Testicular tumor

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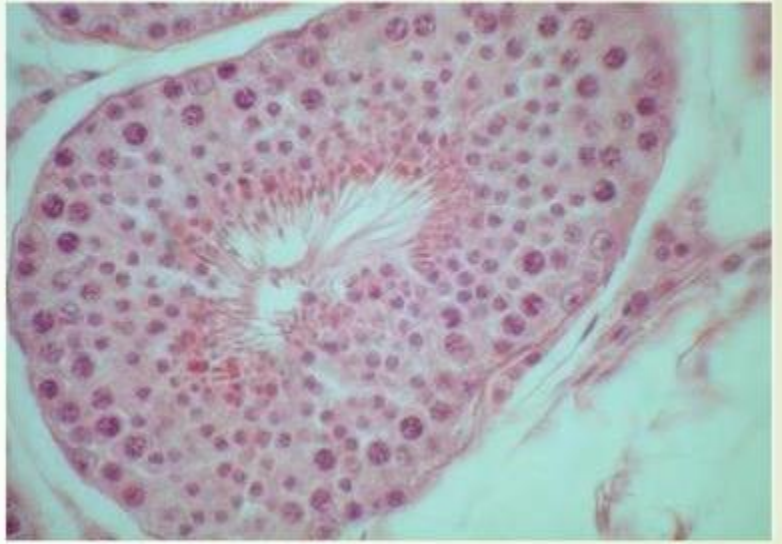
Anatomy of the testes



✓The male gonads are the testes , located in the scrotum .

✓ They serve **two important functions :**

1 hormon production (androgen) , such as testosterone .

2 sperm production . The male cells needed to fertilize female egg.

✓ Covered by **Tunica Albuginea** (white fibrous layer)

✓Each lobule contain up to 4 **seminiferous tubules** where sperm is synthesized

✓ **Three main cells** :

1- germ cells (spermatogonia) :

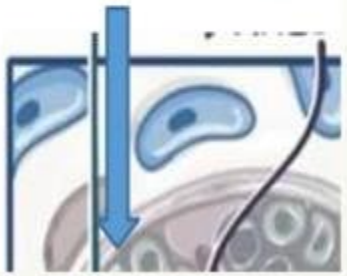
Sperm production

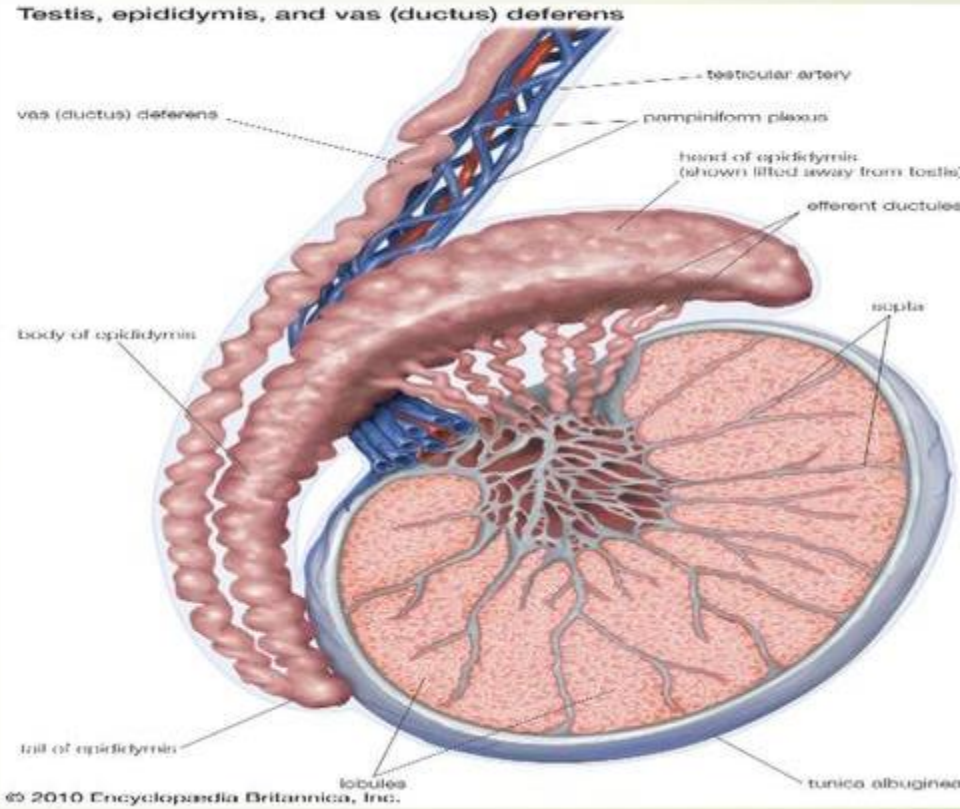
2- sertoli cell :

Provide nutrients to developing sperm

3- leydig cell :

Testosterone hormone synthesis





Incidence and risk factors

- ▪ 99% of testicular neoplasms are malignant .
- ▪ Testicular malignancy represent 1-2% malignant tumours in males .
- ▪ Usually occurs between 20-50 years

➢ **Risk factors :**

1 Age: the commonest affected age group is 20–45y, with germ cell tumours.

2 Race: - white Caucasian people living in Europe and USA have the highest risk.

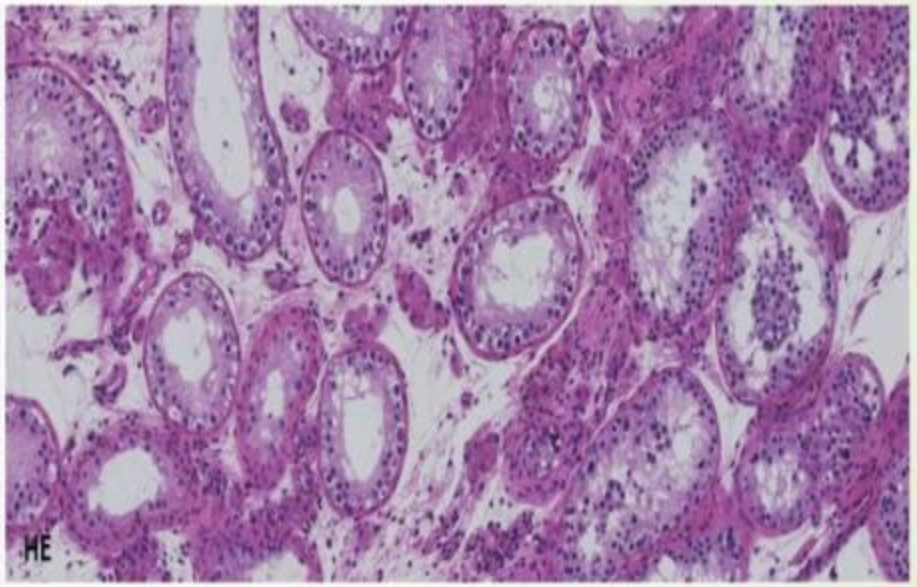
- ▪ Undescended testis especially intra-abdominal type . Malignancy is 15 time more common than in normal testis . It is genetically determined and occur even after successful surgery to descend the testis into the scrotum .
- ▪ Family or personal history of testicular malignancy .
- ▪ Maternal administration of oestrogen.
- ▪ HIV & AIDS .

TIN(testicular interepithelial neoplasia)

- synonymous with **carcinoma in situ**, although the disease arises from malignant change in spermatogonia; 50% of cases develop invasive germ cell TC within 5y.
- The precursor lesion **for most testicular GCTs**, TIN may be observed adjacent to TC.
- **Risk factors include** :

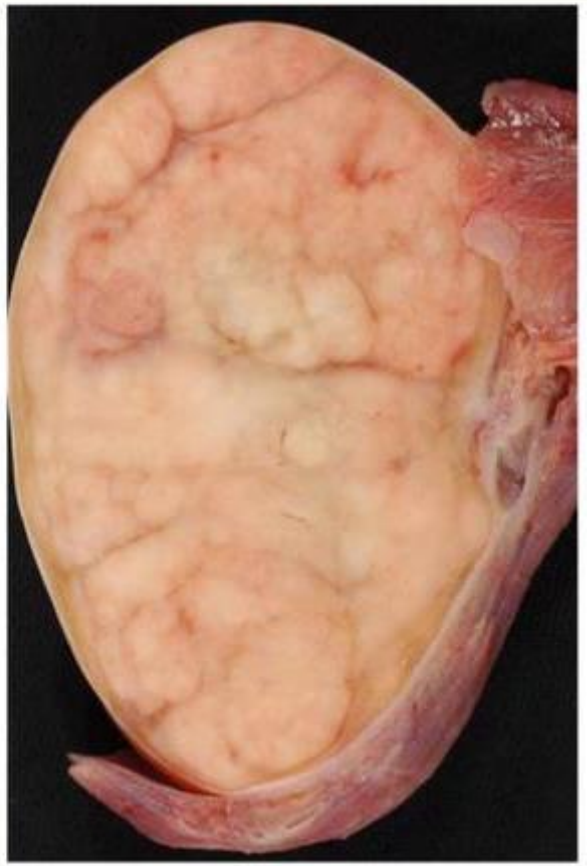
1 cryptorchidism 2- extragonadal germ cell tumour 3-atrophic contralateral testis (<12mL) 4- Klinefelter's syndrome 5- previous or contralateral TC (5%) 6- and infertility.

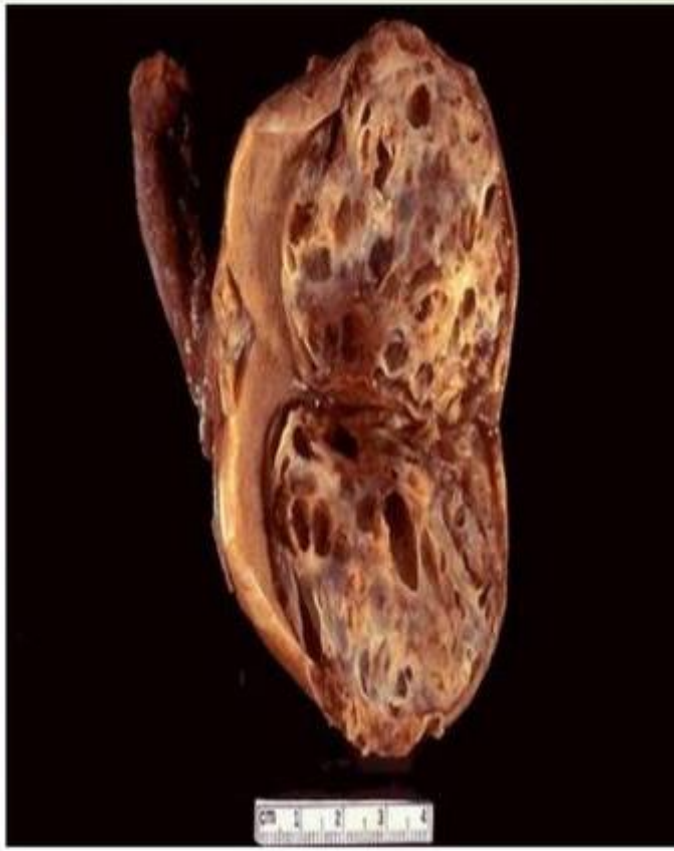
- It is present in the **contralateral testis** of up to 5% of TC patients.
- If TIN is diagnosed, treatment is with **radiotherapy.**



Types of tc

- ▪Seminoma 40%
  ▪Teratoma 30%
  ▪Combined seminoma & teratoma 15%
  ▪Interstitial tumours :
  1- Leydig cell tumour :Usually occur before puberty , secreting
  excess androgens → precocious puberty & extreme muscular
  development (infant Hercules)
  2- Sertoli cell tumour : Usually occur after puberty , secreting excess
  oestrogen → gynaecomastia , loss of libido and aspermia .
  ▪ Other rare tumours e.g. lymphoma .





Sign and symptoms

- Symptoms :

1 Most patients present with a painless scrotal lump.

- ** Delay in presentations not uncommon, particularly those with metastatic disease. This may be due to patient factors (fear, self-neglect, ignorance, denial) or earlier misdiagnosis.

2 5% of patients develop acute scrotal pain due to intratumoural haemorrhage , causing diagnostic ° -- ‘ -'-- 310°oof patients develop symptoms suggestive of advanced disease, including weight loss, lumps i neck, chest symptoms or bone pain.

- '*' More common on the right

- Signs :

1 Observation may reveal asymmetry or slight scrotal skin discoloration.

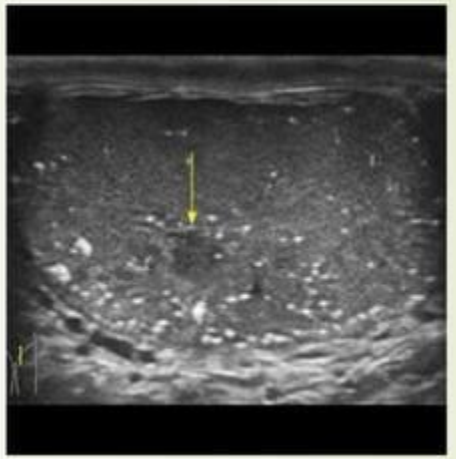
2 palpation may reveal a hard , non-tender , irregular, non-transilluminable mass in the testis or replacing the testis. 3-assess the epididymis, spermatic cord, and overlying scrotal wall, which may be normal or involved in10—15°/oof cases.

4 Rarely , a secondary hydrocele may be present.

5 General examination may reveal cachexia , supraclavicular lymphadenopathy , chest signs hepatomegaly lower limb oedema, or abdominal mass , all suggestive of metastatic disease.

6 Gynaecomastia is seen in about 5°/oof patients with TC due to endocrine manifestations of some tumours.

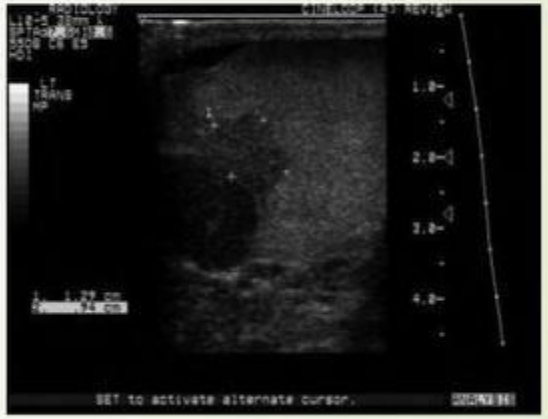
Investigations



➢ **Investigation :**

1 Ultrasound is the **first-line investigation** of any scrotal lump and will confirm whether the palpable lesion is within the testis.

- The sensitivity of USS for detecting a testicular tumor is **almost 100%,** including impalpable lesions of
- 1–2mm and 'occult' primary tumours in patients presenting with systemic symptoms and signs.
- Any **hypoechoic** area within the tunica albuginea should be regarded with suspicion.



2 abdominal and chest CT for staging purpose

- Can identify small nodal deposits <2 cm
- MRI and PET scan no advantage over CT

Tumor markers

- regarding treatment

✓ **Clinical uses**:

- **1-** measured at presentation
- **2-**1-2 weeks after radical orchidectomy
- **3-** and during follow-up to assess response to treatment

4 Elevation after orchidectomy generally represents metastatic disease

5 Conversely normalization does not rule out metastatic disease .

✓ **2 main types** :

1 **oncofetal proteins**

2 **cellular enzymes**

1- oncofetal proteins :

1- alpha fetoprotein :

is expressed by trophoblastic elements within 50–70% of teratomas and yolk sac tumours. The presence of elevated serum AFP strongly suggests a **non-seminomatous element** , normally <10ng/mL.
Half-life: 4-6 days
Falsely elevated in liver dysfunction, viral hepatitis and ETOH

2- human chorionic gonadotrophin : *is expressed by syncytiotrophoblastic* elements of : choriocarcinomas (100%),
teratomas (40%), and
seminomas (10%) Half life 24-36 hours
Falsely elevated in hypogonadism and marijuana use

2-Cellular enzymes

Cellular enzymes

1 **Lactic Acid Dehydrogenase:**

- Presents normally in smooth, cardiac and skeletal muscle, liver and brain(**therefore, less specific**)
- Most useful in monitoring treatment response in advanced seminoma or tumors where other markers are not elevated
- Many false positives
- LDH correlates to tumor burden

2 ***Placental alkaline phosphatase* (PLAP):**

- *is a fetal isoenzyme, elevated in up* to 40% of patients with advanced germ cell tumours. It is not widely used as **it is non-specific**, may be elevated in smokers.

5- Testicular biopsy (see initial treatment) (never incision or needle
biopsy as it allows spread to skin of scrotum & superficial inguinal lymph
nodes).

Ddx

Differential diagnosis :

- causes of painless scrotal swellings :
  1. Hydrocele
  2. Spermatocele
  3. Indirect inguinal Hernia
  4. Syphilitic gumma
  5. TB

- most presentations of acute scrotal pain:
  1. Epididimoorchitis
  2. Epididymitis
  3. testicular Torsion

Spread:

-1TC spreads by local extension into the epididymis, spermatic cord, and rarely, the scrotal wall.

-2 Lymphatic spread occurs via the testicular vessels, initially to the para-aortic nodes. Involvement of the epididymis, spermatic cord, or scrotum may lead to pelvic and inguinal node metastasis.

-3 hematogenous metastasis to the lungs(most common), liver, and bones is more likely once the disease has breached the tunica albuginea.

TNM Staging :

➢Tumor: (pathological)
➢ Node: clinical (physical examination, imaging with CT abdomen and chest)
➢ Metastasis: involves physical examination, imaging(with CT), and biochemical investigations.

➢Stage 1 disease : disease limited to the testis
➢Stage 2 disease disease limited to lymph node
➢Stage 3 disease disease involves distant areas

Stage I	• Limited to the testicles without lymph node involvement
Stage II	• Retroperitoneal (beneath the diaphragm) lymph node involvement ◦ Stage IIa: affected lymph nodes < 2 cm ◦ Stage IIb: affected lymph nodes 2–5 cm ◦ Stage IIc: affected lymph nodes > 5 cm
Stage III	• Distant metastases or nonregional lymph node involvement, or retroperitoneal lymph node involvement with moderately to highly elevated tumor markers

TNM staging

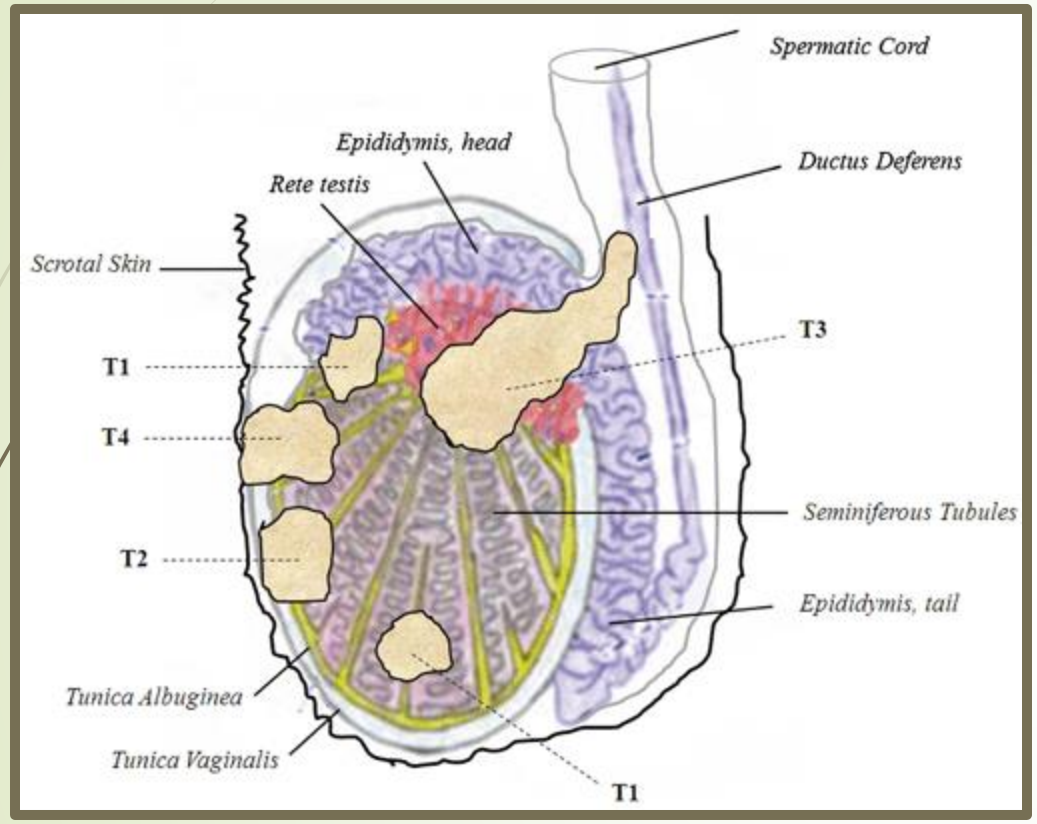
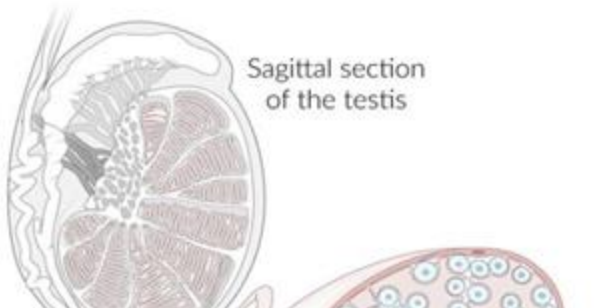
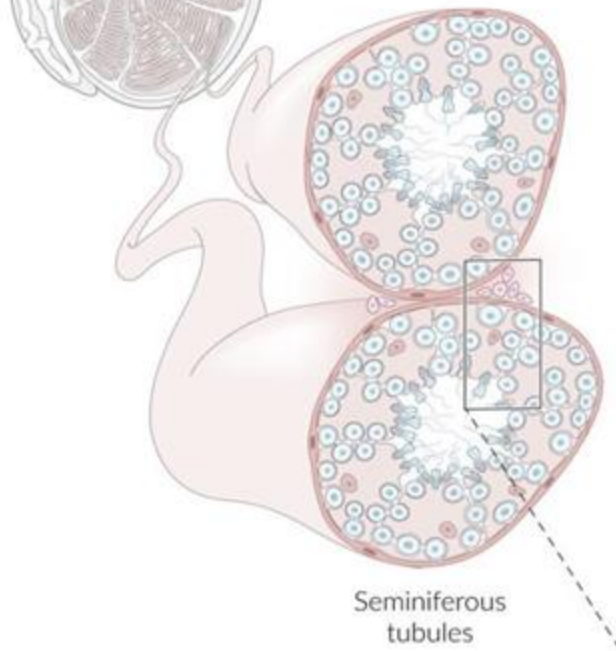
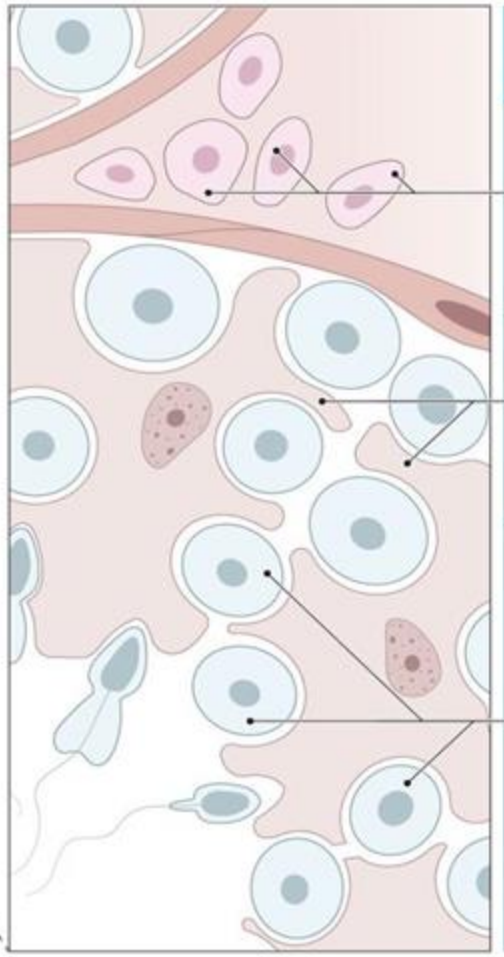


Table 6.16 TNM staging of testicular germ cell tumors. S staging is presented on p. 305

Tx	The primary tumor has not been assessed (no radical orchiectomy)
T0	No evidence of primary tumor
Tis	Intratubular germ cell neoplasia (carcinoma in situ)
T1	Tumor limited to testis and epididymis without vascular invasion; may invade tunica albuginea but not tunica vaginalis
T2	Tumor limited to testis and epididymis with vascular/lymphatic invasion, or tumor involving tunica vaginalis
T3	Tumor invades spermatic cord with or without vascular invasion
T4	Tumor invades scrotum with or without vascular invasion
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis with a lymph node ≤2 cm or multiple lymph nodes, none >2 cm
N2	Metastasis with a lymph node size 2–5 cm or multiple lymph nodes, collected size 2–5 cm
N3	Metastasis with a lymph node mass >5 cm
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1a	Nonregional lymph node or pulmonary metastasis
M1b	Distant metastasis other than to nonregional lymph node or lungs







Cell type	Distribution of primary tumors (%)	Tumor type
Leydig cells	Non-germ cell tumors (5%)	**Leydig cell tumor**
Sertoli cells		**Sertoli cell tumor**
Germ cells	Germ cell tumors (95%)	**Seminoma**
		Nonseminomas: Embryonal carcinoma Teratoma Testicular choriocarcinoma Yolk sac tumor

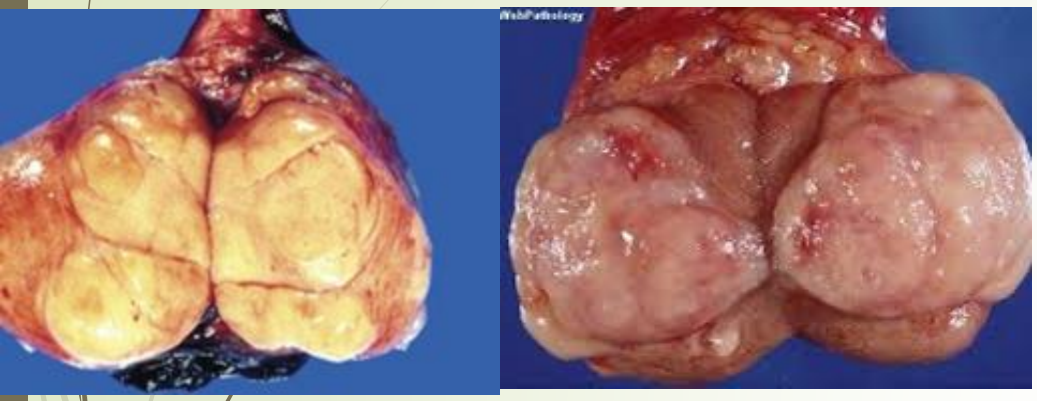
➢**Seminoma:**

Most common testicular tumor ,and most common germ cell tumor,
Never occur in infant.
Malignant tumor that has slow growth and late metastases,
Better overall prognosis compared to nonseminomas,
Most common testicular tumor,
Increased placental ALP
Clinical presentation:painless enlargement of testis(Any solid testicular mass should be considered neoplastic unless proved otherwise).
At diagnosis: %75-65confined to the testis,
%15-10 with regional retroperitoneal nodes,
%10-5 with advanced juxtorenal or visceral disease.
Tumor markers : Pure seminomas never secrete AFP,
%10-5 secrete HCG (usually classic).

Age of presentation :according to the type of seminoma (mostly male in 30s as most common seminoma subtype is classical one).

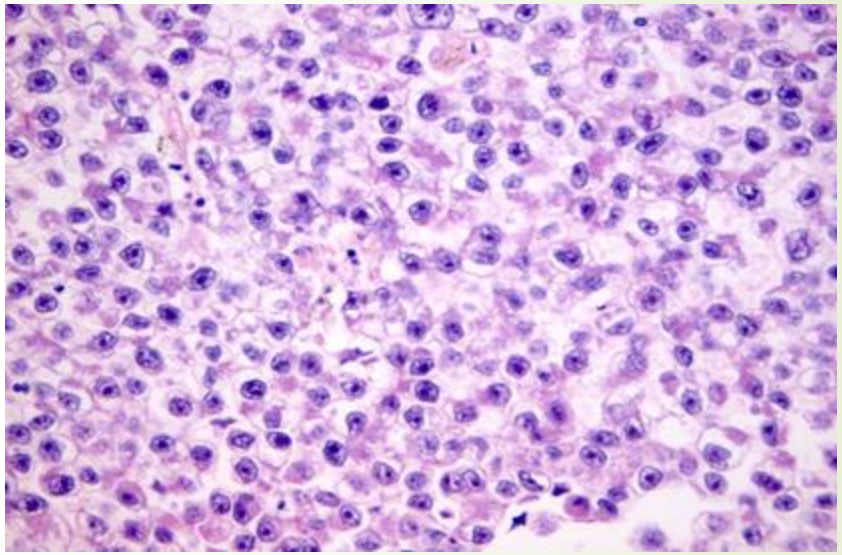
Types of seminoma : (%85-82) cissalc -1on age 30s,
-2anaplastic, (%10-5)
-3spermatocytic : (%12-2) in older population , low metastasis potential.

Gross appearance : bulky , sometimes ten time the testicular size,
well circumscribed, homogeneous mass ,pale ,fleshy and lobulated ,
devoided of necrosis and hemorrhage .



Microscopic appearance:

The classic seminoma cell is large and round to polyhedral and has a distinct cell membrane; a clear or watery-appearing cytoplasm; and a large, central nucleus with one or two prominent nucleoli "fried egg" appearance.



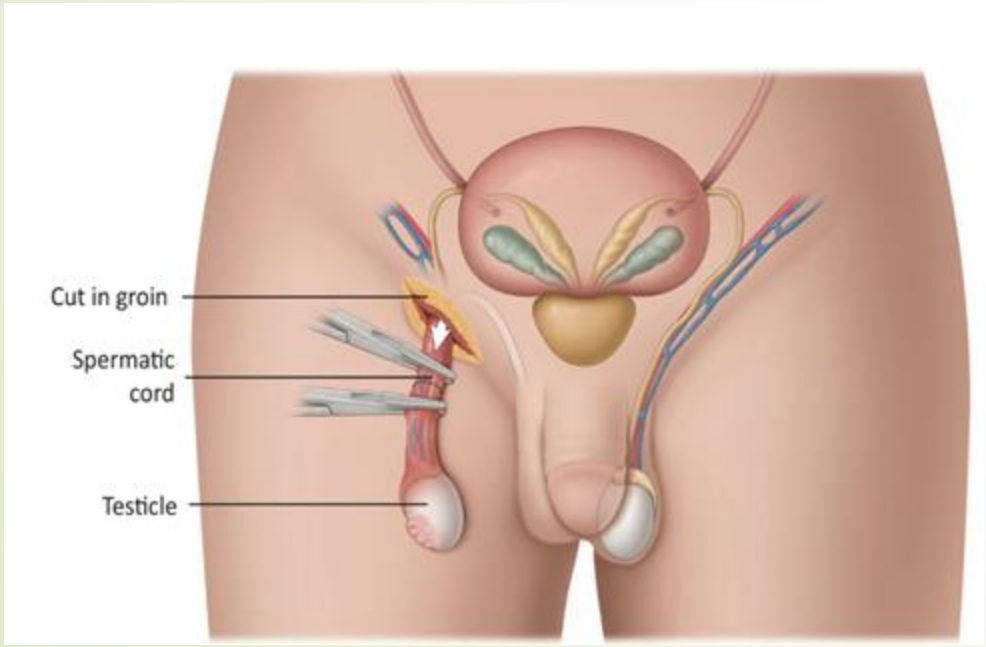
Treatment options of seminoma:

-1radical inguinal orchiectomy .

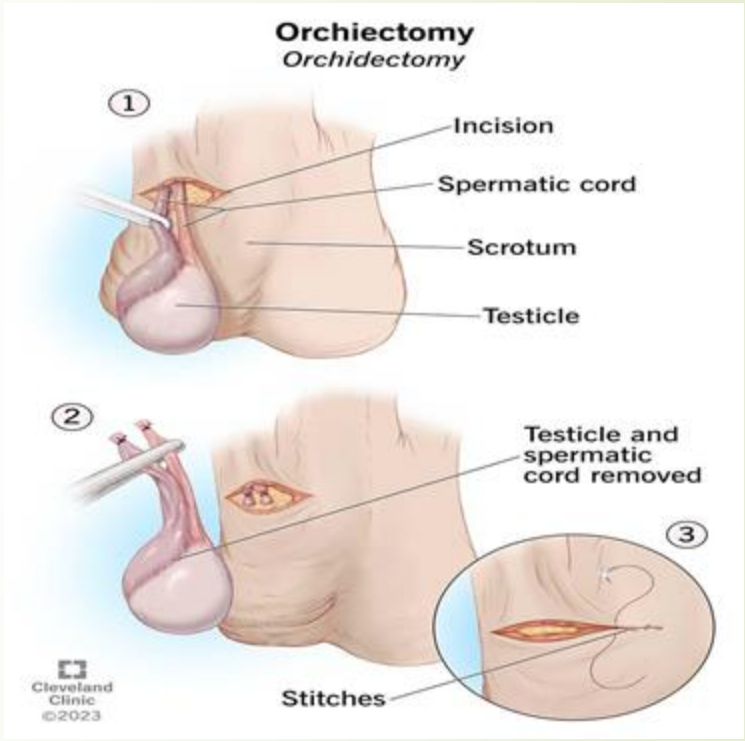
-2radiotherapy (Classic seminoma is highly sensitive to radiation).

Radical inguinal orchiectomy : Surgical removal of spermatic cord and testicle through inguinal canal with early occlusion of the spermatic cord at the internal inguinal ring to avoid hematogenous dissemination of tumor cells.

Radical inguinal orchiectomy : Inguinal approach to avoid seeding the scrotum and disrupting lymphatics
Wait 5 half lives before re- checking tumor markers.



Simple Orchiectomy: The testicle is removed through the scrotum atrophic testis and non-viable testis due to trauma, torsion, or infection.

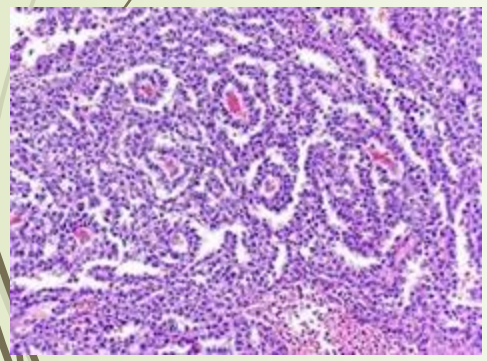


NSGCT(non Seminoma germ cell tumor):

-1Yolk Sac (Infantile embryonal)

MOST COMMON TUMOR IN INFANTS AND CHILDREN,

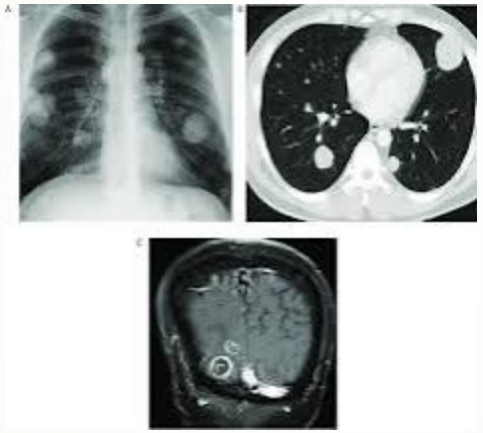
Peak age: infants and children (mostly less than 3 years)
may spread hematogenously
Secretes AFB and B-HCG (hallmark is AFB),
Presentation: child with testicular mass.
Microscopic appearance :
Epithelial like cells arranged in glands with vacuolated cytoplasm, resembles primitive glomeruli (SCHILLER-DUVAL bodies)

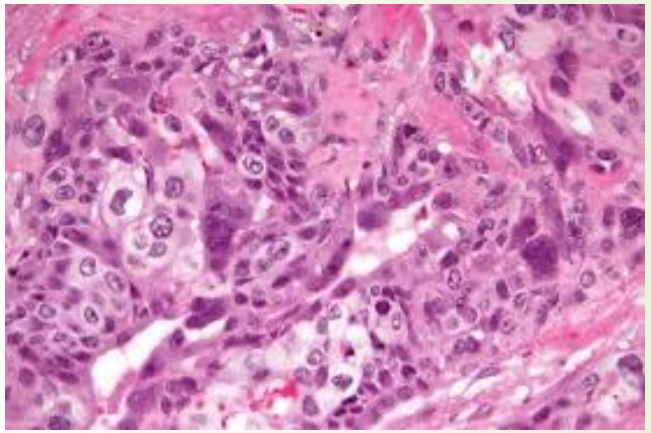


Child with testicular mass + AFP+
primitive glomeruli = yolk sac

Choriocarcinoma:

Peak age)30-20young men, (
Worst prognosis of all testicular tumors
Tumor marker :Always secrete B-HCG ,(100%)
Clinical presentation:testicular mass with hyperthyroidism and gynecomastia.
Mets : early hematogenous spread (especially to the lung ,cannon ball).
Microscopically : discorded syncytiotrophoblasts (eosinophilic cytoplasm) and cytotrophoblasts (closely packed, clear cytoplasm, single nuclei).

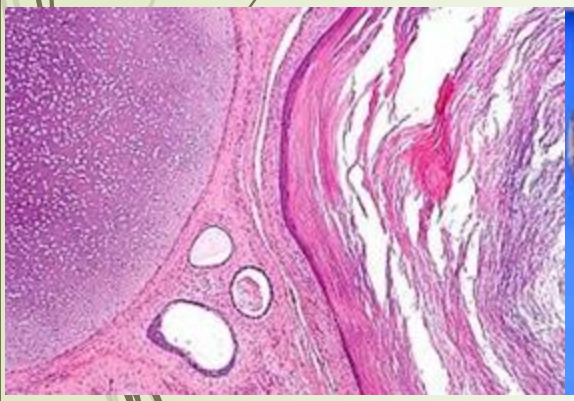




Teratoma :

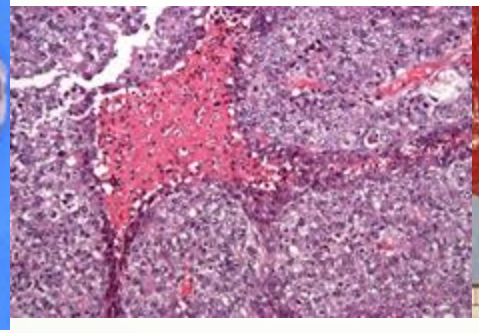
Peak age:)35-25young male and children,(
Malignant in male unlike female,
Tumor marker : none (Pure forms should not secrete AFB or B-HCG),
Gross appearance: large mass with hair ; muscle and cartilage .
Microscopic appearance: Contains all 3 germ layers in the mature form and is undifferentiated in immature form.

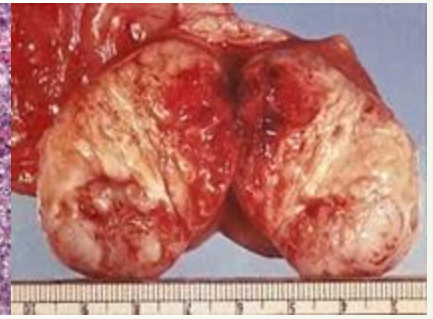
Can arise from malignant transformation after chemotherapy for NSGCT
Poor response to chemotherapy and XRT



Embryonal:

Aggressive tumor with high malignant potential and early mets ,
Worse prognosis than seminoma
Peak age:)35-25young male,(
Tumor marker: May secrete both AFP and B-HCG,
Clinical presentation: painful unilateral scrotal mass,
Gross appearance : grey-white regressive changes with hemorrhage, necrosis, and cysts,
Microscopic appearance:glandular or papillary (Epitheloid cells in glands or tubules with pale cytoplasm,(sllec tnaig dna iloelcun +1





Treatment of stage 1 :

1 RPLND

- Retroperitoneal lymphadenopsthy is usually the **first and only evidence** of extragonadal metastasis of NSGCT .

- **Allows for more accurate staging .**

  30% clinical stage I is pathologic stage II

- **Definitive treatment for N1** .

  N2 will need post RPLND chemotherapy

Relapse rate 5-13% (5-10% outside of RPLND field: primarily in the lungs)

Treat relapses with chemotherapy

RPLND :

Major morbidity is **ejaculatory dysfunction**

Modified nerve sparing RPLND preserves function in 90-99%

Identify the sympathetic nerves

Dissection is limited to below the level of the IMA on the ipsilateral side only

2- Chemotherapy

Traditionally not used for **lower stages**

2 cycles of BEP(bleomycin, etoposide, platinum).

Added advantage of treating **metastatic disease** that RPLND misses

Initial data promising but long term unconfirmed

Surveillance :

Surveillance requires the following:

Year 1:

monthly clinic visit, serum markers and chest X-ray, abdominal CT – months 3 and 12 .

Year 2:

2 monthly clinic visit with serum markers and chest X-ray, abdominal CT –months 24 .

Years 3, 4, and 5: 3-monthly clinic visit, serum markers, and chest x-ray .

Annual clinic visit, serum markers, and chest X-ray thereafter to 10y

Relapse rate 25% and usually occurs in first 8-10 months (commonly outside of the retroperitoneum)

Treatment IIA-IIB

1- RPLND

Advocated for lower volume disease
Cures 50-70% of stage IIa/b without further intervention

2- Chemotherapy

Favored for patients with nodes >3cm
If markers normalize but residual mass is seen on CT, RPLND is advocated

20% residual cancer
40% teratoma
40% fibrosis

Relapse or residual cancer is treated with salvage chemotherapy (VIP) – vinblastin, ifosfamide, cisplatin

Treatment IIC-III

Primary chemotherapy

In IIC disease with partial response, may proceed to RPLND

Salvage chemotherapy or high dose chemotherapy with autologous bone marrow transplant

No response to first line chemotherapy
Incomplete resection after RPLND

Summary of treatment in NSGCT :

After orchiectomy :

1- stage 1 :

RPLND +/- chemotherapy (if relapse)

2- stage 2A+2b :

RPLND + chemotherapy

3- stage 2C+ stage 3 :

Chemotherapy

Prognosis :

Seminoma (at 5 years)

- **I: 98%**
- **IIA: 92-94%**
- **IIB-III: 33-75%**

NSGT (at 5 years)

- **I: 96-100%**
- **IIA: >90%**
- **IIB-III: 55-80%**

	Notes :	Histolopathology
Seminoma	1 M . C germ cell tumor 2 never secrete AFP	Fried egg appearance
Yolk sac	1 M.C in children	Schiller-duval bodies
Choriocarcinoma	1 most aggressive 2 100% beta HCG 3 spread hematogenously	Two cells L 1 cytotrophoblast 2 syncytiotrophoblast
teratoma	Mature vs immature	Three germ cell layers
Embryonal		Epitheloid cell and giant cells with pale cytoplasm

Lyding cell tumor

usually secret androgen causing precocious puberty in children or gynecomastia in adults.

1-3% of all testis tumors

Bimodal age distribution: ages 5-9 and 25-35

Bilateral in 5-10%

No association with cryptorchidism

Prepubertal children may present with virilization and elevated urinary 17-ketosteroid levels,

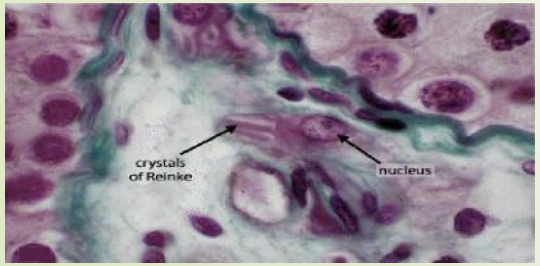
adults are usually asymptomatic (25°ogynecomastia)

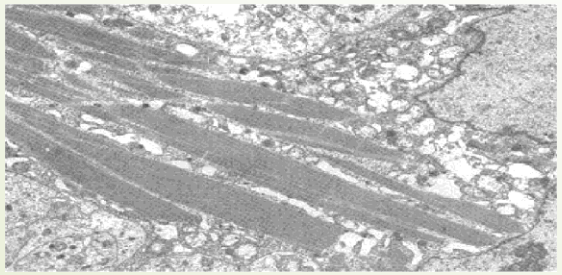
Treatment: radical orchiectomy and RPLND for malignant tumors (10°ofTialignant)

HistopAathology :

Solid sheets of cells with oval nuclei

Reinke crystals (fusiform shaped cytoplasmic inclusion) are pathognomic al though rare





sertoli cell :

Less than 1% of all testicular tumors
Bimodal age of distribution: < 1 year and 20-45 years old
10% lesions are malignant
Virilization seen in children and gynecomastia in adults
Radical orchiectomy with RPLND in malignant disease

Gonadoblstoma :
0.5% of testicular tumors
Seen in patients with gonadal dysgenesis
4/5 patients are phenotypic females with streak gonads
Radical orchiectomy with gonadectomy of the contralateral gonad (bilateral in 50%)

testicular lymphoma :
Old age more than 60 years
Usually bilateral

Thank you