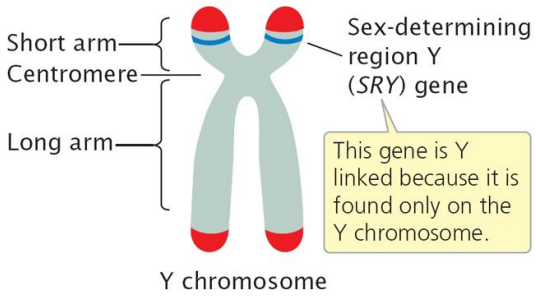
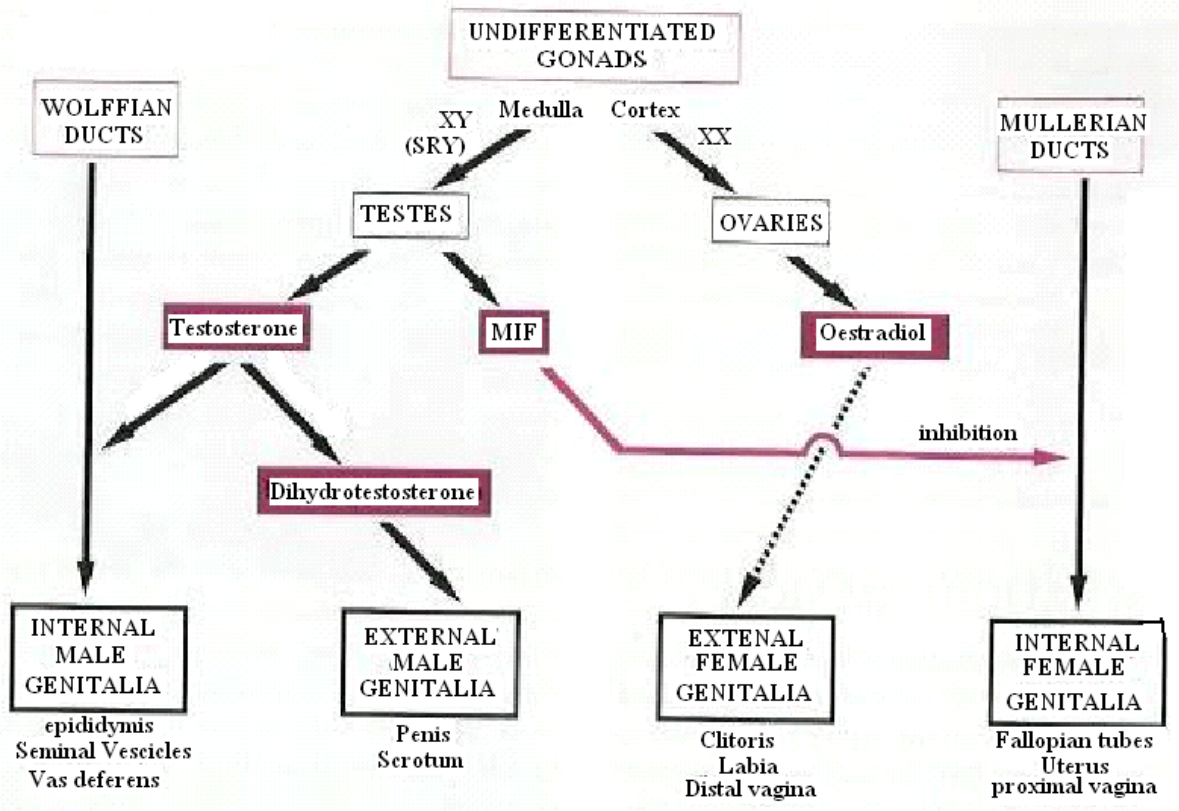
Unit IV – Problem 7 – Genetics: Sexual Differentiation

- **Sex chromosomes**
  - **Male**: 46 XY
  - **Female**: 46 XX

  Notes:
    - ✓ That the (Y) chromosome has the: testis-determining factor (SRY gene) on its short arm. SRY gene must be outside the pseudoautosomal region because it should not be involved in cross-over with the (X) chromosome.



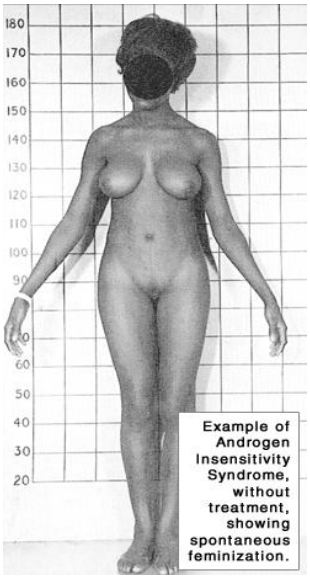
      - ❖ If a person with (XX) chromosome and has one (X) chromosome which is abnormally carrying the SRY-gene: the person will have a male instead of a female phenotype.
      - ❖ If a person with (XY) chromosome and SRY-gene is abnormally deleted from the (Y) chromosome: the person will have a female instead of a male phenotype.
    - ✓ Sex chromosomes of the fetus (either XY or XX) is determined very early during fertilization of the sperm with the ovum but gonads do not undergoe sexual differentiation into male or female until approximately 6 weeks.



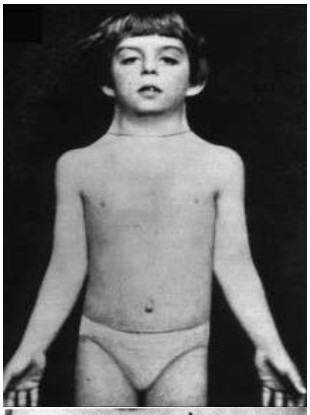
- **(XY) chromosome leads to:**
  - **Undifferentiated gonadal medulla develops into testes which have two types of cells:**
    - ✓ Leydig cells: producing testosterone which stimulates Wolffian ducts to form the male internal genitalia (epididymis, seminal vesicles and vas deferens). The enzyme 5α-reductase converts testosterone to dihydrotestosterone which enhances the development of male external genitalia (penis, scrotum and prostate).

- ✓ Sartoli cells: producing Mullerian Inhibitory Factors (MIF) which causes degeneration of Mullarian duct system.

- **(XX) chromosome leads to:**
  - **Undifferentiated gonadal cortex develops into an ovary** which will produce estradiol that –in turn- enhances the development of female external genitalia (clitoris, labia majora, labia minora and distal part of the vagina).
  - Notice that Mullerian ducts will produce female internal genitalia (fallopian tubes, uterus and proximal part of the vagina).
- **Disorders of sexual differentiation:**
  - **Male pseudohermaphrodite (XY):** testes present but external genitalia are female of ambiguous. Most common form is androgen insensitivity syndrome (testicular feminization).
  - **Androgen insensitivity syndrome (46, XY: see the image):** defect in androgen receptor resulting in normal-appearing female; female external genitalia with rudimentary vagina; uterus and fallopian tubes generally absent; present with scant sexual hair; develops testes (often found in labia majora; surgically removed to prevent malignancy). There will be ↑ testosterone, estrogen and LH.



  - **5α-reductase deficiency**: autosomal recessive, sex limited to genetic males (46, XY). inability to convert testosterone to dihydrotestosterone (DHT). ambiguous genitalia until puberty, when ↑ testosterone causes musculinization/ ↑growth of external genitalia. testosterone/ estrogen levels are normal; LH is normal or ↑. Internal genitalia are normal.
  - **Turner syndrome (45, X: see the image):** it is the most common cause of primary amenorrhea (menopause before menarche!); there is no Barr body and it is characterized by the following:
    - ✓ Short stature.
    - ✓ Ovarian dysgenesis.
    - ✓ Shield chest.
    - ✓ Bicuspid aortic valve.
    - ✓ Webbed neck.
    - ✓ Horseshoe kidney.



- **X-inactivation (see the image):**
  - It occurs early in embryonic life (15-16 days).
  - The inactivation is random (either paternal or maternal).
  - The inactivation is permanent and propagated to all progeny of that cell.
  - The inactive X exist in a condensed form during interphase and appears as darkly staining mass known as Barr body.
  - Notice that not all genes on X-chromosome are inactivated.