



# Lecture 3: Testicular Pathology

## Objectives:

Have a working knowledge of the normal histology of the testis and epididymis.

B. Know the predisposing factors and pathology of epididymitis.

Epididymitis and orchitis

- Non specific Epididymitis and orchitis
- Granulomatous/Autoimmune Orchitis
- Gonorrhoea
- Tuberculosis

C. Be familiar with the basic classification and pathology of testicular tumors.

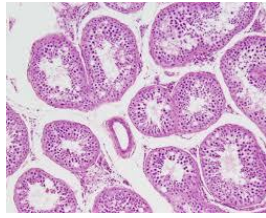
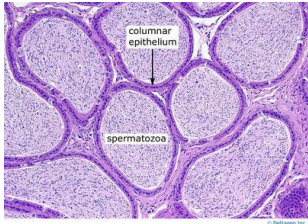
Testicular tumors

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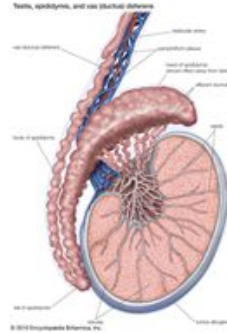
seminoma

yolk sac tumor embryonal carcinoma Teratoma choriocarcinoma.

# Introduction



Normal testis & epididymis



Section of normal testis

## Histology of the: testis:

- 1) Tunica **vaginalis**: a) visceral layer. b) parietal layer.
- 2) Tunica **albuginea**: Fibrous capsule.
- ☆ Parenchyma:
  - 1) seminiferous tubules. Consist of: a) **germ** cells. b) **sertoli** cells.
  - 2) interstitium. Consists of: Leydig cells.
- Epididymis: consists of tubules full of spermatozoa (**sperms**).

- *Epididymitis*: inflammation of epididymis
- *Orchitis*: inflammation of testis
- Inflammatory conditions are generally **more common in the epididymis** than in the testis. *Start in the epididymis then involve the testis*
- However, some infections, notably **syphilis**, may begin in the testis with secondary involvement of the epididymis

## 1) Granulomatous (autoimmune) epididymitis and orchitis:

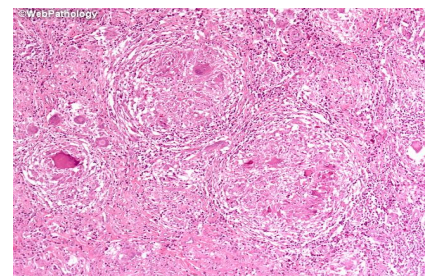
middle-aged men present with unilateral testicular mass.

**mimic testicular tumor.**

autoimmune basis is suspected.

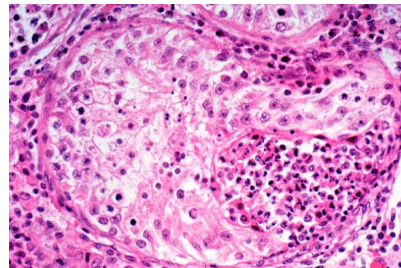
May be in response to: disintegrated sperm<sup>(1)</sup>, post-infectious, due to trauma, Sarcoidosis (inflammatory disease that affects multiple organs).

microscopy: **granulomatous inflammation with plasma cells and lymphocytes.**  
<sup>(1)</sup>: There's a rupture in one of the seminiferous tubules and the sperms will go to interstitium, they're foreign to the interstitium so there will be granulomatous inflammation surround it.



## 2) Non specific epididymitis and orchitis: usually caused by bacteria arising from the urethra or bladder.

Are commonly related to:	<b>infections in the urinary tract</b> (cystitis, urethritis and genitoprostatitis (inflammation of the prostate)).
Infections reach the epididymis/testis through:	the vas deferens or the lymphatics of the spermatic cord.
Causative organisms vary with age:	<ul style="list-style-type: none"><li>● <b>Children:</b> it is uncommon. associated with a congenital genitourinary abnormality and infection with <b>Gram -ve rods</b>.</li><li>● In men <b>younger than age 35</b> years: <b>Chlamydia trachomatis</b> and <b>Neisseria</b> are common causative organisms.(STDs)</li><li>● In men <b>older than 35</b> years: <b>E.coli</b> and <b>Pseudomonas</b>.</li></ul>
Microscopic findings:	congestion, edema and <b>infiltration by neutrophils</b> ,orchitis macrophages and lymphocytes. initially involves the interstitium but later involves seminiferous tubules may progress to <b>frank abscess</b> . Heals by fibrous scarring. Leydig cells are not usually destroyed.



## 3) Gonorrhoea: (Sexually transmitted disease)

Gonococcal infection can spread from urethra to prostate, seminal vesicles and then to epididymis and testis leading to suppurative “full of pus” orchitis and even abscess.

## 4) Tuberculosis:

Begins in the epididymis and spreads to the testis.

There is associated tuberculous prostatitis and seminal vesiculitis.

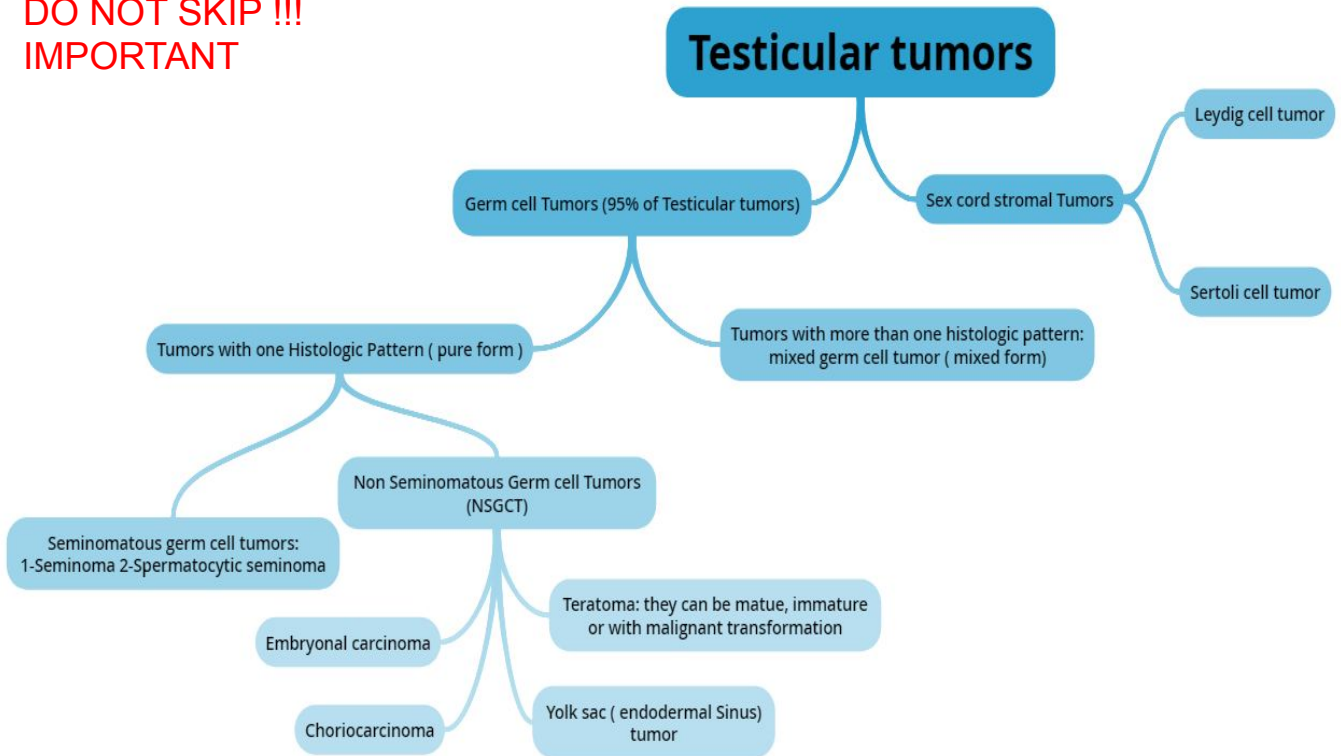
Microscopy: **Caseating Granulomas.**

# Testicular Tumors

- Testicular tumors are the most important cause of a **firm, painless** enlargement of testis.
- The peak incidence is between the ages of **20 and 34 years**.

## Classification of testicular tumors:

**DO NOT SKIP !!!  
IMPORTANT**



- In adults, 95% of testicular tumors are germ cell tumors, and all are malignant.
- Sertoli or Leydig cells (sex cord/stromal tumors) are uncommon and are usually benign.

## Germ cell tumor:

### Age

They occur between 15-30 years of age.

### Prevalence

these are the most **common** tumor in men.

### General Information

Most germ cell tumors are highly **aggressive** cancers, capable of extensive dissemination.

Germ cell tumors may have:

- a single component.
- or as in 60% of cases a mixture of components e.g. mixtures of seminomatous and non-seminomatous components.

Most GCTs originate from precursor lesions called **intratubular germ cell neoplasia** (it is like carcinoma-in-situ).

### Risk Factors

- **Cryptorchidism**: there is a 3 to 5 fold increase in the risk of cancer in the **undescended testis** and in the contralateral descended testis. About 10% cases of testicular cancer have cryptorchidism.
- Testicular dysgenesis.
- Genetic factors.
- Strong family predisposition: brothers, fathers and sons of testicular cancer patients are at risk.
- There is a high risk of developing cancer in one testis if the contralateral testis has cancer.
- Testicular tumors are **more common in whites than in blacks**. Remember that prostate cancer is more common in black.

# Seminoma :

## Age

- The peak incidence is in the 30s.
- It almost **never occurs in infants.**

## Prevalence

- It is the most **common** type of testicular tumors.
- It is also the most common type of testicular GCT (50%).

## General Information

- An **identical tumor** occurs in the **ovary** (called **dysgerminoma**).
- Classic seminoma is **highly sensitive to radiation therapy**, and the overall 5-year survival is 90 to 95%.

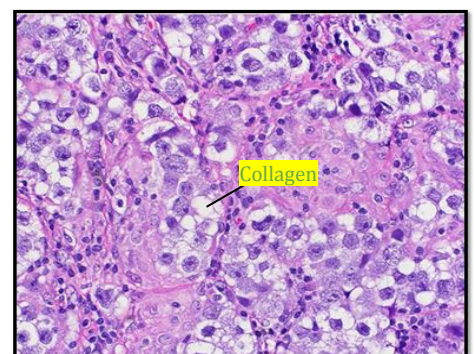
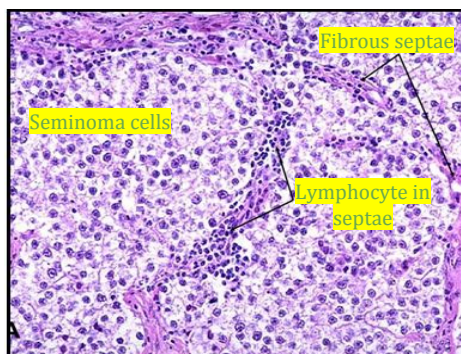
## Gross Morphology

- Bulky masses, sometimes very large
- Homogenous ,gray-white, lobulated cut surface. **Well demarcated.**
- **No** necrosis or hemorrhage



## Morphologic Features

- Sheets of **uniform cells** divided into lobules by delicate **fibrous septa** containing **lymphocytes**.
- **Cells are large** and round with **large nucleus** and **prominent nucleoli**.
- The cytoplasm of tumor cell contains **glycogen**.
- Tumor cells are positive for PLAP, OCT4 and c-kit (CD117).



## Spermatocytic Seminoma (It was called previously spermatocytic seminoma but now spermatocytic tumor.):

### Age and Prevalence

- It affects men over the age of **65 years**.
- **Uncommon**: 1-2 % of testicular GCTs.

### General Information

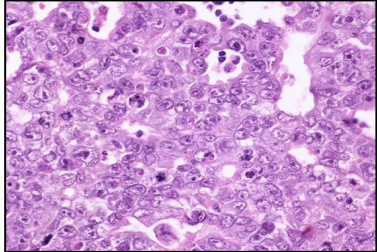
- It is not associated with intratubular germ cell neoplasia.
- It is slowly growing tumor that does not metastasize.
- The prognosis is **excellent**. It's behave in a **benign way**.

## Non seminomatous germ cell tumors

### Choriocarcinoma

- Highly **malignant** tumor. **Very aggressive**.
- Patients have elevated serum human chorionic gonadotropin (**HCG**). it's **organ specific in pregnant woman but tumor specific in non pregnant and males**.
- Small sized lesions
- Prominent **hemorrhage and necrosis**
- Made up of malignant trophoblastic (placental) tissue (**cyto-trophoblastic and syncytio-troblastic cells**)
- Tumor cells positive for human chorionic gonadotropin (HCG) stain
- Pure choriocarcinoma of the testis is extremely rare, and the **tumor is much more common as a component of mixed GCT.**

## Embryonal carcinoma

<b>Age</b>	The age group: 20 to 30 years.
<b>Prevalence</b>	They account for about 15 to 35% of testicular GCTs. <b>Second most common after seminoma.</b>
<b>General Information</b>	<ul style="list-style-type: none"><li>• They are <b>more aggressive</b> than seminomas.</li><li>• They <b>metastasizes</b> early via both lymphatic and hematogenous routes.</li><li>• They are not radiosensitive, <b>they are chemosensitive.</b> New chemotherapeutic agents are very effective and greatly improve prognosis.</li><li>• They can be seen combined with other GCTs (in mixed GCTs).</li></ul>
<b>Gross Morphology</b>	<ul style="list-style-type: none"><li>• They are smaller than seminomas and poorly demarcated.</li><li>• They have variegated surfaces with foci of necrosis and hemorrhage.</li></ul>
<b>Microscopic</b>	<p>No lobules. No fibrous septae. No lymphocytes. Very ugly cells.</p> 
<b>Test</b>	Tumor cells are positive for cytokeratin (CK) and CD30 stain.



# Yolk Sac Tumor

## General information

- Also called Endodermal sinus tumor
- Testicular yolk sac tumors occur in two forms:
  - as a **pure** form seen in young **children** (pure YST of the adult testis is rare)
  - as in **combination** with other NSGCTs seen in **adults**.
- In adults it occurs as a part or component of mixed GCT (commonly mixed with embryonal carcinoma)
- Patients have elevated serum **alpha fetoprotein (AFP)** "it's tumor specific not organ specific". AFP may be used as a marker of disease progression in the patient's serum and also aid in diagnosis.
- The biologic behavior of YST is **similar** to that of embryonal carcinoma

## Prevalence

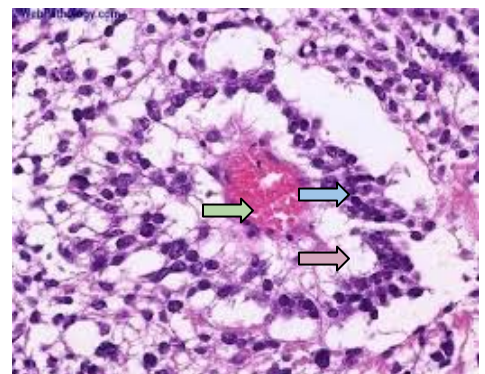
It is the most **common tumor in infant and children** up to 3 years of age and it has a very **good prognosis** in infants and children.

## Gross

Non encapsulated, homogenous, yellow white, mucinous

## Microscopic

- Tumor shows structure resembling endodermal sinuses called as **Schiller-Duval bodies** "consist of blood vessel then empty space then tumor cells surround it, making circle shape" are characteristic.
- Hyaline-pink globules
- Positive for **alpha-fetoprotein** and **alpha-1-antitrypsin stain**.



# Teratoma

General information	<ul style="list-style-type: none"><li>● It is a tumor composed of various different types of cells or organ components. <b>Arising from all 3 germ cell layers of the embryo endoderm, mesoderm and ectoderm.</b></li></ul>
Prevalence	<ul style="list-style-type: none"><li>● Any age, infancy to adult life</li><li>● In its <b>pure</b> form it is common in <b>infants and children</b> second to yolk sac tumor (in this age group)</li><li>● In <b>adult</b> the pure form is rare. It occurs as part of <b>mixed GTC</b></li></ul>
Gross morphology	<ul style="list-style-type: none"><li>● Usually large 5 -10 cm</li><li>● Heterogeneous appearance with solid and cystic areas. Can show <b>bone, cartilage and teeth grossly.</b></li><li>● Composed of bizarrely distributed collection of different type of cells or organ structures (heterogenous)</li><li>● Any of the following <b>cell types of various organs</b> can be present: neural/brain, cartilage, bone, squamous epithelium, hair, glandular cells, smooth muscle, thyroid tissue, bronchial epithelium of lung, pancreatic tissue etc.</li></ul>



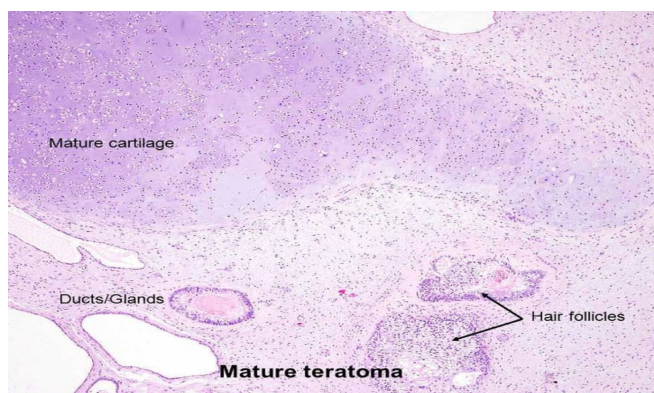
# Teratoma(cont)

## Microscopic morphology

- If the cells/tissue is mature looking it is called as **mature teratoma**.
- If some of the cells/tissue component is immature it is called as **immature teratoma**.
- If any of the cells/tissue undergoes non germ cell type of malignant transformation it is called as **teratoma with malignant transformation** (rare) e.g squamous cells develop squamous cell carcinoma or the glandular cells develop adenocarcinoma.

## Prognosis

- **In prepubertal males, teratomas are benign, whereas the majority of teratomas in postpubertal males are malignant, being capable of metastasis regardless of whether they are composed of mature or immature elements. Remember that in females, mature is benign/ immature is malignant.**



# Mixed GCTs

## General information

- Mixed Germ Cell Tumors are quite common.
- About half of testicular tumors are composed of a mixture of GCTs.
- The common combinations/mixtures are:
  - Teratoma + embryonal carcinoma +/- yolk sac tumor
  - Seminoma + embryonal carcinoma

## Clinical features

- Present as a **painless** enlarging mass in the testis. Generally any solid testicular mass should be considered neoplastic.
- Germ cell tumors secrete hormones and enzymes that can be detected in blood (HCG "choriocarcinoma", AFP "yolk-sac", and lactate dehydrogenase "seminoma")
- **Biopsy** of a testicular tumor is associated with a risk of tumor spillage therefore it is **not recommended**. Biopsy is not recommended in ovaries and testis. .
- The standard management of solid testicular tumors is radical **orchiectomy** removal of testicles
- GCTs can spread by:
  - direct extension to the epididymis, spermatic cord, or scrotal sac.
  - Lymphatic spread is common. Retroperitoneal and para-aortic nodes are first to be involved.
  - Hematogenous spread to Lung, liver, Brain, and bones.
- **Seminomatous** tumors are **radiosensitive**.
- **Non-seminomatous** tumors are chemo sensitive and respond very well to **chemotherapy**.

## Mixed GCTs(cont..)

### Prognosis

- More than 95% of patients with seminoma can be cured
- 90% of patients with non-seminomatous tumors can achieve complete remission with aggressive chemotherapy, and most can be cured
- The rare pure choriocarcinoma is the most aggressive non-seminomatous tumor. Pure choriocarcinoma has a poor prognosis

## Summary

Seminomas	Nonseminomatous germ cell tumor
Seminoma	embryonal, yolk sac, choriocarcinoma, teratoma
<b>Radiosensitive</b> (important)	Not radiosensitive
Chemosensitive	<b>Chemosensitive</b>
Late metastasis	Early metastases to retroperitoneal lymph nodes
Excellent prognosis	Not aggressive

# Doctors notes

- Testicular tumors is the **most important part** in our lecture!
- Seminoma is the only tumor that responds to **radiation, the rest are chemosensitive.**
- Seminoma is **well-demarcated** homogenous tumor on cut surface, there is **no** necrosis or hemorrhage.
- On microscope you will see **sheets of uniform cells divided into lobules by delicate fibrous septa containing lymphocytes**, cells are large and round with large nucleus and prominent nucleoli.
- Spermatocytic tumor is not associated with intratubular germ cell neoplasia, slowly growing tumor that does not metastasize> **prognosis is excellent.**
- Embryonal carcinoma is **more aggressive** than seminoma and metastasize early, smaller and poorly demarcated, **has foci of necrosis and hemorrhage.**
- Yolk sac tumor seen **pure** in children **less than 3 years**, and seen in **mixed** form in **adults**, on microscope you will see Schiller-Duval bodies, Hyaline–pink globules, Tumor cell are **positive for AFP and alpha-1-antitrypsin stain.**
- CHORIOCARCINOMA is **very malignant** tumor, mostly seen as mixes for, prominent hemorrhage and necrosis.
- Teratoma is tumor composed of various different types of cells or organ components, seen **pure in children and mixed in adults.**
- If any of the cells/tissue undergoes non germ cell type of malignant transformation it is called as **teratoma with malignant transformation.**
- In **prepubertal** males, teratomas are **benign**, whereas the majority of teratomas in **postpubertal** males are **malignant**, being capable of metastasis **regardless** of whether they are composed of mature or immature elements.
- A biopsy of a testicular tumor is associated with a risk of tumor **spillage** therefore it is **not recommended.**
- **THE TUMORS secrete hormones and enzymes that can be detected in blood (HCG, AFP, and lactate dehydrogenase).**
- **HCG>CHORIOCARCINOMA**
- **AFP> YOLK SAC TUMOR.**
- **Lactate dehydrogenase> SEMINOMA.**
- **إذا جاء سؤال حط لك اثنين معناته انه ميكسد واكثر من تيومر وضروري تعرفون كل واحد يخص مين**

# Pathoma summary

## I. ORCHITIS

A. Inflammation of the testicle

B. Causes

1. Chlamydia trachomatis (serotypes D-K) or Neisseria gonorrhoeae-Seen in young adults. Increased risk of sterility, but libido is not affected because Leydig cells are spared.
2. Escherichia coli and Pseudomonas-Seen in older adults; urinary tract infection pathogens spread into the reproductive tract.
3. Mumps virus (teenage males)-increased risk for infertility; testicular inflammation is usually not seen in children < 10 years old.
4. Autoimmune orchitis- characterized by granulomas involving the seminiferous tubules

## II. TESTICULAR TUMORS

### I. BASIC PRINCIPLES

A. Arise from germ cells or sex cord-stroma

B. Present as a firm, painless testicular mass that cannot be transilluminated

C. Usually not biopsied due to risk of seeding the scrotum; removed via radical orchiectomy

1. Most testicular tumors are malignant germ cell tumors.

### II. GERM CELL TUMORS

A. Most common type of testicular tumor (> 95% of cases)

B. Usually occur between 15- 40 years of age

C. Risk factors include cryptorchidism and Klinefelter syndrome.

D. Divided into seminoma and nonseminoma

1. Seminomas (55% of cases) are highly responsive to radiotherapy, metastasize late, and have an excellent prognosis.
2. Nonseminomas (45% of cases) show variable response to treatment and often metastasize early.

E. Seminoma is a malignant tumor comprised of large cells with clear cytoplasm and central nuclei (resemble spermatogonia); forms a homogeneous mass with no hemorrhage or necrosis. Most common testicular tumor; resembles ovarian dysgerminoma.

2. Rare cases may produce  $\beta$ -hCG
3. Good prognosis; responds to radiotherapy

F. Embryonal carcinoma is a malignant tumor comprised of immature, primitive cells that may produce glands; forms a hemorrhagic mass with necrosis.

1. Aggressive with early hematogenous spread
2. Chemotherapy may result in differentiation into another type of germ cell tumor (e.g., teratoma).
3. Increased AFP or  $\beta$ -hCG may be present.

G. Yolk sac (endodermal sinus) tumor is a malignant tumor that resembles yolk sac elements.

1. Most common testicular tumor in children
2. Schiller-Duval bodies (glomerulus-like structures) are seen on histology
3. AFP is characteristically elevated.

# Pathoma summary continued

H. Choriocarcinoma is a malignant tumor of syncytiotrophoblasts and cytotrophoblasts (placenta-like tissue, but villi are absent)

1. Spreads early via blood
2.  $\beta$ -hCG is characteristically elevated; may lead to hyperthyroidism or gynecomastia ( $\alpha$  subunit of hCG is similar to that of FSH, LH, and TSH)

I. Teratoma is a tumor composed of mature fetal tissue derived from two or three embryonic layers.

1. Malignant in males (as opposed to females)
2. AFP or  $\beta$ -hCG may be increased.

J. Mixed germ cell tumors

1. Germ cell tumors are usually mixed.
2. Prognosis is based on the worst component.

## III. SEX CORD-STROMAL TUMORS

A. Tumors that resemble sex cord-stromal tissues of the testicle;; usually benign

B. Leydig cell tumor usually produces androgen, causing precocious puberty in children or gynecomastia in adults.

1. Characteristic Reinke crystals may be seen on histology.

C. Sertoli cell tumor is comprised of tubules and is usually clinically silent.

## IV. LYMPHOMA

- A. Most common cause of a testicular mass in males > 60 years old; often bilateral
- B. Usually of diffuse large B-cell type



# Questions

1- A 60-year-old man with a history of nodular prostatic hyperplasia and recurrent cystitis presents with pain in the scrotum. His temperature is 38°C (101°F). Physical examination reveals a small, tender nodule attached to the testis. Which of the following is the most likely diagnosis?

- (A) Epididymitis
- (B) Orchitis
- (C) Spermatocele
- (D) Urethritis

2- An 8-year-old boy is brought to the physician because his parents noticed a mass on his left testicle. Physical examination reveals a solid mass that cannot be transilluminated, and biopsy shows a haphazard arrangement of benign differentiated tissues, including squamous epithelium, glandular epithelium, cartilage, and neural tissue. The left testicle was removed surgically, and the patient is symptom free 5 years later. Which of the following is the most likely diagnosis?

- (A) Embryonal Carcinoma
- (B) Mature teratoma
- (C) Mixed germ cell tumor
- (D) Seminoma

3- A 32-year-old man presents with a testicular mass that he first noticed 2 weeks ago. The mass cannot be transilluminated and appears solid and homogeneous on ultrasound examination. No tumor markers are detected on serologic testing. An orchiectomy is performed, and the surgical specimen is shown in the image. Which of the following is the most likely diagnosis?

- (A) Choriocarcinoma
- (B) Embryonal carcinoma
- (C) Lymphoma
- (D) Seminoma

1- A  
2- B  
3- D

4- A 25-year-old man presents with a 4-week history of a painless mass in the scrotum. Physical examination reveals a testicular mass that cannot be transilluminated. Serum levels of AFP and hCG are normal. A hemiorchiectomy is performed. On gross examination, the testicular tumor shows foci of hemorrhage and necrosis. Microscopic examination of the tumor is shown in the image. The patient was cured by orchiectomy followed by chemotherapy. Which of the following is the most likely diagnosis?

- (A) Choriocarcinoma
- (B) Embryonal carcinoma
- (C) Lymphoma
- (D) Mature Teratoma

5- A 2-year-old boy is brought to the physician because his parents noticed a mass on his right testicle. Physical examination confirms the parents' observation. An orchiectomy is performed. Microscopic examination of the surgical specimen shows neoplastic cells forming glomeruloid Schiller-Duval bodies. Which of the following serum markers is most useful for monitoring the recurrence of tumor in this patient?

- (A) CA-125
- (B) Carcinoembryonic antigen
- (C) Estrogen
- (D)  $\alpha$ -Fetoprotein

6- Which of the following is correct about testicular tumors?

- (A) They are more common in females.
- (B) Painful masses.
- (C) Seminomas metastasis are late.
- (D) Nonseminomatous tumor metastasis are late.

7- Which of the following is False regarding Inflammatory lesion of the testis and epididymis?

- (A) Epididymitis is more common than orchitis.
- (B) Commonly related to blood infections.
- (C) Orchitis rarely occurs in children.
- (D) Granulomatous inflammation of the testis is commonly caused by TB.

4- B  
5- D  
6- C  
7- B

8- A 33-year-old man has noted asymmetric enlargement of the scrotum over the past 4 months. On physical examination, the right testis is twice its normal size and has increased tenderness to palpation. The right testis is biopsied. The epididymis and the upper aspect of the right testis have extensive granulomatous inflammation with epithelioid cells, Langhans giant cells, and caseous necrosis. Which of the following infections is the most likely cause of these findings?

- (A) Gonorrhoea.
- (B) Mumps.
- (C) Syphilis.
- (D) Tuberculosis.

9- An isochromosome of the short arm of which chromosome is pathognomonic of GCT?

- (A) 11
- (B) 12
- (C) 13
- (D) 14

10- Which of the following statements is true regarding testicular tumors?

- (A) Are embryonal cell carcinomas in 95% of cases
- (B) Bilateral in up to 10% cases
- (C) Teratomas are more common than seminomas
- (D) Usually present after 50 years of age

8- D  
9- B  
10- B



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## References:



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