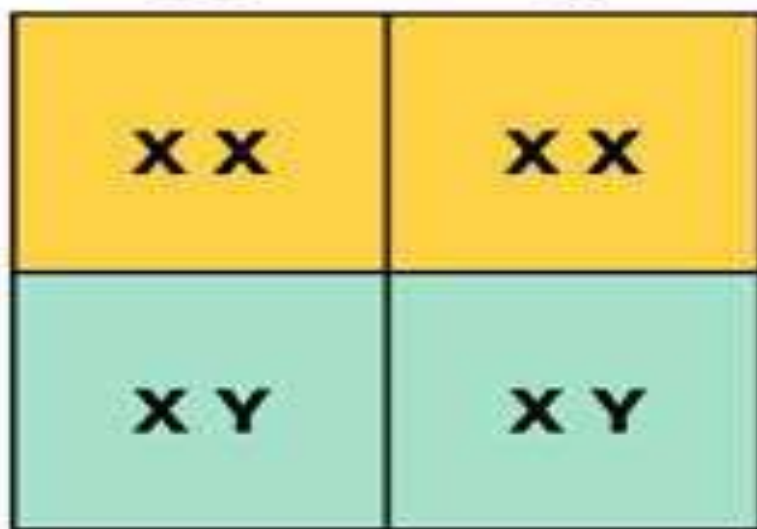
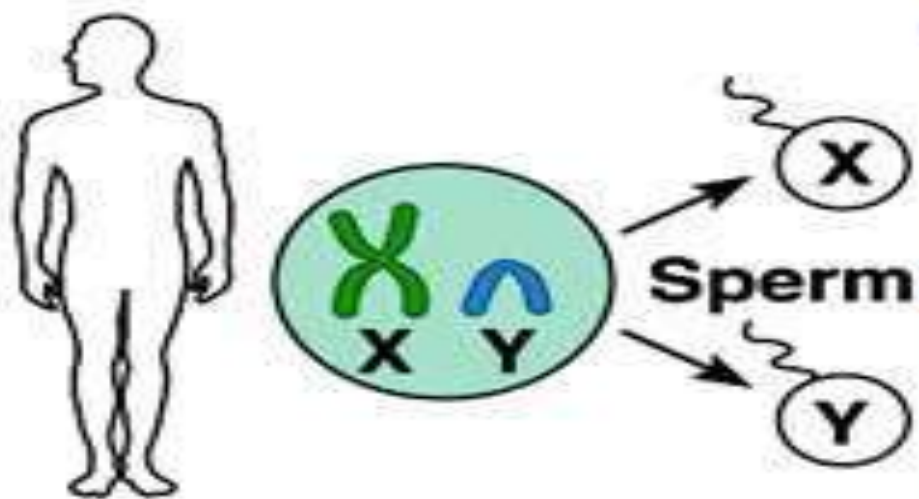
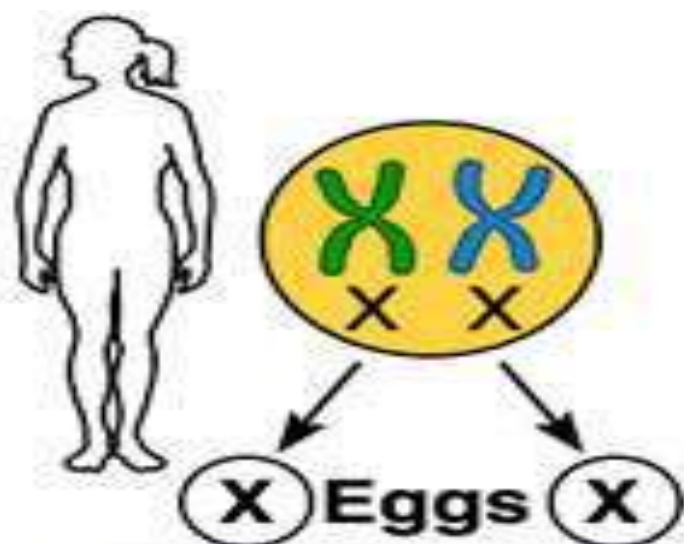
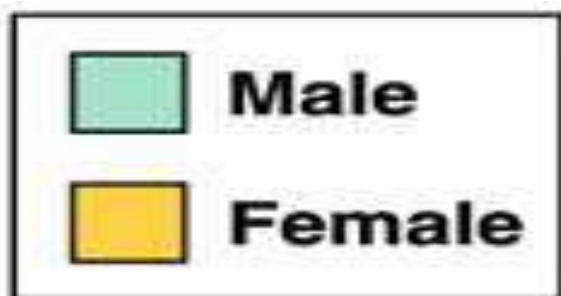
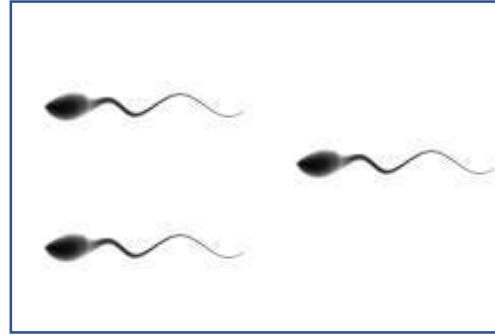
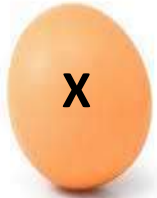
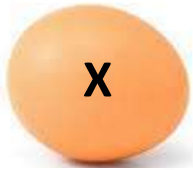


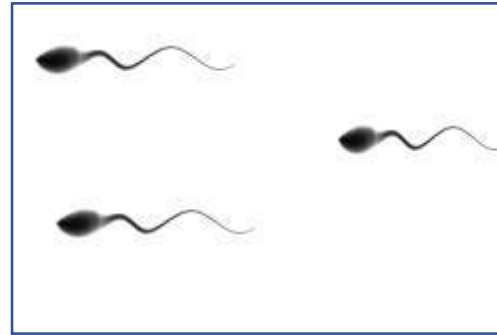
Sexual Differentiation, Its Abnormality & Puberty

Dr. Sanhita Mukherjee

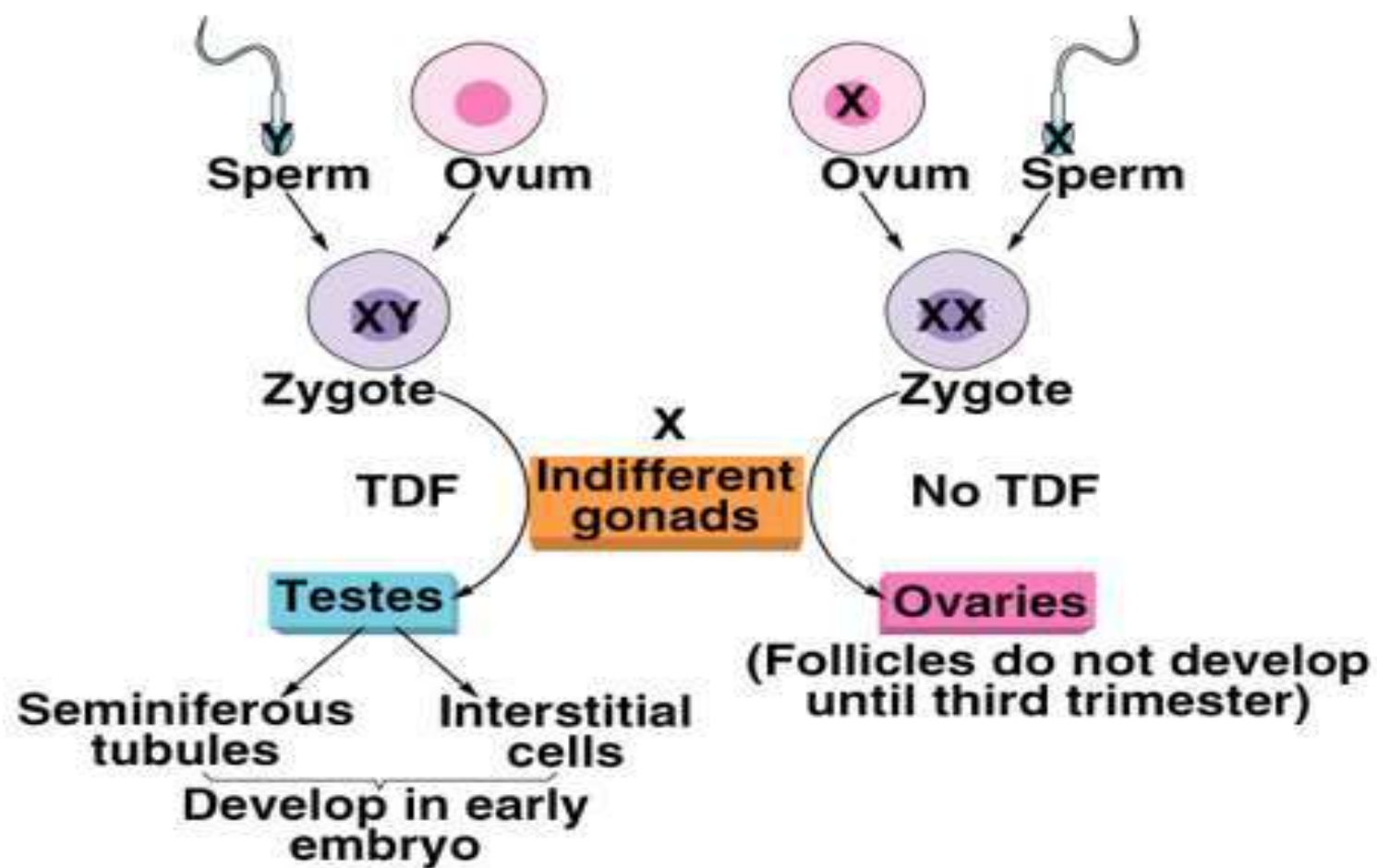




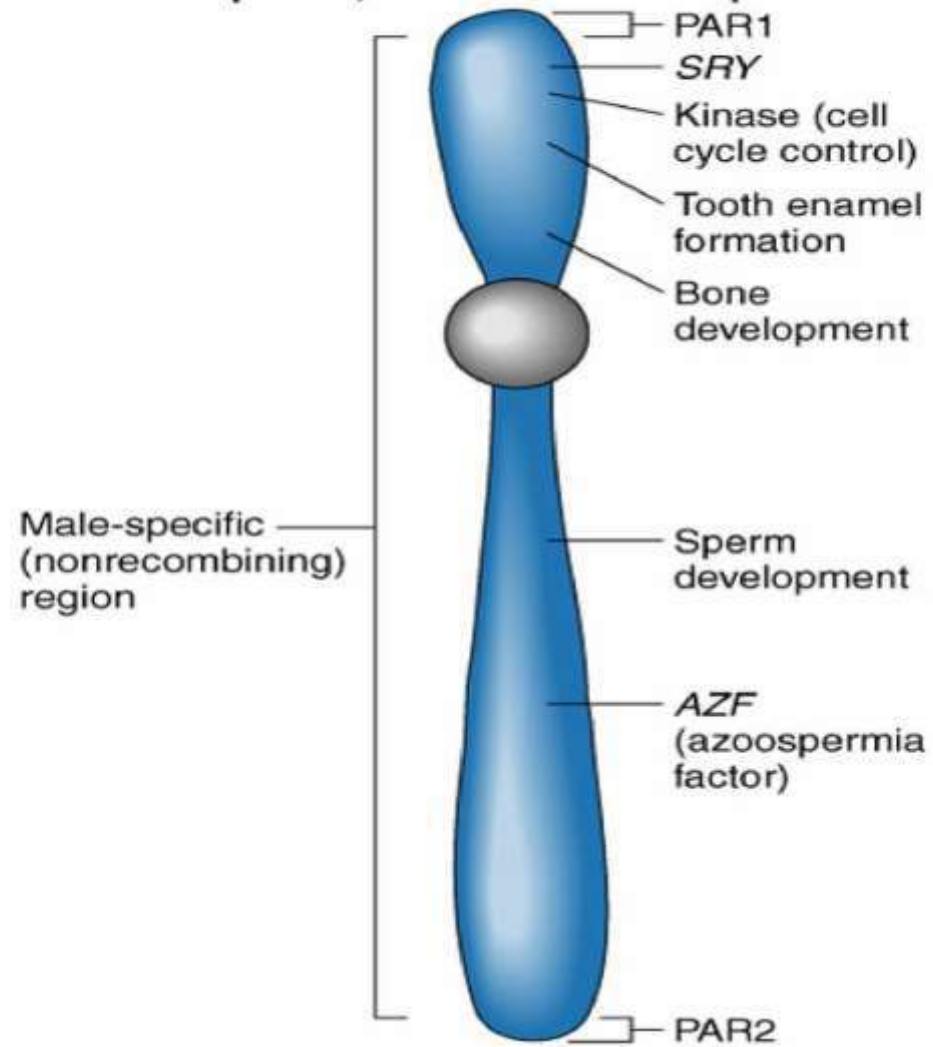
X

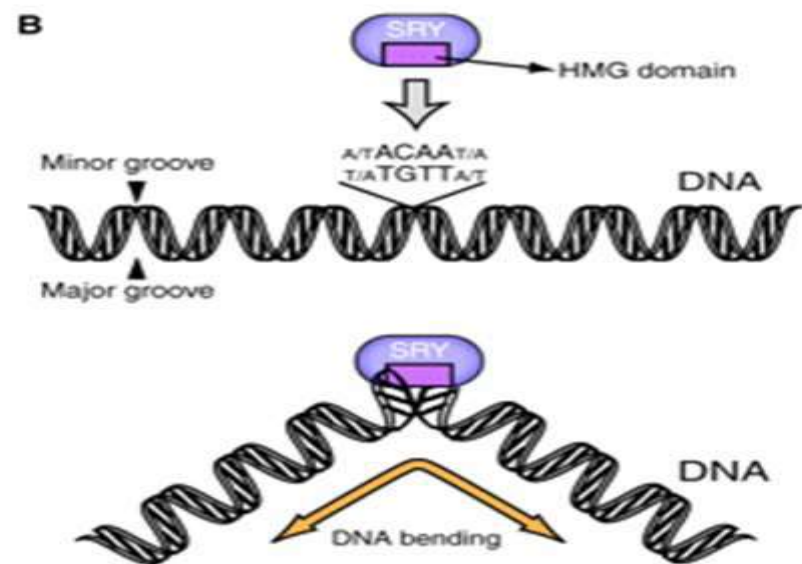
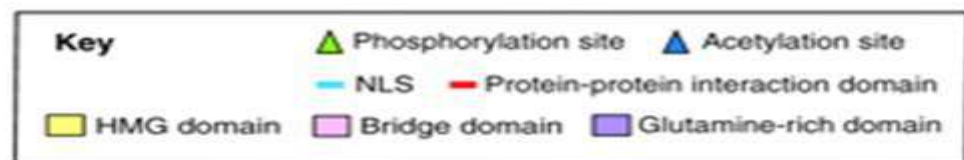
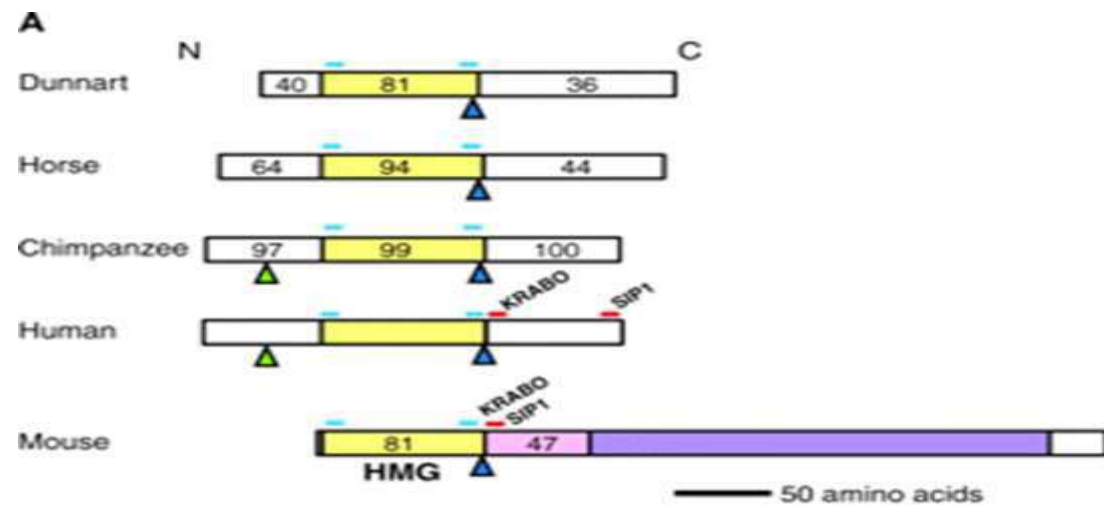
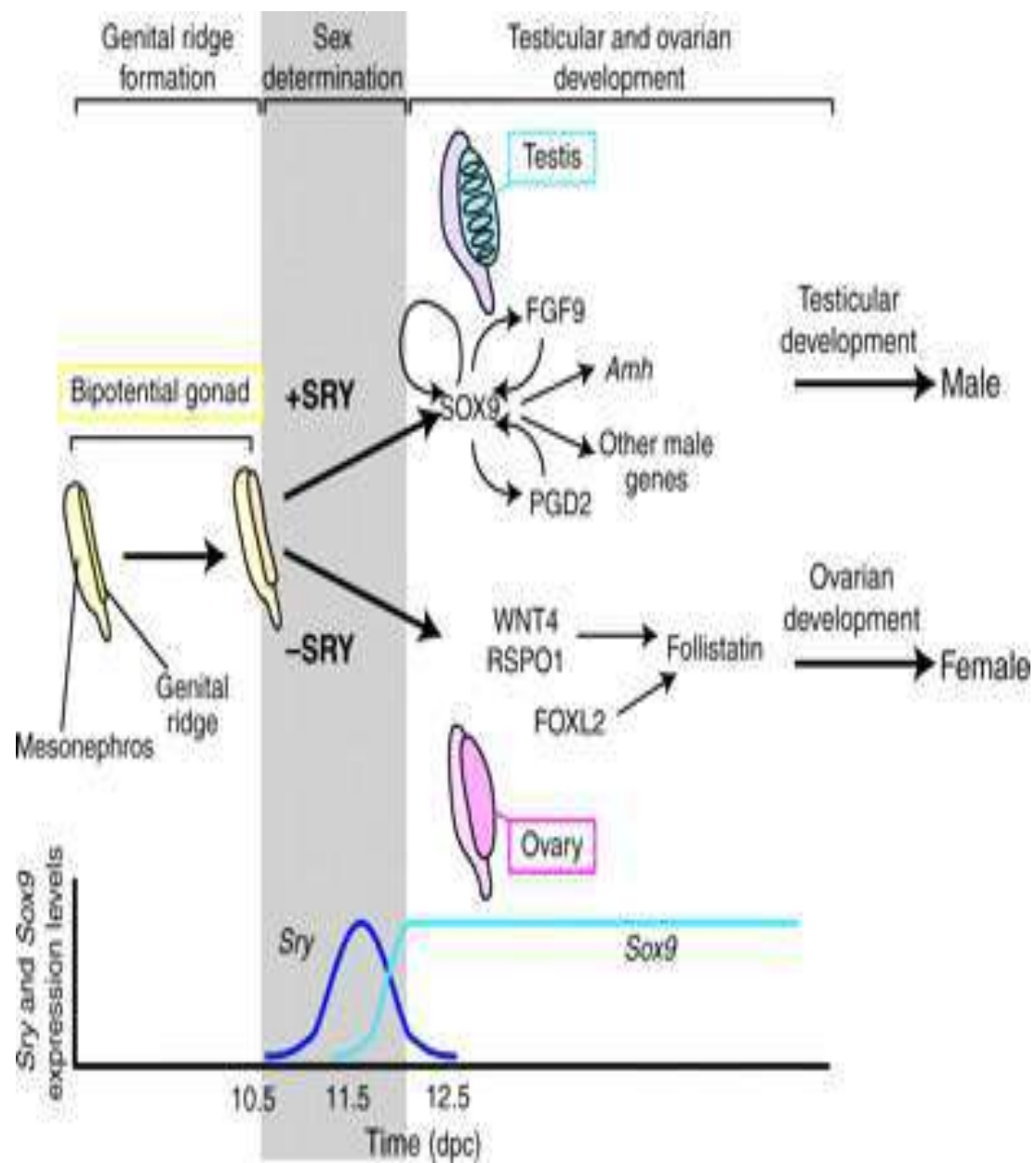


Y



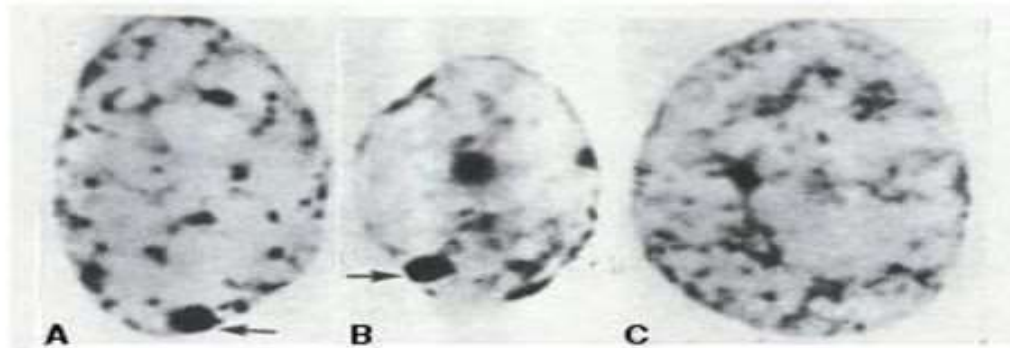
Y Chromosome





X-chromosome inactivation in female mammals occurs through heterochromatin formation

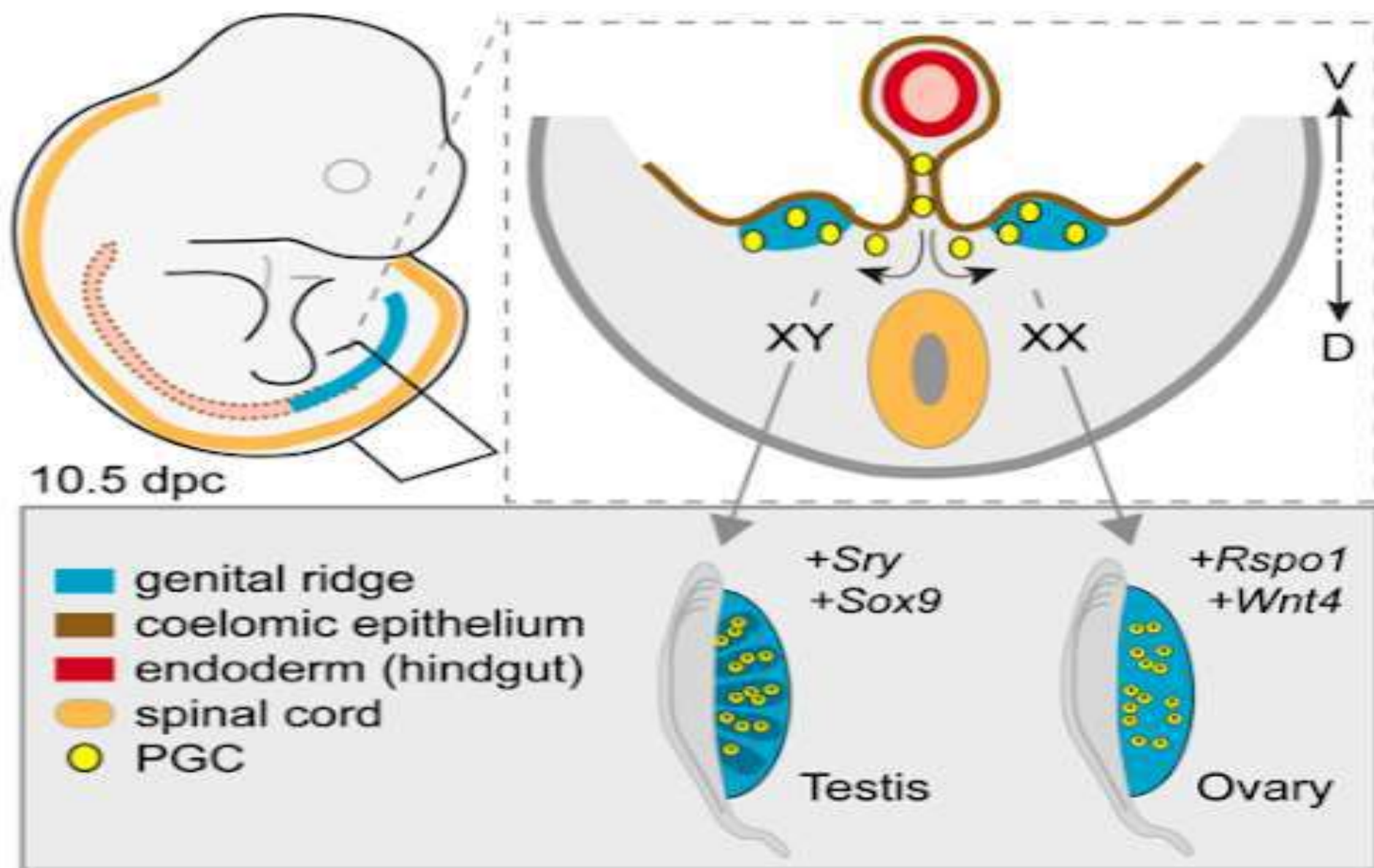
- **Dosage compensation in mammals** so that X-linked genes in XX and XY individuals are expressed at same level
- **Random inactivation** of all except one X chromosome in XX

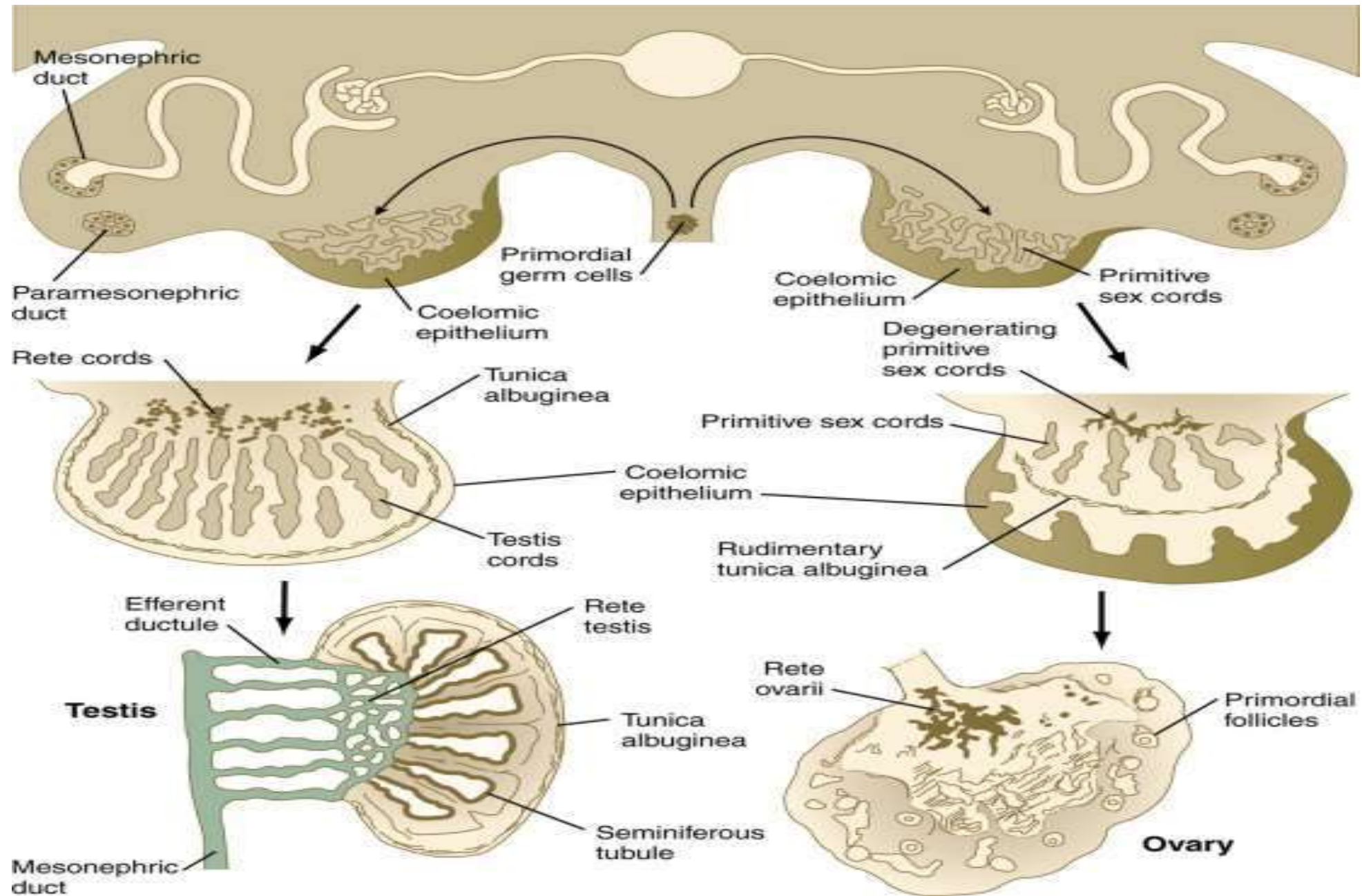


A and B are the nuclei obtained from a female. Notice the dark stained area in the lower portion of the nucleus of A and B, this is the Barr body. The nuclei C is from a male and has no Barr body.

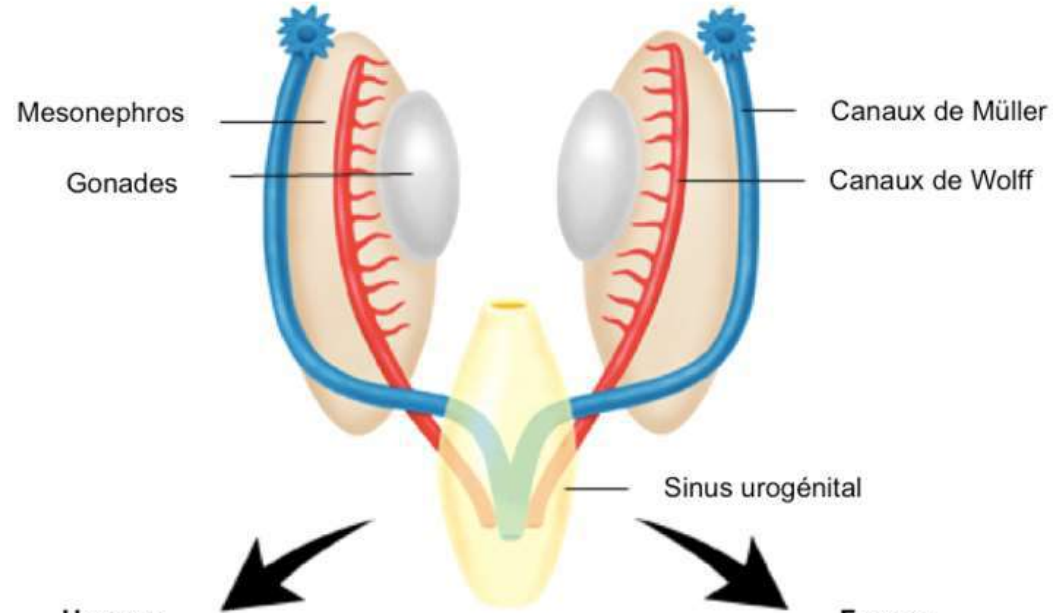
Barr bodies – darkly stained heterochromatin masses observed in somatic cells at interphase

- XX person has one Barr body
- XXX person has two Barr bodies
- XXY person has one Barr body

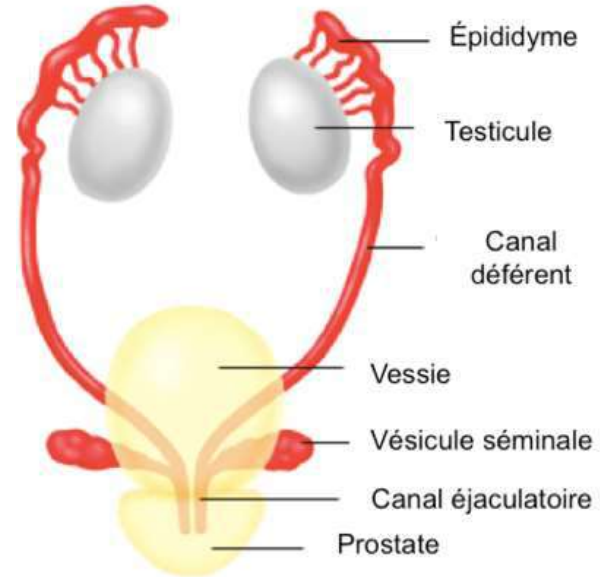




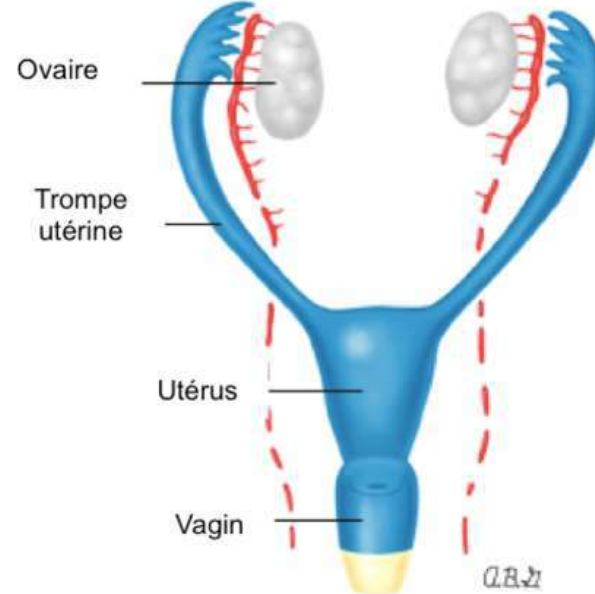
Stade indifférencié



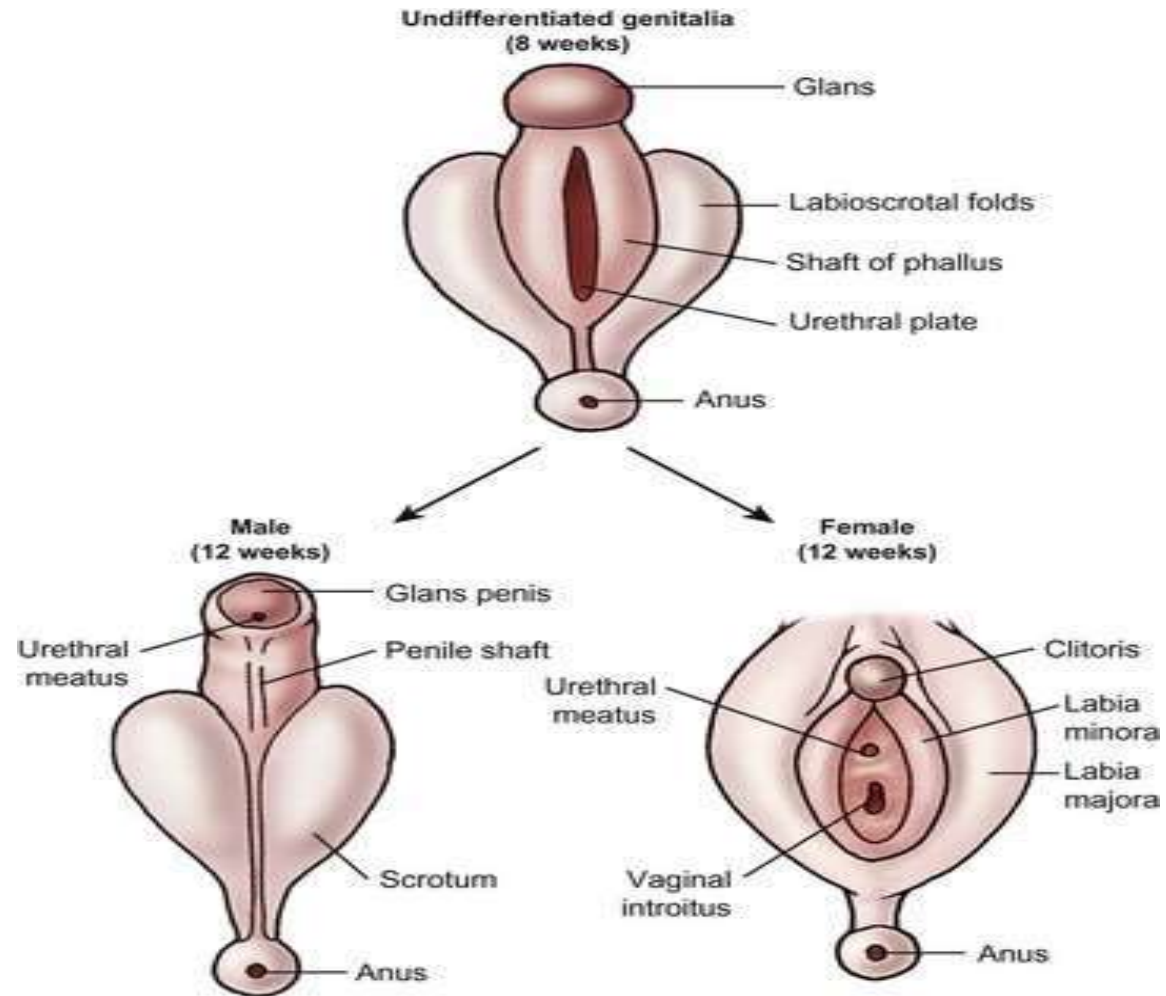
Homme



Femme

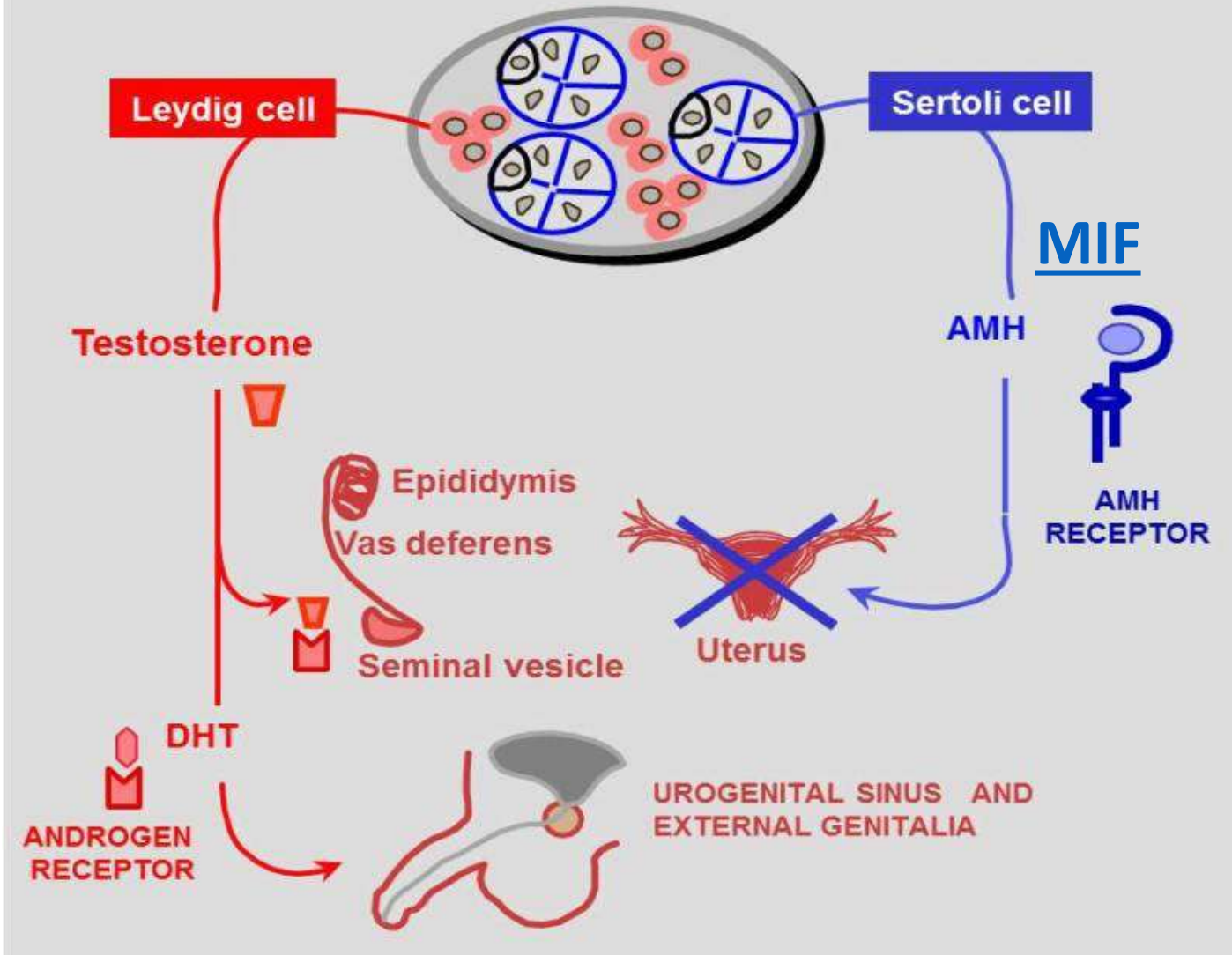


Q.B.J.

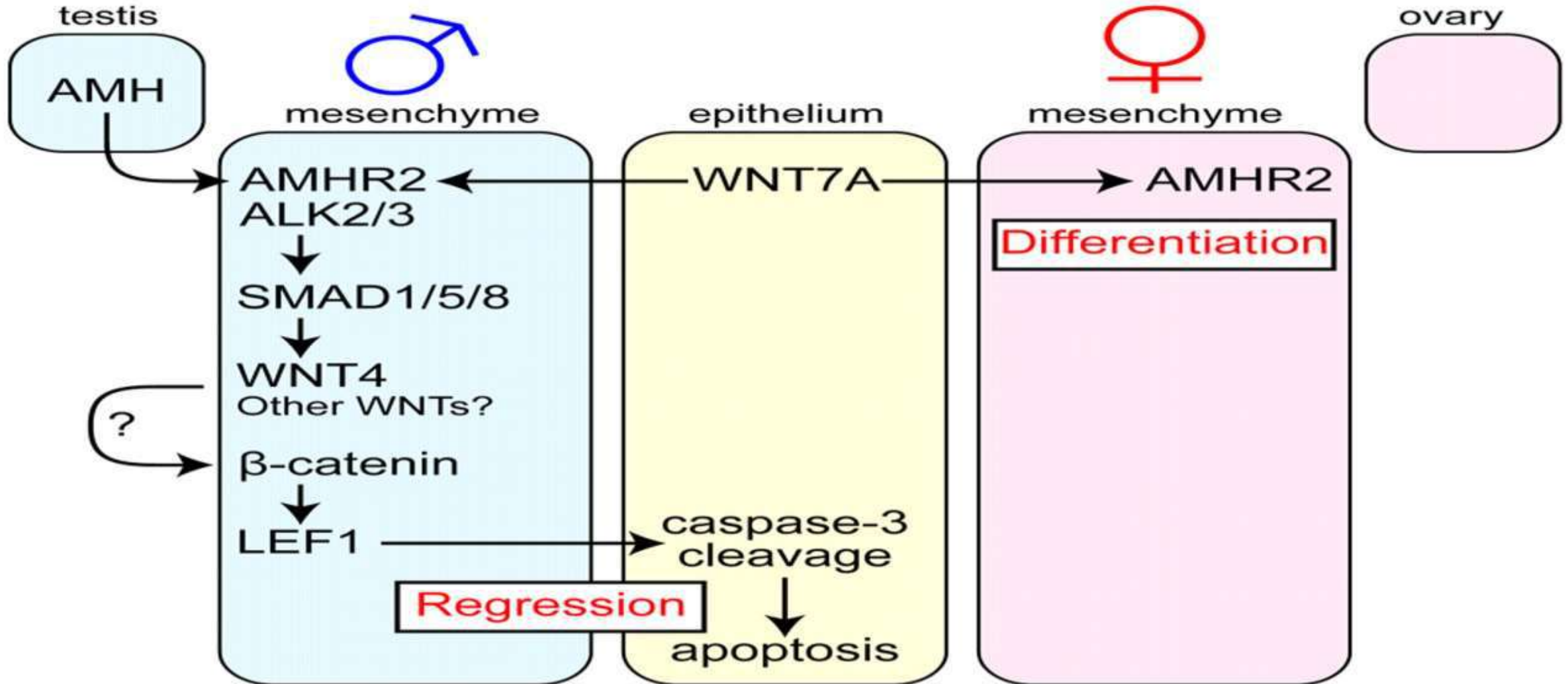


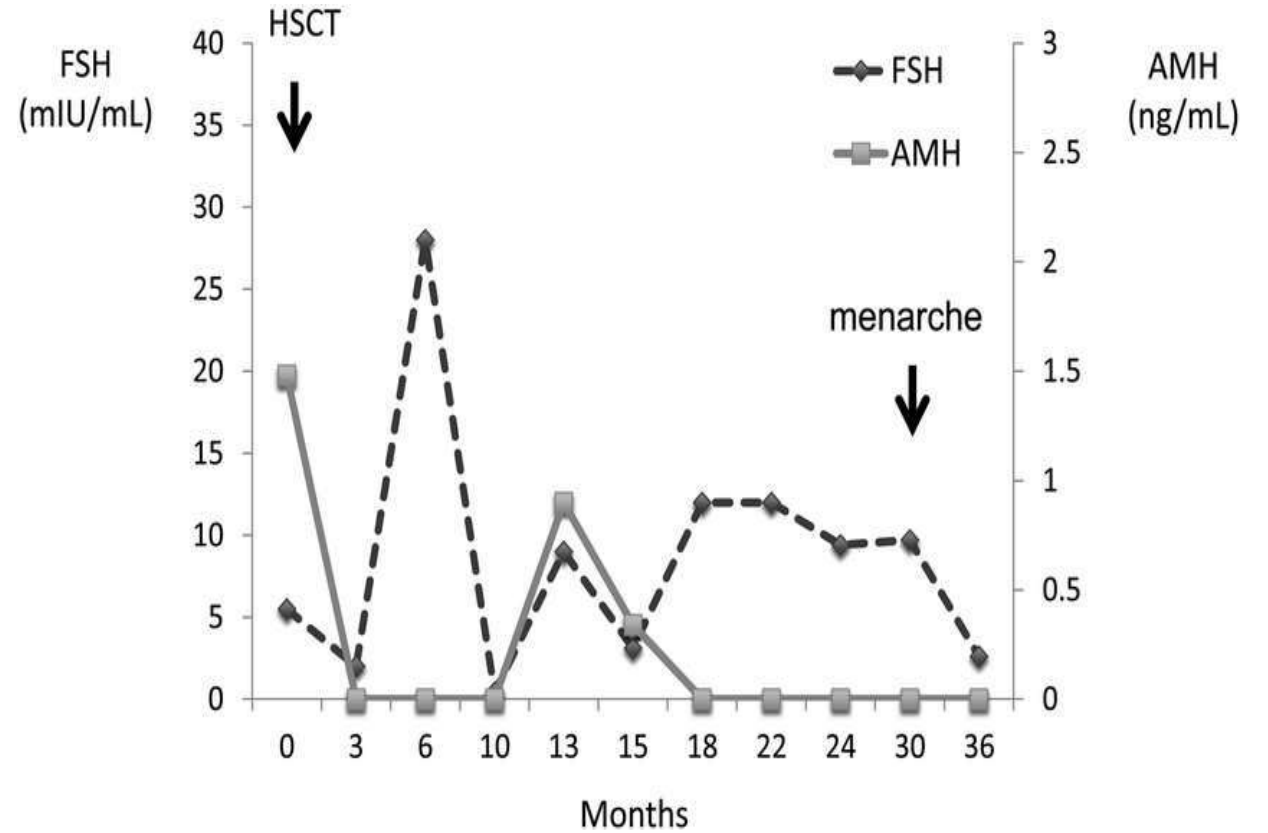
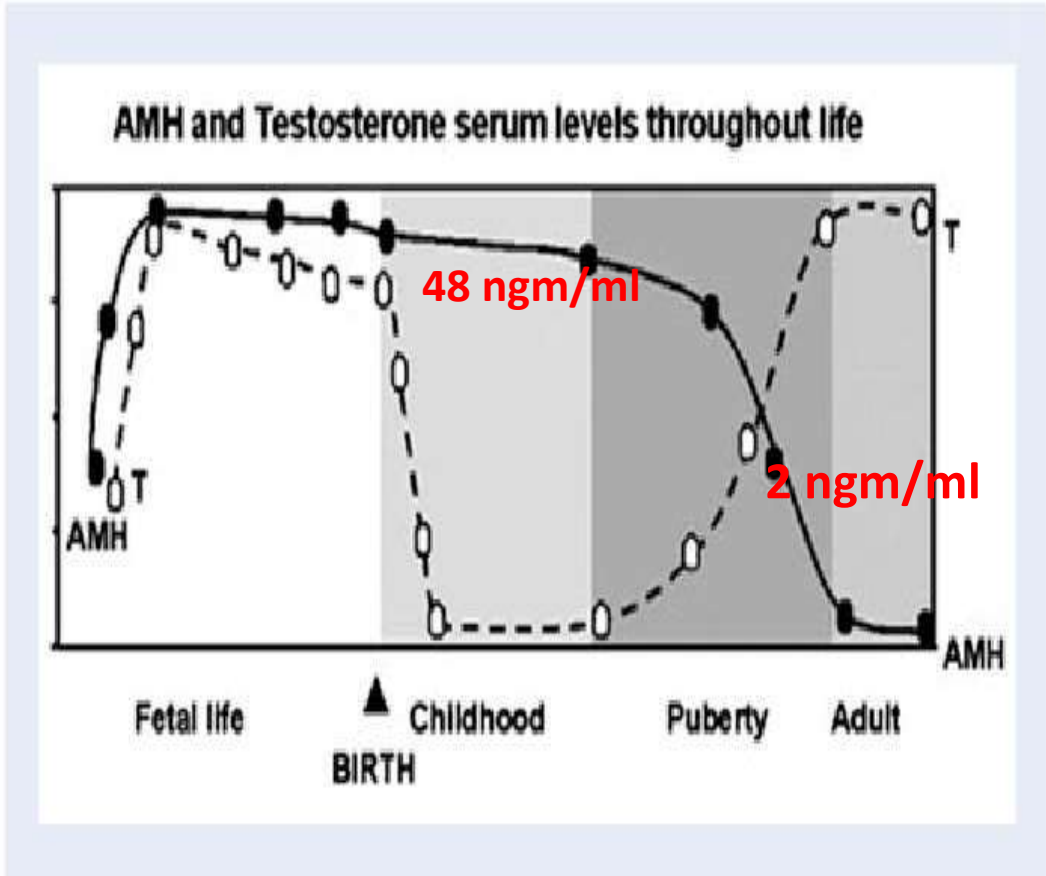
The external genitalia is Bipotential until 8th Week

Hormonal regulation of sex differentiation



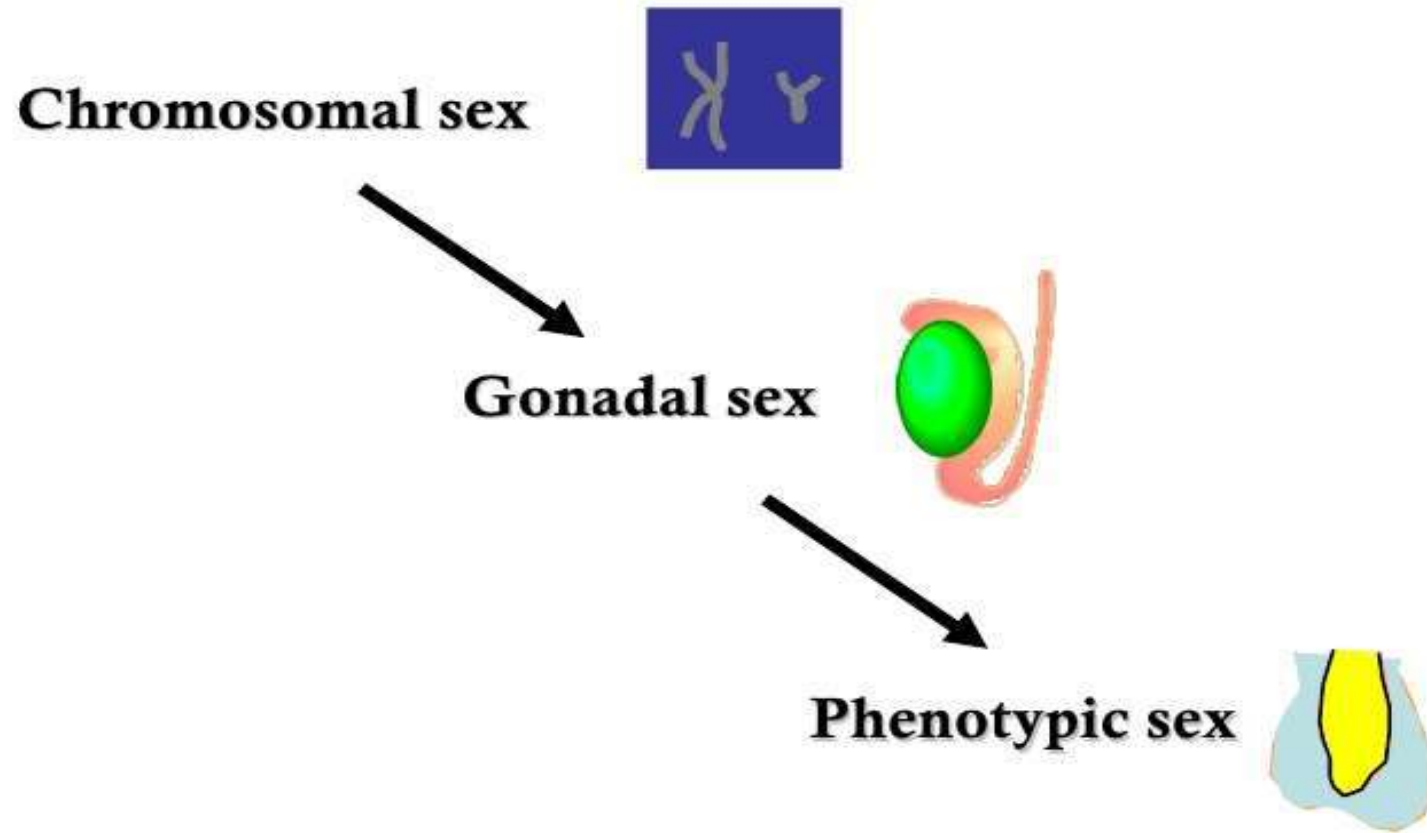
- 536 amino acid, Homodimer
- TGF Beta Super family





After Embryonic life: Germ cell maturation in both sexes & testicular descent in Boys

Sexual Differentiation



SEXUAL DIFFERENTIATION:

- ▶ Genetic Sex

XX-Female

XY-Male

- ▶ Gonadal Sex

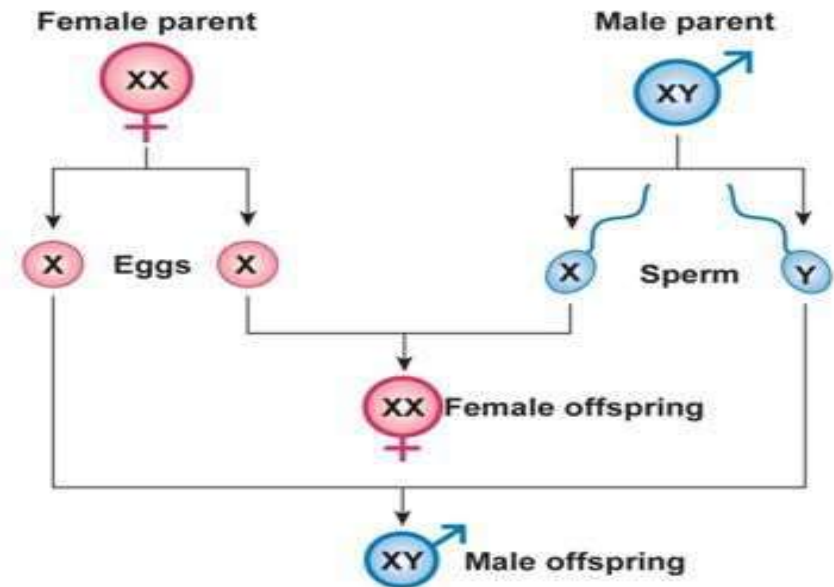
Testes-Male

Ovaries-Female

- ▶ Phenotypic Sex

Characteristics of internal genital tract and external genitalia,

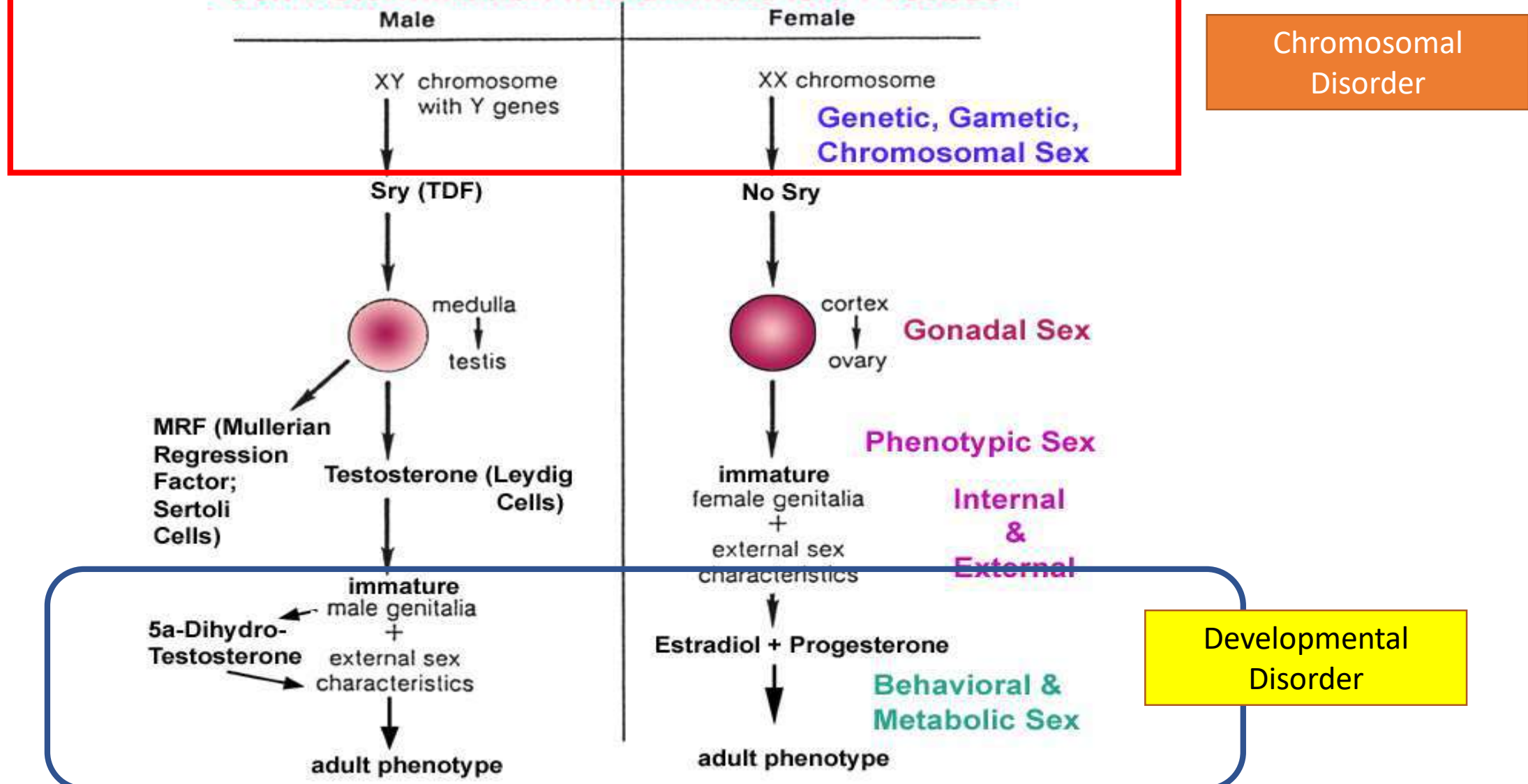
differentiation into male depends on **Testosterone**



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Sex Determination in Mammals Is a Process



Pseudohermaphrodite: Genetic pattern and gonads of one sex, genitalia of other

Chromosomal Disorder

Gonadal
Dysgenesis

Super
Female
XXX

True
Hermaphrodi
tism

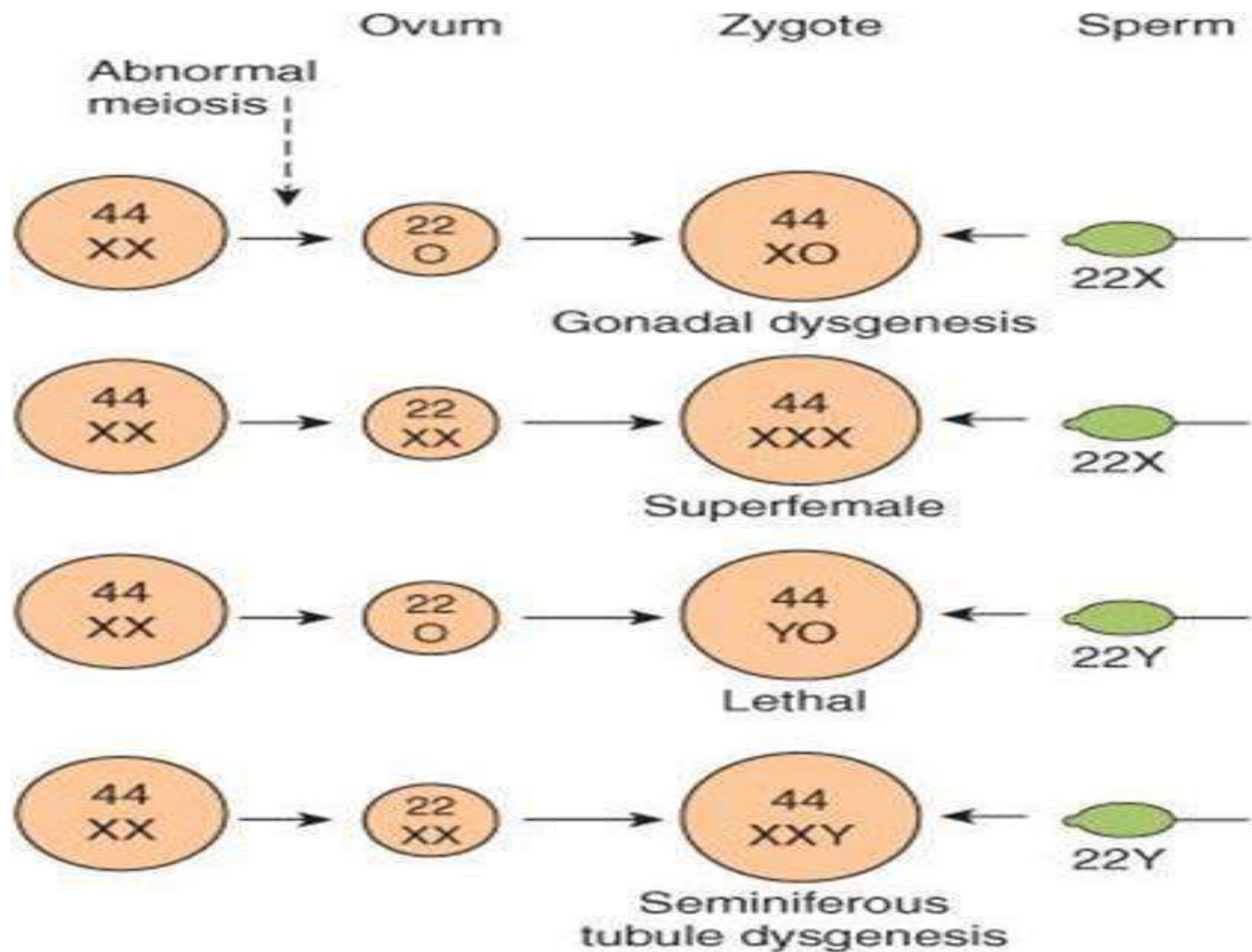
Developmental Disorder

Female
Pseudo
Hermaphroditism

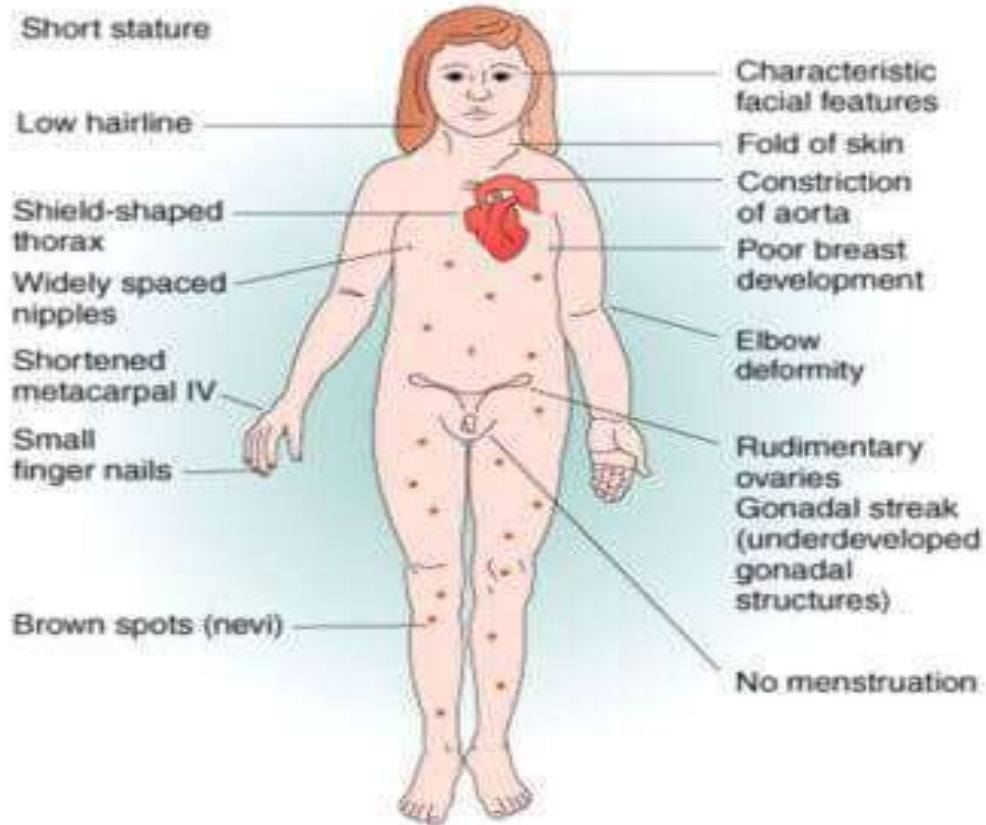
1. Congenital
Virilizing Adrenal
Hyperplasia
2. Maternal
Androgen Excess
3. Virilizing Ovarian
Tumour

Male
Pseudo
Hermaphroditism

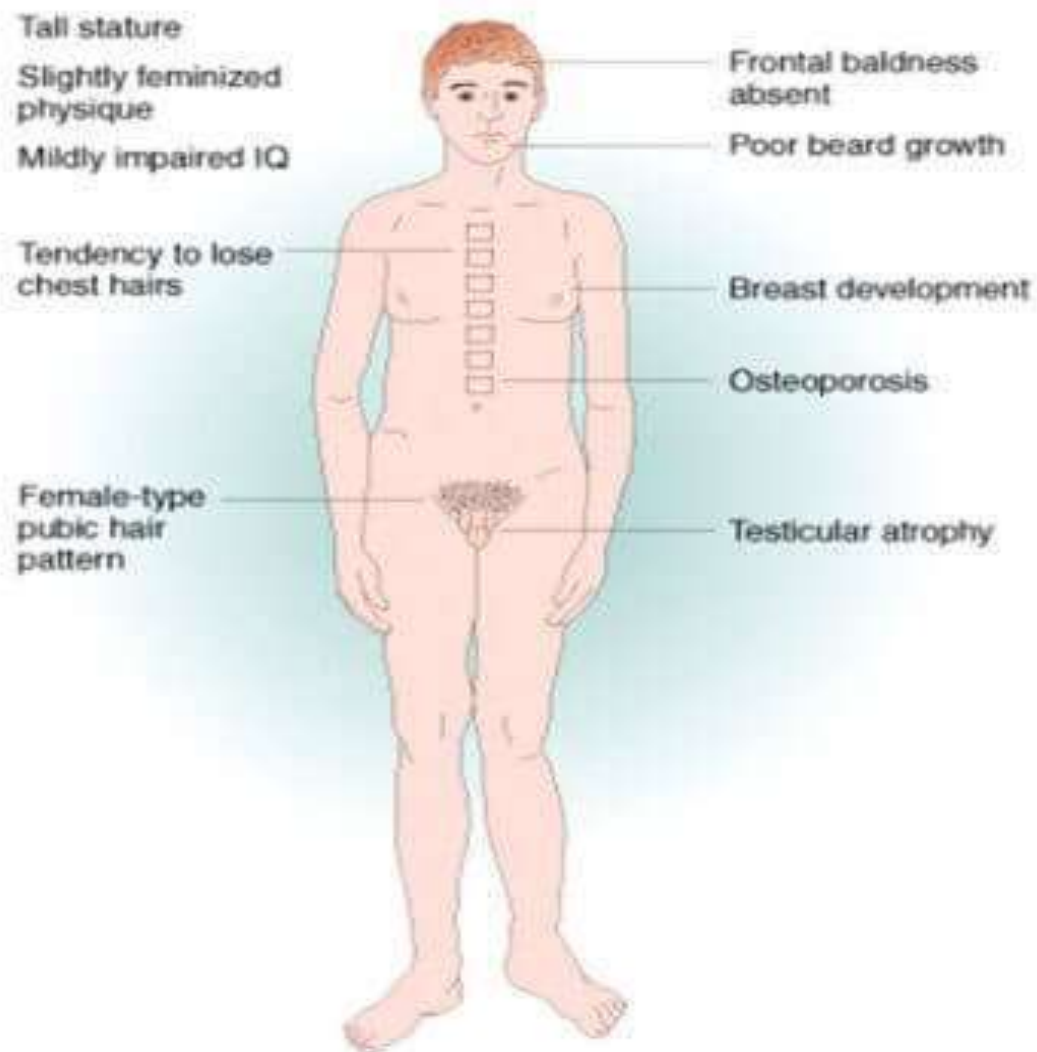
1. Androgen
Resistance
2. 5 alpha
reductase
deficiency

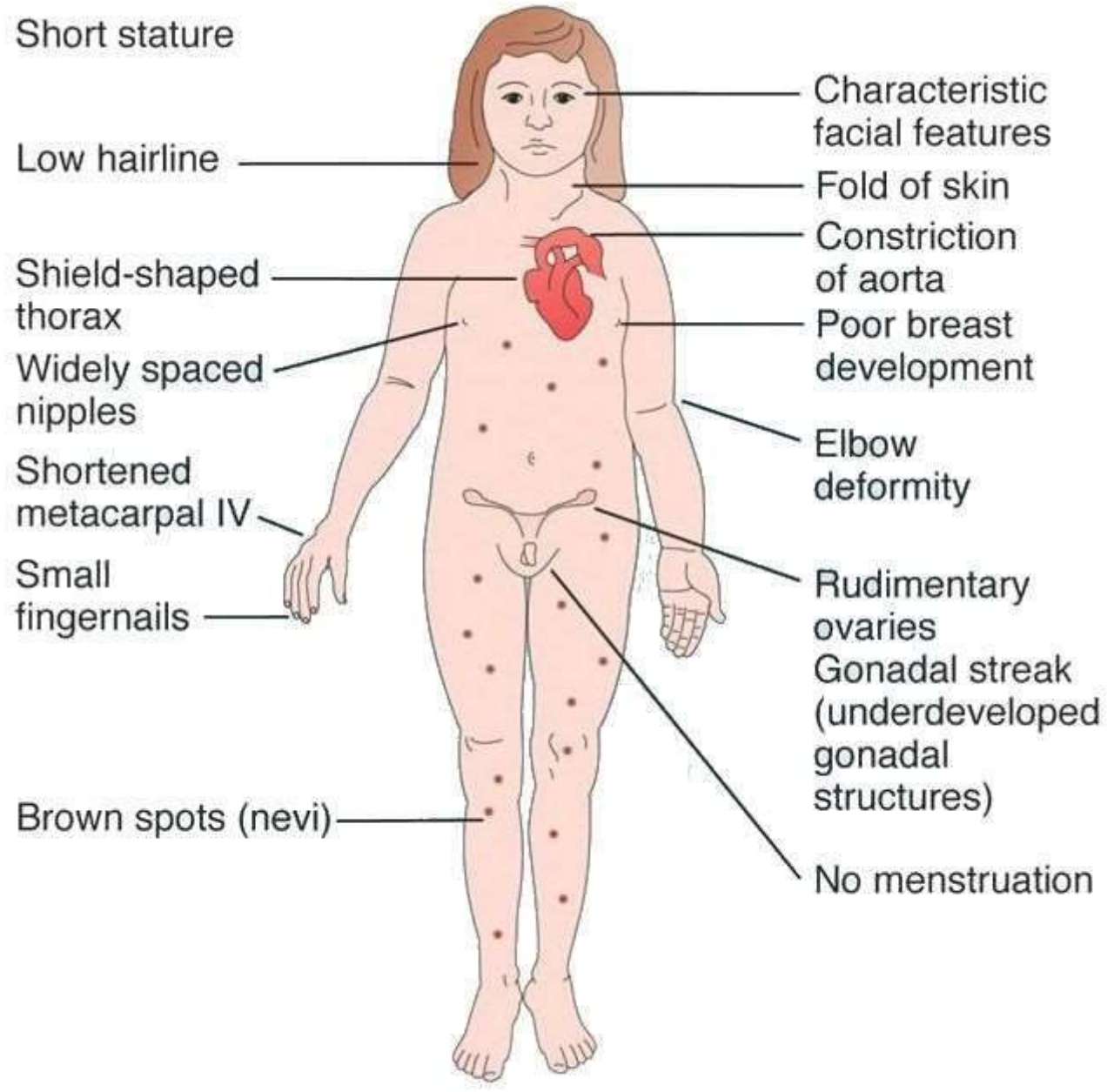


Turner Syndrome XO



Klinefelter Syndrome XXY





Short stature

Low hairline

Shield-shaped thorax

Widely spaced nipples

Shortened metacarpal IV

Small fingernails

Brown spots (nevi)

Characteristic facial features

Fold of skin

Constriction of aorta

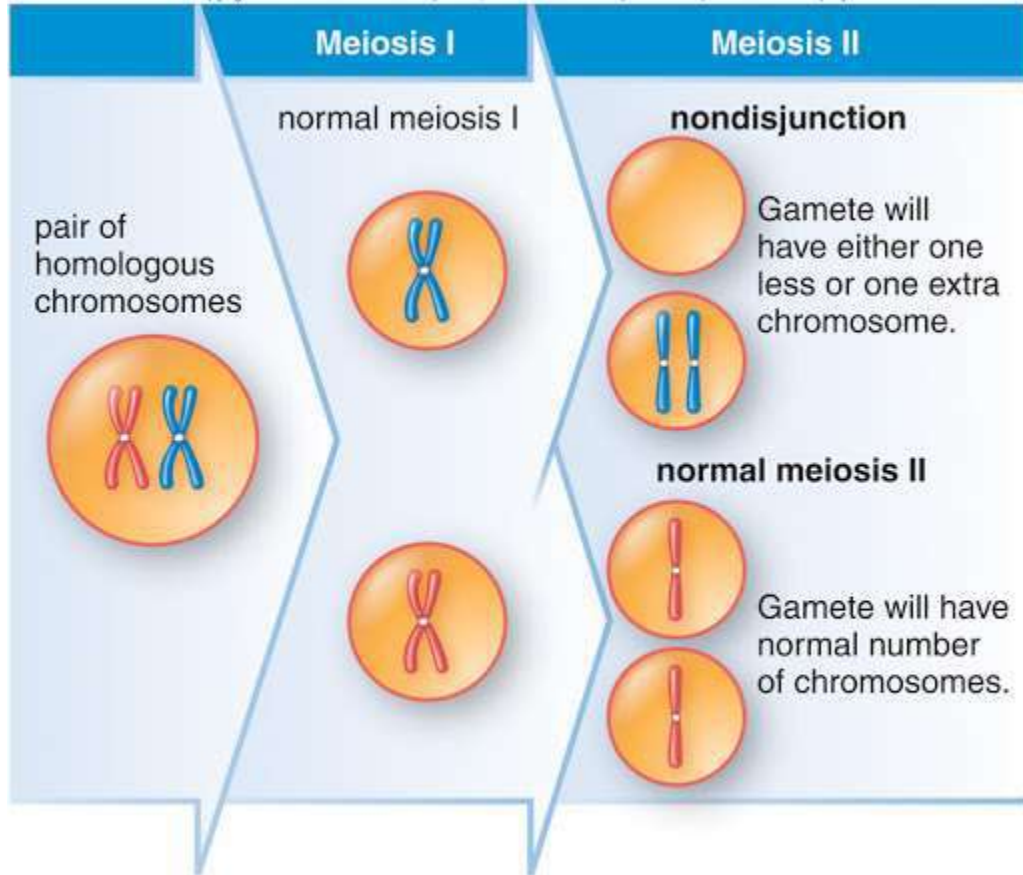
Poor breast development

Elbow deformity

Rudimentary ovaries

Gonadal streak (underdeveloped gonadal structures)

No menstruation

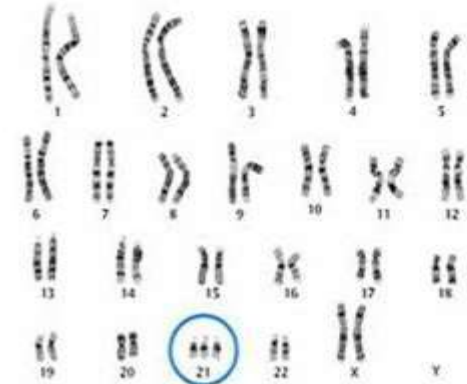


b. Nondisjunction during meiosis II

Down Syndrome (trisomy 21): 47, XX, +21 or 47, XY, +21

The result of an extra copy of chromosome 21.

Down syndrome alters the child's physical appearance either moderately or severely.



- characteristic facial features, short stature; heart defects, shorter lifespan

Chromosomal Disorder

Gonadal
Dysgenesis

Super
Female
XXX

True
Hermaphrodi
tism

Developmental Disorder

Female
Pseudo
Hermaphroditism

1. Congenital
Virilizing Adrenal
Hyperplasia
2. Maternal
Androgen Excess
3. Virilizing Ovarian
Tumour

Male
Pseudo
Hermaphroditism

1. Androgen
Resistance
2. 5 alpha
reductase
deficiency

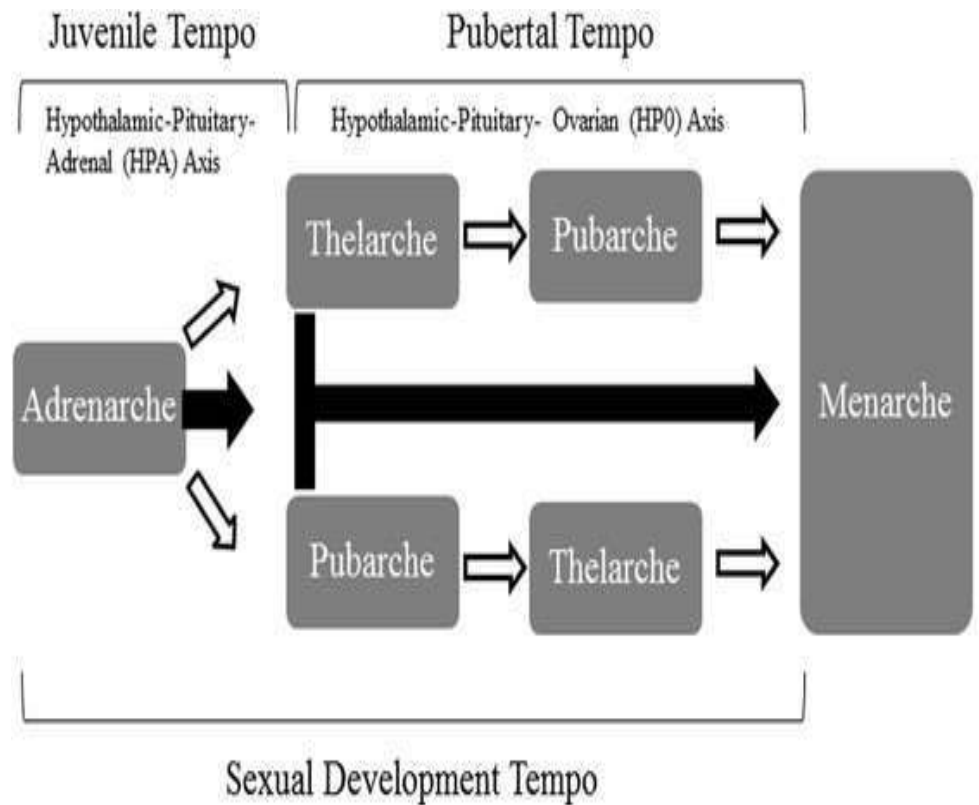
Complete androgen insensitivity syndrome

- **Phenotypically female**
- **Symptoms do not appear until puberty**
- **Absent menses**
- **External genitalia is normal**
- **Vaginal depth is short**
- **Not ovaries - atrophic testes**
- **Slightly longer limbs and larger hands and feet, minimal or no acne, larger teeth, well developed breasts.**
- **Greater incidence of meibomian gland dysfunction (dry eye syndromes and light sensitivity)**

Karyotype
46 XY

PUBERTY

- Definition: It is the period when the endocrine and gametogenic functions of the gonads have first developed to the point where reproduction is possible.



Puberty – Terms & Events

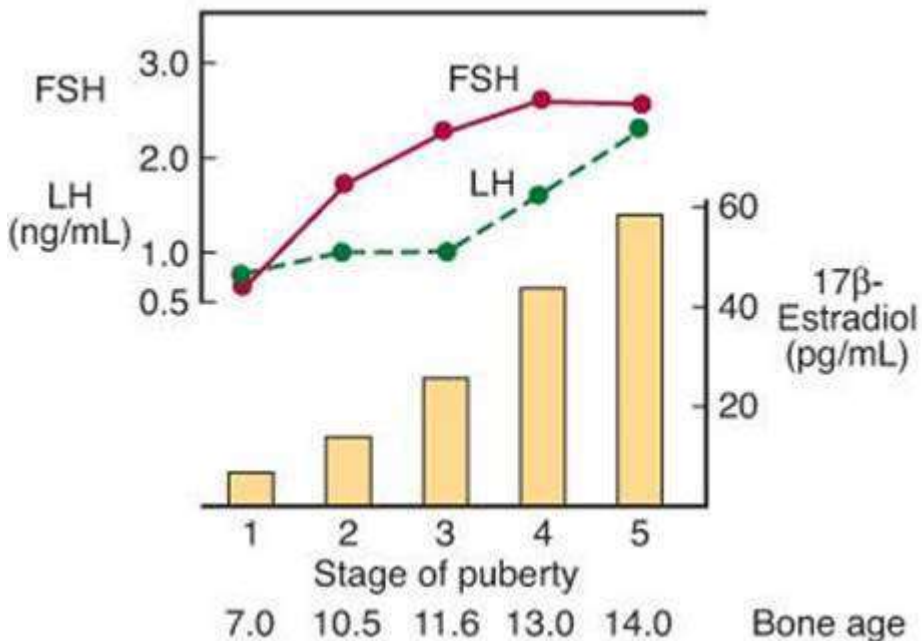
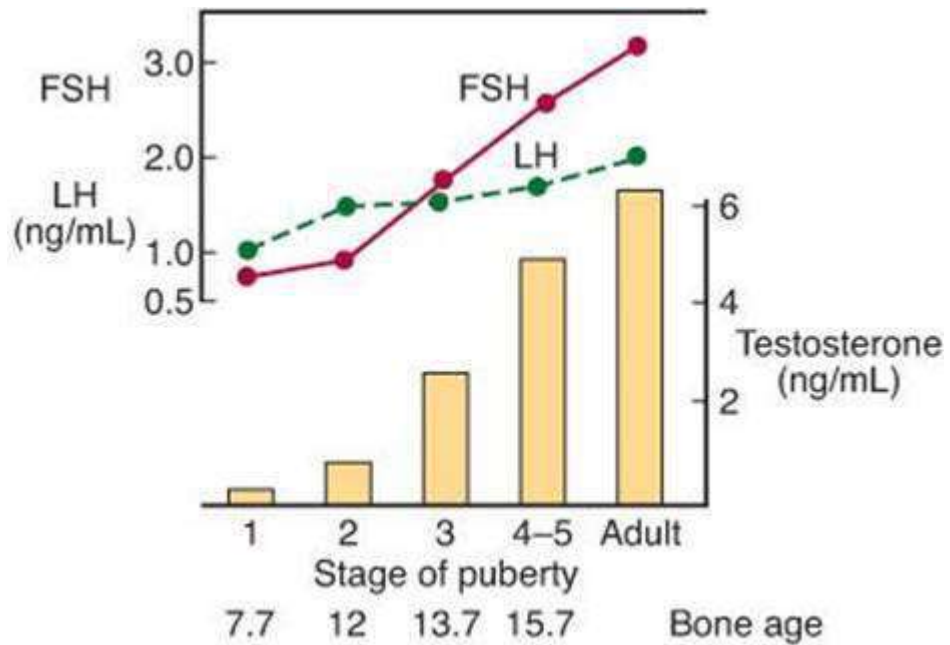
- Thelarche: development of breast
- Puberarche: development of axillary & pubic hair
- Menarche: the first menstrual period
- Adrenarche: the onset of an increase in the secretion of androgens, responsible for development of pubic and axillary hair, body odour and acne.



8-13 Years

	African American	Mexican American	Caucasian
Pubertal milestone			
Mean age in years			
Pubarche	9.5	10.3	10.5
Thelarche	9.5	9.8	10.3
Menarche	12.1	12.2	12.7

Data from: Anderson SE, Must A. Interpreting the continued decline in the average age at menarche: results from two nationally representative surveys of U.S. girls studied 10 years apart. J Pediatr 2005 Dec;147(6):753–60



Stage 1 of puberty is preadolescence in both sexes.

In boys,

- stage 2 is characterized by beginning enlargement of the testes,
- stage 3 by penile enlargement,
- stage 4 by growth of the glans penis, and
- stage 5 by adult genitalia.

In girls,

- stage 2 is characterized by breast buds,
- stage 3 by elevation and enlargement of the breasts, stage 4 by projection of the areolas, and
- stage 5 by adult breasts.
- (Modified and reproduced with permission from Berenberg SR [editor]: *Puberty: Biologic and Psychosocial Components*. HE Stenfoert Kroese BV, 1975.)

Control of Onset of Puberty

- A burst of testosterone secretion occurs in male fetuses before birth
- In the neonatal period there is another burst, with unknown function,
- But thereafter the Leydig cells become quiescent.
- There follows in all mammals a period in which the gonads of both sexes are quiescent until they are activated by gonadotropins from the pituitary to bring about the final maturation of the reproductive system.

Leptin

Control of Onset of Puberty

- It seems clear that **pulsatile secretion** of GnRH brings on puberty.
- During the period from birth to puberty, a neural mechanism is operating to prevent the normal pulsatile release of GnRH.
- The nature of the mechanism inhibiting the GnRH pulse generator is unknown.
- However, one or more genes produce products that stimulate secretion of GnRH, and inhibition of these genes before puberty is an interesting possibility

Precocious Puberty

- **True precocious puberty** due to an early but otherwise normal pubertal pattern of gonadotropin secretion from the pituitary.
- Early development of secondary sexual characteristics without gametogenesis is caused by abnormal exposure of immature males to androgen or females to estrogen. This syndrome should be called **precocious pseudopuberty** .

True precocious puberty

Constitutional

Cerebral: Disorders involving posterior hypothalamus

Tumors

Infections

Developmental abnormalities

Gonadotropin-independent precocity

Precocious pseudopuberty (no spermatogenesis or ovarian development)

Adrenal

Congenital virilizing adrenal hyperplasia

Androgen-secreting tumors (in males)

Estrogen-secreting tumors (in females)

Gonadal

Leydig cell tumors of testis

Granulosa cell tumors of ovary

Miscellaneous

Delayed OR Absent Puberty

- Puberty cannot be considered to be pathologically delayed until the menarche has failed to occur by the age of 17 or testicular development by the age of 20.
- Failure of maturation due to panhypopituitarism is associated with dwarfing and evidence of other endocrine abnormalities.
- Patients with the XO chromosomal pattern and gonadal dysgenesis are also dwarfed.