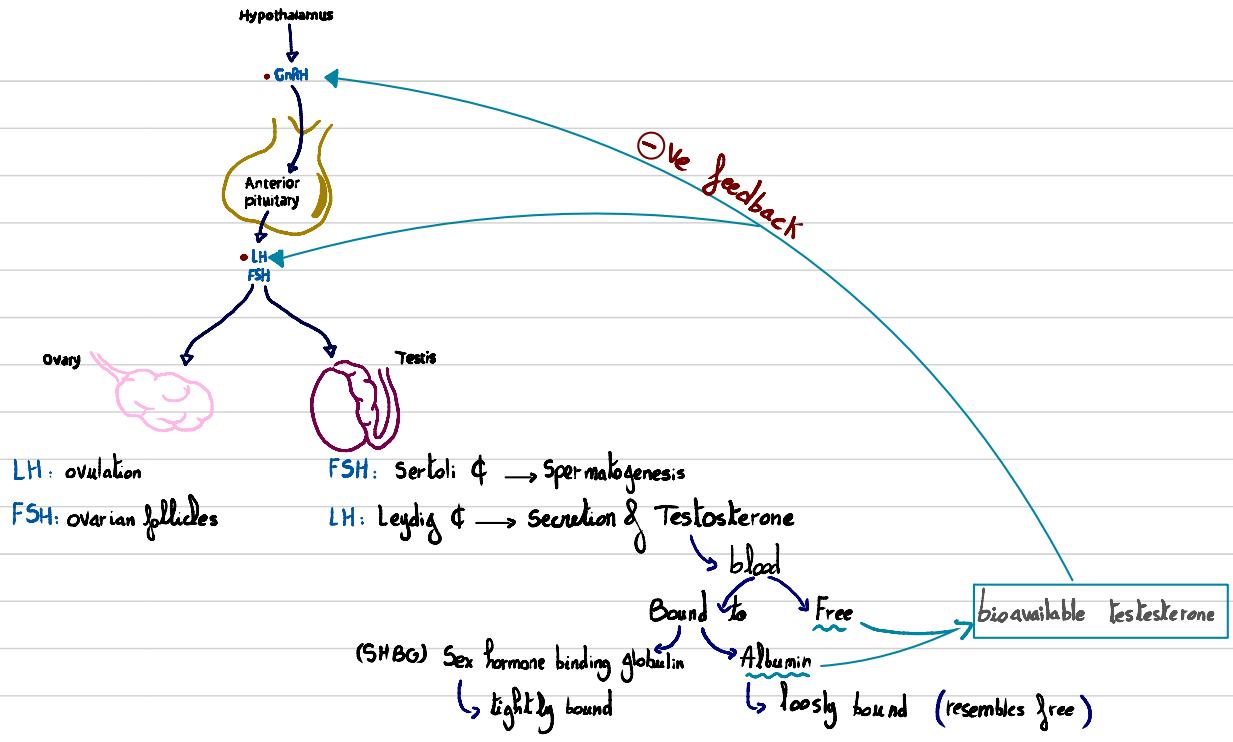
Hypogonadism

↳ ♀: ↓ funct° of ovaries → ① Estrogen \ Progesterone ② Ovulation
↳ ♂: ↓ funct° of gonads → ① Testosterone ② Spermatogenesis

* Manifestations of ↓ Estrogen:
  - Fatigue & insomnia
  - Mood swings & irritability
  - Tender breast
  - Irregular menstrual cycles or amenorrhea
  - Dry skin
  - Osteoporosis
  - Belly fat
  - ↓ lipido

* Manifestations of ↓ Testosterone (mostly non specific)
  - Fatigue & weakness
  - Depression
  - Mood swings
  - ↓ confidence
  - Day time sleepiness
  - Loss of Lipido
  - Erectile dysfunction
  - ↓ hair growth

* How to Dx hypogonadism in ♂
  - ↳ Hx
  - ↳ PEx: hair growth - gynecomastia (due to imbalance btw estrogen & Testosterone, can be idiopathic) - Size & consistency of testicles...
  - ↳ Labs: Bioavailable Testosterone
    - ↳ Testosterone has a circadian cycle → ↑ in morning, ↓ at night → should be measured in the morning
    - ↳ Testosterone is secreted in a pulsatile fashion → we take pooled blood sample (Sample at 8-9-10 Am, all mixed together & measured)

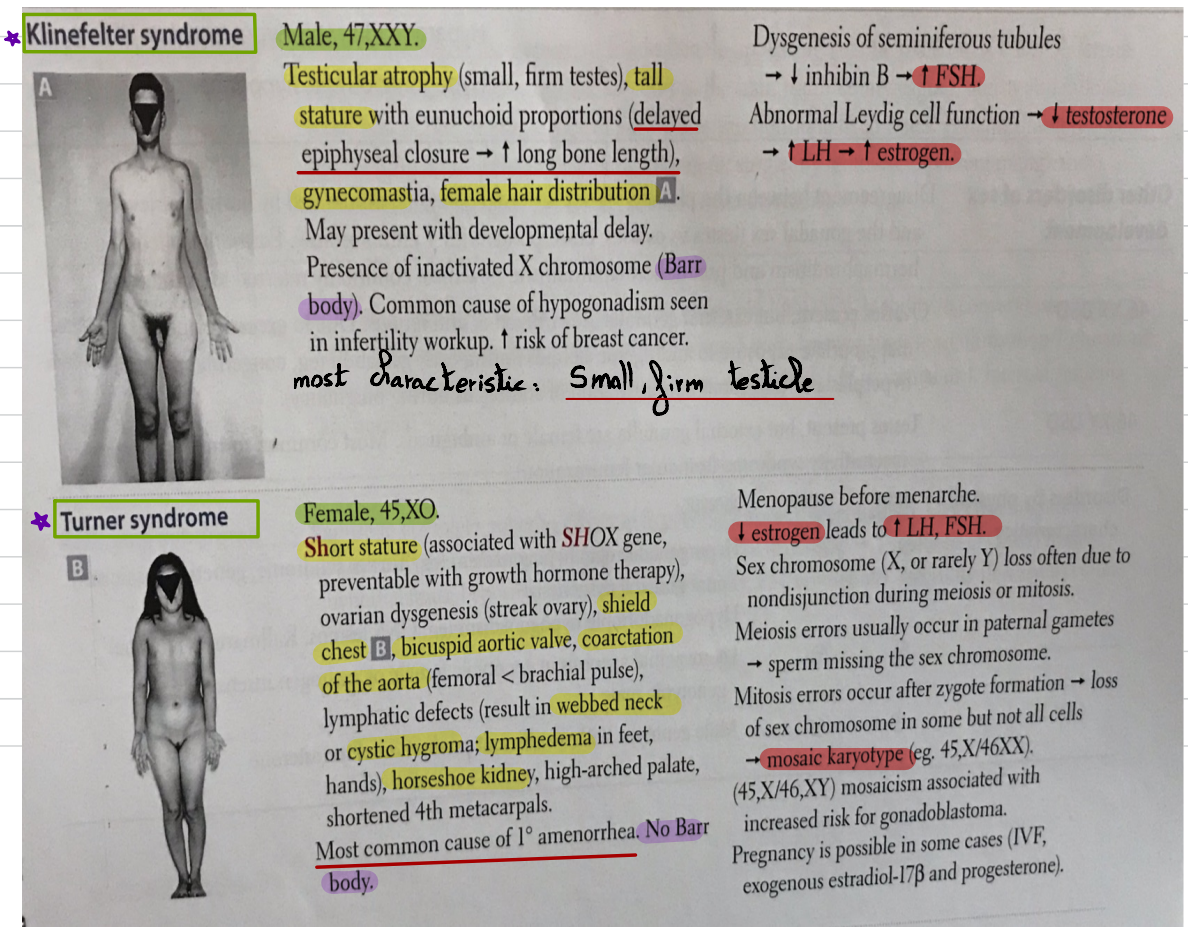


* Types of hypogonadism
  - ↳ Primary: the problem is in testicles\ovaries → high FSH & LH due ↓ testosterone \ Estrogen (No ⊖ve feedback)
    - ↳ Kline felter syndrome - Turner syndrome
  - ↳ Central: the problem is in hypothalamus \ pituitary → low \ Normal LH \ FSH
    - ↳ Tertiary ↳ secondary
    - ↳ Dx: MRI & Prolactin
      - ↳ ⊖ LH & FSH

* Hirsudism: excessive male pattern hair growth in females, mainly due to ↑ serum total testosterone - ↓ SHBG ...
  - ↳ Common causes: PCOS - idiopathic - Congenital adrenal hyperplasia - peri\post menopause - Cushing disease - Hypothyroidism...
    - ↳ Dx by exclusion

* Congenital adrenal hyperplasia: (CAH): Autosomal recessive defects in enzymes responsible for Cortisol production
  - ↳ 3 subtypes: 21 β-hydroxylase (mc) 11β-hydroxylase 17α-hydroxylase
    - ↳ Zona reticularis of medulla in adrenal gland is affected
    - ↳ ↑ 17α-hydroxyprogesterone
    - ↳ ↓ Cortisol → ↓ ⊖ve feedback to the pituitary → ↑ ACTH → ↑ Androgens, ↓ Aldosterone
  - ↳ Manifestations → Classical: deficiency is very severe, at birth → ambiguous genitalia
    - → Non classical: mild deficiency, not obvious at birth, Teenager → hirsutism due to ↑ adrenal androgens

* Amenorrhea
  - ↳ 1°: absence of menarche at 15 years of age despite normal development of 2° sexual characteristics, or absence of menses at 13 with no 2° sexual characteristics.
  - ↳ 2°: absence of menses for > 3 months with individuals with previously regular cycles, of >6 months if irregular



Klinefelter syndrome

Male, 47,XXY.

Testicular atrophy (small, firm testes), tall stature with eunuchoid proportions (delayed epiphyseal closure → ↑ long bone length), gynecomastia, female hair distribution A.

May present with developmental delay.

Presence of inactivated X chromosome (Barr body). Common cause of hypogonadism seen in infertility workup. ↑ risk of breast cancer.

Dysgenesis of seminiferous tubules → ↓ inhibin B → ↑ FSH.

Abnormal Leydig cell function → ↓ testosterone → ↑ LH → ↑ estrogen.

most characteristic: Small, firm testicle

Turner syndrome

Female, 45,XO.

Short stature (associated with SHOX gene, preventable with growth hormone therapy), ovarian dysgenesis (streak ovary), shield chest B, bicuspid aortic valve, coarctation of the aorta (femoral < brachial pulse), lymphatic defects (result in webbed neck or cystic hygroma; lymphedema in feet, hands), horseshoe kidney, high-arched palate, shortened 4th metacarpals.

Most common cause of 1° amenorrhea. No Barr body.

Menopause before menarche.

↓ estrogen leads to ↑ LH, FSH.

Sex chromosome (X, or rarely Y) loss often due to nondisjunction during meiosis or mitosis.

Meiosis errors usually occur in paternal gametes → sperm missing the sex chromosome.

Mitosis errors occur after zygote formation → loss of sex chromosome in some but not all cells → mosaic karyotype (eg. 45,X/46XX).

(45,X/46,XY) mosaicism associated with increased risk for gonadoblastoma.

Pregnancy is possible in some cases (IVF, exogenous estradiol-17β and progesterone).

* Polycystic ovaries syndrome (PCOS)
  - ↳ hyperandrogenism in female, ovulatory dysfunction

Clinical features

Onset of symptoms typically occurs during adolescence.

- **Menstrual irregularities**
  - Primary or secondary amenorrhea
  - Oligomenorrhea
  - Menorrhagia
  - **Infertility** or difficulties conceiving
- **Insulin resistance and associated conditions**
  - Metabolic syndrome (especially **obesity**) → ↑ risk of sleep apnea
  - Nonalcoholic fatty liver disease
- **Skin conditions**
  - **Hirsutism**
  - Androgenic alopecia
  - Acne vulgaris
  - Oily skin
  - Acanthosis nigricans
- **Psychiatric conditions**
  - Depression
  - Anxiety disorders

! Voice change may occur in severe forms of PCOS. However, it typically suggests a different underlying cause of hyperandrogenism.