Testes

Cryptorchidism

A failure of testicular descent into the scrotum, testis is situated in the normal path of descent, abdomen or inguinoscrotal region.

Normally, the testes descend from the abdominal cavity into:

- the **pelvis** by the **third** month of gestation ((transabdominal/insulin-like factor 3 and anti-Müllerian hormone-dependent))
- then through the **inguinal** canals into the scrotum ((inguinoscrotal/androgen-dependent)) during the last **2** months of intrauterine life.

In the vast majority of cases, the **cause** is **unknown**. Hormonal effect probably that are responsible for the descending.

Environmental factors likely play a role: **diethylstilbestrol** and **pesticide** exposure, and maternal and paternal **smoking** may increase risk.

Causes of cryptochidism:

1. Unknown - hormonal, m/c
2. Diethylstilbestrol - environmental, m/c
3. Pesticide - environmental
4. Smoking - environmental

Causes of atrophi**c** testes:
5. **C**ryptorchidism
6. **C**hronic ischemia
7. **C**rush injury - trauma
8. **C**ancer therapy - Irradiation
9. **C**hemotherapy anti-cancer
10. **C**irrhosis due to chronic elevated estrogen
11. **C**hronic alcoholism
12. **C**hronic use of high doses of anabolic steroids
13. Atherosclerosis
14. Viral infection, mumps is the m/c cause of orchitis, that has a patchy pattern and it does not lead to sterility, and it the m/c cause of focal testicular atrophy in children
15. Hypopituitarism

Cryptorchidism (undescended testicles)
Descent failure of one or both testes.
Absence of one or both testes in the scrotum.
The most common congenital abnormality of the genitourinary tract
80% are palpated within the inguinal canal or high scrotal area.

Cryptorchidism (undescended testicles)
20% not palpated (50% lie in the abdomen, and 50% are atrophic)
Impaired spermatogenesis (since sperm develop best at temperatures < 37°C) subfertility.
Can have normal testosterone levels (Leydig cells are mostly unaffected by temperature) in unilateral (90% of the cases) cryptorchidism but ↓ in bilateral (10% of the cases are bilateral).
Associated with ↑ risk of germ cell tumors.
Affects 1-4% of **full-term** male infants at birth.
Prematurity ↑ risk of cryptorchidism, higher than 1-4%. More common in preterm/low-weight infants = premature birth.
(Sertoli cells are mostly affected by temperature), so inhibin B ↓, LH and FSH ↑
Most cases resolve spontaneously; otherwise, orchiopexy performed before 2 years of age, maximum by the 6th month after birth. Observation for spontaneous descent until **6 months of age**. Surgical placement of the undescended testis into the scrotum (orchiopexy) is **recommended between 6-12 months** to decrease the likelihood of testicular **atrophy/infertility, and testicular seminomas cancer** but NOT completely.
In the bilateral cases (10%), **a small subset** of these cases have chromosomal aberrations and other developmental abnormalities, including: 1. **Klinefelter** syndrome (47, XXY), 2. **Prader**-Willi syndrome, 3. **Testicular** dysgenesis syndrome
COMPS including: 1. Testicular **atrophy** and sterility: Bilateral cryptorchidism results in sterility. (The cryptorchid testis may be of normal size early in life. Some degree of atrophy usually is evident by the onset of puberty. Tubular atrophy **begins by 5 to 6 years of age** advanced by the time of puberty.) For unclear reasons, even unilateral cryptorchidism may be associated with atrophy of the **contralateral** descended gonad. 2. Testicular **torsion**. 3. Testicular **cancer**: **3- to 5-fold increased risk** for testicular cancer (germ cell germ cell tumors). (Increased risk for germ cell neoplasia in-situ: a precursor of subsequent germ cell tumors.) Patients with unilateral cryptorchidism also are at increased risk for the development of cancer in the **contralateral**, normally descended testis (intrinsic abnormality).

Testicular neoplasms:

Germ cell tumors	Sex cord-stromal tumors
Arise from primordial germ cells.	Derived from Sertoli cells (supporting cells) or Leydig cells (testosterone-producing cells).
Common (95% of all testicular tumors).	Uncommon (5% of all testicular tumors).
Almost all malignant in postpubertal males.	Usually benign.
The most common tumors in young males (age **15-34 years**). But recall from the penis disorders: SCC is the most common malignant tumor of the penis, at age of **58** (**40-70 years**).	Leyding cell tumors: Occur at any age with 2 peaks: (Dua**L** = **L**eydig) **5 - 10 years and 30 - 60 years.** Sertoli cell tumor: **Rare before age 20; mean age 45 years**.
Painless testicular mass (mostly unilateral).	

Germ cell tumors	Sex cord-stromal tumors
Some tumours, especially **nons**eminomatous germ cell neoplasms, may have metastasized widely by the time of diagnosis in the **absence** of a palpable testicular lesion.	
The levels of lactate dehydrogenase (LDH) correlate with the GCT burden (size, volume, number of tumors, mets).	

Germ cell tumors - risk factors
More common in whites than in blacks. Recalling from the SCC in penis where it was way more common in Hispanics and blacks
Cryptorchidism increases the risk of germ cell neoplasia in situ (**precursor** lesion). (**3-5 folds increased risk**). Early orchiopexy reduces the risk of testicular cancer. However, it does not eliminate the risk entirely Patients with unilateral cryptorchidism also are at increased risk for the development of cancer in the **contralateral**, normally descended testis (intrinsic abnormality).
Disorders of sex development (androgen insensitivity syndrome and **testicular** dysgenesis) increases the risk of germ cell neoplasia in situ (**precursor** lesion). Recalling from the cryptorchidism, that a small subset of the 10% of the cases (bilateral) are associated with many chromosomal abnormalities including: 1. **Klinefelter** syndrome (47, XXY), 2. **Prader**-Willi syndrome, 3. **Testicular** dysgenesis syndrome
Family history increases the risk of the family members for this type of neoplasm

Testicular germ cell tumours classification:

Germ cell tumors are **derived** from germ cell neoplasia in situ	Description
Seminomas	Most common (accounting for 50% of testicular germ cell neoplasms). Malignant. Painless, homogenous testicular enlargement. Counterparts in the ovary are called **dysgerminomas** a**nd in CNS/other extrag**onadal sites called germinomas. Age: 35-45 years. Does not occur in infancy. But in a general range for the germcell tumor is the (age **of 15-34 years**). Good prognosis, despite that, almost all malignant in postpubertal males. -**Extremely radiosensitive**.- Tends to remain localized/confined to the testis for long periods.- **Metastases most commonly in the iliac and paraaortic lymph nodes**.- Hematogenous metastases occur late in the course of the disease.- Has the best prognosis with 95% cure rate for early stages (I and II).
Non-seminomatous	1- Embryonal carcinoma. 2- Yolk sac tumour (postpubertal, prepubertal types). 3- Teratoma (postpubertal, prepubertal types). 4- Choriocarcinoma. Age: 25-35 years. But in a general range for the germcell tumor is the (age **of 15-34 years**).

Germ cell tumors are derived from germ cell neoplasia in situ	Description
	Bad prognosis -**Treated with aggressive chemotherapy** (the histologic subtype does not influence the therapy). - Tend to metastasize earlier, by lymphatic as well as **hematogenous routes (most common in the liver and lungs)**.- 90% of patients achieve complete remission with aggressive chemotherapy, and most are cured; except Choriocarcinoma is associated with poorer prognosis (worst prognosis). - Metastatic lesions may be identical to the primary testicular tumour or may contain elements of other germ cell tumours
Mixed germ cell tumour	Non-seminomatous different type or Non-seminomatous and seminomatous type

Seminomatous	Non-seminomatous
Soft, well-demarcated, gray white tumour. A *lymphocytic* infiltrate in intervening fibrous septa. *Granulomatous* reaction.	Ill-defined mass with hemorrhage and necrosis
Large, uniform cells with **distinct cell borders**, **clear, glycogen-rich cytoplasm**, round nuclei, and conspicuous nucleoli. Large cells in lobules with watery cytoplasm and “fried egg” appearance on histology	Embryonal carcinoma; The tumour cells are **large and have basophilic cytoplasm** **indistinct cell borders**, large nuclei, and prominent nucleoli. It has primitive tubules Malignant. Painful, hemorrhagic mass with necrosis. “Pure” embryonal carcinoma is rare most commonly mixed with other tumor types. May present with metastases. May be associated with **hCG** and normal AFP levels when pure (AFP when mixed). Worse prognosis than seminoma.
Syncytiotrophoblasts are present in **15**% of cases--- elevated **HCG** elevated placental alkaline phosphatase (PLAP)	Choriocarcinoma; Cells resembling placental trophoblasts: Cytotrophoblastic cells (with single Nuclei) and syncytiotrophoblastic cells (multiple nuclei) + H CG. + H emorrhage and necrosis are prominent. +Early H ematogenous spread to the lung, liver and bone. May produce gynecomastia, symptoms of hyperthyroidism (hCG and TSH share an identical α subunit and a similar β subunit, which determines their hormonal function)
	Yolk sac tumor; (postpubertal, prepubertal types) **Cuboidal to columnar epithelial cells** that form **microcysts, lacelike (reticular) patterns, sheets, glands, and papillae.** Schiller-Duval bodies (resemble primitive glomeruli). + A FP
	Teratoma; (postpubertal, prepubertal types) Contain (mature/immature) 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.

Seminomatous	Non-seminomatous
	Mature teratoma may be malignant in adult males. Benign in children and females. cells from endodermal (e.g. glandular), mesodermal (e.g. cartilage), and ectodermal (e.g. neural) lines. Teratoma with malignant transformation: non–germ cell tumors may arise in teratoma (e.g. SCC).

Germ cell tumors **unrelated** to germ cell neoplasia in situ	Description
Prepubertal yolk sac tumor	Is the most common primary testicular neoplasm in **children younger than 3** years of age; in this age group, it has a very good prognosis. Has no germ cell neoplasia in situ (since all post-pubertal ones are malignant) - thus benign behavior and good prognosis, even if histology is malignant
Prepubertal teratoma	Prepubertal teratoma is the 2nd most common primary testicular **neoplasm in infants and children**; it is benign in this age group.
Spermatocytic tumours	(previously spermatocytic seminoma)----- **older men >50 years old**, do not metastasize, benign behavior. Excellent prognosis

So Testicular germ cell tumors are associated with/arise from germ cell neoplasia in situ except:

- Spermatocytic tumors.
- Prepubertal type of yolk sac tumor.
- Prepubertal type of teratoma.

In germ cell tumours are due to:
Extra copies of the short arm of chromosome 12, usually due to the presence of an isochromosome 12 [i(12p), a chromosome with two copies of the short arm (12p) and no long arm], are found in postpubertal germ cell tumors and germ cell neoplasia in situ. But not in spermatocytic seminoma, Oncogenic mutations in KIT which are found in up to 25% of tumours.

Treatment: Radical orchiectomy (Biopsy of a testicular neoplasm is associated with a risk for tumour spillage, which would necessitate excision of the scrotal skin in addition to orchiectomy). Chemotherapy AND radiotherapy

Prognosis: Depends on the histologic type and stage and treatment.

Do not transilluminate. Usually not biopsied (risk of seeding scrotum), removed via radical orchiectomy.