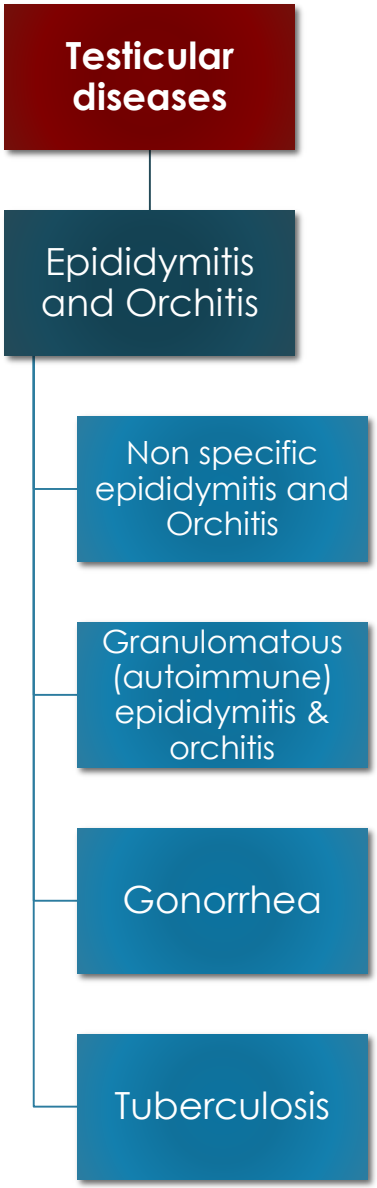
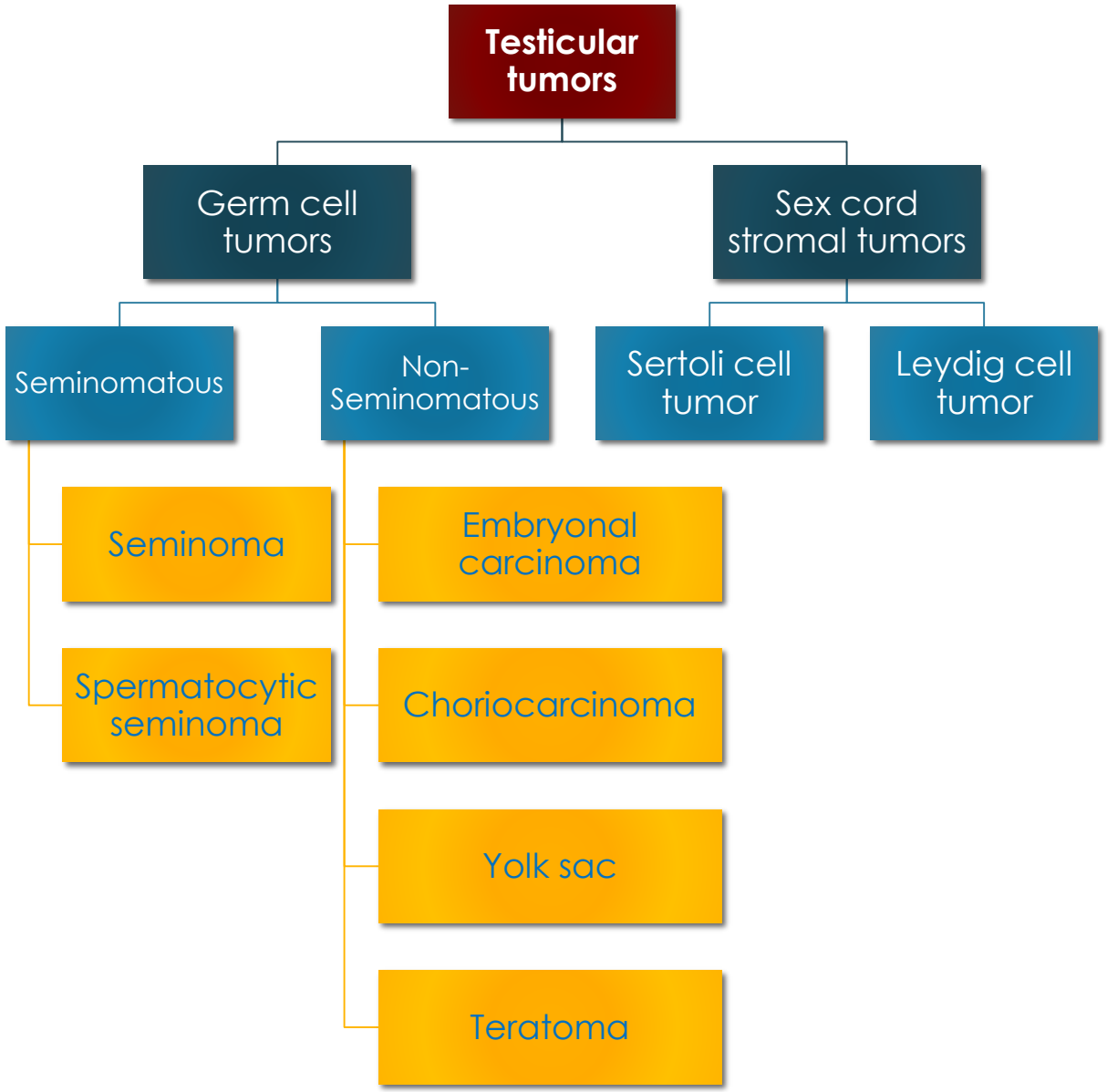
Lecture 1:
Diseases of the Epididymis & Testicular Tumors

▫ Important ▫ Notes ▫ Explanation


Testicular diseases
Epididymitis and Orchitis
Non specific epididymitis and Orchitis
Granulomatous (autoimmune) epididymitis & orchitis
Gonorrhea
Tuberculosis


Testicular tumors
Germ cell tumors
Sex cord stromal tumors
Seminomatous
Non-Seminomatous
Sertoli cell tumor
Leydig cell tumor
Seminoma
Spermatocytic seminoma
Embryonal carcinoma
Choriocarcinoma
Yolk sac
Teratoma

Testicular Diseases

Epididymitis and Orchitis:

- Epididymitis: inflammation of epididymis.
- Orchitis: inflammation of testis.
- 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. Non Specific Epididymitis and Orchitis:

- Commonly related to infections in the urinary tract (cystitis, urethritis and genitoprostatitis).
- Infections reach the epididymis/testis through the vas deference or the lymphatics of the spermatic cord.
- **Causative organisms** vary with age;

Children	It is uncommon. Usually associated with a **congenital genitourinary abnormality** and **infection with Gram –ve rods** (e.g. E.coli).
In men < 35 years	**Chlamydia trachomatis** and **Neisseria** are common causative organisms.
In men > 35 years	**E.Coli** and **Pseudomonas**.

Microscopic Findings:

- Congestion, edema and infiltration by neutrophils, macrophages and lymphocytes.
- Initially involves the interstitium but later involves seminiferous tubules.
- May progress to frank abscess.
- Heals by **fibrous scarring**.
- Leydig cells are not usually destroyed.

2. Granulomatous (Autoimmune) Epididymitis & Orchitis:

- Middle–aged men present with unilateral testicular mass.
- Mimic testicular tumor.
- **Microscopy:** granulomatous inflammation with plasma cells and lymphocytes.
- Autoimmune basis is suspected.
- May be in response to disintegrated sperm, post-infectious, due to trauma or sarcoidosis.

3. Gonorrhea:

- Gonoccocal infection can spread from urethra to prostate, seminal vesicles and then to epididymis and testis leading to suppurative 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 firm, **painless** enlargement of testis.
- Peak incidence between the ages of 20 and 34 years.

Testicular tumors are a heterogeneous group of tumors **divided into:**

1) Germ Cell Tumors (95%)

A- Tumors with One Histologic Pattern (Pure Form)

1. **Seminomatous Germ Cell Tumors:**
   - Seminoma
   - Spermatocytic seminoma

1. **Non-Seminomatous Germ Cell Tumors (NSGCT):**
   - Embryonal carcinoma
   - Choriocarcinoma
   - Yolk sac (endodermal Sinus) tumor
   - Teratoma: they can be mature, immature or with malignant transformation

* In adults, 95% of testicular tumors are germ cell tumors, and all are malignant.

B- Tumors with More Than One Histologic Pattern: (Mixed Form)

Mixed Germ Cell Tumor.

2) Sex Cord Stromal Tumors

A- Sertoli Cell Tumor

B- Leydig Cell Tumor

* Sertoli or Leydig cells (sex cord/stromal tumors) are uncommon and are usually benign.

1) Germ Cell Tumors (GCT)

- Between 15 to 30 years of age, these are the most common tumor of men.
- Most of gem cell tumors are highly aggressive cancers, capable of extensive dissemination.
- Good news is that with current therapy most of them can be cured.

Germ cell tumors may have

- a single tumor type component.
- or as is 40% 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:

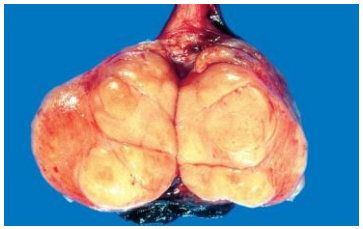
- **Cryptorchidism** About 10% cases of testicular cancer have cryptorchidism.
  - Cyptorchidism refers to incomplete descent of the testis from the abdomen to the scrotum and is present in about 1% of 1-year-old male infants.
  - Cryptorchidism is associated with a 3 to 5 fold increase in the risk of cancer in the undescended testis and in the contralateral descended testis.
- 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.

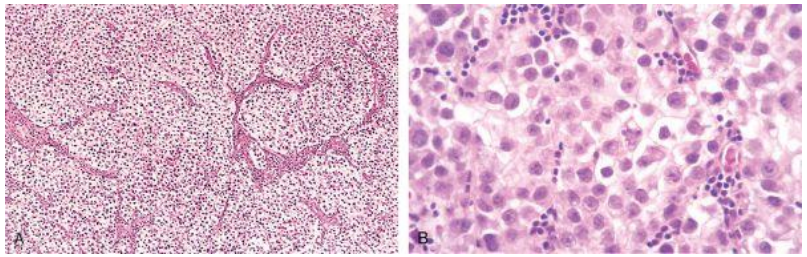
A. Seminomatous Germ Cell Tumors

- Seminoma

- The **most common type** of testicular tumors.
- It is also **the most common type of testicular GCT** (50%)
- Almost never occur in infants
- Peak incidence in **the 30ies**
- 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	Microscopic Morphology
• Bulky masses, sometimes very large • Homogenous ,gray-white, lobulated cut surface • No necrosis or hemorrhage	• 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 • Positive for **PLAP**, **OCT4** stain and **c-kit (CD117)**.



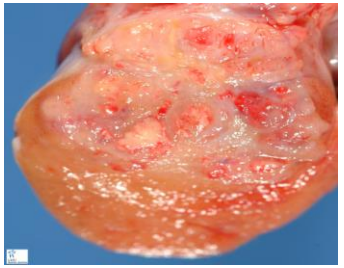


- Spermatocytic Seminoma

- Uncommon: 1-2 % of testicular GCTs
- **Over age 65**
- Slow growing tumor, does not metastasize
- Prognosis is excellent

B. Non-Seminomatous Germ Cell Tumors (NSGCTs)

- Embryonal Carcinoma



- It accounts for about 15 to 35% of testicular GCTs
- Group age: 20 to 30 years
- More aggressive than seminomas.
- Metastasizes early via **both** lymphatic and hematogenous routes.

Size & Features:	Stains:	Treatment:
Smaller than seminoma • Poorly demarcated • Variegated with foci of necrosis & hemorrhage • Can be seen combined with other GCTs • (in mixed GCTs)	Tumor cells are positive for: Cytokeratin (CK) - CD30 -	Chemotherapy (radiation is not effective like seminoma)

- Choriocarcinoma:

- Highly malignant tumor

Tumor size & features:	Components:	Serum level:	Stain:
- Small sized lesions. - Prominent hemorrhage and necrosis.	Made up of malignant trophoblastic (placental) tissue. (cyto-trophoblastic and syncytio-troblastic cells)	Patients have elevated serum human **chorionic gonadotropin (HCG)**.	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.

- Yolk Sac Tumor

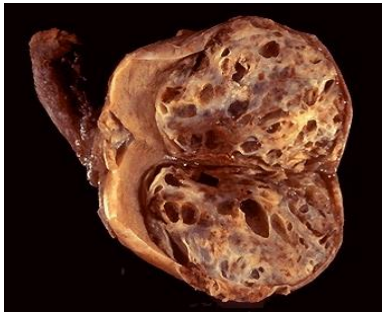
- Also called Endodermal sinus tumor.
- Forms of testicular yolk sac tumor:

	Pure YST:	**Combination with other NSGCTs:**
Adults :	Rare	Occurs as a part or component of mixed GCT (commonly mixed with embryonal carcinoma)
Children :	It is the **most common** tumor in infant and children up to 3 years of age. It has a very good prognosis in infants and children.	Rare
Serum AFP level & stain :	Patients have elevated serum alpha fetoprotein (AFP) Tumor cell are positive for alphafetoprotein (AFP) and alpha-1-antitrypsin stain.	

- 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.

Gross morphology:	**Microscopic morphology:**
- Non encapsulated - homogenous - yellow white - mucinous	- Tumor shows structure resembling endodermal sinuses called as **Schiller-Duval bodies** are characteristic. - Hyaline–pink globules

- Teratoma:



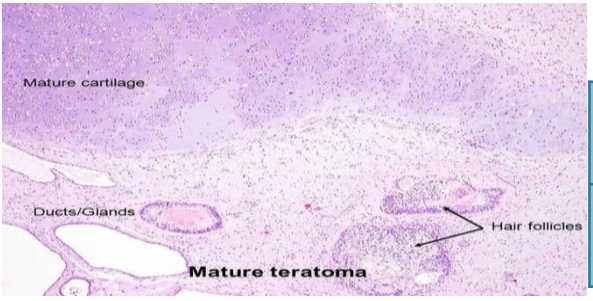
- It is a tumor composed of various different types of cells or organ components.
- Any age, infancy to adult life
- In it's pure form:
  - **common in infants and children secondry to yolk sac tumor (in this age group).**
  - Rare in adults, but it It occurs as part of mixed GTC.

Size & features:	**Components:**
Usually large 5 -10 cm - Heterogenous appearance - with solid and cystic areas	Composed of bizzarely distributed collection of different type of cells or organ structures (heterogenous): neural/brain, cartilage, bone, squamous epithelium, hair, glandular cells, smooth muscle, thyroid tissue, bronchial epithelium of lung, pancreatic tissue, teeth etc.

Types of Teratoma:

Mature teratoma:	If the cellular/organ tissue is mature looking
Immature teratoma:	If some of the cellular/organ tissue component is immature
Teratoma with malignant transformation:	- If any of the cellular/organ tissue undergoes non germ cell type of malignant tranformation - Rare, e.g squamous cell carcinoma or adenocarcinoma

Behavior of Teratoma:



	Mature teratoma	**Immature teratoma**
Infants & children:	Benign	Malignant
Adults :	all teratomas are regarded as **malignant**, and capable of metastasis, regardless of whether the elements are mature or not.	

Mixed Germ Cells Tumors:

- 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 + embyronal carcinoma

We have to know the elements to decide the line of treatment

Clinical features of GCTs:

- 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
  - ✓ lactate dehydrogenase
- The standard management of solid testicular tumors is radical orchiectomy, biopsy in **not** recommended due to the risk of having tumor spillage.
- GCTs can spread by three ways :
  - ✓ **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** but non-seminomatous tumors are **chemosensitive** and respond very well to chemotherapy.

Prognosis:

- **Patients with seminomatous tumors:** more than 95% can be cured.
- **Patients with non-seminomatous tumers:** can achieve complete remission with aggressive chemotherapy, and most can be cured.
- **Patients with pure choriocarcinoma:** the most aggressive non-seminomatous tumor. It has a poor prognosis.

Difference between seminoma and non-seminomatous germ cell tumors:

Seminomas	Nonseminomatous Germ Cell Tumors
Seminoma	Embryonal, yolk sac, choriocarcinoma, teratoma
Radiosensitive	Not radiosensitive
Chemosensitive	Chemosensitive
Late metastasis	Early metastases to retroperitoneal lymph nodes
Excellent prognosis	More aggressive

Table 17–1 Summary of Testicular Tumors

Tumor	Peak Patient Age (yr)	Morphology	Tumor Marker(s)
Seminoma	40–50	Sheets of uniform polygonal cells with cleared cytoplasm; lymphocytes in the stroma	10% of patients have elevated hCG
Embryonal carcinoma	20–30	Poorly differentiated, pleomorphic cells in cords, sheets, or papillary formation; most contain some yolk sac and choriocarcinoma cells	Negative (pure embryonal carcinoma)
Yolk sac tumor	3	Poorly differentiated endothelium-like, cuboidal, or columnar cells	90% of patients have elevated AFP
Choriocarcinoma	20–30	Cytotrophoblast and syncytiotrophoblast without villus formation	100% of patients have elevated hCG
Teratoma	All ages	Tissues from all three germ cell layers with varying degrees of differentiation	Negative (pure teratoma)
Mixed tumor	15–30	Variable, depending on mixture; commonly teratoma and embryonal carcinoma	90% of patients have elevated hCG and AFP

AFP, alpha fetoprotein; hCG, human chorionic gonadotropin.

Summary

(from Robbin's basic pathology)

SUMMARY

Testicular Tumors

- Testicular tumors are the most common cause of painless testicular enlargement. They occur with increased frequency in association with undescended testis and with testicular dysgenesis.
- Germ cells are the source of 95% of testicular tumors, and the remainder arise from Sertoli or Leydig cells. Germ cell tumors may be composed of a single histologic pattern (60% of cases) or mixed patterns (40%).
- The most common "pure" histologic patterns of germ cell tumors are seminoma, embryonal carcinoma, yolk sac tumors, choriocarcinoma, and teratoma. Mixed tumors contain more than one element, most commonly embryonal carcinoma, teratoma, and yolk sac tumor.
- Clinically, testicular germ cell tumors can be divided into two groups: seminomas and nonseminomatous tumors. Seminomas remain confined to the testis for a long time and spread mainly to paraaortic nodes—distant spread is rare. Nonseminomatous tumors tend to spread earlier, by both lymphatics and blood vessels.
- HCG is produced by syncytiotrophoblasts and is always elevated in patients with choriocarcinomas and those with seminomas containing syncytiotrophoblasts. AFP is elevated when there is a yolk sac tumor component.

Thank You!

We hope you found this helpful and informative.

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