



# GENITOURINARY SYSTEM

SUBJECT : Male genital tract

LEC NO. : 9

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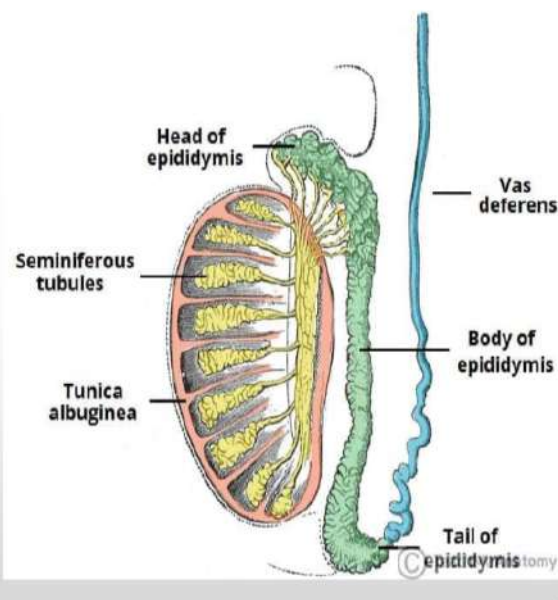
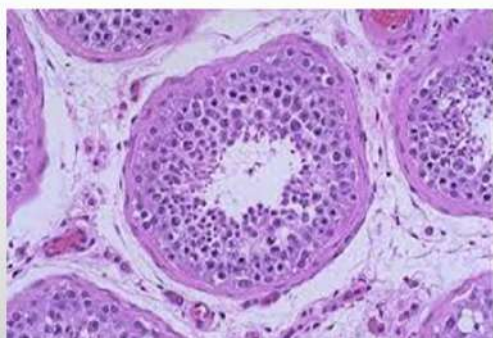
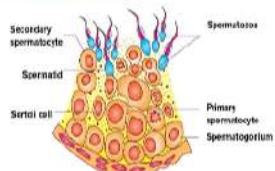
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# GENITOURINARY SYSTEM

## TESTIS

### SEMINIFEROUS TUBULE



## Testicular tumors (T)

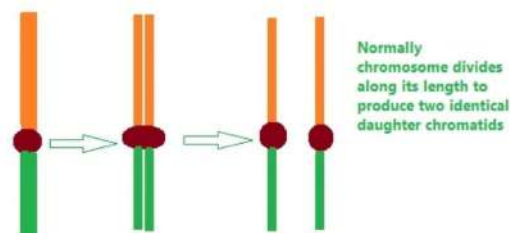
- ❑ Testicular T are the most important cause of firm, painless enlargement of the testis with a peak incidence in **20-34 years age group. Reproductive age**
- ❑ In adults, **95% of testicular T arises from germ cells & all are malignant.**
- ❑ **Sertoli or Leydig cells T (sex cord/stromal tumors) are uncommon & are usually benign.**
- ❑ **Cryptorchidism** associated with a 3-to 5-fold increase risk of cancer. In the undescended testis, as well as increase risk of cancer in the contralateral descended testis,
- ❑ **Intersex syndromes, including androgen insensitivity syndrome & gonadal dysgenesis, are also associated with an increase frequency of testicular cancer.**
- ❑ For unknown reasons, the risk of cancer is increase in siblings of males with testicular cancers.



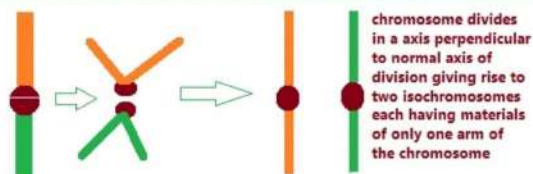
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- ❑ Testicular T are more common in whites than in blacks & the incidence has increase in Caucasian populations in recent decades.
- ❑ Cytogenetic studies show a wide range of abnormalities in testicular germ cell T, the most common of these is an isochromosome of the short arm of chromosome 12, but their role in the pathogenesis of these cancers remains unclear.

Q . how does isochromosome forms ?



[A] NORMAL CHROMOSOME DIVISION ALONG AXIS OF THE CHROMOSOME

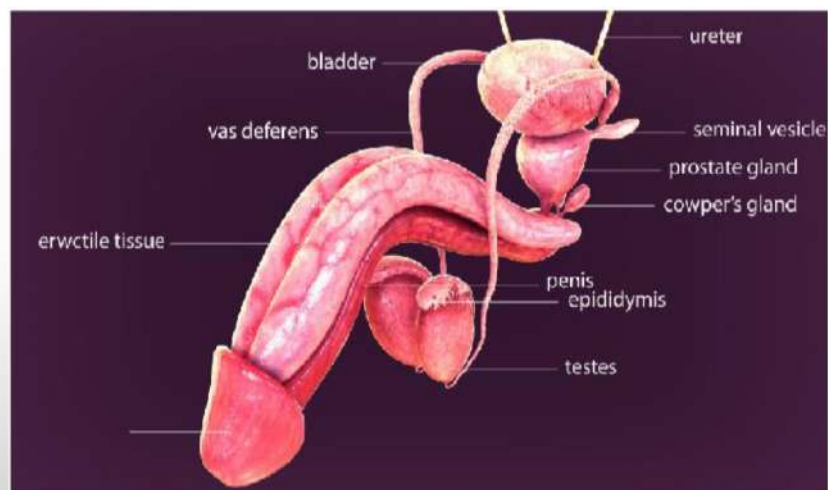


[B] ABNORMAL CHROMOSOME DIVISION PERPENDICULAR TO NORMAL AXIS OF DIVISION

NOTE : AXIS OF CH DIVISION ALWAYS PASSES THROUGH CENTROMERE



للمعرفة فقط



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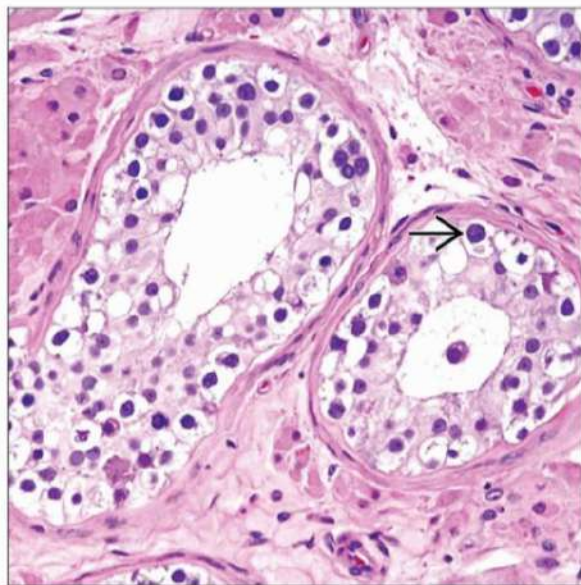


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- ❑ **Testicular germ cell tumors (TGCTs)** demonstrate a wide variety of histopathologic, genetic, pathogenetic, and immunocytochemical characteristics and various clinical-biologic profiles and prognoses.
- ❑ Most TGCTs arise from an **intratubular precursor cell** referred to as germ cell neoplasia in situ (GCNIS), which is an embryonic germ cell with the potential to differentiate into a plethora of embryonic and extraembryonic lineages.

**Intratubular precursor cell:** indicates that the tumors originate from a specific type of cell that is found within the seminiferous tubules of the testicles. These cells are considered precursors because they have the potential to develop into cancerous cells.

GCNIS refers to the presence of abnormal germ cells **within** the seminiferous tubules that have **not** yet developed into invasive cancer but have the potential to do so

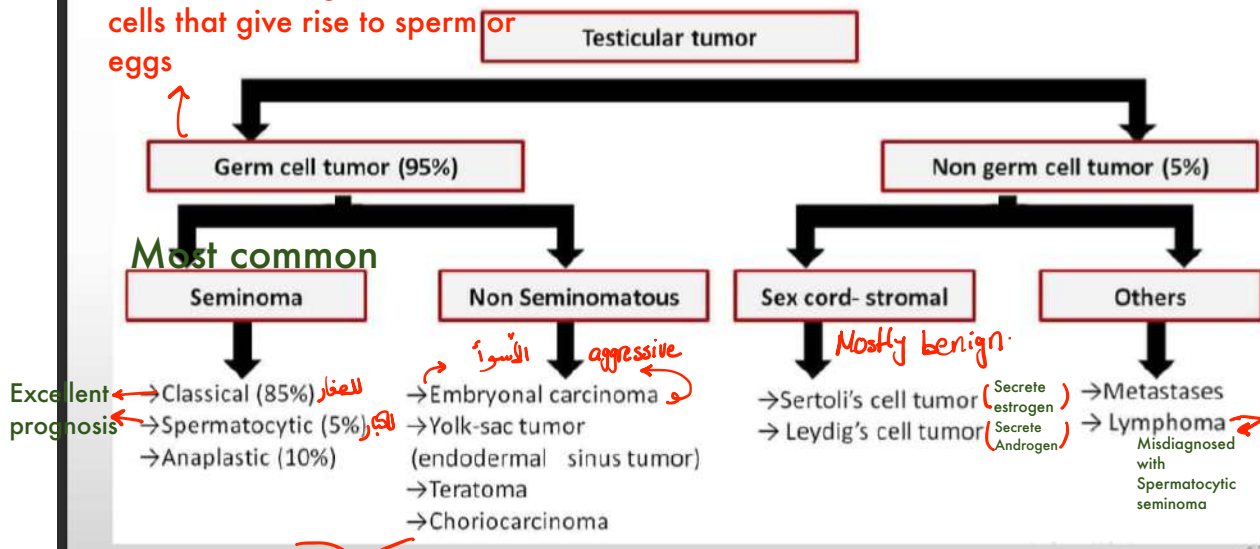


- intratubular germ cell neoplasia (IGCN): Beautiful picture showing cells (within seminiferous tubule) having enlarged nuclei, prominent nucleoli, and clear cytoplasm along the basal aspect of a seminiferous tubules lacking spermatogenesis. Sertoli cells are displaced toward the lumen.
- The TGCT of young adults originate from a common precursor, germ cell neoplasia in situ (GCNIS), initially termed carcinoma in situ (CIS) testis .
- GCNIS is considered to originate from developmentally arrested immature germ cells (gonocytes) that fail to differentiate to spermatogonia .

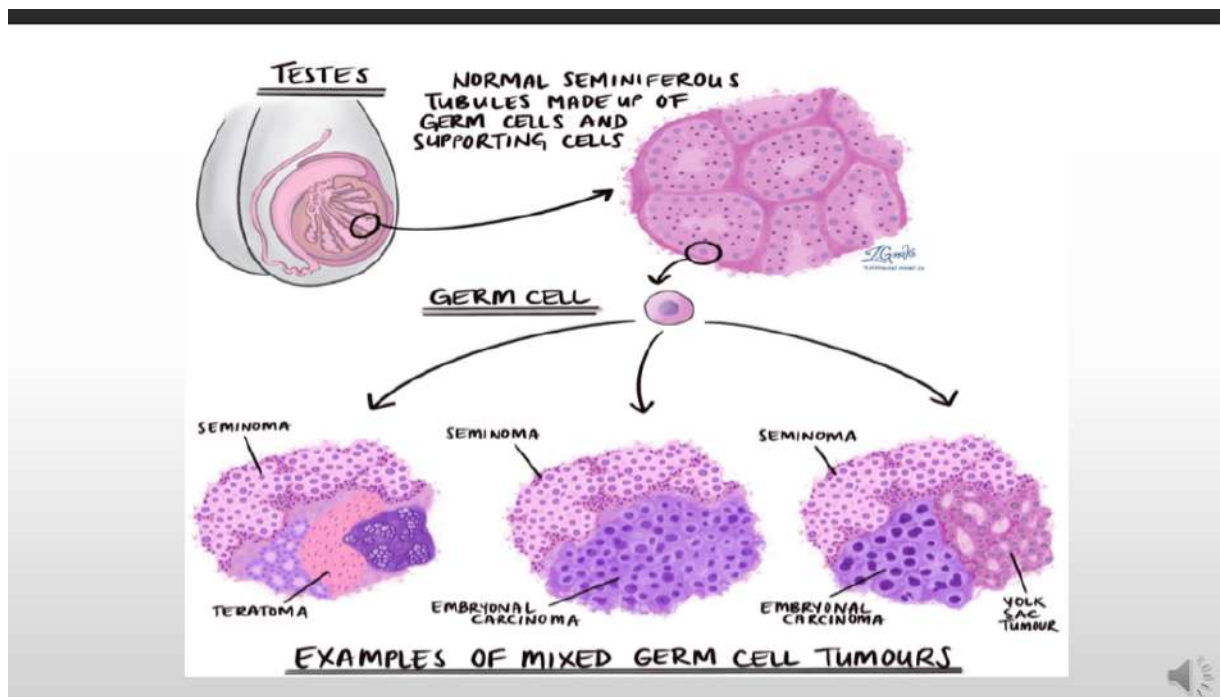


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A germ cell tumor is a type of a tumor that originates in the cells that give rise to sperm or eggs



The patient complains from hard firm mass in his testis



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## Classification & Histogenesis

- In the WHO classification, which is the most widely used in the US the germ cells T of the testis are divided into two broad categories, based on whether they contain a **single histologic pattern (60% of cases)** or **multiple histologic patterns (40% of cases)**.

### ▪ WHO Classification of Testicular Germ Cell T

- ❑ Tumors with **One Histologic Pattern (60% of cases)** **40% mixed**

#### (I) Seminoma,

#### (II) Non-seminomatous T including:

- Embryonal carcinoma,
- Yolk sac tumor,
- Choriocarcinoma,
- Teratomas - Mature & Immature & with malignant transformation of somatic elements.



- ❑ **Tumors with More Than One Histologic Pattern (40%)**

- ❑ This classification is based on the view that testicular germ cell T arise from primitive cells that may either differentiate along

(I) Gonadal lines to produce seminomas.

(II) Transform into a totipotential cell population, giving rise to non-seminomatous germ cell T. Such totipotential cells:

- (a) may remain **undifferentiated** to form **embryonal ca, or**
- (b) may **differentiate along extra-embryonic lines to form yolk sac tumors & choriocarcinomas.**
- (c) may **differentiate along somatic cell lines to produce teratomas.**

→ We don't consider it benign in testis (immature)

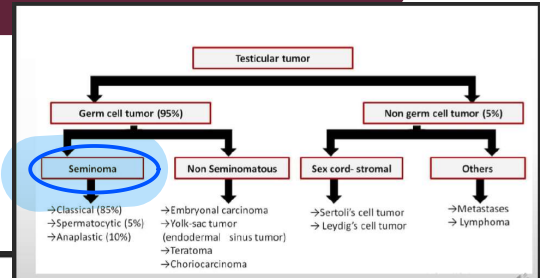
عكس ovarian teratoma

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## حفظ Seminomas "classic"

- Seminomas account for 50% of testicular germ cell T. Most common
- They are histologically identical to ovarian dysgerminomas & to germinomas occurring in the CNS & other extra-gonadal sites.
- GROSSLY, seminomas are "potato" like, large, soft, well-demarcated, homogeneous, gray-white T that bulge from the cut surface of the affected testis, typically confined to the testis by an intact tunica albuginea.
- Large seminoma may contain foci of coagulation necrosis, usually without hemorrhage; But the presence of hemorrhage should prompt careful scrutiny (examination) for an associated non-seminomatous germ cell component to the T.

## Seminoma

يحدث عادة في testis، وتحديدًا في أنسجة testis التي تنتج الحيوانات المنوية

Seminoma is a type of testicular germ cell tumor that **arises from the cells that develop into sperm**. It is one of the most common types of testicular cancers, comprising about 50% of all testicular germ cell tumors.

**Dysgerminoma** is a type of germ cell tumor that primarily occurs in the **ovaries**. It is the ovarian counterpart of seminoma, which occurs in the testes

(بمعنى Seminoma كثير بتشبهه Dysgerminoma سواء كان grossly or histologically)

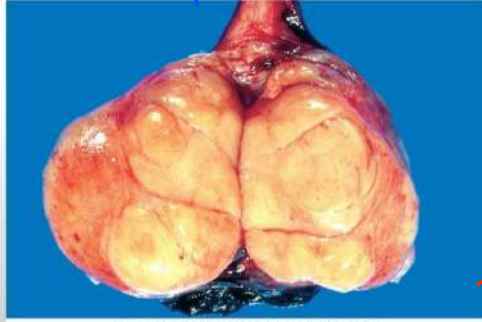
Seminomas can grow rapidly, leading to inadequate blood supply to the tumor cells. This results in ischemia, causing the affected cells undergo coagulation necrosis

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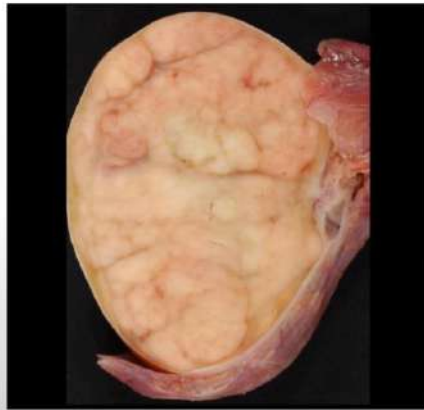


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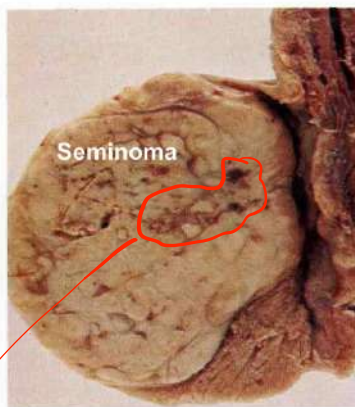
Seminoma of the testis. Well circumscribed, pale, fleshy, homogenous mass.



Seminoma:  
testis.



Lobulated, potato like, Bulky, solid, rubbery, firm, sharply demarcated



**Seminoma: testis.**

- A lobulated, pale-grey opaque tumor of the testis, which is firm & "potato" looking on section.

the presence of hemorrhage should prompt careful (examination) for an associated non-seminomatous germ cell component

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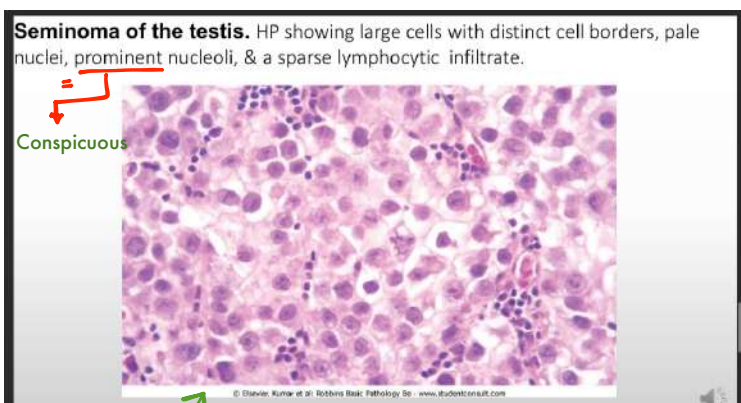
## Histologically

1. seminomas composed of large, uniform cells with distinct cell borders, clear, glycogen-rich cytoplasm, & round nuclei with conspicuous nucleoli.
2. Cells are arranged in small lobules with intervening fibrous septa infiltrated by lymphocytes.
3. A granulomatous inflammatory reaction may also be seen.
4. In as many as 25% of cases, cells staining positively for human chorionic gonadotropin (hCG). **choriocarcinoma** هاد لا يعني انه في
5. These hCG-expressing cells are morphologically similar to  
\* syncytiotrophoblasts, & they are presumably the source of the elevated  
\* serum hCG concentrations that may be encountered in some males with  
\* pure seminoma.

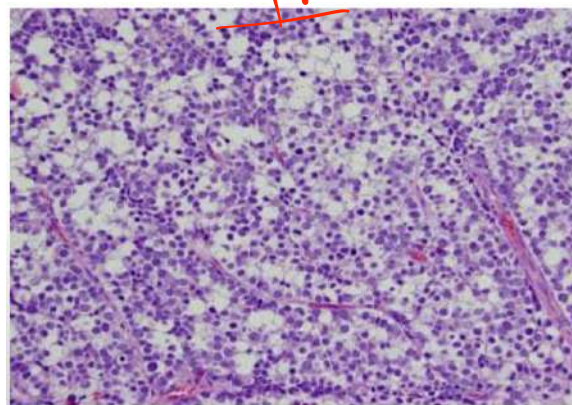
٢٣ جردا

In seminoma, the immune system may react to tumor antigens or debris, leading to the formation of

The syncytiotrophoblast is a specialized layer of cells that forms part of the outermost layer of the placenta during pregnancy. syncytiotrophoblast secretes hormones essential for maintaining pregnancy and supporting fetal development. These hormones include human chorionic gonadotropin (hCG (هرمون الحمل))



Clear uniform cells  
Clear cytoplasm cause it contains glycogen



لاحظوا انها lobulated  
fibrous septa

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❖ **Spermatocytic seminoma** is a less common morphologic variant of seminoma, which tend to occur in: حفظ

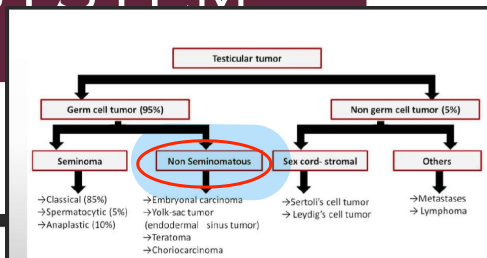
1. **Older patients** → **uniform** يعني مش
2. It contain a mixture of medium-sized, **large** → **uninucleate or multinucleate T cells, & small cells with round nuclei that are reminiscent of secondary spermatocytes.** → مرات بصير في miss diagnosis كونها بتصير بالكبار كمان with lymphoma
3. In contrast to the behavior of classic seminoma,
  - 1) there is **no association with intratubular germ cell neoplasia.**
  - 2) metastases are **exceedingly rare,** (Best prognosis in all Sonoma)

spermatocytic seminoma and seminoma are distinct subtypes of testicular **germ cell tumors** that differ in terms of **age** of onset, histological features, growth pattern, and prognosis. **Spermatocytic** seminoma is typically **less aggressive** and occurs in **older** men, while **seminoma** is **more common** in **younger** men and may **grow more rapidly**.





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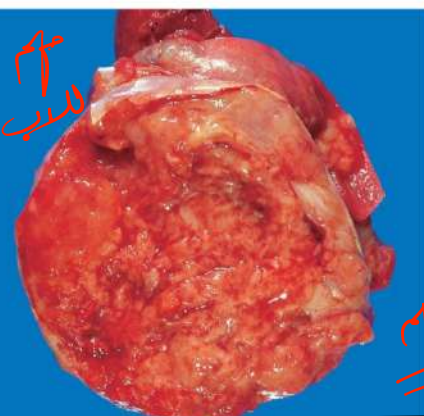


## Not well circumscribed Embryonal carcinomas

- highly malignant, ill-defined, invasive T containing foci of hemorrhage & necrosis. The primary lesions may be small, even in patients with systemic metastases.
- Larger lesions may invade the epididymis & spermatic cord.

### Histologically : Undifferentiated cells

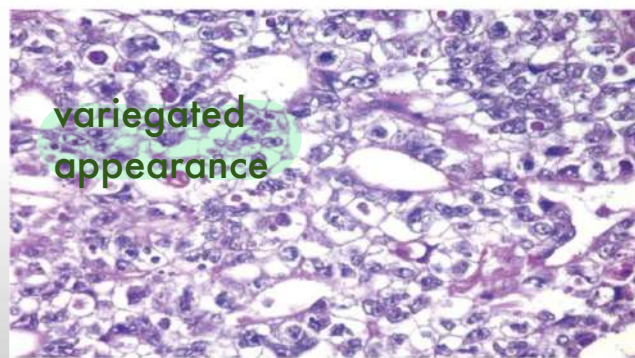
- the T cells are large & primitive looking, with basophilic cytoplasm, indistinct cell borders, & large nuclei with prominent nucleoli.
- Tumor cells may arranged in undifferentiated solid sheets or may contain (glandular structures & irregular papillae) → pleomorphism, atypia
- In most cases of embryonal carcinoma, other patterns of germ cell T (e.g., teratoma, yolk sac ca, choriocarcinoma) are admixed with the embryonal areas.
- Pure embryonal carcinomas are rare, comprise 2% to 3% of all testicular germ cell T.



## Embryonal carcinoma of the testis.

In contrast to the seminoma, the embryonal carcinoma is a hemorrhagic mass

Embryonal carcinoma of the testis. Sheets of undifferentiated cells, as well as primitive glandular differentiation. The nuclei are large & hyperchromatic



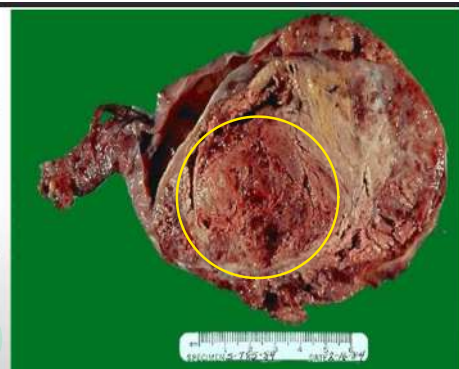
variegated appearance

Embryonal carcinoma is a type of aggressive (very poor prognosis) testicular germ cell tumor that arises from embryonic stem cells and characterized by the presence of primitive, undifferentiated cells resembling early embryonic tissue

A small testicular carcinoma is shown here. There is a mixture of bluish cartilage with red and white tumor tissue. This neoplasm microscopically contained mainly teratoma, but areas of embryonal carcinoma were also present.



- Here is an even larger testicular neoplasm. It is composed mostly of embryonal carcinoma, but there are scattered firmer white areas that histologically are teratoma.
- Thus, this testicular neoplasm is mixed embryonal carcinoma plus teratoma (sometimes called teratocarcinoma).
- Embryonal carcinoma is more aggressive than seminoma.







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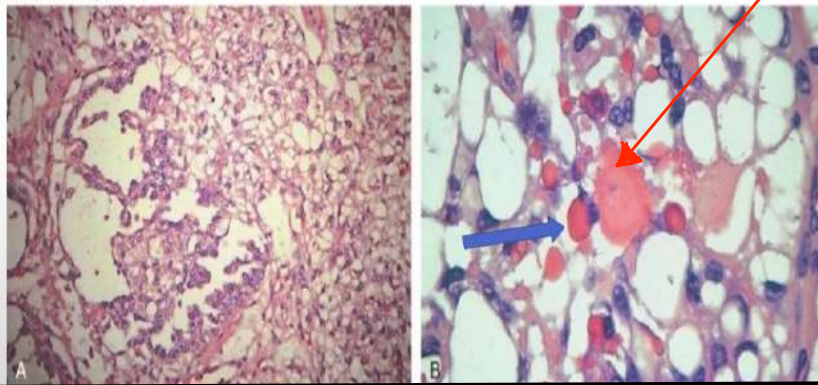
## Yolk sac tumors

- Represents **endodermal sinus** differentiation of totipotential neoplastic cells, hence the other name **endodermal sinus T**.

They are the **most common primary testicular cancer in children younger than 3 years of age**.

- In adults, they are mostly seen **admixed** with embryonal ca. → Worse than pure yolk sac tumors
- **Grossly**, these T are often large & may be well demarcated.
- **Histologically**
  1. cuboidal to columnar epithelial cells forming microcysts, sheets, glands, & papillae, often associated with **eosinophilic hyaline globules**.
  2. A distinctive feature is the presence of structures resembling primitive **glomeruli**, the so-called **Schiller-Duval bodies**.\*
  3. **α-fetoprotein (AFP)** can be demonstrated within the cytoplasm of the T cells by immunohistochemical techniques.

**Yolk sac tumor "carcinoma"**. A, LP view showing areas of loosely textured, microcystic tissue & papillary structure resembling a developing glomerulus (**Schiller-Duval body**)  
B, HP view showing characteristic hyaline droplets within the microcystic areas of the tumor. **Alfa-fetoprotein** is present within the droplets.



## Yolk sac

هو كيس صغير يتكون في الجنين خلال مرحلة التطور المبكرة و يعمل كمصدر للتغذية والدعم للجنين خلال فترة تطوره

Yolk Sac tumors ( primitive **endodermal** tumors or endodermal sinus tumors) are derived from malignant germ cells that are differentiating along the extraembryonic yolk sac lineage.

The tumor cells elaborate α-fetoprotein (like normal yolk sac)

Due to their histological resemblance to the yolk sac and their origin from germ cells, these tumors are termed "yolk sac tumors." While the yolk sac itself is not present in human embryos beyond the very early stages of development, the term is used to describe these tumors because of their similarity to the yolk sac histologically and their association with germ cell development.

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## Choriocarcinomas placental cells

➤ represent differentiation of pluripotential neoplastic germ cells along trophoblastic lines.

➤ **Grossly**, the primary T are often small, non palpable lesions, even with extensive systemic metastases!

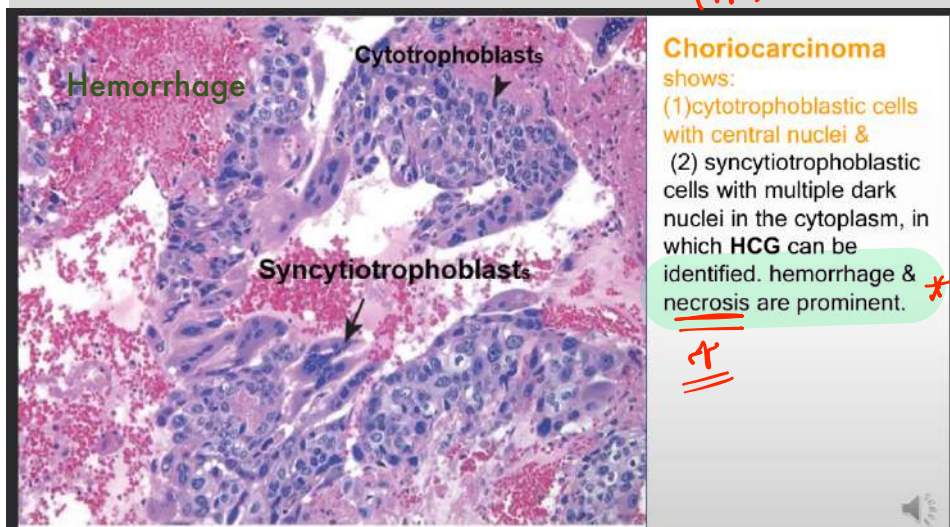
### Histologically :

- composed of (1) cytotrophoblasts; sheets of small cuboidal cells capped by (2) Syncytiotrophoblasts ; large, eosinophilic syncytial cells containing multiple dark, pleomorphic nuclei.

- Well-formed placental villi are never seen. (٢٣)

- **hCG** hormone can be identified by immunohistochemical staining, particularly within the cytoplasm of the syncytiotrophoblastic elements. (٢٣)

بكون تنبير عاللي



Choriocarcinoma in males is an extremely rare and aggressive type of cancer that originates from germ cells, specifically from trophoblastic cells. Trophoblastic cells are normally found in the placenta during pregnancy, but in choriocarcinoma, these cells develop abnormally and can form tumors in the testes

choriocarcinoma in males may include testicular swelling or enlargement, pain or discomfort in the testes, a palpable mass in the scrotum, or symptoms related to metastasis, such as hemoptysis

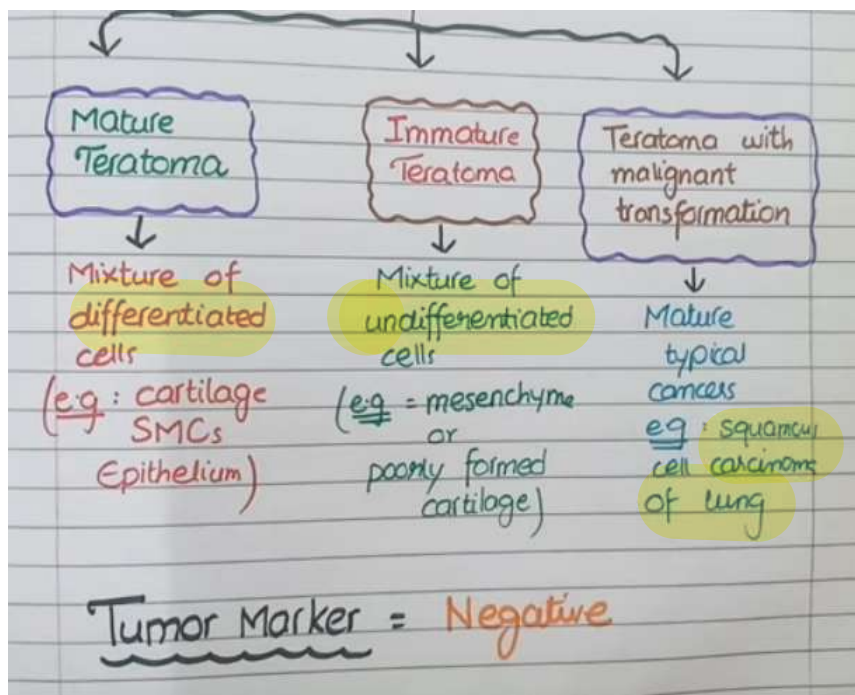
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Teratoma = cells of multiple lineages , it has the potential to develop into cells of all types such as endothelium, epithelium ,bones , hair cartilage ...



## Teratomas (TT)

- ❑ Represent differentiation of pluripotential neoplastic germ cells along **somatic** cell lines.
- ❑ TT form firm masses that on cut surface, often contain **cysts** & areas of **cartilage**.

**Histologically** : 3 major variants of **pure** teratomas are recognized:

(I) **Mature TT** contain **fully differentiated** tissues from one or more germ cell layers (neural tissue, cartilage, adipose tissue, bone, & epithelium) in a haphazard array.

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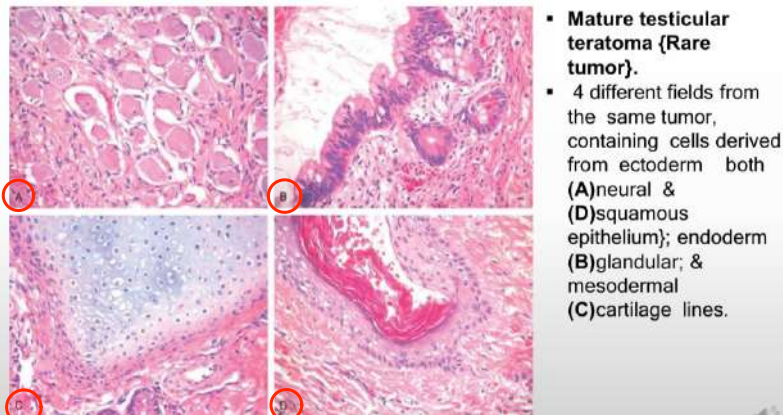
**Immature TT** ,contain **immature** somatic elements reminiscent of those in developing fetal tissue.

## TT with somatic-type malignancies

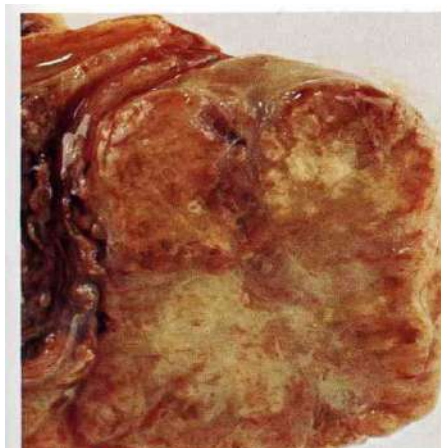
are characterized by the development of frank malignancy (usually in the form of a SCCa or adenocarcinoma) in preexisting TT elements.

➤ Pure TT in **prepubertal males** are usually benign, BUT...

**All testicular TT in adults should be regarded as malignant T because they are:** (1) often contain other malignant germ cell elements & (2) they metastasize in 37% of cases.



عكس ال ovaries \*



**Teratoma: testis**, from a man aged 44years.

- Solid testicular mass, 6X4 cm.
- C/S is pinkish-white with yellow areas of necrosis & hemorrhage. No cysts are present.

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## Germ cell tumors arise from the cells that give rise to sperm

A mixed germ cell tumor in the testis is a type of testicular cancer that contains two or more types of germ cell elements . When multiple types of germ cell elements are present within the same tumor, it is referred to as a mixed germ cell tumor

So as not to get confused, the difference between mixed germ cell tumors and testicular teratoma is that mixed germ cell tumors contain two or more types of germ cell elements such as seminoma embryonal carcinoma etc. While testicular teratomas are germ cell tumors that typically contain a variety of differentiated tissues derived from two or more embryonic layers (Ectoderm, mesoderm and endoderm).

## Mixed germ cell tumors

- ❖ Account for 40% of all testicular germ cell T. Combinations of any of the described patterns may occur in mixed T
- ❖ the most common of which is a combination of teratoma, embryonal carcinoma, & yolk sac tumors.

## Clinical Features

1. All testicular germ cell T present mostly as a
  - ❖ \* (1) painless enlargement of the testis. \*
  - ❖ (2) Unfortunately some T, especially nonseminomatous germ cell T, may present with widespread metastases at diagnosis, in the absence of a palpable testicular lesion!
  - ❖ **Clinically**, it is best to consider testicular germ cell T under 2 broad categories:

**Seminomas & non-seminomatous T.**

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❖ **Seminomas** often remain confined to the testis **for long time** & may reach considerable size before diagnosis.

So good prognosis

لأنه بنلاحظها بسرعة و يتكون كبيره قبل ما يصير لها metastasis

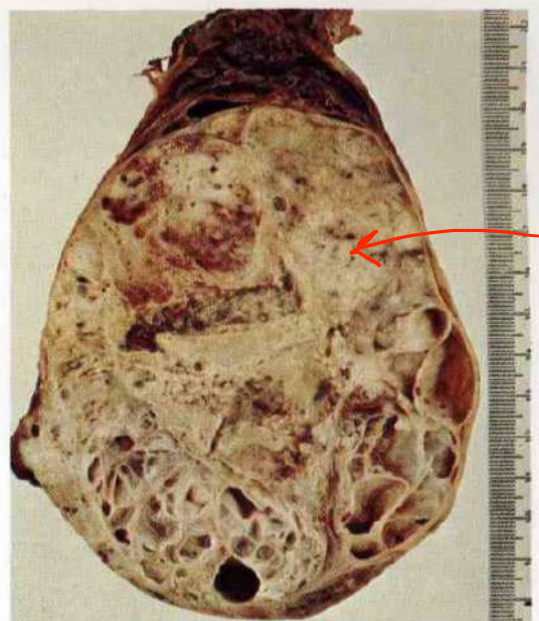
❖ **Lymphatic metastases** are most commonly encountered in the iliac & para-aortic LN, particularly in the upper lumbar region.

❖ Hematogenous metastases occur later.

❖ In contrast, **nonseminomatous germ cell T** tend to metastasize **earlier**, by both blood (most commonly to the liver & lungs) & by lymphatics.

❖ Seminomas have **good prognosis**, as they are **very radiosensitive**, & **respond well to chemotherapy**.

reproductive مشان هيك الاشخاص اللي بكونوا في مرحله ال sperms age ينصح انهم يجمدوا ال sperms تبعونهم احتياط لأنه لو chemotherapy صار معه كانسر بال testis رح ياخذ affect spermatogenesis



11.21 Teratoma: testis

## Combined testicular seminoma & teratoma.

- A large, ovoid mixed tumor, with
- (1) **seminomatous**, yellowish-white solid element, with necrosis & hemorrhages in the upper 2/3 of tumor &
- (2) an almost entirely cystic **teratomatous** element in the lower

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- ❑ Nonseminomatous germ cell T prognosis is generally **poor**, but it has improved dramatically in some cases with the introduction of platinum-based chemotherapy regimens.
- ❑ **Testicular germ cell T are staged in to:**
  - ❑ Stage I: T confined to the testis.
  - ❑ Stage II: Regional LN metastases only.
  - ❑ Stage III: Non-regional LN &/or distant organ metastases
- Assay of tumor markers secreted by T cells is important in the clinical evaluation & staging of germ cell T.

Follow up

## (I) hCG,

1. produced by neoplastic syncytiotrophoblastic cells, is always elevated in patients with **choriocarcinoma**.
2. Germ cell tumors, including **seminoma**, may also contain foci of syncytiotrophoblastic cells (without cytotrophoblastic element) & hence may elaborate hCG. **Approximately 10% to 25% of seminomas elaborate hCG.**

اكادت عليها الدكتور انه هاد لا

## (II) $\alpha$ -fetoprotein (AFP)

is a glycoprotein normally synthesized by the fetal yolk sac & several other fetal tissues.

لانه choriocarcinoma لما يكون في  
cytotrophoblast (unineuclear cell)

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1. Nonseminomatous germ cell T containing elements of yolk sac (endodermal sinus) often produce AFP (AFP is **also elevated in hepatocellular ca**); & in contrast to hCG,...
2. The presence of **AFP** is a reliable indicator of the presence of a **nonseminomatous component** in the germ cell T, as yolk sac elements are not found in pure seminomas.
3. As mixed patterns are common, most nonseminomatous T have elevations of both hCG & AFP.
4. Serial determinations of **hCG & AFP** are useful in the (A) primary **diagnosis** (B) **staging** (C) **monitoring** patients with testicular germ cell T for **persistent or recurrent** T after therapy

على عكس HCG

لأنه  
عنه  
تكونه  
Pure  
Seminoma



## الأسئلة

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## Question 2

A 30-year-old man has had a feeling of heaviness in his left testis for the past 6 months. Physical examination reveals enlargement of the left testis, while the right testis appears normal. There is a palpable left inguinal lymph node. An ultrasound reveals a 4 cm solid mass within the body of the left testis. Laboratory findings included a serum beta-HCG of 5 IU/L and alpha-fetoprotein of 2 ng/mL. The left testis is removed and with on sectioning reveals a firm, lobulated light tan mass without hemorrhage or necrosis. He receives radiation therapy. Which of the following neoplasms is he most likely to have?

- A  Choriocarcinoma
- B  Embryonal carcinoma
- C  Seminoma
- D  Yolk sac tumor
- E  Leydig cell tumor

## Answer

(C) CORRECT. The most common pure form of testicular cancer is seminoma, a type of germ cell tumor which is radiosensitive. The tumor markers are not markedly elevated. This form of testicular carcinoma has the best prognosis overall, when not mixed with other elements.

## Question 11

A 31-year-old man has had a feeling of heaviness in his scrotum for over 6 months. On exam he has an enlarged right testis. An ultrasound reveals a solid 5 cm mass in the body of the right testis. Laboratory studies show a serum alpha-fetoprotein (AFP) of 81 ng/mL and human chorionic gonadotrophin (HCG) of 15 IU/L. A right orchiectomy is performed, and on gross examination the testicular mass is soft and reddish brown. Microscopic examination shows cords and sheets of primitive cells with large nuclei. Which of the following is the most likely diagnosis?

- A  Teratoma
- B  Embryonal carcinoma
- C  Mumps orchitis
- D  Leydig cell tumor
- E  Squamous cell carcinoma
- F  Choriocarcinoma

## Answer

(B) CORRECT. The embryonal carcinoma is likely to have an elevated AFP. Many malignant testicular neoplasms produce some detectable HCG, but this does not mean that choriocarcinoma is present.





# GENITOURINARY SYSTEM

## Question 29

A clinical study is conducted to determine the survival following treatment for testicular neoplasms utilizing subjects recorded into a hospital tumor registry. Treatments included surgery, chemotherapy, and radiation therapy. The patient records are reviewed to determine the pathologic diagnosis and the 5 year survivals for these patients. Which of the following types of testicular neoplasm is most likely to have responded best to radiation therapy?

- A  Choriocarcinoma
- B  Embryonal carcinoma
- C  Seminoma
- D  Teratoma
- E  Yolk sac tumor

**Answer**

(C) CORRECT. Seminomas are the most radiosensitive of testicular carcinomas.

## Question 32

A 2-year-old boy is brought to the physician because his mother (a geometry teacher) has observed that his scrotum is no longer symmetrical. On physical examination the child has enlargement of the left testis. An ultrasound scan shows a 2 cm solid mass within the body of the testis. Laboratory studies show a serum alpha-fetoprotein of 226 ng/mL. Which of the following neoplasms is this child most likely to have?

- A  Leydig cell tumor
- B  Neuroblastoma
- C  Rhabdomyosarcoma
- D  Teratoma
- E  Yolk sac tumor

**Answer**

(E) CORRECT. The most common testicular tumor under the age of 3 is a yolk sac tumor (infantile embryonal carcinoma). However, finding any testicular tumor in children is uncommon. The prognosis is good in most cases.

 كل التوفيق  
وَقَلِّدْ بَزْرِنِي عَلِمًا

هيك بنكون انهينا مادة المييد  
ازا عندكم اي سؤال ابعتولي