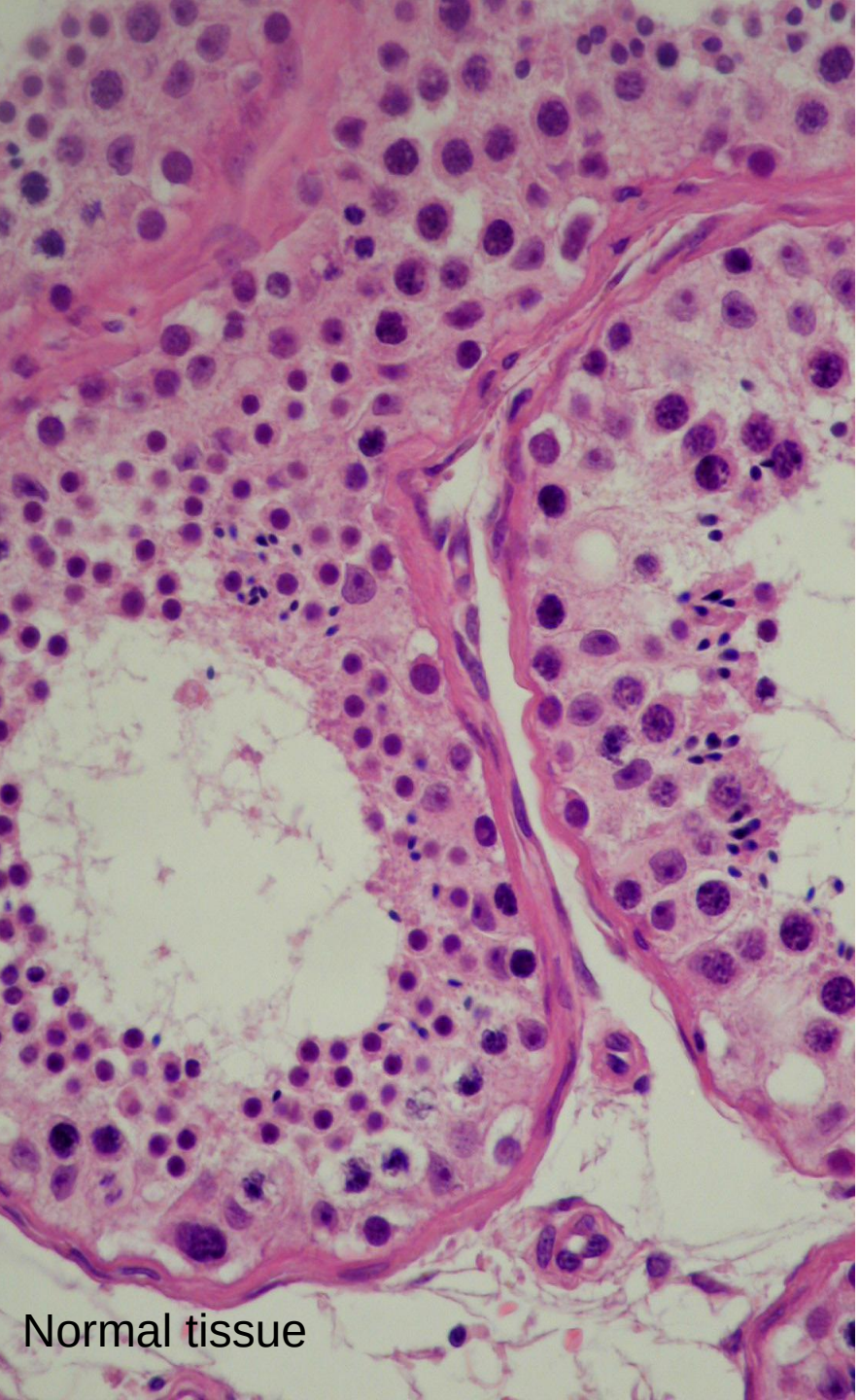
Seminoma macroscopy

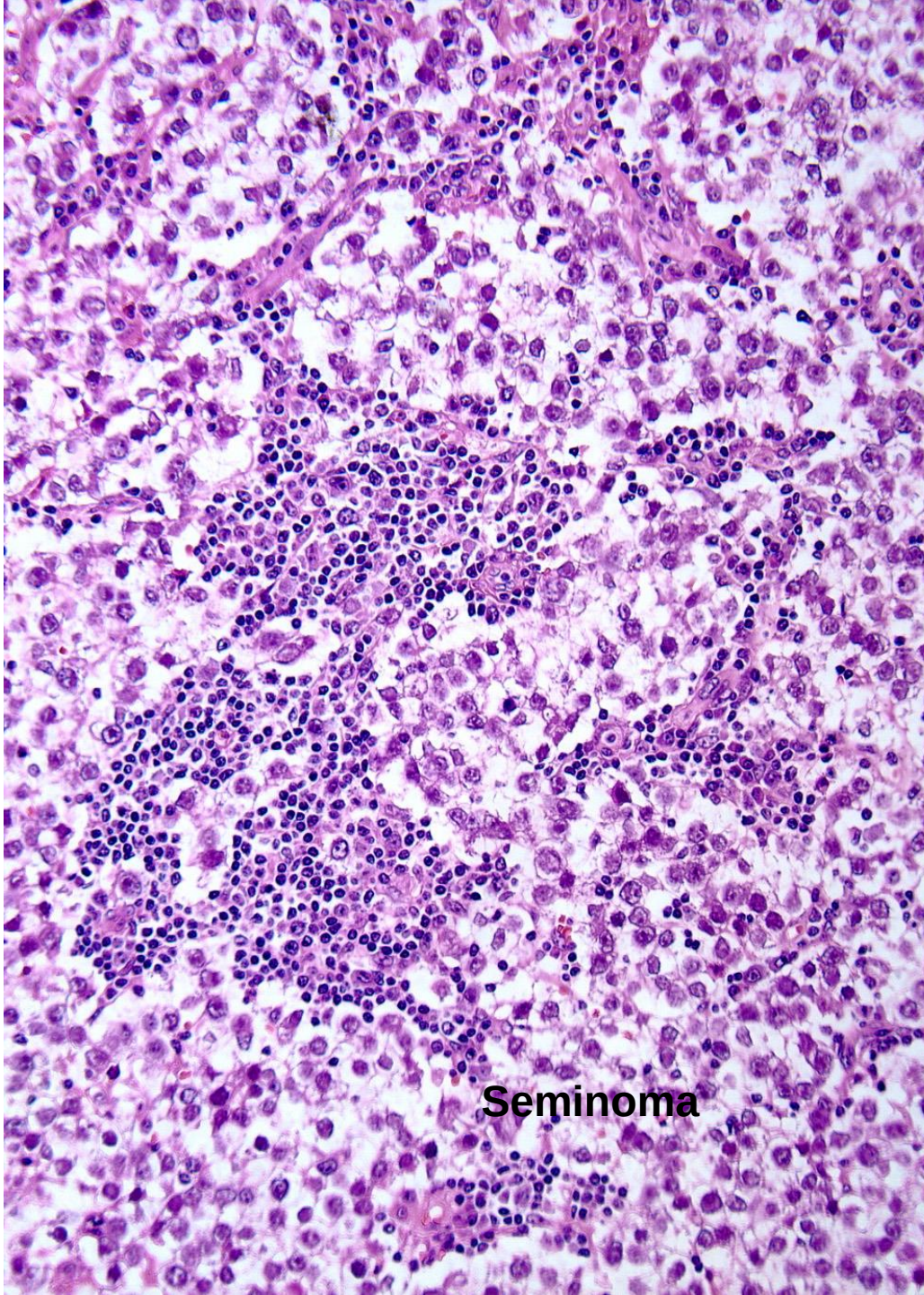


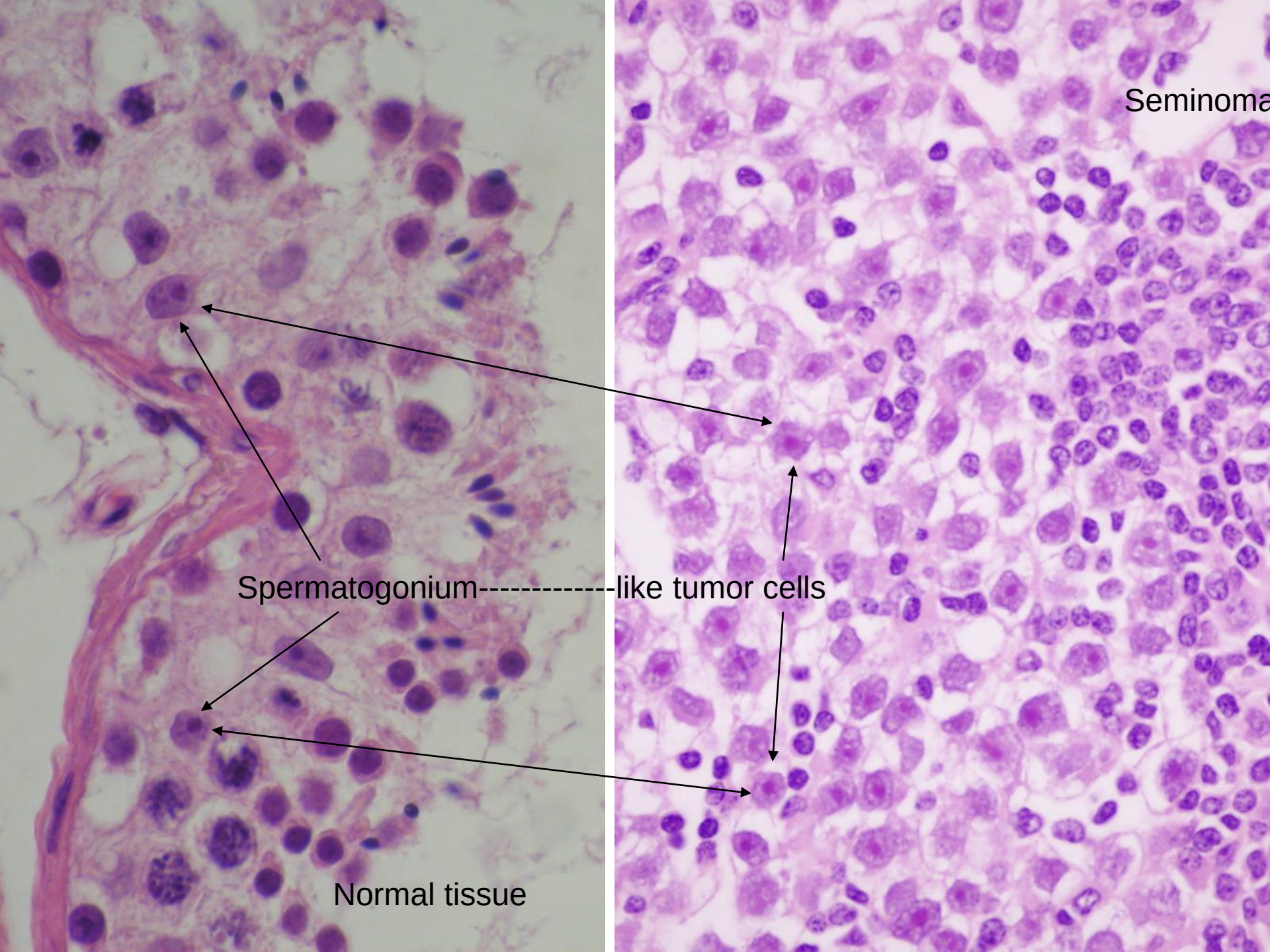
Seminoma microscopic features

- Large, monomorph cells with distinct cell borders
- Clear, glycogen rich cytoplasm
- Round nuclei, prominent nucleoli
- Fibrotic septi
- Lymphocytic infiltration


Fibrosis - regression
seminoma

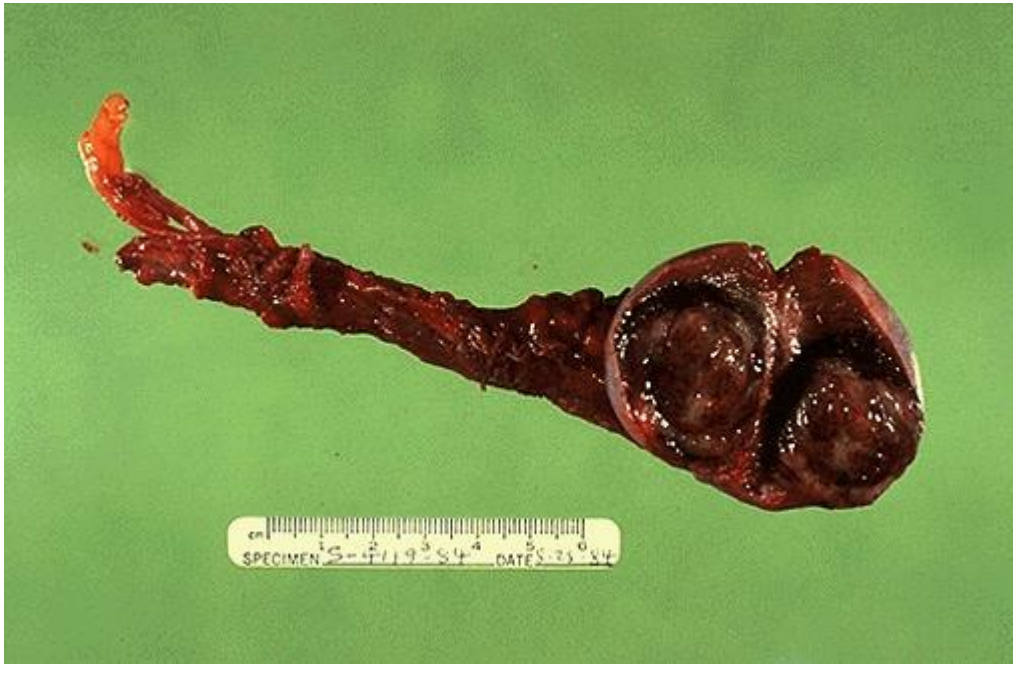

Normal tissue

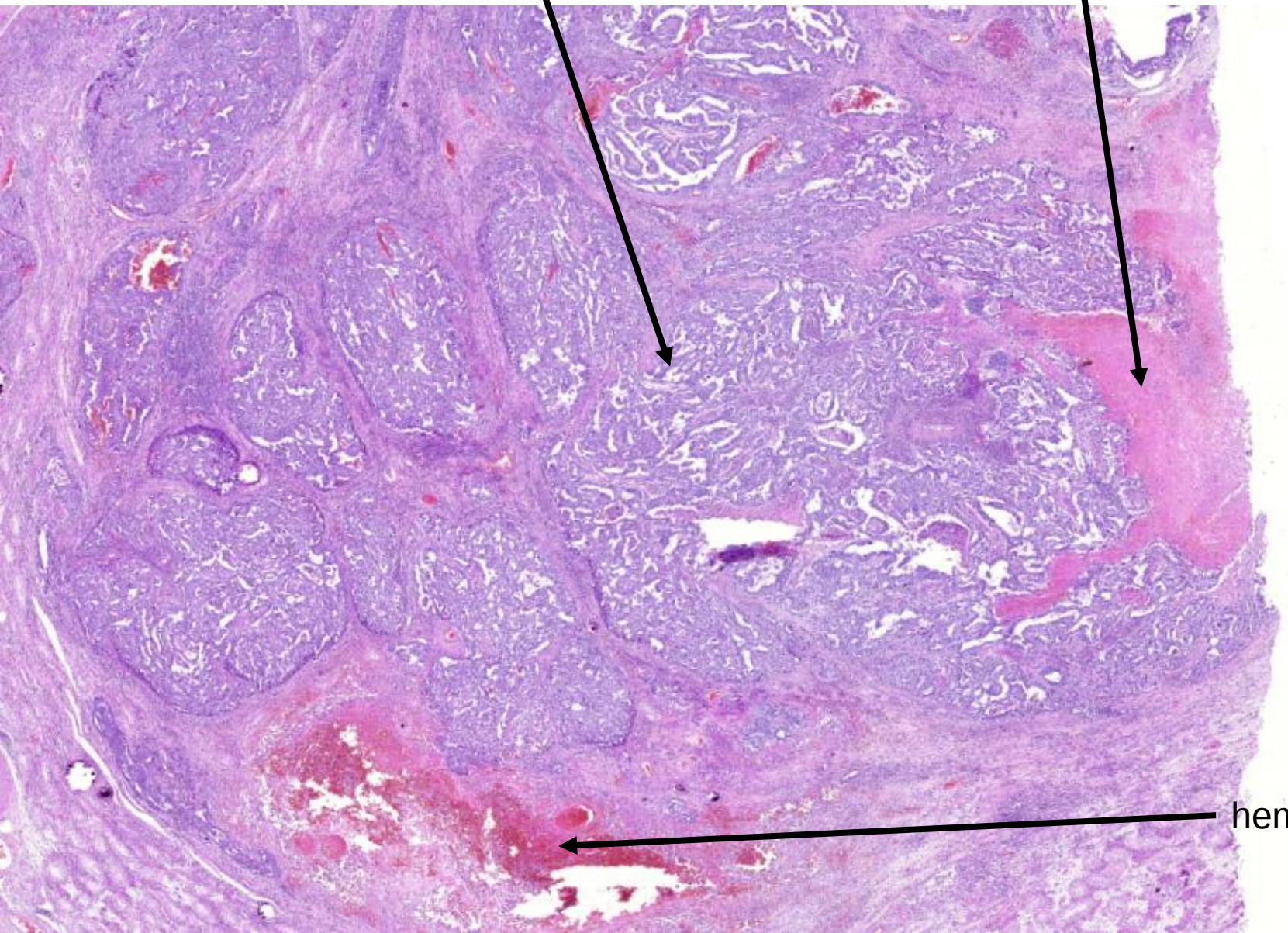

Seminoma


Seminoma
Spermatogonium----------like tumor cells
Normal tissue

Embryonal Carcinoma

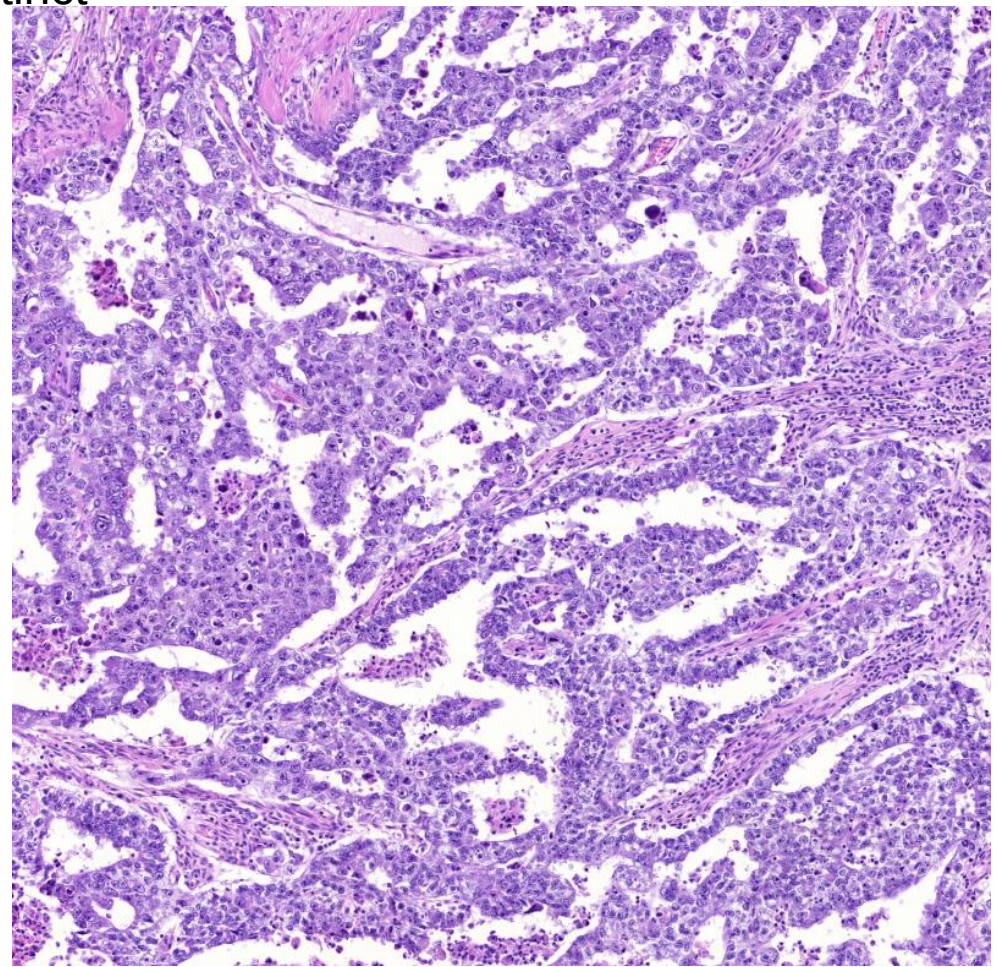
- more agressive tumor than seminoma
- usually mixed (85%)
- Therapy: Orchiectomy, Chemotherapy (PVB, BEP, VIP)
- resistant to radiotherapy
- Macroscopy: white gray, necrosis, haemorrhage




embryonal carcinoma
necrosis
hemorrhage

Embryonal Carcinoma

- solid, pseudoglandular, papillary, alveolar areas
- primitive epithelial tumor cells, indistinct cell borders
- definitive nuclear polymorphism
- prominent nucleoli
- mitotic figures are frequently seen
- fibrotic septi are absent



Metastasis spreading

- Lymphatic spread
  - Retroperitoneal lymphnodes → supradiaphragmatic lymphnodes
  - ((((((Inguinal lymphnodes are only effected exceptionally))))))
    - After inguinal hernia surgery, orchidopexia
    - Tumor infiltrates tunica albuginea
- Hematogenous spread
  - Lungs, less often: liver and brain
  - Choriocarcinoma!