

Testicular Pathology

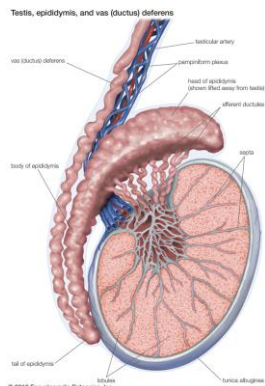
Objectives:

- Have a working knowledge of the normal histology of the testis and epididymis.
- Know the predisposing factors and pathology of epididymitis.
- Epididymitis and orchitis: Non specific Epididymitis and orchitis, Granulomatous/Autoimmune Orchitis, Gonorrhoea, Tuberculosis.
- Testicular tumors: Seminoma, yolk sac tumor, embryonal carcinoma, Teratoma, choriocarcinoma.

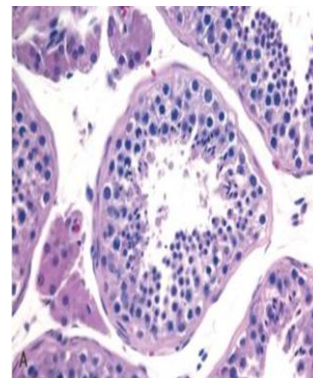
Normal testis and epididymis



Normal testis & epididymis



Section of normal testis



Section of Seminiferous tubule

Testicular disease: Epididymitis and orchitis:

- *Epididymitis*: inflammation of epididymis we will ask you about tumors more than inflammation so focus on that.
- *Orchitis*: inflammation of testis Orchitis is mainly seen in TB or syphilis.
- Inflammatory conditions are generally **more common in the epididymis** than in 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. (we don't know how it occurred it could be due to the following)

autoimmune basis is suspected.

May be in response to:

- disintegrated sperm (broken down into smaller parts and lodged into spaces).
- post-infectious,
- due to trauma
- Sarcoidosis (inflammatory disease that affects multiple organs).

microscopy:

granulomatous inflammation with plasma cells and lymphocytes

2) Non specific epididymitis and orchitis:

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

3) Gonorrhea: (Sexually transmitted disease)

Gonococcal infection can spread from urethra to prostate, seminal vesicles and then to epididymis and testis leading to → suppurative* orchitis and even abscess. (*pus producing) It is a sexually transmitted infection.

4) Tuberculosis:

Begins in the epididymis and spreads to the testis.

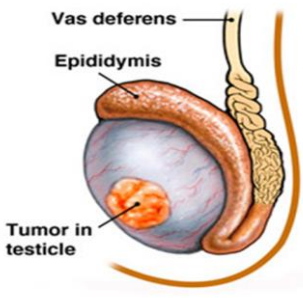
There is associated tuberculous prostatitis and seminal vesiculitis (inflammation of the seminal vesicle).

Microscopy: Caseating Granulomas.

Testicular tumors:

- Testicular tumors are the **most important cause** of firm, painless enlargement of the testis. (if there is a mass in the testis, most likely it will be a tumor)
- Peak incidence between the ages of 20 and 34 years.

Tumors are important



Classification of testicular tumors:

(Classification is like ovarian tumors but there is NO surface epithelium tumors).

Testicular tumors are a heterogeneous group of tumors divided into **germ cell tumors** and **sex cord stromal tumors**:

- 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**.

classification	1) Germ cell tumors (95% of testicular tumors): Could be in a pure or mixed form	a) Tumors with One Histologic Pattern (pure form):	Seminomatous germ cell tumors (Seminomatous germ cell tumors are radio-sensitive) Respond well to radio therapy	<ol style="list-style-type: none"> 1. Seminoma (Seminoma is the classical type of seminomatous germ cell tumors) 2. Spermatocytic seminoma (very good prognosis hardly metastasize)
			Non-seminomatous germ cell tumors They are radio-resistant but chemosensitive.	<ol style="list-style-type: none"> 1. Embryonal carcinoma 2. Yolk sac (endodermal Sinus) tumor 3. Choriocarcinoma 4. Teratoma: they can be mature, immature or with malignant transformation
		b) Tumors with more than one Histologic Pattern: mixed germ cell tumor (mixed form)		
	2) Sex cord stromal tumors:	1) Leydig cell tumor	Stroma of the interstitium	
	2) Sertoli cell tumor	Stroma of the seminiferous tubules		

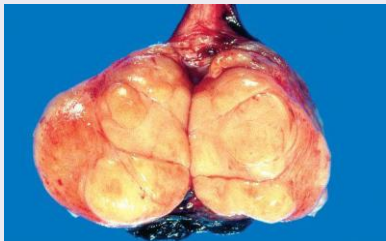
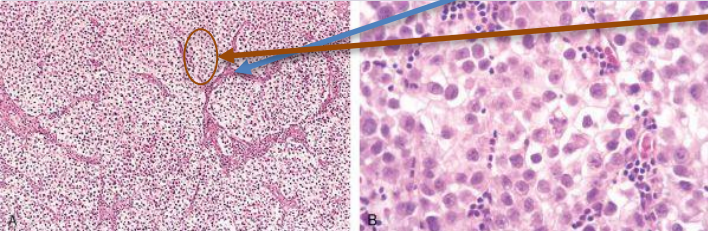
Germ cell tumors could have everything under the microscope we call it mixed or just the specific histological feature we call it pure form also good response to therapy.

GERM CELL TUMORS (GCT)

Age group	Between 15-30 years of age
Prevalence	these are the most common tumor in men. it is important to know that mixed tumors are more common than single tumors in germ cell tumors
general information	<ul style="list-style-type: none">• Most of gem cell tumors are highly aggressive cancers, capable of extensive Dissemination. As in they metastasize quickly• The Good news is that with current therapy most of them can be cured.• Germ cell tumors may have:<ol style="list-style-type: none">1.a single tumor type component2.or as 60% of cases a mixture of tumor types 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)
Predisposing factors: factor that might lead to GCT	<ul style="list-style-type: none">• Cryptorchidism¹ is associated with a 3 to 5 fold increase in the risk of cancer in the undescended testis and in the contralateral descended testis. The undescended and descended are at equal risk of developing germ cell tumor.• Testicular dysgenesis (genetic disorientation)• genetic factors• Strong family predisposition. Brothers, fathers and sons of testicular cancer patients are at risk too.• 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.

¹ a condition in which one or both testes fail to descend from abdomen into scrotum

Seminoma

Age group	<ul style="list-style-type: none">• Peak incidence in the 30ies• Almost never occur in infants (if she give a history in the exam remember age groups)
Prevalence	<ul style="list-style-type: none">• It is the most common type of testicular tumors.• It is also the most common type of testicular GCT (50%)
General information	<ul style="list-style-type: none">• An identical tumor occurs in the ovary (dysgerminoma).• classic seminoma is highly sensitive to radiation therapy, and the overall 5-year survival is 90% to 95%
Gross morphology 	<ul style="list-style-type: none">• Bulky masses, sometimes very large• homogenous, gray-white,• lobulated cut surface• No necrosis or hemorrhage (it is the clue for seminoma)
Microscopic morphology 	<ul style="list-style-type: none">• sheets of uniform cells divided into lobules by delicate fibrous septa containing lymphocytes.• cells are large and round with large nucleus and prominent nucleoli.• Cytoplasm of tumor cell has glycogen.
teste	Positive for PLAP, OCT4 stain and c-kit (CD117).

Spermatocytic Seminoma (slowly growing never metastasize and good prognosis)

Age group and Prevalence	<ul style="list-style-type: none">• Uncommon 1-2 % of testicular GCTs• Over age 65
General information	Slow growing tumor, doesn't metastasize prognosis is excellent

Embryonal Carcinoma	
Age group	20 to 30 year age group
Prevalence	Less common It accounts for about 15 to 35% of testicular GCTs
General information	<ul style="list-style-type: none"> • It is More aggressive than seminomas • It metastasizes early via both lymphatic and hematogenous routes • Can be seen combined with other GCTs (in mixed GCTs) • Radiation is not as effective as with seminoma, but newer chemotherapeutic agents are very effective with greatly improved prognosis.
Gross morphology	<ul style="list-style-type: none"> • smaller than seminoma • poorly demarcated • Variegated with foci of necrosis and hemorrhage
Teste	Tumor cells are positive for cytokeratin (CK) and CD30 stain it is the clue teste

Yolk Sac Tumor(YST) also called endodermal sinus tumor

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
General information	<ul style="list-style-type: none">• Testicular yolk sac tumors occur in two forms:<ol style="list-style-type: none">1. as a pure form in young children (pure YST of the adult testis is rare)2. as in combination with other NSGCT (mainly embryonal carcinoma, in adults)• Patients have elevated serum alpha fetoprotein (AFP) it is the clue for YST. 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 <p>If the tumor contained both AFP and PLAP then it's a mix between yolk-sac and seminoma</p>
Gross morphology	<ul style="list-style-type: none">• Non encapsulated homogenous yellow white mucinous
Microscopic morphology	<ul style="list-style-type: none">• Tumor shows structure resembling endodermal sinuses called Schiller-Duval bodies (characteristic for yolk sac tumor) <p>On histology these bodies will appear like a flower with a circle in the center.</p> <ul style="list-style-type: none">• hyaline–pink globules• tumor cell are positive for alpha fetoprotein (AFP) and alpha-1-antitrypsin stain.

Choriocarcinoma (from placental tissue)

It occurs due to the pluripotent cells found in the tissue

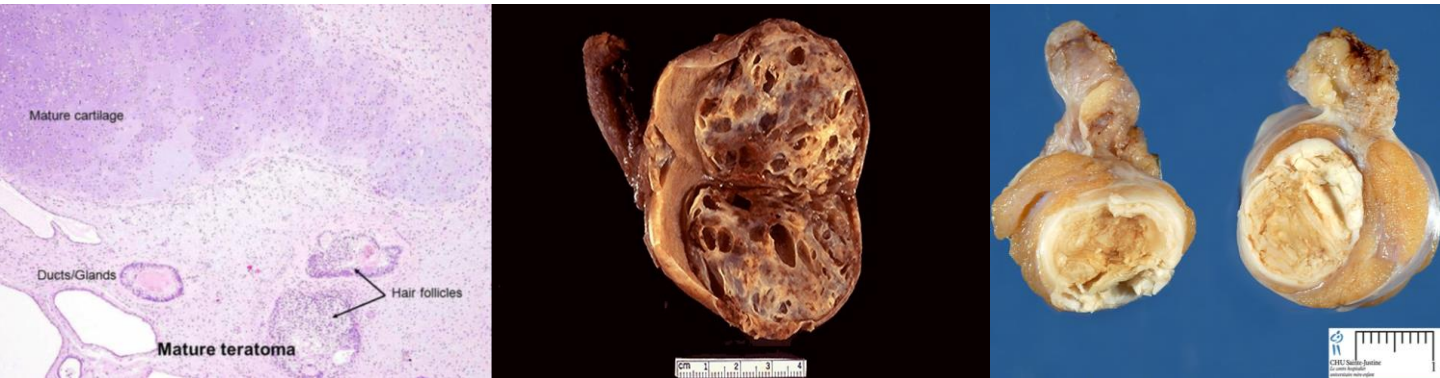
- Highly malignant tumor choriocarcinoma is the worst type due to its aggressiveness.
- Patients have **elevated serum human chorionic gonadotropin (HCG)** (also seen in pregnancy, trophoblastic tumors and ovarian tumors which have a component of chorionic carcinoma)
- Small sized lesions
- Prominent 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.

Teratoma Teratoma is always in OSPE (imp)

- It is a tumor composed of various different types of cells or organ components
- Any age, infancy to adult life
- **In its pure form it is common in infants and children second to yolk sac tumor (in this age group)**
- **In adult the pure form is rare. It occurs as part of mixed GTC**
Once you've found it, try to look for other components since its very unlikely for it to occur by itself.
- Usually large 5 -10 cm
- **Heterogenous appearance with solid and cystic areas. Can show bone, cartilage and teeth grossly.**
- Composed of bizzarely distributed collection of different type of cells or organ structures (heterogenous)
- Any of the following cell types of various organs can be present: neural/brain, cartilage, bone, squamous epithelium, hair, glandular cells, smooth muscle, thyroid tissue, bronchial epithelium of lung, pancreatic tissue etc.
- 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 tranformation** it is called as **teratoma with malignant transformation** (rare) e.g **squamous cells develop squamous cell carcinoma or the glandular cells develop adenocarcinoma.** (Even if it is mature and in adult we consider it malignant e.g, squamous cell carcinoma in the teratoma.)

Teratoma cont...

- Behavior of teratomas:
 - In infants and children, mature teratomas are benign and immature teratoma is considered malignant.
 - In post pubertal male, all teratomas are regarded as malignant (since they're most likely mixed), and capable of metastasis, regardless of whether the elements are mature or not. In females mature teratomas are benign



Mixed Germ Cell Tumors

- Mixed Germ Cell Tumors are quite common. common in adults
- 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 of GCTs Remember the combination & the stain for each tumor

- 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, AFP, and lactate dehydrogenase)
- Biopsy of a testicular tumor is associated with a risk of tumor spillage therefore it is not recommended. never do biopsy for testicular tumors because of (tumor spillage). This spillage doesn't happen in breast, liver or kidney.
- The standard management of solid testicular tumors is radical orchiectomy

The female doctor emphasized here that u know the tests for each just to revise it for u seminoma is PLAP (pos) embryonal carcinoma is CD30 (pos) Yolk sac tumor is Alpha feto protein (pos) choriocarcinoma has HCG (pos)

Clinical features of GCTs cont..

- 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 chemosensitive and respond very well to chemotherapy.

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

Even though choriocarcinoma is very hard to manage the good thing is in the testes it has very little components.

Summary Difference between seminoma and non-seminomatous GCTs

seminomas	non-seminomatous GCTs
seminoma	Embryonal, yolk sac, Choriocarcinoma, teratoma
radiosensitive	Not radiosensitive
Chemosensitive	Chemosensitive
Late metastasis	Early metastases to retroperitoneal lymph nodes
Excellent prognosis	More aggressive

Summary

Germ cell Tumor	Incidence	Morphology		Tests	Treatment	Notes
		gross	Microscopic			
Seminoma	30's	- Bulky - No necrosis - No hemorrhage	- Sheets of uniform cells with cleared cytoplasm - Cells are large	- PLAP - OCT4 stain - c-kit (CD117)	Radiation therapy	Best prognosis of all GCT
Spermatocytic Seminoma	Older than 65 yrs	Same as seminoma But with less lymphocytic infiltration and metastasis		-	Radiation therapy	-
Embryonal Carcinoma	20-30 yrs	- Foci of hemorrhage & necrosis - Smaller than seminoma	-	- Cytokeratin (CK) - CD30 stain	Chemotherapy Radioresistant	- Can be mixed - More aggressive than seminomas
Yolk Sac Tumor (Endodermal sinus tumor)	Pure < 3 yrs Mixed: adults	Non-encapsulated, homogenous, yellow white, mucinous	- Endodermal sinuses called Schiller-Duval bodies - Hyaline-pink globules	- Alpha fetoprotein (AFP) - Alpha-1-antitrypsin stain	Very good prognosis Chemotherapy	Most common in children and infants
Choriocarcinoma	-	- Small sized lesions - Prominent hemorrhage and necrosis	Made up of malignant (placental) trophoblastic tissue.	Human chorionic gonadotropin (HCG)	Chemotherapy	- Highly malignant - Extremely rare as pure usually mixed
Teratoma	All ages	Heterogenous appearance with solid and cystic areas	Composed of bizarrely distributed collection of different type of cells (neuronal tissue, muscles bundle, cartilage, etc)	-	Chemotherapy	2nd most common GCT in children and infants

Difference between seminoma and nonseminomatous germ cell tumors:

Seminomas	Nonseminomatous Germ Cell tumors
Seminoma	Embryonal, yolk sac, choriocarcinoma, teratoma
Radiosensitivity	chemosensitive
Late metastasis	Easy metastases to retroperitoneal lymph nodes
Excellent prognosis	More aggressive

Questions

1- 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.

ANS: B, commonly related to urinary tract infection.

2- A 26-year old male came to the hospital with a right testicular mass and history of cryptorchidism. which of the following is most likely diagnosis?

A- Sex cord tumors.

B- Germ cell tumors.

C- Tuberculoma of the intrascrotal cord.

D- Vascular aneurysm.

ANS: B

3- A 26-year-old man has occasionally felt pain in the scrotum for the past 3 months. An ultrasound scan shows a 1.5-cm mass within the right testis. A right orchiectomy is performed, and gross examination shows the mass to be hemorrhagic and soft. A retroperitoneal lymph node dissection is done. Microscopic examination shows that areas of viable tumor are composed of cuboidal cells intermingled with large eosinophilic syncytial cells containing multiple dark, pleomorphic nuclei. Immunohistochemical staining of syncytial cells is most likely to be positive for which of the following?

A- α -Fetoprotein.

B- CD20.

C- Carcinoembryonic antigen.

D- Human chorionic gonadotropin.

ANS: D

4-A 32-year-old man has noticed an increased feeling of heaviness in his scrotum for the past 10 months. On physical examination, the left testis is three times the size of the right testis and is firm on palpation. An ultrasound scan shows a 6-cm solid mass within the body of the left testis. Laboratory studies include an elevated serum α -fetoprotein level. Which of the following cellular components is most likely to be present in this mass?

A- Cytotrophoblasts.

B- Embryonal carcinoma cells.

C- Seminoma cells.

D- Yolk sac cells.

ANS: D

5- 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- Gonorrhea.

B- Mumps.

C- Syphilis.

D- Tuberculosis.

ANS: D

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.

ANS: C

7-A 64-year-old man noted pain with burning on urination a week ago. He has had discomfort in his scrotum for the past 2 days. On examination, the right testis is swollen and tender. Which of the following organisms is the most likely cause?

A- E coli.

B- Mumps virus.

C- TB.

D- Human papillomavirus.

ANS: A, Time course suggests bacterial infection. And mumps is more likely to be bilateral and doesn't cause UTI.

حسبي الله لا إله إلا هو عليه توكلت وهو رب العرش العظيم

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