MALE GENITAL TRACT

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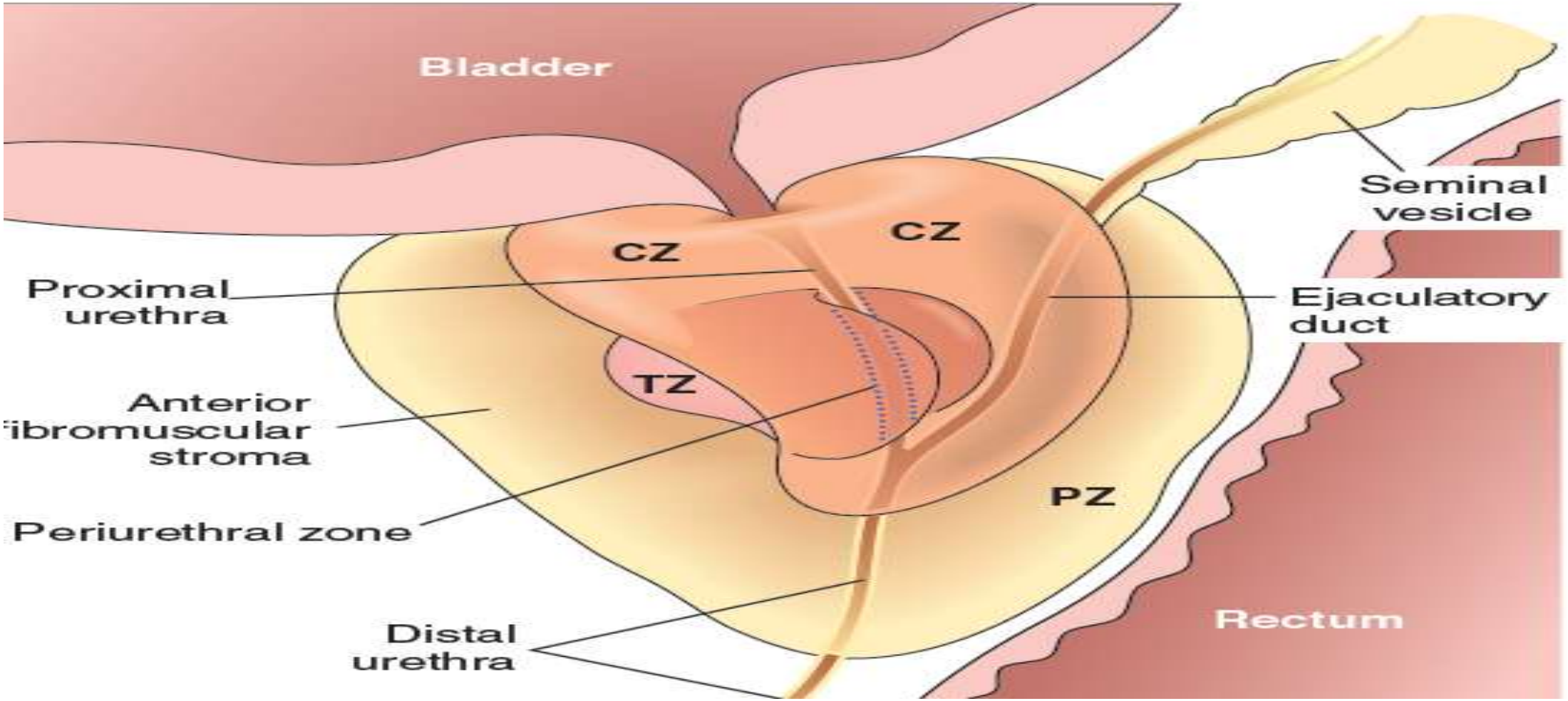
Prostate

- **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.**

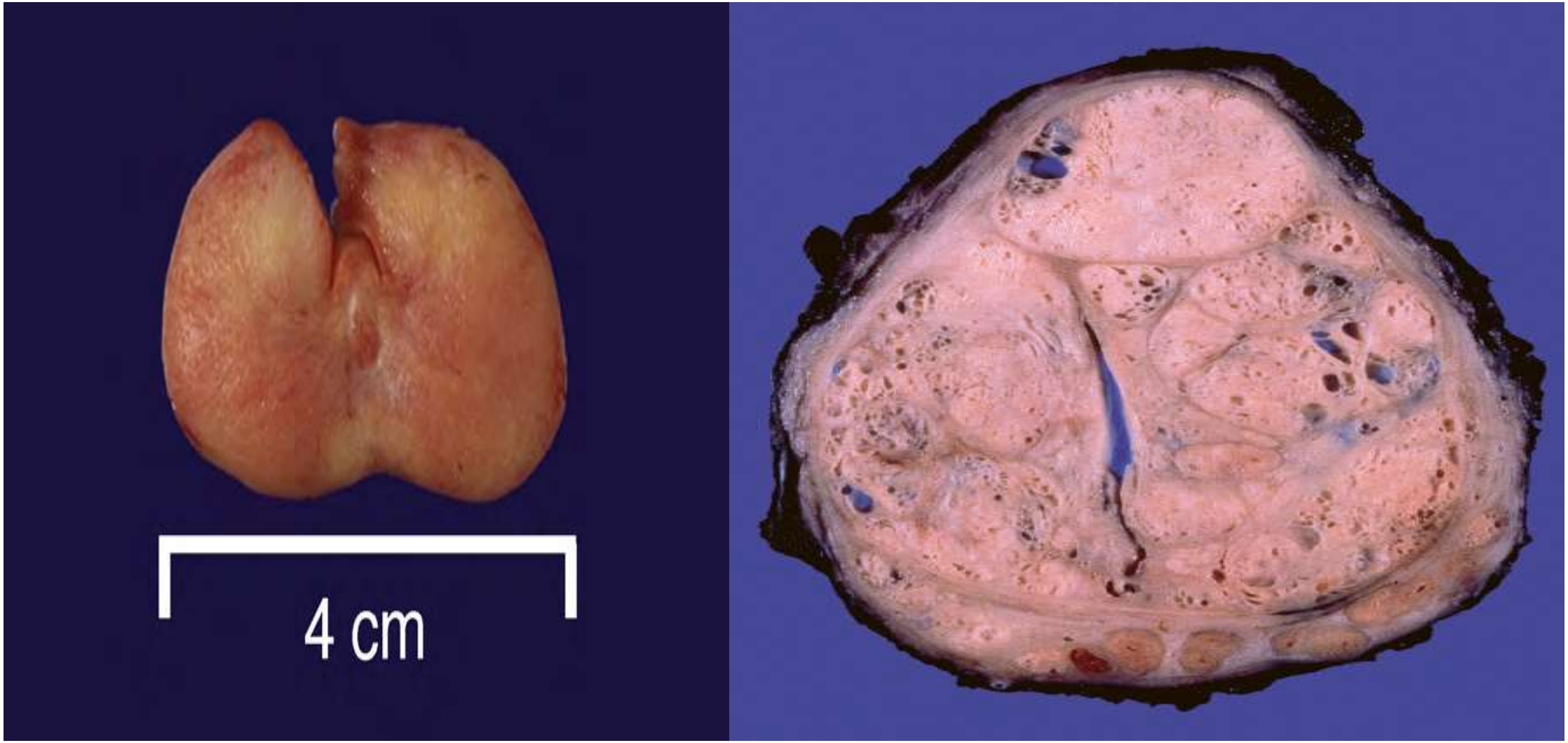
Benign Prostatic Hyperplasia

- **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**

- **Complete urinary obstruction with resultant painful distention of the bladder**
- **Hydronephrosis**

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**

- **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**

- **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

- **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)

Testicular Neoplasms

- **Testicular neoplasms occur in roughly 6/100,000 males.**
- **Peak in incidence 15-34-year-old age group**
- **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

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

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)

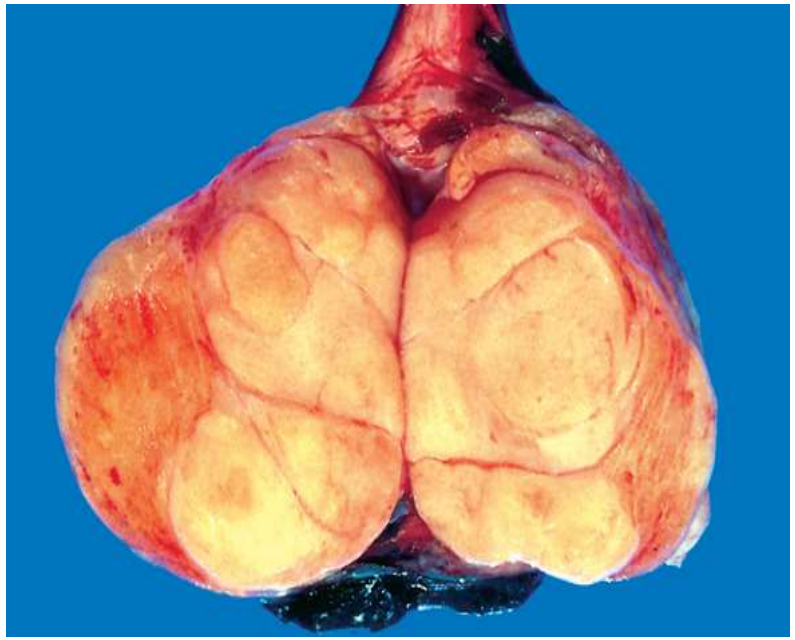
- embryonal carcinoma
- yolk sac tumor
- choriocarcinoma
- teratoma

Pure or Mixed

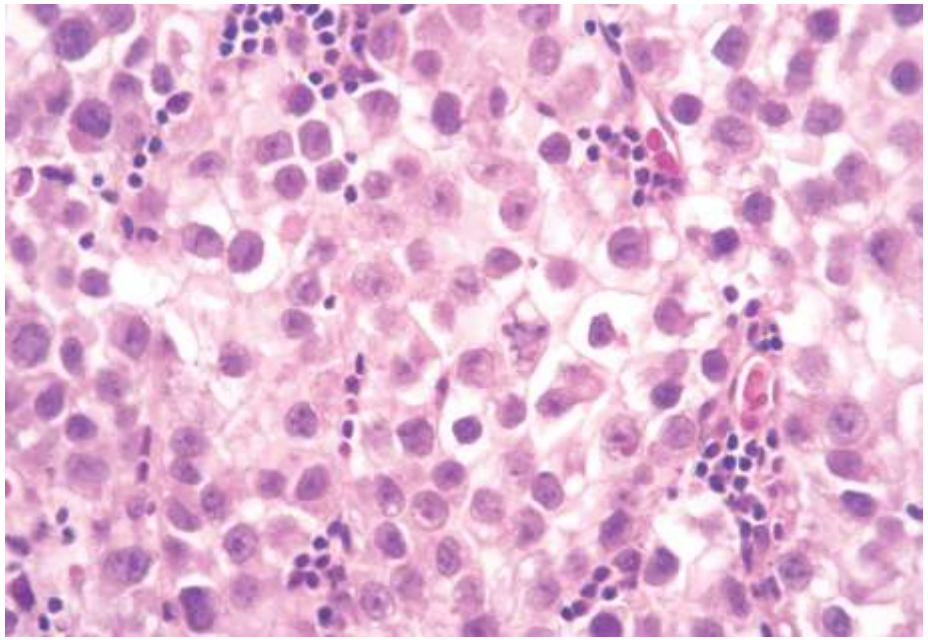
Seminoma

- **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

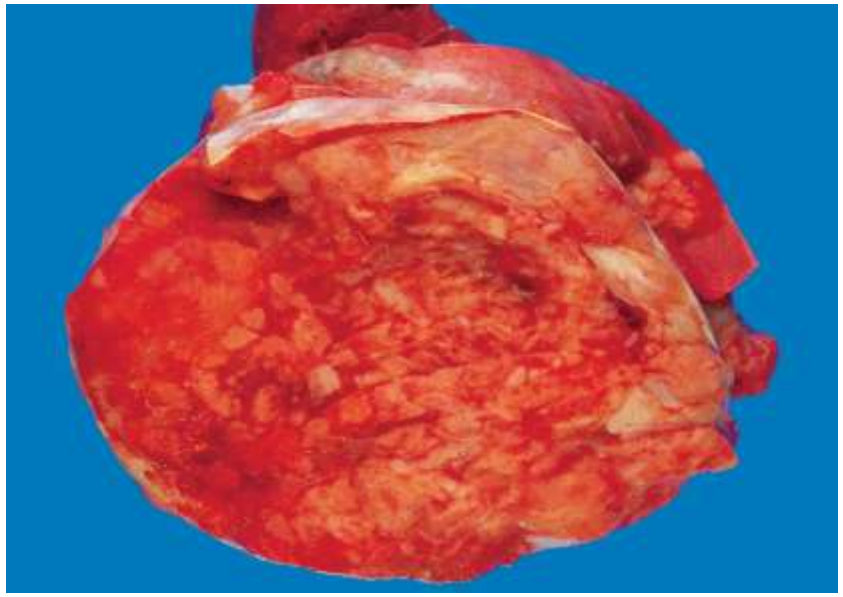


Seminoma :circumscribed, pale, fleshy, homogeneous mass; usually without hemorrhage or necrosis.

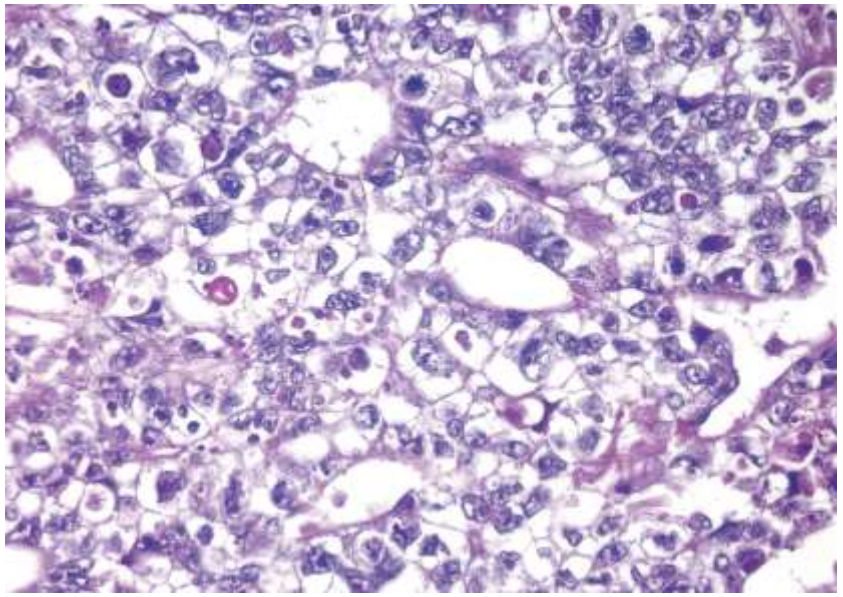


Microscopic examination reveals large cells with distinct cell borders, pale nuclei, prominent nucleoli, and lymphocytic infiltrate.

2. Embryonal carcinoma



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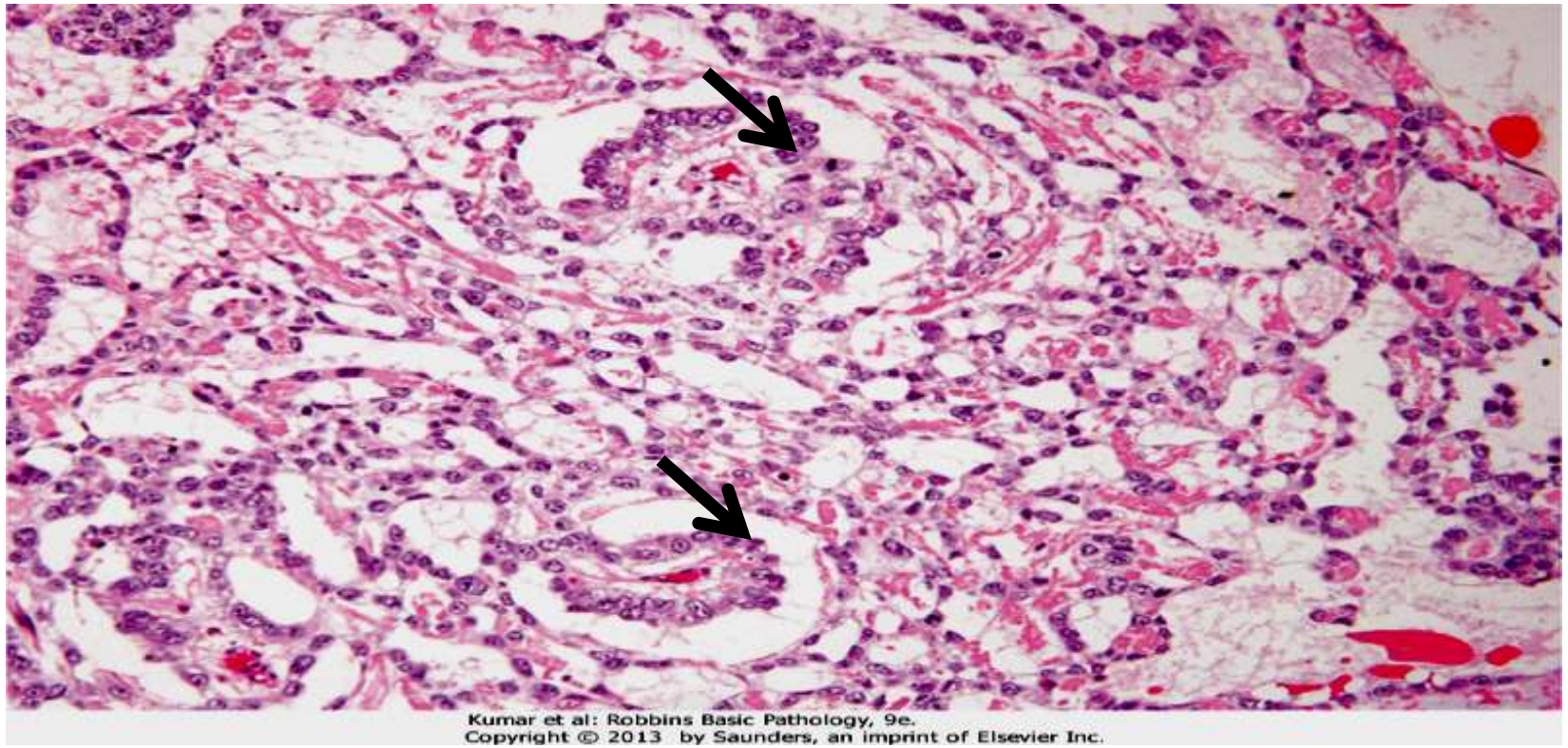
3. Yolk sac tumor (arrows: Schiller-Duvall bodies)



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**

Macroscopically:

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

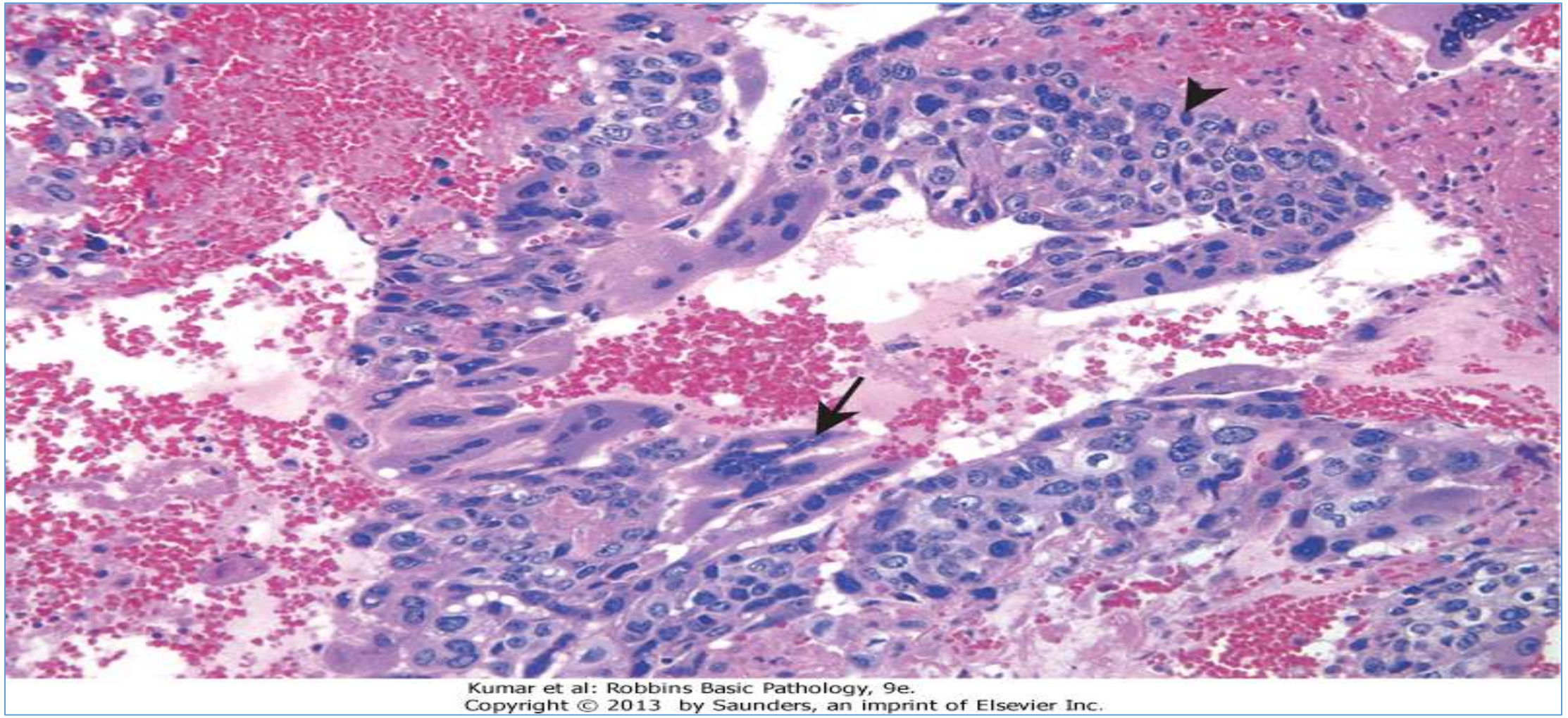
Microscopic examination:

- **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:

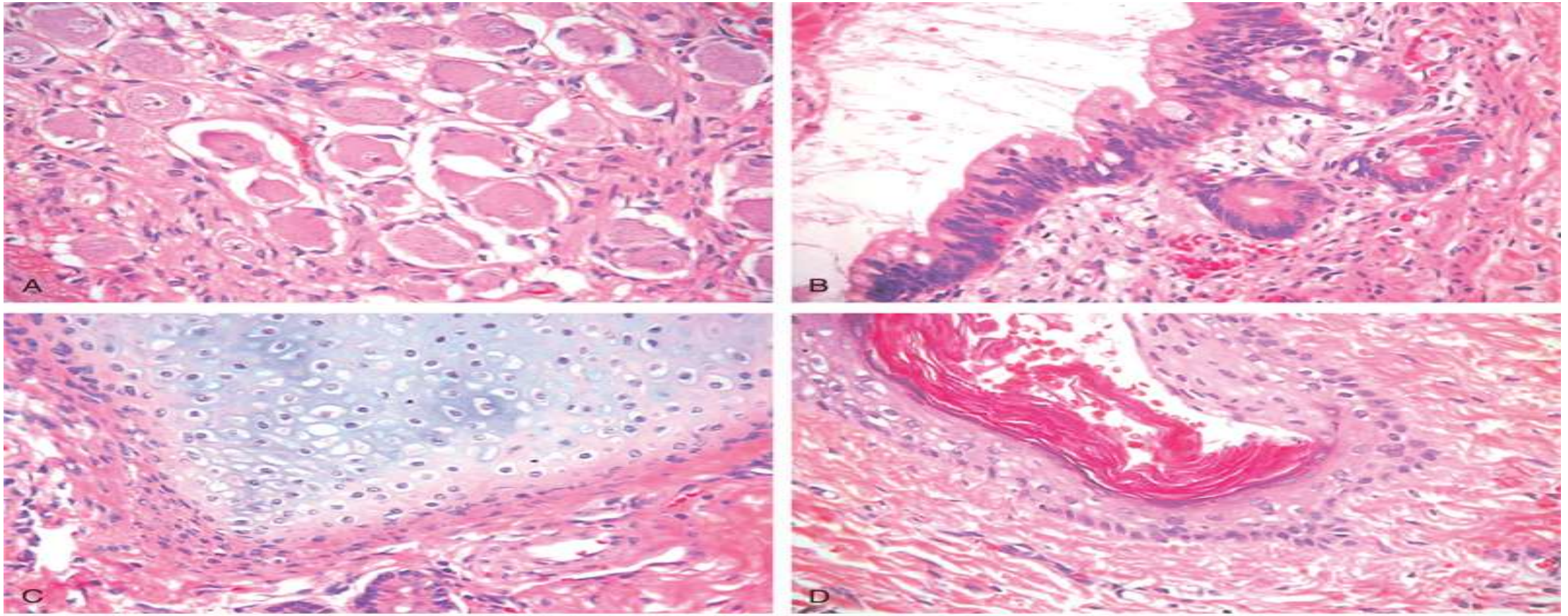
a heterogeneous collection of differentiated cells, such as neural tissue, muscle bundles, islands of cartilage, clusters of squamous epithelium, etc.

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