

Testicular and prostatic tumors

Maram Abdaljaleel, MD

Dermatopathologist &

Neuropathologist

**Faculty of Medicine, University of
Jordan**

Testicular Neoplasms:

- Peak incidence at 15-34 years old
- The most common tumors in men and causes 10% of cancer deaths
- include:
 - I. **Germ cell tumors** : (95%); *all are malignant in postpubertal males*
 - II. **Sex cord-stromal tumors**: generally benign.

RISK FACTORS:

- 1. whites > blacks**
- 2. Cryptorchidism :**
3- to-5 folds risk of cancer in the undescended testis, and an increased risk of cancer in the contralateral descended testis.
- 3. Intersex syndromes:**
-Androgen insensitivity syndrome; Gonadal dysgenesis
- 4. Family history:** RR is 4X higher than normal in fathers and sons of affected patient and 8-10X in their brothers

5. The development of cancer in one testis

markedly increased risk of neoplasia in the contralateral testis.

6. An isochromosome of the short arm of chromosome 12, i(12p), is found in virtually all germ cell tumors, regardless of their histologic type.

7. Most testicular tumors in postpubertal males arise from the in situ lesion *intratubular germ cell neoplasia*

Testicular germ cell tumors are sub-classified into:

- I. Seminomas**
- II. Non-seminomatous germ cell tumors(NSGCT)**

- **The histologic appearances may be:**
 - 1. Pure** (i.e., composed of a single histologic type 40% of cases)
 - 2. Mixed** (60% of cases).

I. Seminomas:

- Make up to 50% of all testicular tumors
- ***Classic seminoma:***
 - 40-50 years old
 - Rare in prepubertal children
 - Progressive painless enlargement of the testis
 - Histologically identical to ovarian dysgerminomas and to germinomas occurring in the CNS and other extragonadal sites.

MORPHOLOGY

Grossly:

- soft, well-demarcated tumors, usually without hemorrhage or necrosis.

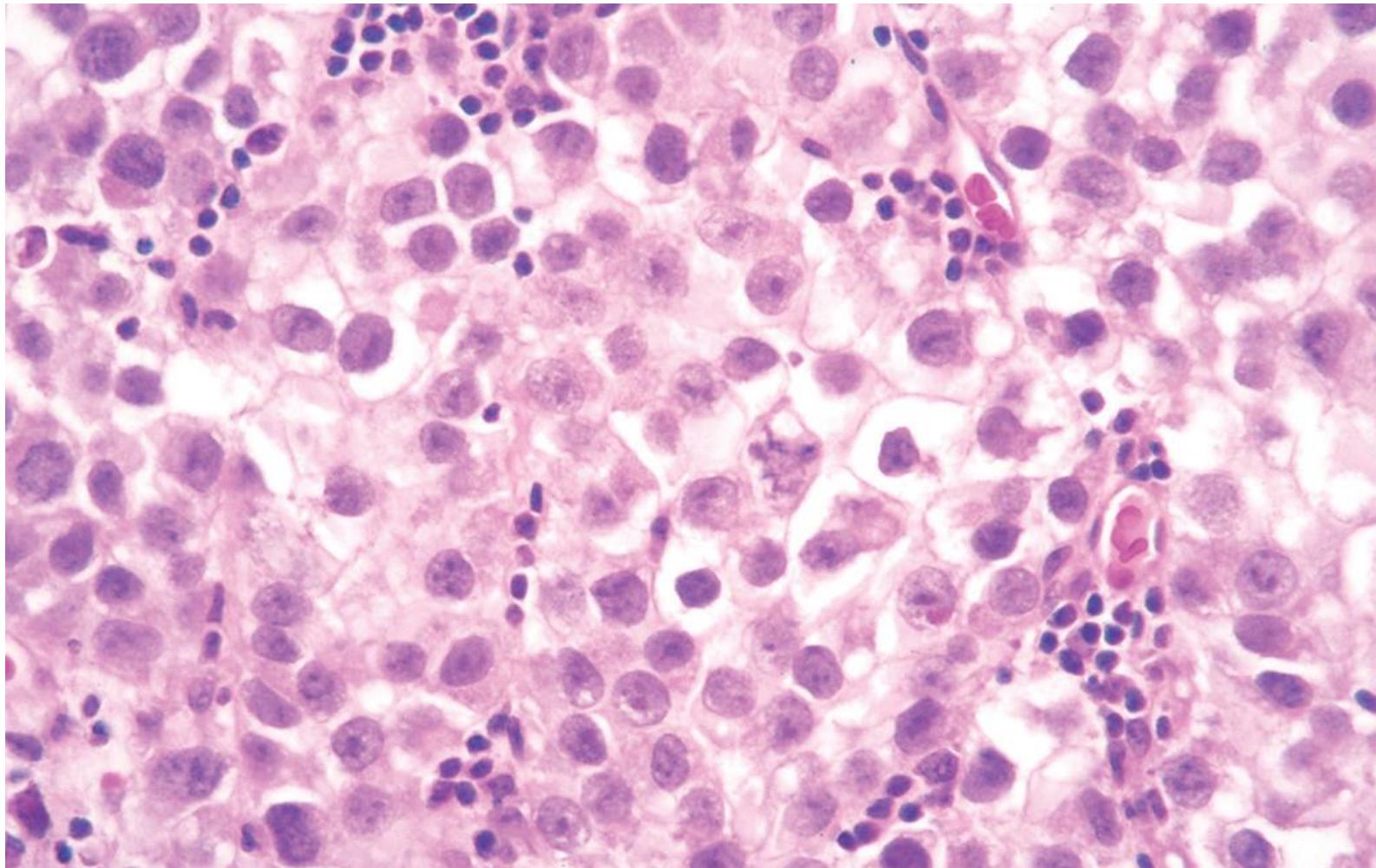
Histologically:

- **large, uniform cells with distinct cell borders, clear, glycogen-rich cytoplasm, round large nuclei, and 1-2 conspicuous nucleoli**
- The cells arrayed in small lobules with intervening delicate fibrous septa.
- A lymphocytic infiltrate usually is present

Seminoma of the testis appearing as a well circumscribed, pale, fleshy, homogeneous mass



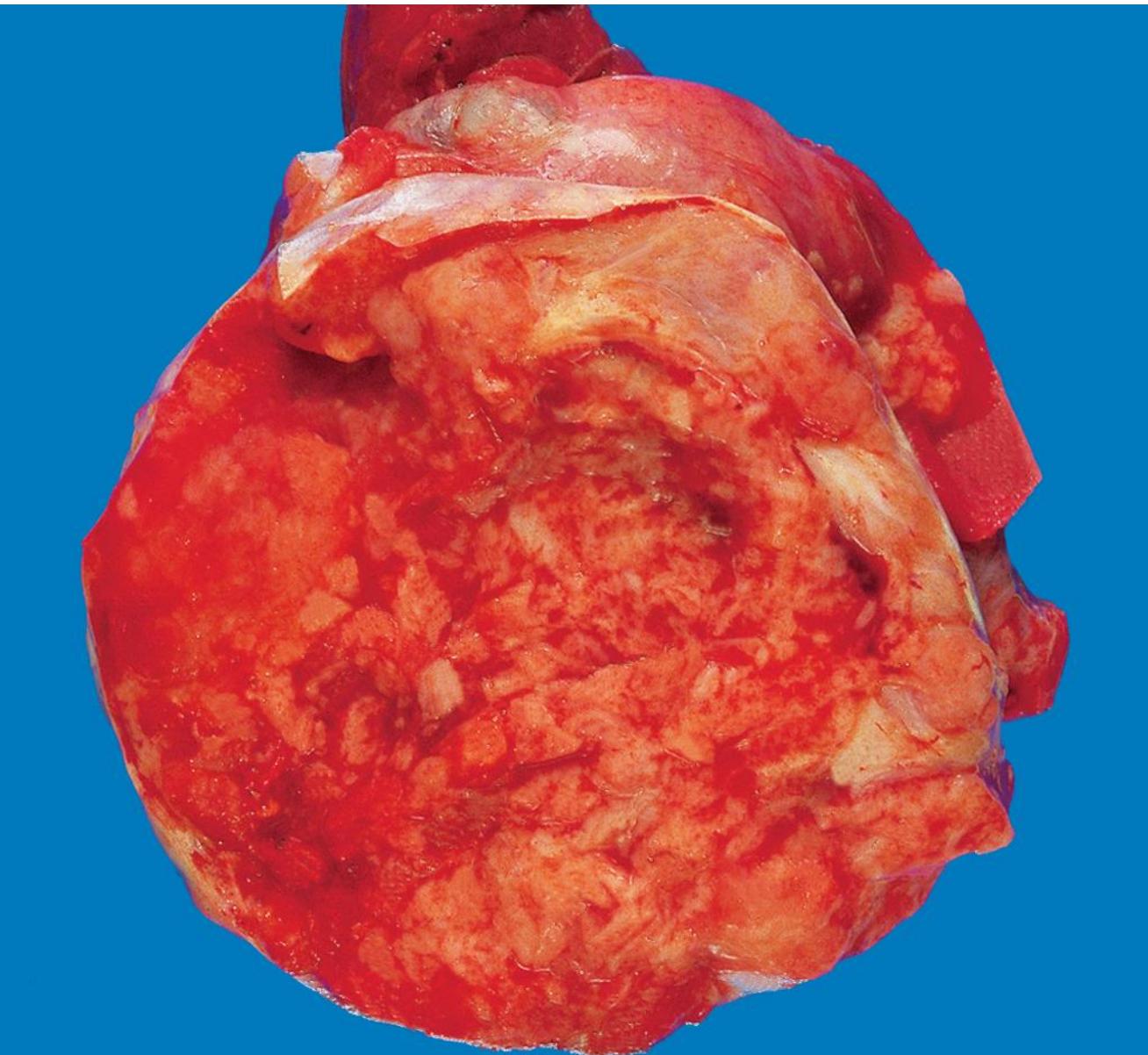
Microscopic examination reveals large cells with distinct cell borders, pale nuclei, prominent nucleoli, and lymphocytic infiltrate.



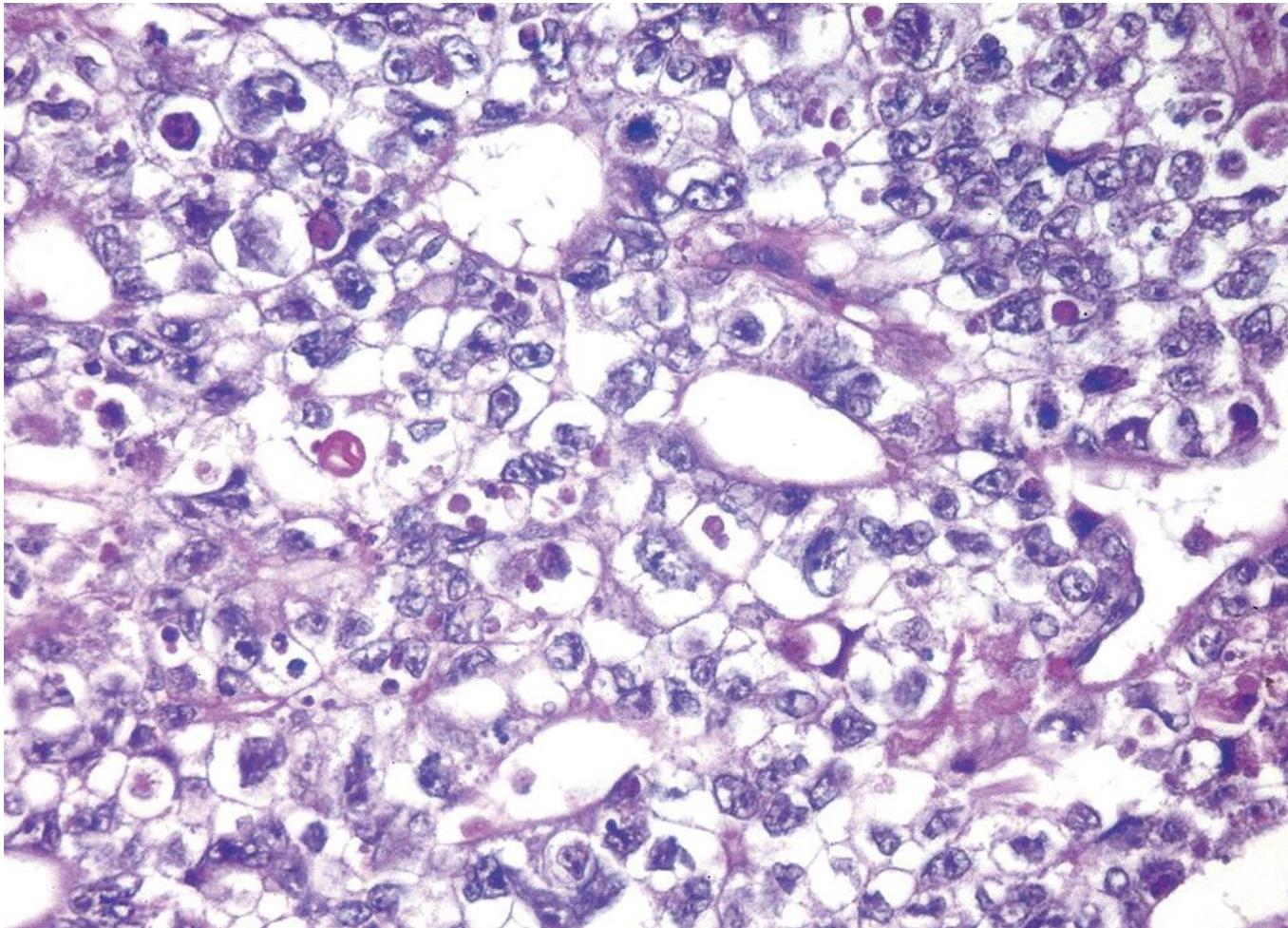
2. Embryonal carcinomas :

- **20-30 years old**
- **More aggressive than seminoma**
- **Grossly:**
 - Are ill-defined masses containing foci of hemorrhage and necrosis
- **Microscopically:**
 - The tumor cells are large and primitive-looking. With basophilic cytoplasm, indistinct cell borders, large nuclei, prominent nucleoli, pleomorphic, and increased mitotic activity

The tumor is hemorrhagic



Sheets of undifferentiated cells & primitive gland -like structures. The nuclei are large and hyperchromatic



3. Yolk sac tumors

- The most common primary testicular neoplasm in **children** <3 yr with very good prognosis
- In adults pure form of yolk sac tumors is rare and have a worse prognosis

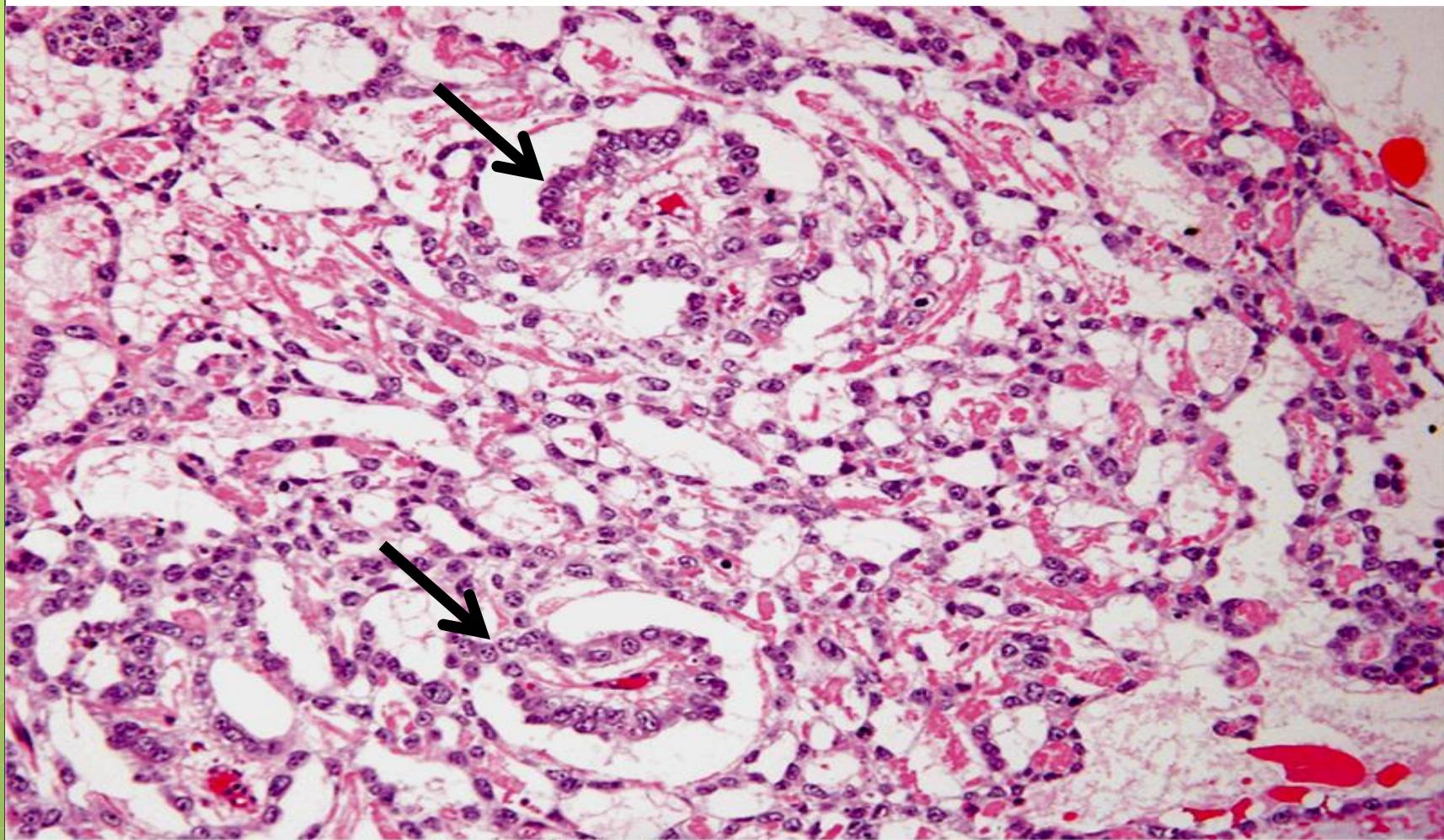
- **Grossly:**

- large and may be well demarcated.

- **Histologically:**

- The tumor is composed of low cuboidal to columnar epithelial cells forming Microcysts, Lacelike (reticular) patterns.
- A distinctive feature is the presence of structures resembling primitive glomeruli, called **Schiller-Duvall bodies**.
- AFP can also be detected in the serum.

Schiller-Duvall bodies.



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4. Choriocarcinomas

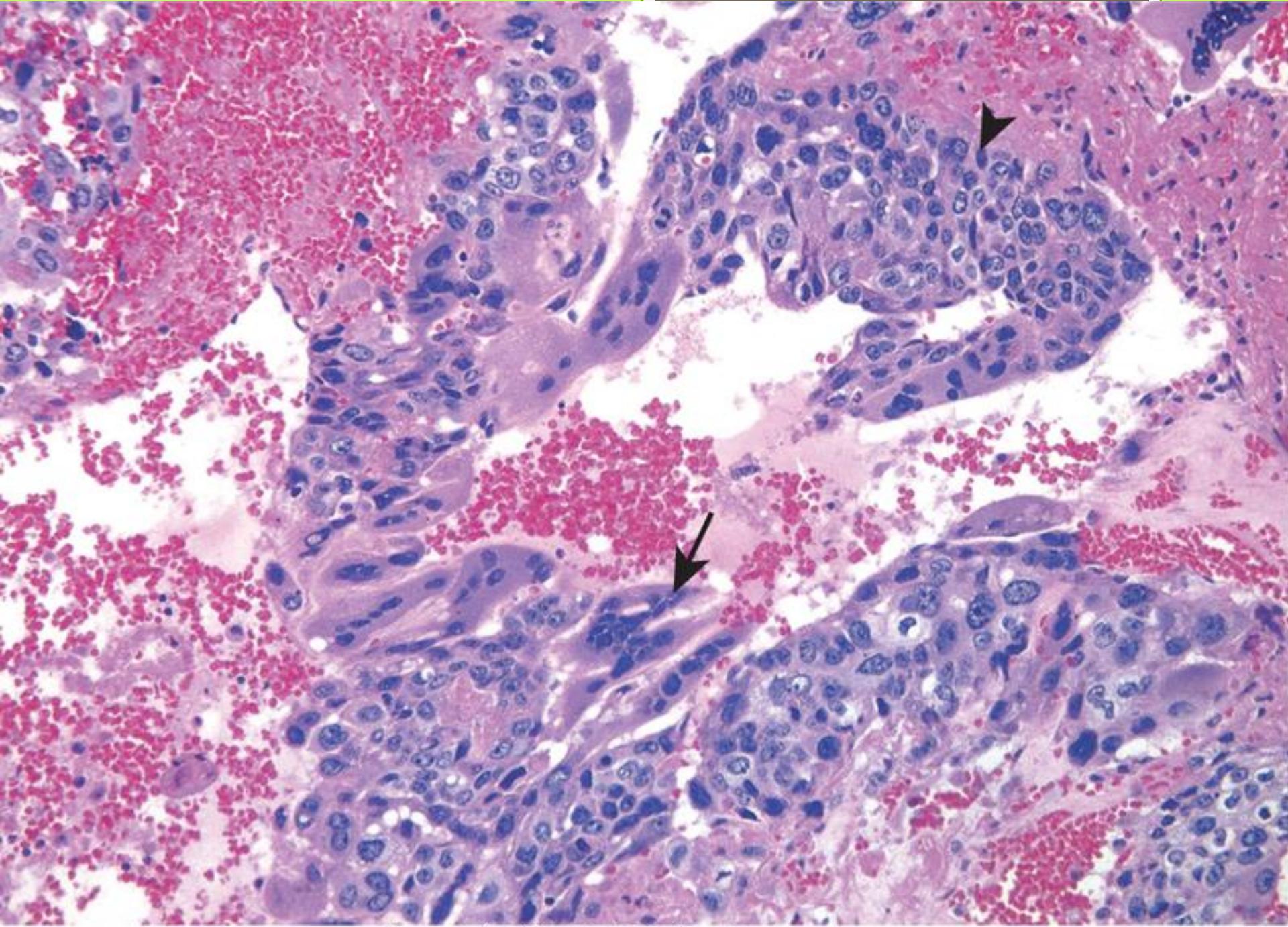
- 20-30 years old
- highly malignant form of testicular tumor.
- its “pure” form is rare, constituting less than 1% of all germ cell tumors
- This neoplasm can also arise in the female genital tract
- Elevated serum level of HCG.

Grossly:

- The primary tumors often are small (<5cm) , palpable nodule with no testicular enlargement, even in patients with extensive metastatic disease.
- necrosis and hemorrhage are extremely common

Microscopic examination:

- Syncytiotrophoblasts: large multinucleated cells with abundant eosinophilic vacuolated cytoplasm containing HCG.
- Cytotrophoblasts: regular polygonal, with distinct borders and clear cytoplasm; grow in cords or masses and have a single, fairly uniform nucleus.



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5. Teratomas

- The neoplastic germ cells differentiate along somatic cell lines showing various cellular or organoid components
- Reminiscent of the normal derivatives of more than one germ layer.
- All ages

- Pure forms of teratoma are common in infants and children , being second in frequency only to yolk sac tumors
- In adults, pure teratomas are rare, constituting 2% to 3% of germ cell tumors. However, the frequency of teratomas mixed with other germ cell tumors is approximately 45%.

- **Grossly:**

firm masses containing cysts and recognizable areas of cartilage

- **Histologically:**

1. **Mature teratomas:**

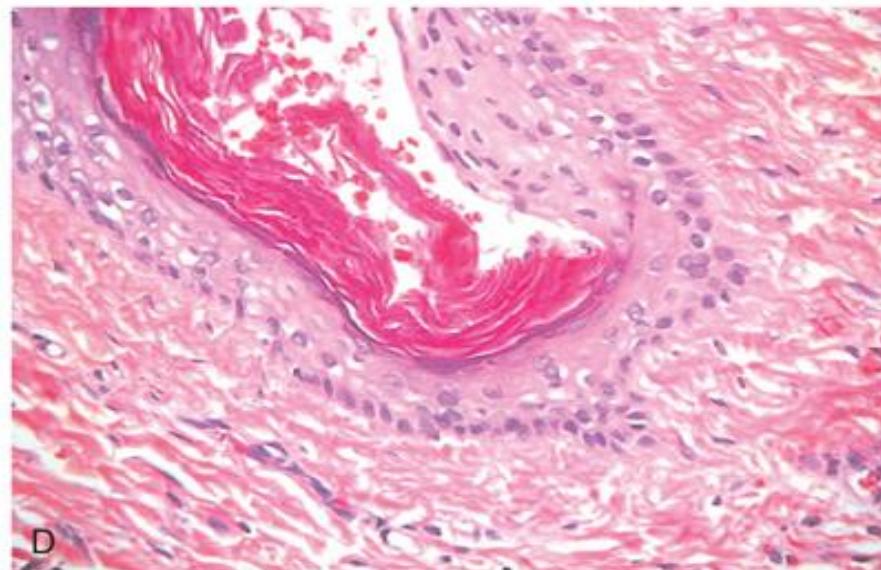
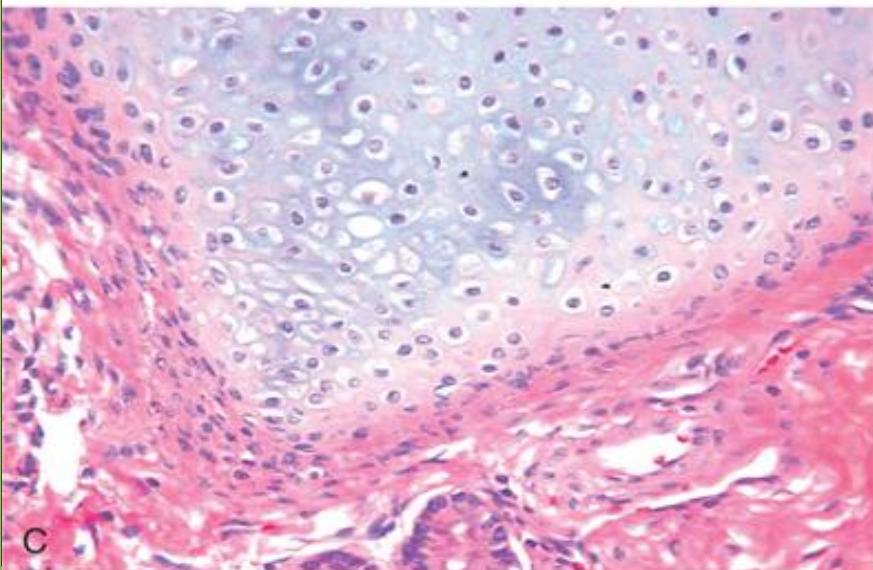
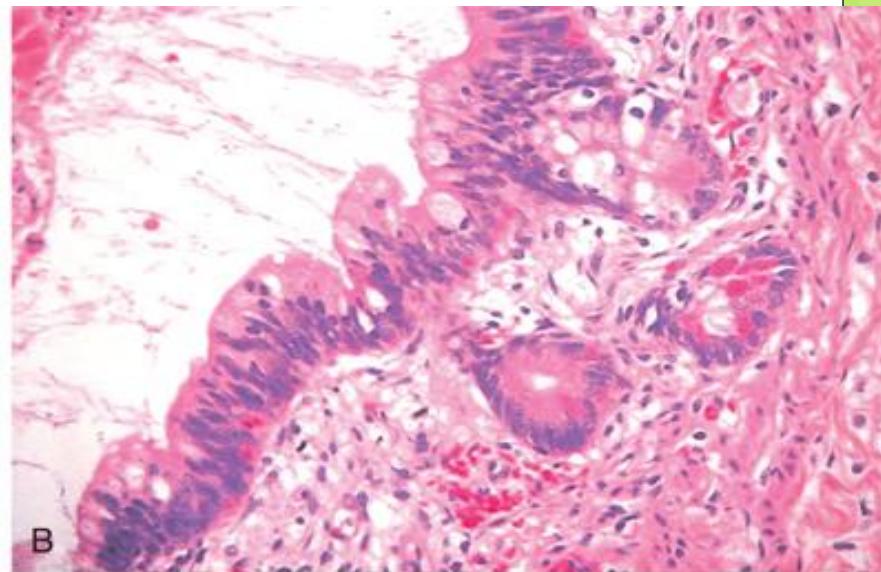
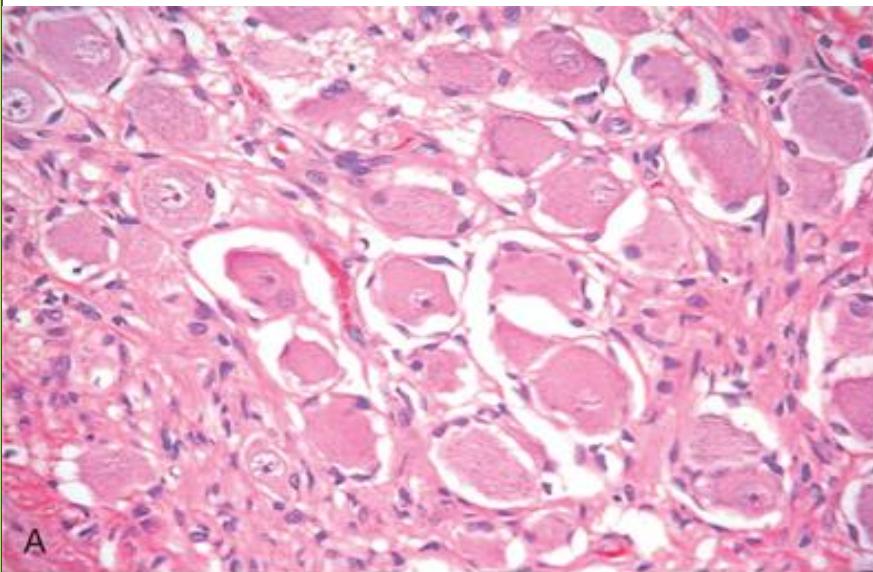
a heterogeneous, collection of differentiated cells or organoid structures, such as neural tissue, muscle bundles, islands of cartilage, clusters of squamous epithelium, etc

2. **Immature teratomas:**

- Share histologic features with fetal or embryonal tissues

- **In prepubertal males**, mature teratomas usually follow a benign course.
- **In postpubertal males**, all teratomas are malignant, being capable of metastasis regardless of whether they are composed of mature or immature elements.
- it is not critical to detect immaturity in a testicular teratoma of a postpubertal male.

teratoma



Clinical Features of testicular germ cell neoplasms:

- present most frequently with a **painless testicular mass** that is non-translucent
- Some tumors, especially NSGCT, may have metastasized widely by the time of diagnosis in the absence of a palpable testicular lesion.

- Biopsy of a testicular neoplasm is **contraindicated**, because it's associated with a risk of tumor spillage
- The standard management of a solid testicular mass is **radical orchectomy**, based on the presumption of malignancy.

Seminomas and nonseminomatous tumors differ in their behavior and clinical course:

I. **Seminomas:**

- often remain confined to the testis for long periods and may reach considerable size before diagnosis.
- Metastases most commonly in the iliac and paraaortic lymph nodes, particularly in the upper lumbar region.
- Hematogenous metastases occur late in the course of the disease.

II. Nonseminomatous germ cell neoplasms:

- tend to metastasize earlier, by lymphatic & hematogenous (**liver and lung** mainly) routes.
- Metastatic lesions may be identical to the primary testicular tumor or different containing elements of other germ cell tumors

Assay of tumor markers secreted by germ cell tumors:

- helpful in diagnosis and following up
 - HCG is **always elevated** in patients with **choriocarcinoma**
 - ✓ HCG may be **minimally elevated** in individuals with other GCTs containing **syncytiotrophoblastic cells**.
 - ✓ AFP is increased in lesions with **yolk sac tumor** component.
 - ✓ **lactate dehydrogenase (LDH)** level correlate with the **tumor burden** (tumor size or load).

TREATMENT:

- **Seminoma:**
 - extremely radiosensitive
 - tends to remain **localized** for long periods
 - **best prognosis.**
 - >95% of patients with early-stage disease can be cured.
- **Nonseminomatous germ cell tumors:**
 - histologic subtype **DOES NOT** influence the therapy.
 - 90% of patients achieve complete remission with **aggressive chemotherapy**, and most are cured.
 - The exception is **choriocarcinoma**, which is associated with a **poorer prognosis**.

Prostate gland pathology



4 cm

Benign Prostatic Hyperplasia (Nodular Hyperplasia)

- extremely common cause of prostatic enlargement in men ≥ 40 ; frequency rises with age.
- androgen-dependent proliferation of both stromal and epithelial elements
- does not occur in males with genetic diseases that block androgen activity.

Pathogenesis:

- Dihydrotestosterone (DHT) is synthesized in the prostate from circulating testosterone by the action of the enzyme **5α-reductase, type 2**.
- DHT → support the growth and survival of prostatic epithelium and stromal cells by binding to **androgen receptors**
- Although testosterone can also bind to androgen receptors and stimulate growth, **DHT is 10 times more potent.**

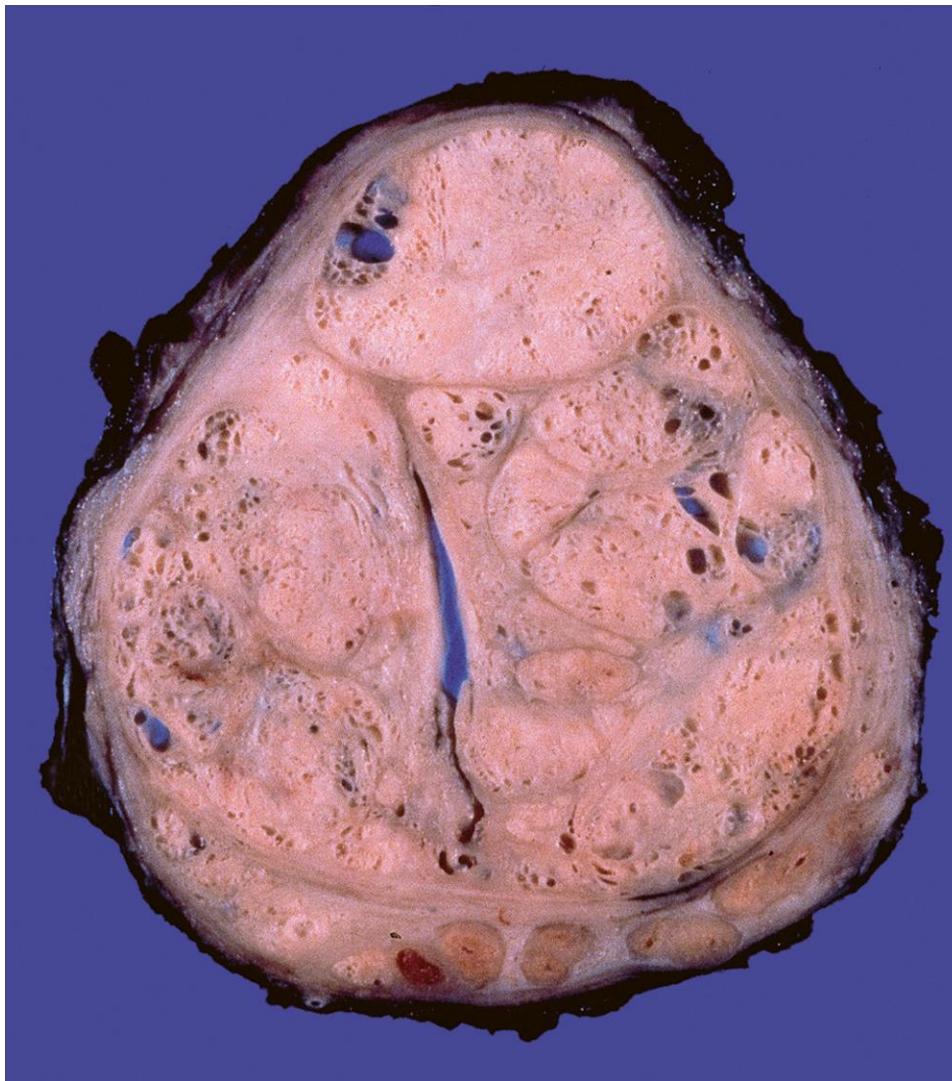
Morphology:

- BPH virtually **always** occurs in the **inner transition zone of the prostate**.
- **Grossly:**
 - Prostatic enlargement (60 and 100 g),
 - many well circumscribed nodules bulging from the cut surface
 - Compressed urethra

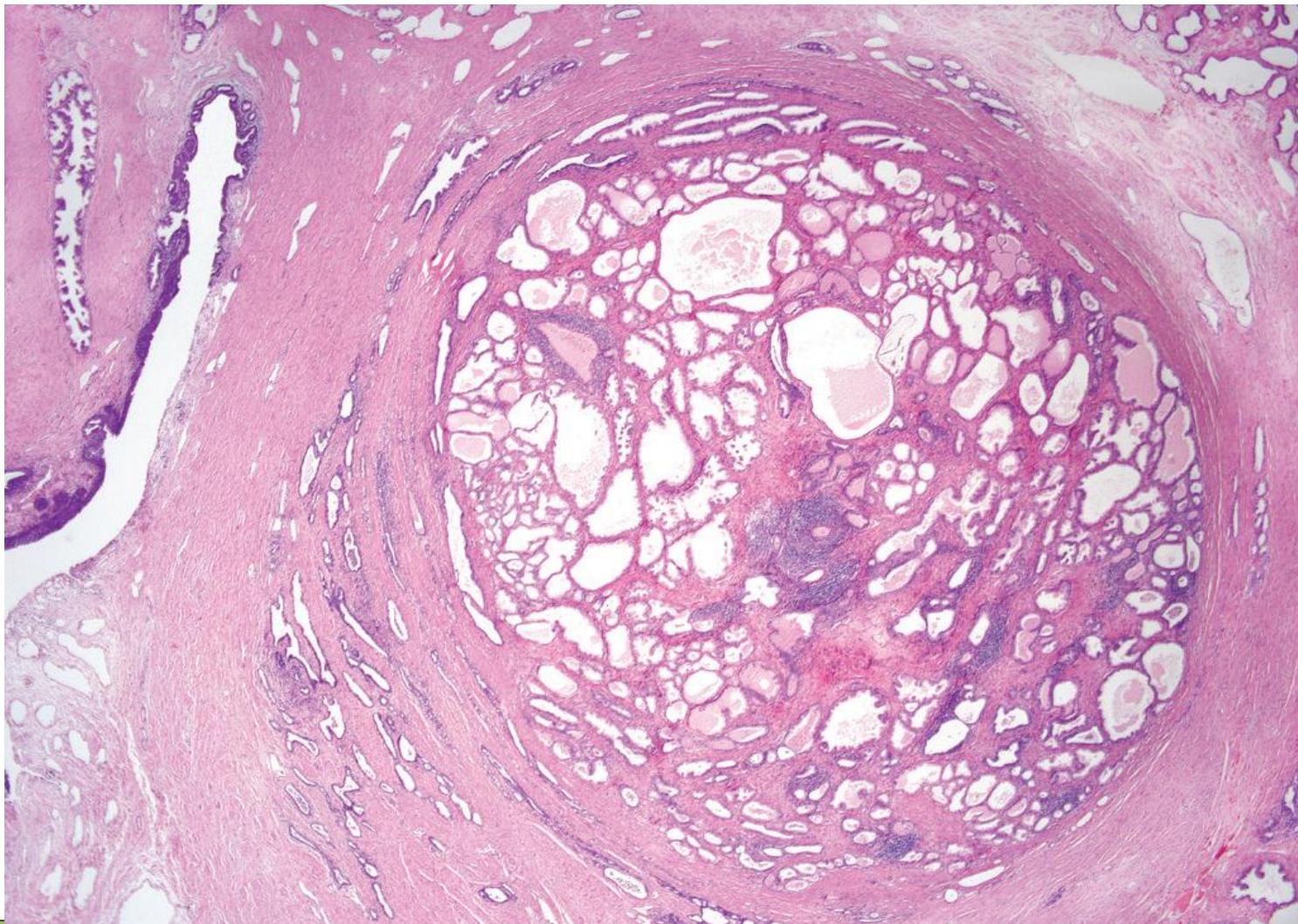
- **Microscopically:**

- hyperplastic nodules composed of proliferating glandular elements and fibromuscular stroma.
- The hyperplastic glands are lined by tall, columnar epithelial cells and a peripheral layer of flattened basal cells.

Nodular prostatic hyperplasia: Well-defined nodules



Nodular hyperplasia of the prostate. →well-demarcated nodule with a portion of urethra.



Clinical features:

- Because BPH preferentially involves the **inner portions of the prostate**, the most common manifestations are **lower urinary tract obstruction**
 - difficulty in starting the stream of urine (hesitancy)
 - intermittent interruption of the urinary stream
 - urinary urgency, frequency, and nocturia, all indicating bladder irritation.
- ↑ risk of urinary tract infections.

- **TREATMENT:** agents that inhibit the formation of DHT from testosterone (5-alpha reductase inhibitors) or that relax prostatic smooth muscle by blocking α 1-adrenergic receptors +/- Surgery

Carcinoma of the Prostate

- >50 years of age.
- **The most common form of cancer in men**
- significant drop in prostate cancer mortality,
due to increased detection of the disease
through screening

PATHOGENESIS

1. Androgens.

- Provide the “soil,” within which prostate cancer develops
- Cancer of prostate does not develop in males castrated before puberty.
- Cancers regress in response to surgical or chemical castration

2. Heredity:

↑risk among first-degree relatives of patients with prostate cancer.

3. Environment:

- Geographical variations → raise of incidence in Japanese immigrants to US
- diet: westernized dietary habits

4. Acquired somatic mutations

- The most common gene rearrangements in prostate cancer → fusion genes consisting of the androgen regulated promoter of the ***TMPRSS2*** gene and the coding sequence of ***ETS*** family transcription factors.
→ ***TMPRSS2-ETS*** fusion genes

Clinical Features

- 70% - 80% arise in peripheral glands → palpable as irregular hard nodules on digital rectal examination.
- elevated serum prostate-specific antigen (PSA) level screening tests.
- Bone metastases (axial skeleton) → osteoblastic (bone-producing) lesions on bone scans

○ References:

- Robbins basic pathology, 10th edition
- Robbins and Cotran Atlas of Pathology, 3rd edition

QUESTIONS!



Thank you!