MALE GENITAL TRACT

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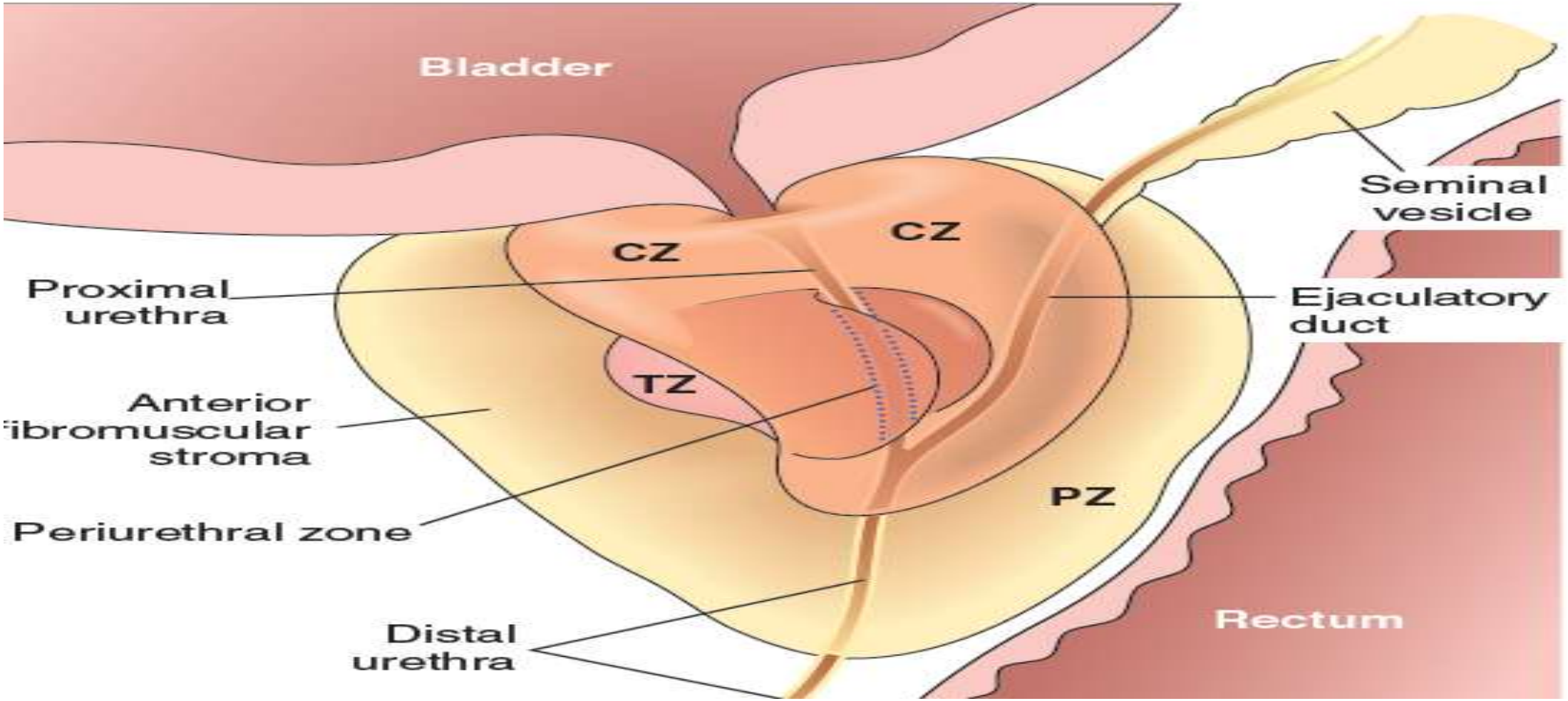
*لا تنسوا أهلنا في غزة من الدعوات والصدقات..

Prostate

- The normal prostate contains glands with two cell layers:
- 1. Flat basal cell layer
- 2. An overlying columnar secretory cell layer
- The surrounding prostatic stroma contains a mixture of smooth muscle and fibrous tissue.

Prostate zones

central zone (CZ), a peripheral zone (PZ), a transitional zone (TZ), and a periurethral zone.



- Most carcinomas arise from the peripheral glands of the organ
- Nodular hyperplasia arises from more centrally situated glands (inner transitional zone
- Most carcinomas (70%–80%) arise in the peripheral zones
- Carcinomas are often detected by rectal exammination
- Hyperplasias are more likely to cause urinary obstruction.

Benign Prostatic Hyperplasia

- **Benign prostatic hyperplasia (BPH) is an extremely common cause of prostatic enlargement**
- **It results from proliferation of of stromal and glandular elements**
- **It is present in a significant number of men by 40 years of age,**
- **Its frequency rises progressively thereafter reaching 90% by the eighth decade of life.**
- **The enlargement of the prostate in men with BPH is an important cause of urinary obstruction.**

- **Excessive androgen-dependent growth of stromal and glandular elements has a central role in the pathogenesis of BPH.**
- **BPH does not occur in males who are castrated before the onset of puberty or in males with genetic diseases that block androgen activity**

- **BPH virtually always occurs in the inner transition zone of the prostate.**
- The affected prostate is enlarged
- Many wellcircumscribed nodules that bulge from the cut surface (Fig.
- 18.11).
- The nodules may appear solid or contain cystic spaces the latter corresponding to dilated glands.
- The urethra is usually compressed, often to a narrow slit, by the hyperplastic nodules.

Benign nodular hyperplasia of prostate

Clinical Features

- **Difficulty in starting the stream of urine (hesitancy)**
- **Intermittent interruption of the urinary stream while voiding**
- **Urinary urgency, frequency, and nocturia, indicative of bladder irritation**
- **The presence of residual urine in the bladder due to chronic obstruction increases the risk for urinary tract infections**

الانسداد الكامل في مجرى البول يؤدي إلى
تمدد مؤلم في المثانة .

- **Complete urinary obstruction with resultant painful distention of the bladder**
- **Hydronephrosis** (استسقاء الكلية) .

* في حالة البول ما يقدر ينزل من الكلية للمثانة بسبب
حصى ، يصير بالكلية انتفاخ وبتبلش تتوسع بسبب
تراكم البول فيها ، "إذا استمر كذا بدون علاج
ممكن يأدي إلى فشل كلوي" .

Carcinoma of the Prostate

- **Adenocarcinoma of the prostate and is the most common form of cancer in men, accounting for 27% of cancer cases in the United States in 2014**
- **> 50 yr of age**

Predisposing factors

- **1. Androgens** (sex hormones)

- **2. Heredity**
- **There is an increased risk among first-degree relatives of patients with prostate cancer.**
- **Prostate cancer is uncommon in Asians**
- **The incidence is highest among African-Americans and in Scandinavian countries.**
- **Aggressive, clinically significant disease is more common in African-Americans than in Caucasians.**

- **3. Environment**
- **The incidence in Japanese immigrants to the United States rises**
- **The diet in Asia becomes more westernized**

لما بتغرب

anomalies

- 4. **Acquired genetic aberrations**
- The most common gene rearrangements in prostate cancer create fusion genes consisting of the androgenregulated promoter of the *TMPRSS2* gene and the coding sequence of *ETS* family transcription factors.
- It occurs in 40-60% of prostate cancers in Caucasian populations, and they occur relatively early in tumorigenesis.
- Tumor suppressor PTEN mutation

- Most prostate cancers are **moderately differentiated adenocarcinomas** that produce well-defined glands. The glands
- typically are smaller than benign glands and are lined by a single
- uniform layer of cuboidal or low columnar epithelium, lacking
- the basal cell layer seen in benign glands. In further contrast with
- benign glands, malignant glands are crowded together and characteristically
- lack branching and papillary infolding.

Prostate adenocarcinoma

- Prostate cancer is graded by the **Gleason system,** created
- in 1967 and updated in 2014.
- According to this system, prostate cancers are stratified into five grades on the basis of glandular patterns of differentiation.
- Grade 1 represents the most well differentiated tumors, and grade 5 tumors show no glandular differentiation.

Clinical features

→ Prostate specific antigen

- **1.Elevated PSA serum levels**
- **2.Palpable nodules on per rectal examination**
- **3. Incidental**
- **4.** Bone metastases, particularly to the axial skeleton (osteoblastic (bone-producing) lesions that can be detected on radionuclide bone scans)

→ Radioactive nuclide.

Testicular Neoplasms

- **Testicular neoplasms occur in roughly 6/100,000 males.** (Rare)
- **Peak in incidence 15-34-year-old age group** (Young)
- **Neoplasms of the testis are heterogeneous and include:**

1. **Germ cell tumors (95%)**
2. **Sex cord–stromal tumors (5%)**

- In postpubertal males, 95% of testicular tumors arise from germ cells, and almost all are malignant
- Sex cord-stromal tumors derived from Sertoli or Leydig cells are uncommon and usually benign

- **Risk factors:**

1. Whites more than blacks
2. Cryptorchidism is associated with a 3-5 fold increase in the risk for cancer in the undescended testis, as well as an increased risk for cancer in the contralateral descended testis

A history of cryptorchidism is present in approximately 10% of cases of testicular cancer

عدم تطابق بين الكروموسوم
والأعضاء التناسلية الخارجية أو
الداخلية أو الوظيفة الهرمونية

* ذكر جينتيا (XY)
لكنه انثى هرمونيا

3. **Intersex syndromes, including androgen insensitivity syndrome and gonadal dysgenesis also are associated with an increased frequency of testicular cancer.**

* خلل في تطور
الاعضاء التناسلية

4. Inherited factors

There is an increased risk of 8-10 folds inbrothers of males with germ cell tumors have an 8-10-fold increased risk

5. The development of cancer in one testis is associated with a markedly increased risk for neoplasia in the contralateral testis

6. Genetics

- Extra copies of the short arm of chromosome 12, usually due to the presence of an isochromosome 12 [i(12p)] are found in virtually all germ cell tumors
- Mutations in *KIT gene* are found in up to 25% of tumors

Classification

I. **Seminomas**

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

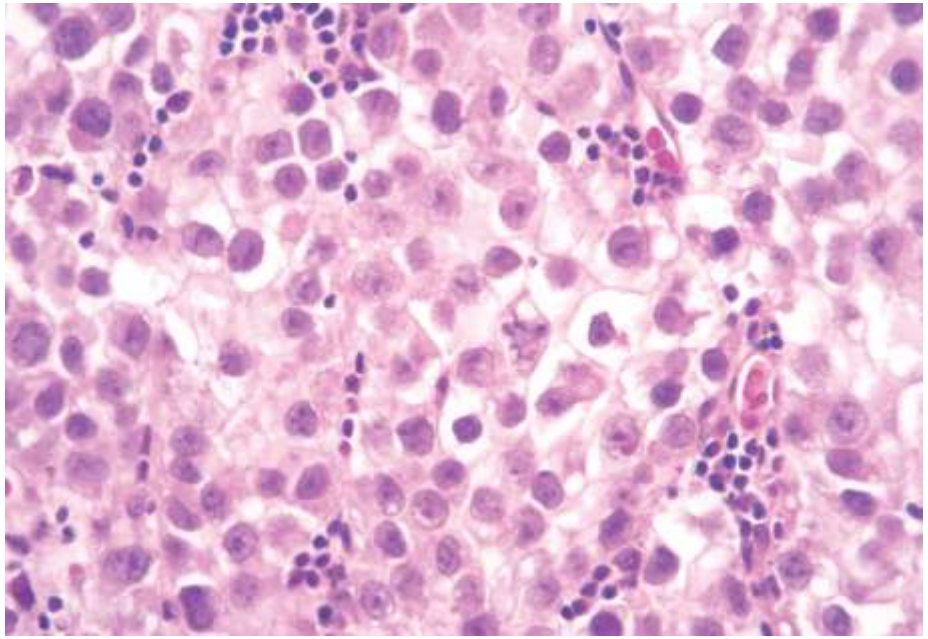
- embryonal carcinoma
- yolk sac tumor
- choriocarcinoma
- teratoma

Pure or Mixed

Seminoma

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

1. Seminoma

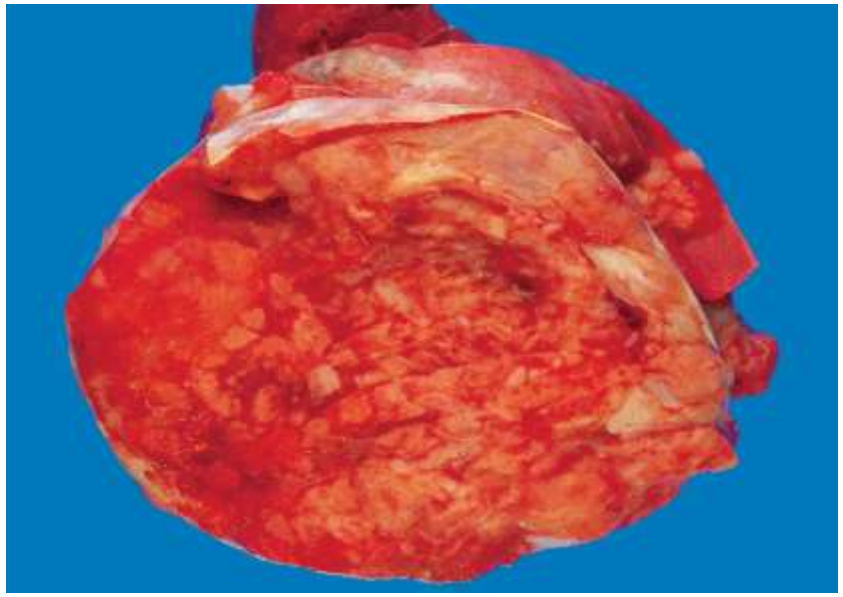


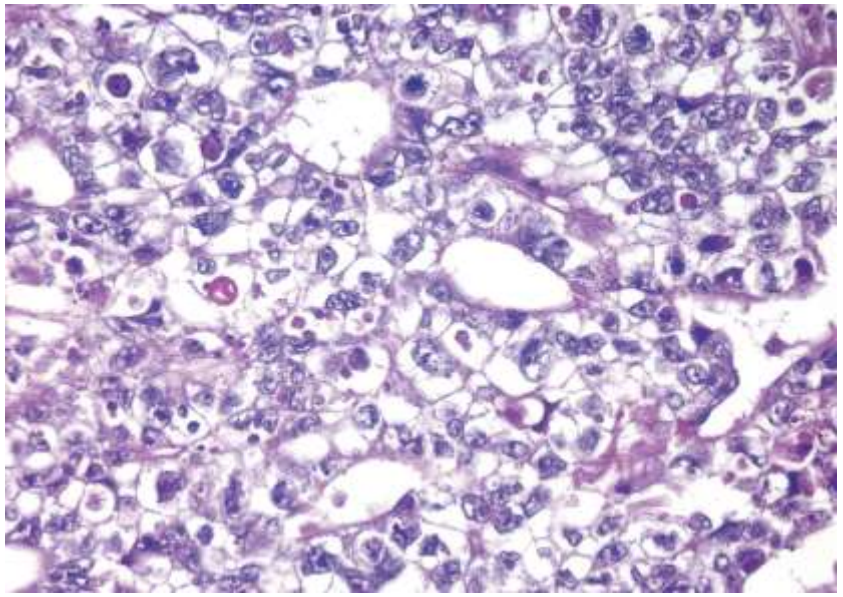
Seminoma :circumscribed, pale, fleshy, homogeneous mass; usually without hemorrhage or necrosis.

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

2. Embryonal carcinoma

non-seminomatous





ill-defined masses containing foci of **hemorrhage** and **necrosis**

Sheets of undifferentiated cells & primitive gland -like structures. The nuclei are large and hyperchromatic with prominent nucleoli, and increased mitotic activity

- **20-30 years old**
- **More aggressive than seminoma**

3. Yolk sac tumors

- The most common primary testicular neoplasm in children <3 year
- Good prognosis in young children
- In adults, pure form of yolk sac tumors is rare and have a worse prognosis

- **Yolk sac tumors**

- **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.**

- **Alpha- feto-protein (AFP)** usually detected in serum.

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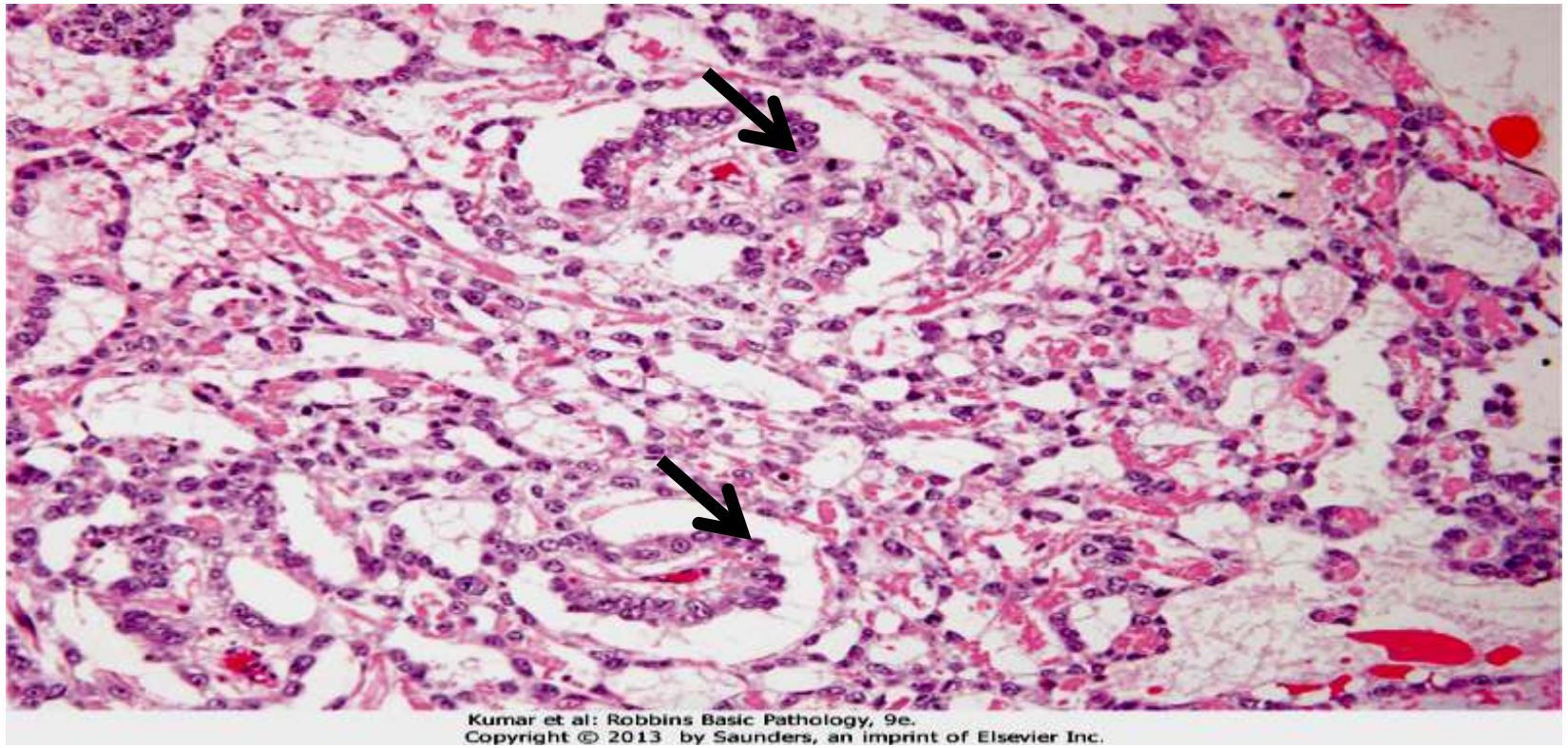
3. Yolk sac tumor (arrows: Schiller-Duvall bodies)



4. Choriocarcinoma

- **Highly malignant form of testicular tumor.**
- **"pure" form is rare, constituting less than 1% of all germ cell tumors**
- **Usually mixed with other germ cell tumors**
- **Characterized: Elevated serum level of HCG**

Human chorionic gonadotropin.

Macroscopically:

- The primary tumors may be small even in patients with extensive metastatic disease.
- necrosis and hemorrhage are extremely common

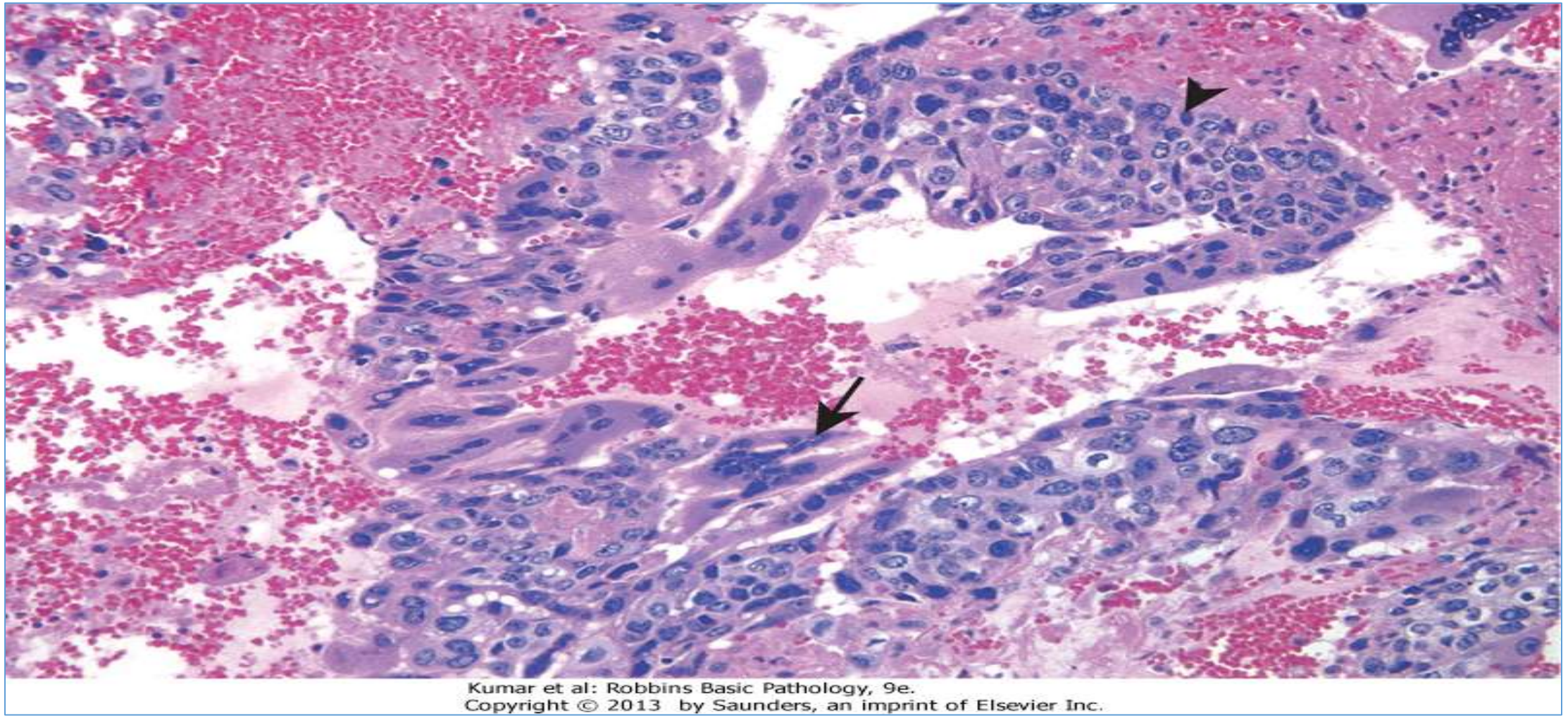
Microscopic examination:

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

Choriocarcinoma

Arrow: **Syncytiotrophoblast**

Arrow head: Cytotrophoblast



5. Teratoma

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

- **In children**

- **Pure forms of teratoma are common being second in frequency to yolk sac tumors**

- **In adults**

- **Pure teratomas are rare (3% of germ cell tumors).**

- **frequency of teratoma mixed with other germ cell tumors is high.**

- **Grossly:**

  Firm masses and cysts with hair, cartilage, bone, and even teeth!

- **Histologically:**

1. **Mature teratomas:**

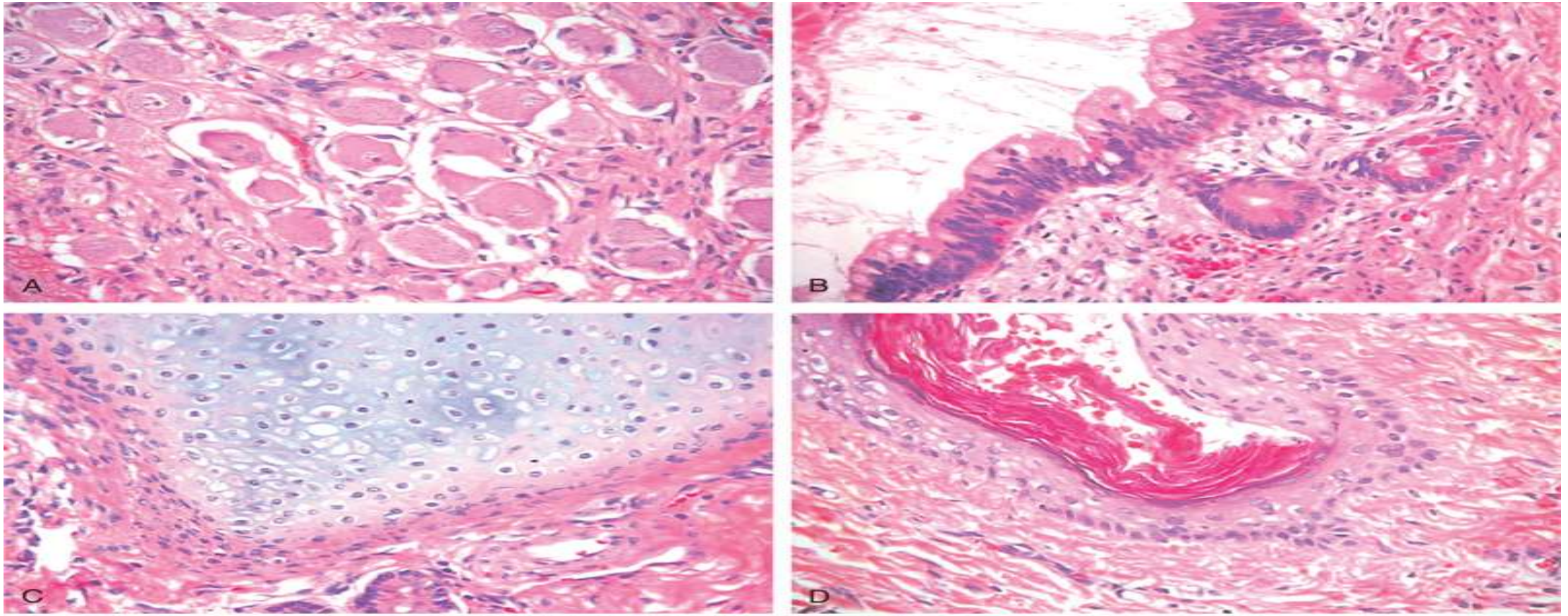
   a heterogeneous collection of differentiated cells, such as neural tissue, muscle bundles, islands of cartilage, clusters of squamous epithelium, etc.

2. **Immature teratomas:**

- Contain fetal primitive tissues

Teratoma

Teratoma



- **In prepubertal males**, mature teratomas usually follow a benign course.
- **In postpubertal males,** all teratomas are regarded as potentially malignant, being capable of metastasis regardless of whether they are composed of mature or immature elements.

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
- 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 orchiectomy**, 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**
- **If metastasize, most commonly in iliac and paraaortic lymph nodes**
- **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**

Serum Assay of tumor markers secreted by germ cell tumors:

- Helpful in diagnosis and follow up (to detect recurrence and response to therapy)
  - ✓**HCG** : **elevated** in patients with **choriocarcinoma**
  - ✓**AFP** : **elevated** in patients with **yolk sac tumor**
  - ✓**lactate dehydrogenase (LDH)**:correlate with the **tumor burden** (tumor size and load); regardless of histologic type

* يعني ممكن يجيني ناتج عن الحجم، والحجم لـ mass بغض النظر عن الـgrade

- لاتنسونا من الدعوات ..