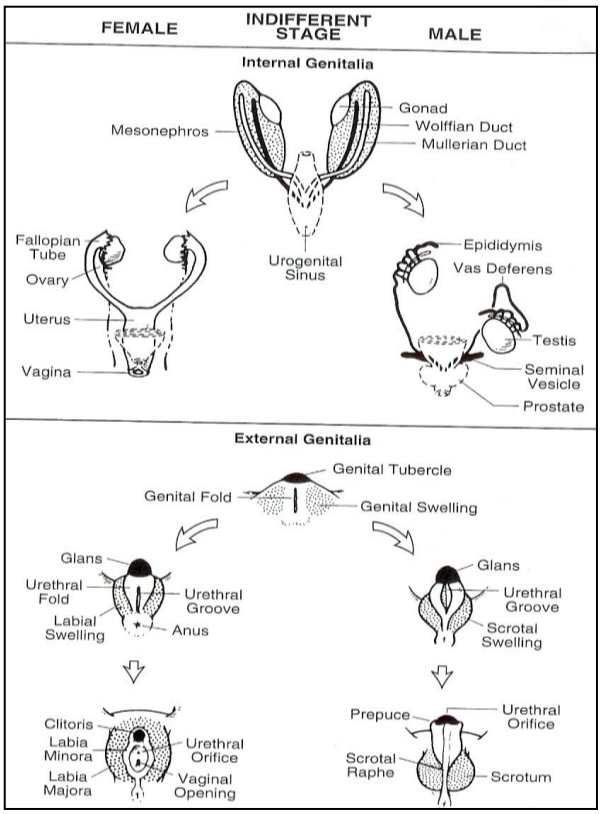
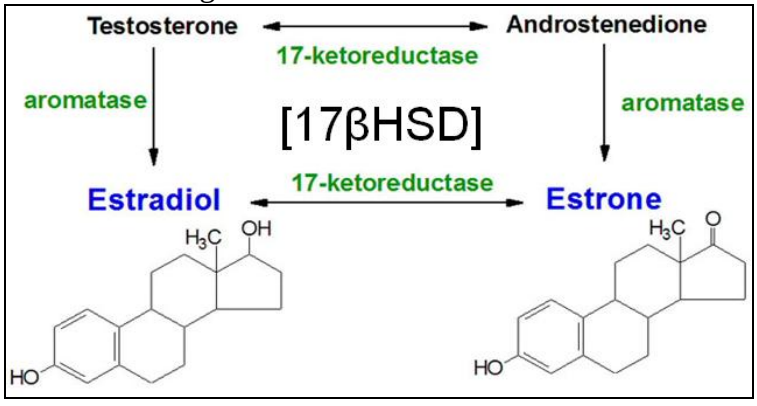
- **Reproductive system consists of:**
  - **Bi-potential gonads (can differentiate into either male or female genitalia):**
    - ✓ They appear as a pair of genital ridges formed by the proliferation of epithelium and underlying mesenchyme.
    - ✓ Primitive Woflian ducts: will differentiate into internal male genitalia under the influence of SRY-gene carried on Y-chromosome:
      - ❖ *Influence of SRY-gene:*
        - ➢ Enhancing the secretion of anti-mullerian hormone from sertoli cells which will lead to the regression of mullerian ducts.
        - ➢ Enhancing the production of testosterone from leydig cells which, in turn, will cause the formation of internal male genitalia. Testosterone is converted to dihydrotestosterone by the enzyme 5α-reductase and this will result in the formation of external male genitalia.

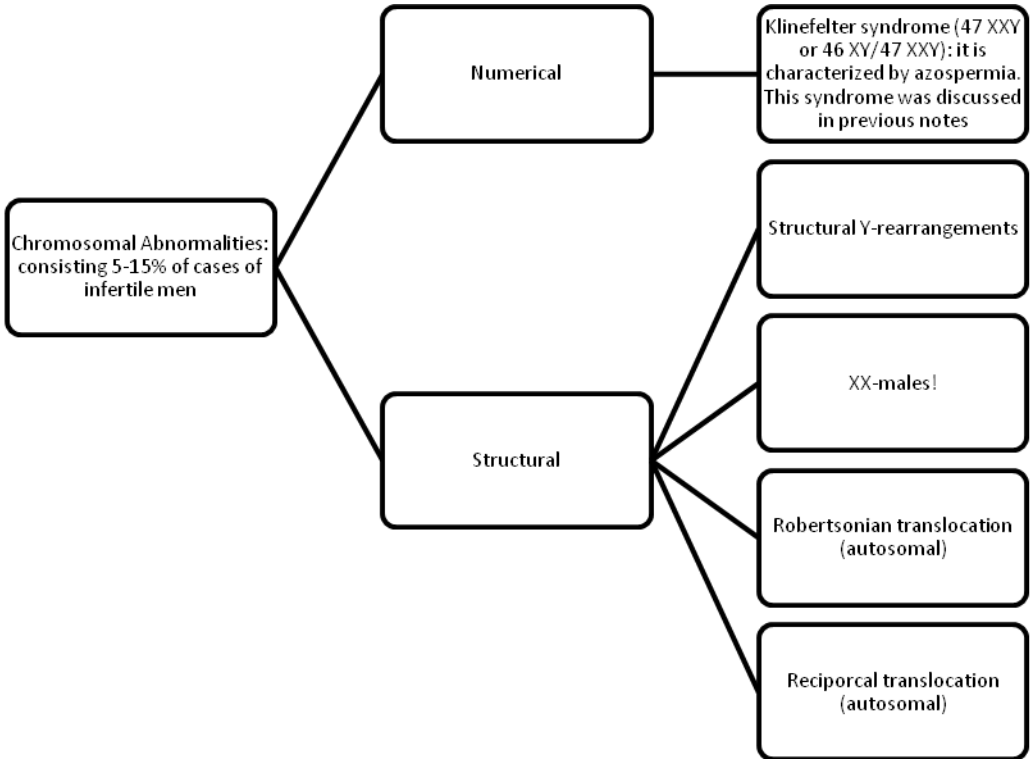


    - ✓ Primitive mullerian ducts: will differentiate into internal female genitalia when Y-chromosome is absent.

- **Gonadal steroid hormone biosynthesis:**
  - LH-hormone (from anterior pituitary) will enhance leydig cells to produce dehydroepiandrosterone and androstendione which will be converted to testosterone. Testosterone is binding to the following:
    - ✓ Androgen binding protein (in sertoli cells).
    - ✓ Sex hormone binding globulin (in plasma) → binding 60% of testosterone.
    - ✓ Albumin (in plasma).
  - Testosterone is converted in peripheral tissues to its more potent and active form → dihydrotestosterone by the action of the enzyme 5α-reductase.
  - FSH-hormone binds to its receptors which are found on the surface of sertoli cells → enhancing spermatogenesis under the influence of testosterone which is secreted by leydig cells.
  - An enzyme known as aromatase is found mainly in ovaries and adipose tissue and converts testosterone to estrogen.



- **The conversion of pregnenolone to testosterone needs the action of five enzymes:**
  - ✓ 17α-hydroxylase.
  - ✓ 17,20 lyase.
  - ✓ 3β-hydroxysteroid dehydrogenase.
  - ✓ 17β-hydroxysteroid dehydrogenase.
  - ✓ 5α-reductase.
- Notice that testosterone is metabolized by the liver to androsterone and etiocholanolone, which, after conjugation with glucouronic or sulfuric acid, are excreted in the urine as 17-ketosteroids.



Hormonal Disorders	
Disorder	**Notes**
Persistent mullerian duct syndrome	-
Defect in androgen receptor	• Testicular feminization syndrome: ✓ Spectrum: from complete or incomplete testicular feminization through genital ambiguity to infertile males. ✓ Characterized by: ❖ Female external genitalia with normal male karyotype (46 XY). ❖ Breasts development during puberty. ❖ Primary amenorrhea (sterility). ❖ Blind-ended vagina, absent uterus and fallopian tubes. ❖ Inguinal hernia: testes with normal androgen production.
5α-reductase deficiency	• Ambiguous external genitalia at birth (undergo virilization at puberty!). • No dihydrotestosterone → patients will have external female genitalia.
LH	• Homozygous mutation in β-subunit of LH leads to: ✓ Delayed puberty. ✓ Spermatogenic arrest. ✓ Complete absence of leydig cells (which are producing testosterone).
Kallmann's syndrome	• Failure to complete puberty (a form of hypogonadotropic hypogonadism). • ↓GnRH, FSH, LH, testosterone and infertility (low sperm count in males; amenorrhea in females).

- **Other disorders:**
  - **Obstructive azospermia:**
    - ✓ Congenital bilateral absence of vas deferens (due to mutation in the gene of cystic fibrosis CFTR).

- **Primary ciliary dyskinesia (also known as Kartagener syndrome):**
  - ✓ Characterized by: abnormal sperm flagella.
- **Noonan syndrome:**
  - ✓ Characteristics:
    - ❖ Short stature.
    - ❖ Congenital heart disease.
    - ❖ Facial dysmorphism.
    - ❖ Azospermia.
- **Myotonic dystrophy:**
  - ✓ Caused by: trinucleotide repeat expansion (CTG).
  - ✓ Characterized by: testicular atrophy.
- **Y-chromosome microdeletions: there are three deletion regions:**
  - ✓ AZFa: complete absence of germ cells (azospermia).
  - ✓ AZFb: maturation arrest at the spermatocyte stage (azospermia).
  - ✓ AZFc (the most common type): more variable phenotype ranging from sertoli cell only (azospermia) to presence of all germ cell types (severe oligospermia).
- **True hermaphroditism (46 XX or 47 XXY):**
  - ✓ Also known as ovotesticular disorder of sex development. It is very rare.
  - ✓ Characteristics:
    - ❖ Both ovary and testicular tissue present (ovotestis).
    - ❖ Ambiguous genitalia.
- **Female pseudohermaphroditism (XX):**
  - ✓ Ovaries are present, but external genitalia are virilized or ambiguous.
  - ✓ Due to excessive and inappropriate exposure to androgenic steroids during early gestation.
- **Male pseudohermaphroditism (XY):**
  - ✓ Testes are present, but external genitalia are female or ambiguous.
  - ✓ Most common form is androgen insensitivity syndrome (testicular feminization).