Sexual Differentiation During Development

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- In somatic cells, chromosomes appear as 23 **homologous** pairs to form the **diploid** number of 46 chromosomes.
- 22 pairs of matching chromosomes called the autosomes and a pair of sex chromosomes.
- If the sex chromosome pair is XX then the individual is genetically female and if it is XY then the individual is genetically male.
- One chromosome of each pair is derived from the maternal gamete **(oocyte)** and one from the paternal gamete **(sperm).**
- Thus each gamete contains a **haploid** number of 23 chromosomes, and on **fertilization** restores the diploid number of 46 chromosome.

Primary and secondary sex determination

(Chromosomal)

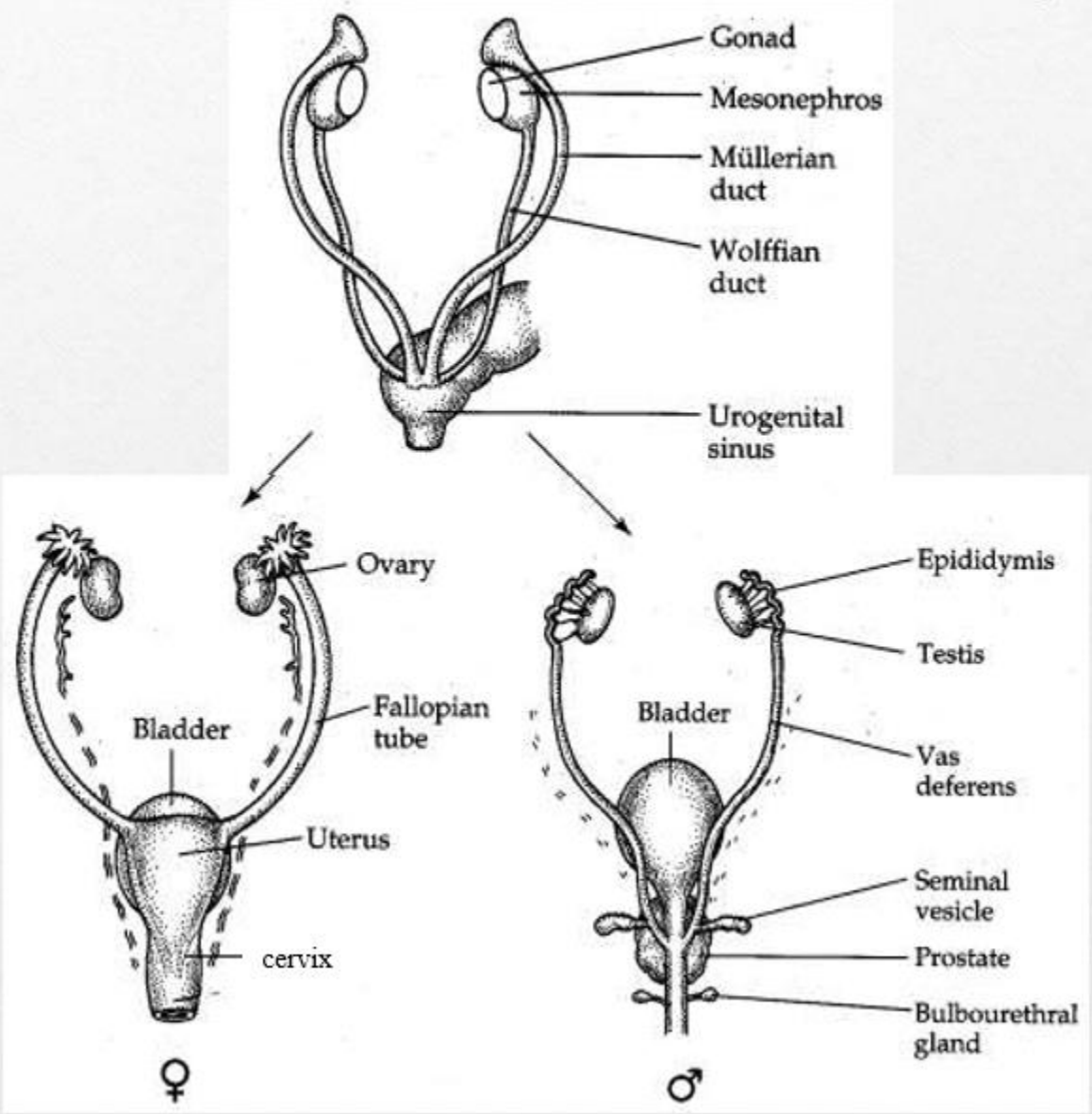
- **Primary sex determination** is the determination of the gonads.
- The female is XX and the male is XY. Every individual must have at least one X chromosome.
- Since the female is XX, each of her eggs has a single X chromosome.
- The male, being XY, can generate two types of sperm: half bear the X chromosome, half the Y chromosome.
- If the egg receives another X chromosome from the sperm, the resulting individual is XX, forms ovaries, and is female.
- If the egg receives a Y chromosome from the sperm, the individual is XY, forms testes, and is male.

- The Y chromosome carries a gene that encodes a testis-determining factor. This factor organizes the gonad into a testis rather than an ovary.
- A person with five X chromosomes and one Y chromosome (XXXXXY) would be male.
- Furthermore, an individual with only a single X chromosome and no second X or Y (i.e.,XO) develops as a female and begins making ovaries, although the ovarian follicles cannot be maintained. For a complete ovary, a second X chromosome is needed.

- Secondary sex determination affects the bodily phenotype outside the gonads.
- A male mammal has a penis, seminal vesicles, and prostate gland.
- A female mammal has a vagina, cervix, uterus, oviducts, and mammary glands.
- The ovaries produce **estrogen**, a hormone that enables the development of the **Müllerian duct** into the uterus, oviducts, and upper end of the vagina.

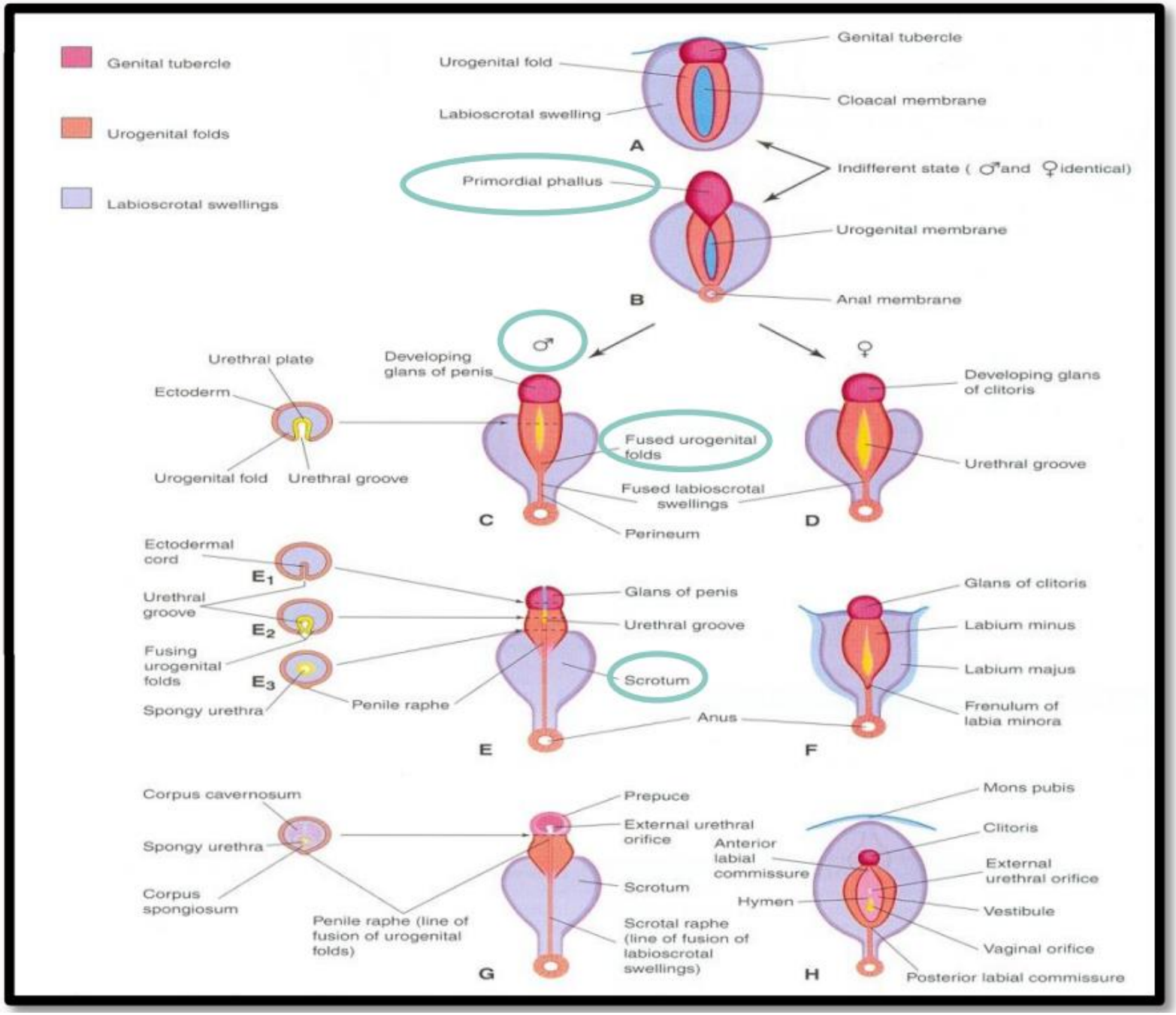
- If the Y chromosome is present, testes form and secrete two major hormones.
- The first hormone **anti-Müllerian duct hormone** (**AMH**; also referred to as Müllerian-inhibiting substance, MIS) destroys the Müllerian duct.
- The second hormone **testosterone** masculinizes the fetus, stimulating Wolffian ducts become vas deferens, seminal vessicles, and prostate gland as well as inhibiting the development of the breast primordia.
- Thus, the body has the female phenotype unless it is changed by the two hormones secreted by the fetal testes.

Mullerian and Wolffian Duct Systems



THE EXTERNAL GENITALIA

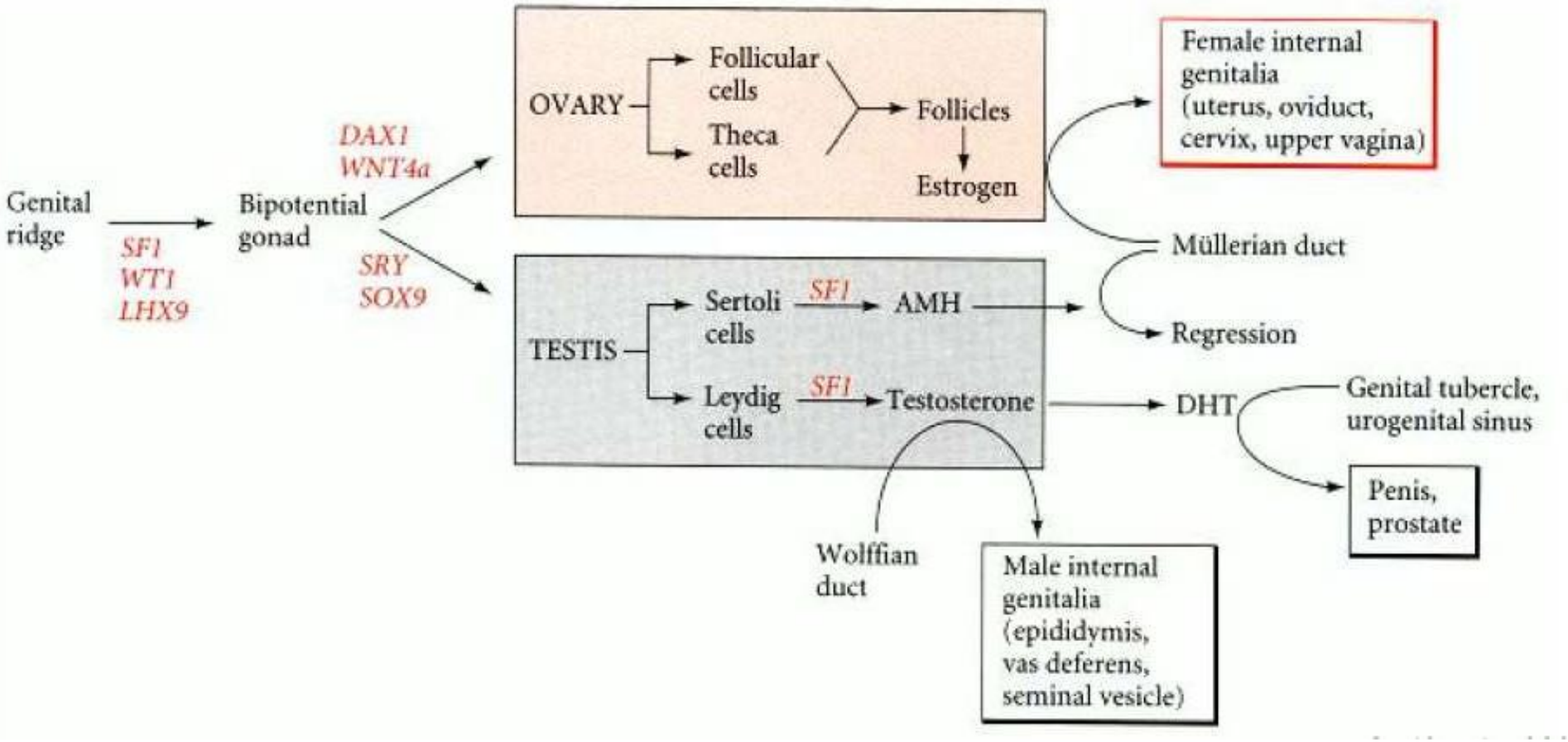
- Until 8 weeks in embryonic life, the external genitalia are bi-potential
- In the presence of testosterone:
  - Testosterone is converted to DHT by 5-alpha reductase
  - DHT promotes the development of bi-potential external genitalia to become Male External Genitalia
- Enlargement of genital tubercle – Penis
- Fusion of urethral fold over uro-genital sinus – Penile urethra
- Fusion of labio-scrotal swelling – Scrotum


Genital tubercle
Urogenital folds
Labioscrotal swellings
Genital tubercle
Urogenital fold
Cloacal membrane
Labioscrotal swelling
A
Indifferent state (♂and ♀identical)
Primordial phallus
Urogenital membrane
B
Anal membrane
♂
♀
Urethral plate
Ectoderm
Developing glans of penis
Developing glans of clitoris
Fused urogenital folds
Urethral groove
Urogenital fold
Urethral groove
Fused labioscrotal swellings
C
D
Perineum
Ectodermal cord
E1
Urethral groove
E2
Fusing urogenital folds
E3
Spongy urethra
Penile raphe
Glans of penis
Urethral groove
Scrotum
Anus
E
Glans of clitoris
Labium minus
Labium majus
Frenulum of labia minora
F
Corpus cavernosum
Spongy urethra
Corpus spongiosum
Penile raphe (line of fusion of urogenital folds)
Prepuce
External urethral orifice
Scrotum
Scrotal raphe (line of fusion of labioscrotal swellings)
G
Mons pubis
Clitoris
Anterior labial commissure
External urethral orifice
Hymen
Vestibule
Vaginal orifice
Posterior labial commissure
H

In females:

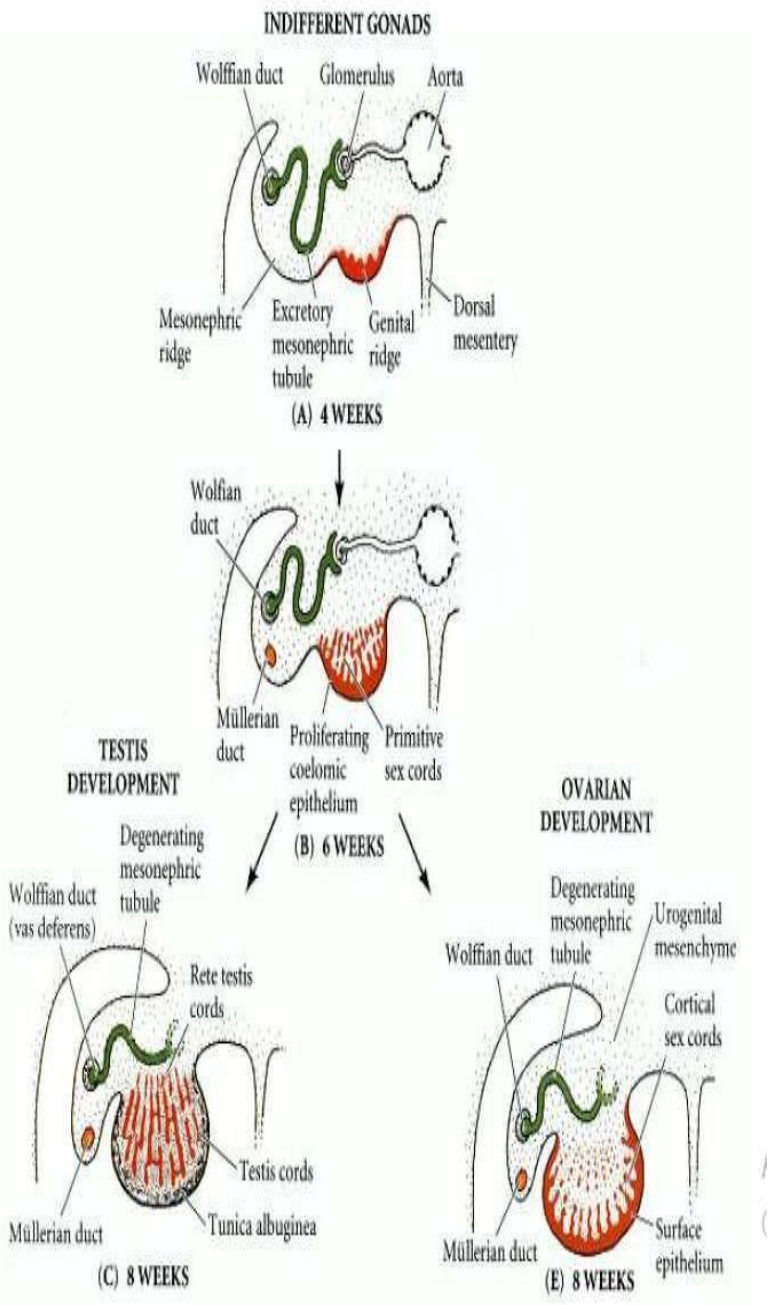
- No Testosterone
- No DHT
- Therefore the bi-potential external genitalia differentiates in to female external genitalia
- Genital tubercle remains – Clitoris
- Non fusion of uro genital sinus – Lower vagina & urethra (vestibule)
- Non fusion of urethral folds – Labia minora
- Non fusion of labio scrotal swelling – Labia majora

General scheme of mammalian sex determination.



gonads

- Although the sex of the embryo is determined genetically at the time of fertilization, the gonads do not acquire male or female morphological characteristics until the seventh week of development.
- Gonads appear initially as a pair of longitudinal ridges called the **genital** or **gonadal ridges.**
- **Germ cells** do not appear in the genital ridges until the sixth week of development.
- Primordial germ cells first appear at an early stage of development among endoderm cells in the wall of the yolk sac.



- They migrate by amoeboid movement along the dorsal mesentery of the hindgut arriving at the primitive gonads at the beginning of the fifth week and invading the genital ridges in the sixth week.

- If they fail to reach the ridges, the gonads do not develop. Hence the primordial germ cells have an inductive influence on development of the gonad into ovary or testis.

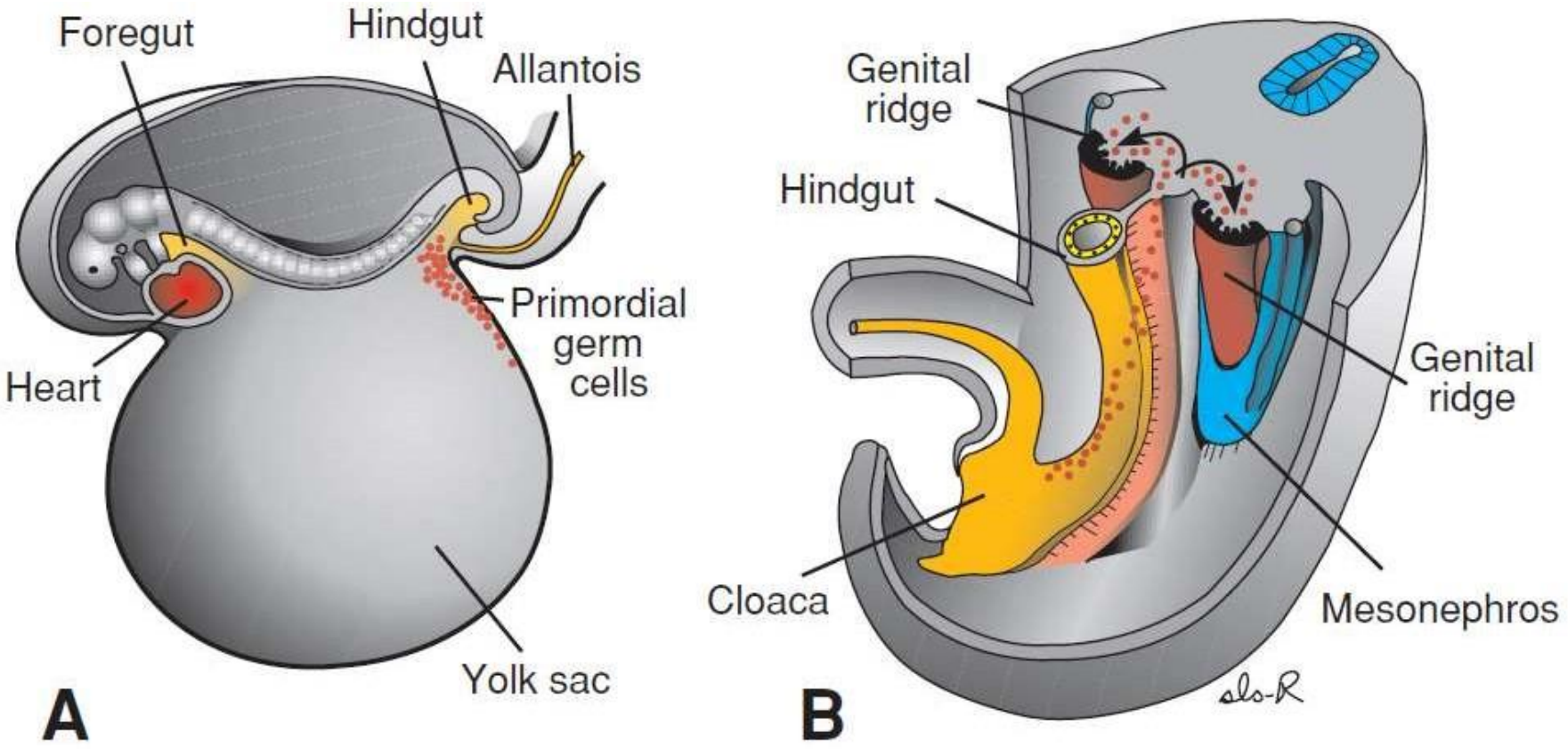


Figure 14.18 A. A 3-week-old embryo showing the primordial germ cells in the wall of the yolk sac close to the attachment of the allantois. **B.** Migrational path of the primordial germ cells along the wall of the hindgut and the dorsal mesentery into the genital ridge.

testis

- If the embryo is genetically male, the primordial germ cells carry an XY sex chromosome complex.
- Under influence of the *SRY (Sex Determining Region on Y)* gene on the Y chromosome, which encodes the testis-determining factor, the primitive sex cords continue to proliferate and penetrate deep into the medulla to form the **testis** or **medullary cords.**
- Toward the hilum of the gland the cords break up into a network of tiny cell strands that later give rise to tubules of the **rete testis.**

- During further development a dense layer of fibrous connective tissue, the **tunica albuginea,** separates the testis cords from the surface epithelium.
- In the fourth month, the testis cords become horseshoe shaped.
- Testis cords are now composed of **primitive germ cells** and **sustentacular cells of Sertoli** derived from the surface epithelium of the gland.
- **Interstitial cells of Leydig** derived from the original mesenchyme of the gonadal ridge, lie between the testis cords.
- They begin development shortly after onset of differentiation of these cords.

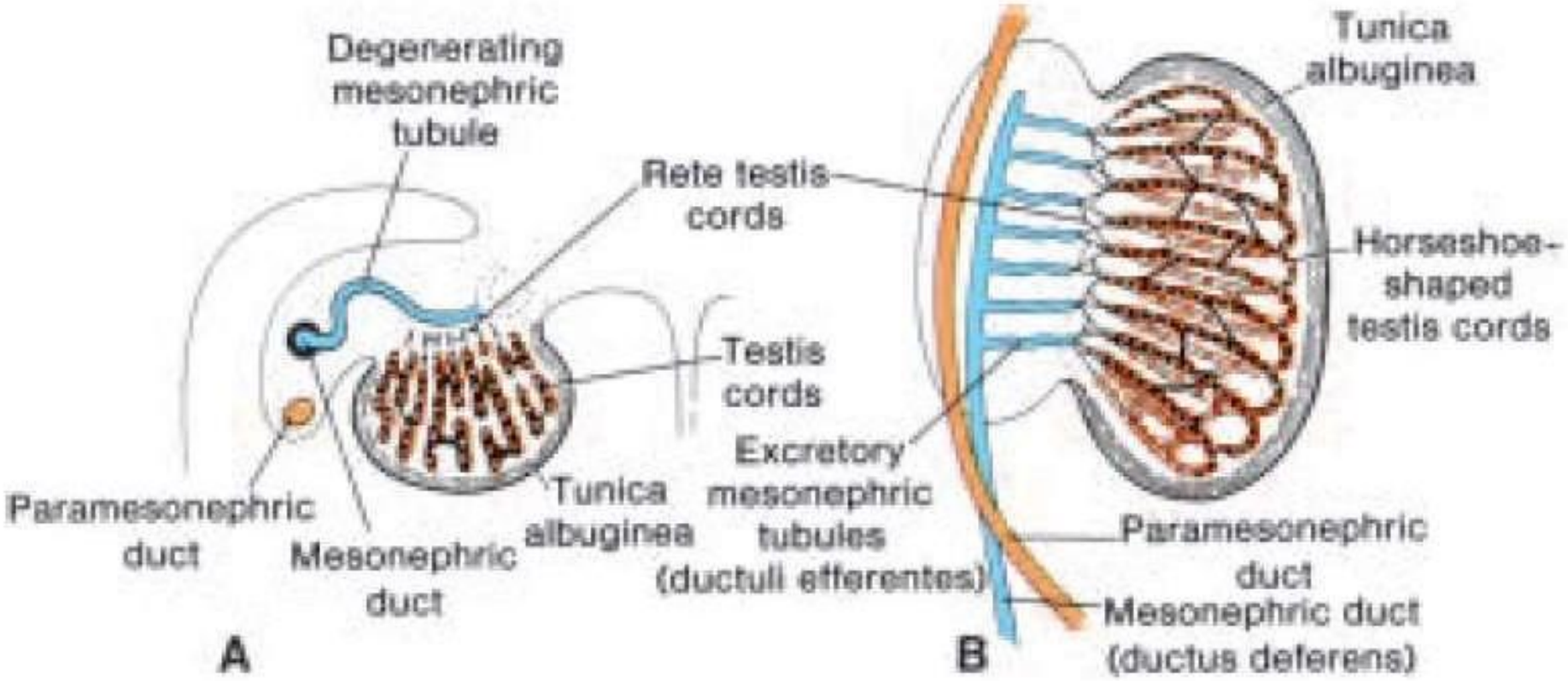
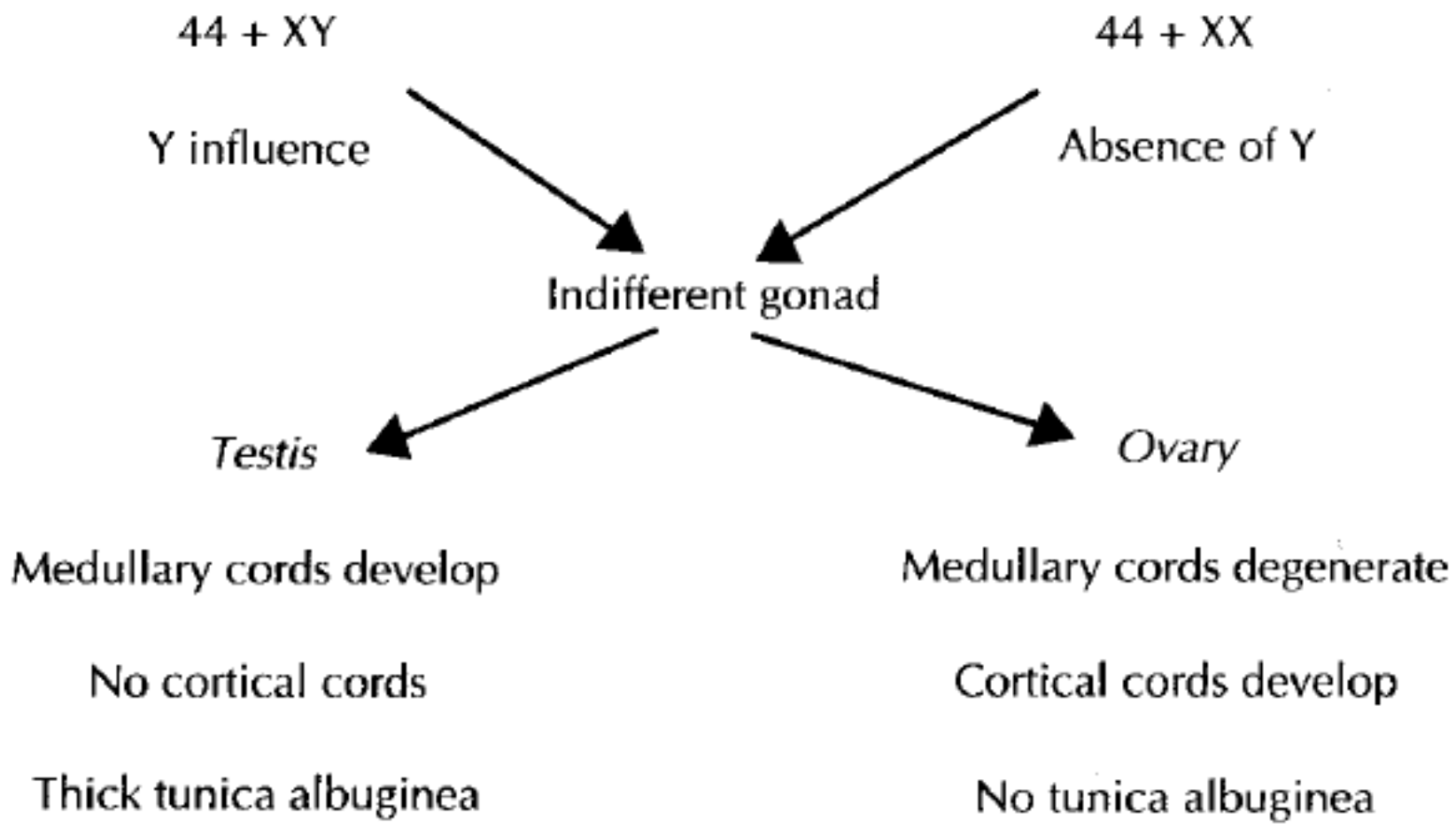


Figure 14.20 A. Transverse section through the testis in the eighth week, showing the tunica albuginea, testis cords, rete testis, and primordial germ cells. The glomerulus and Bowman's capsule of the mesonephric excretory tubule are degenerating. **B.** Testis and genital duct in the fourth month. The horseshoe-shaped testis cords are continuous with the rete testis cords. Note the ductuli efferentes (excretory mesonephric tubules), which enter the mesonephric duct.

- By the eighth week of gestation, Leydig cells begin production of **testosterone** and the testis is able to influence sexual differentiation of the genital ducts and external genitalia.
- Testis cords remain solid until puberty, when they acquire a lumen, thus forming the **seminiferous tubules.**

Influence of primordial germ cells on indifferent gonad



Ovary

- In female embryos with an XX sex chromosome complement and no Y chromosome, primitive sex cords dissociate into irregular cell clusters.

- These clusters, containing groups of primitive germ cells occupy the medullary part of the ovary. Later they disappear and are replaced by a vascular stroma that forms the **ovarian medulla.**

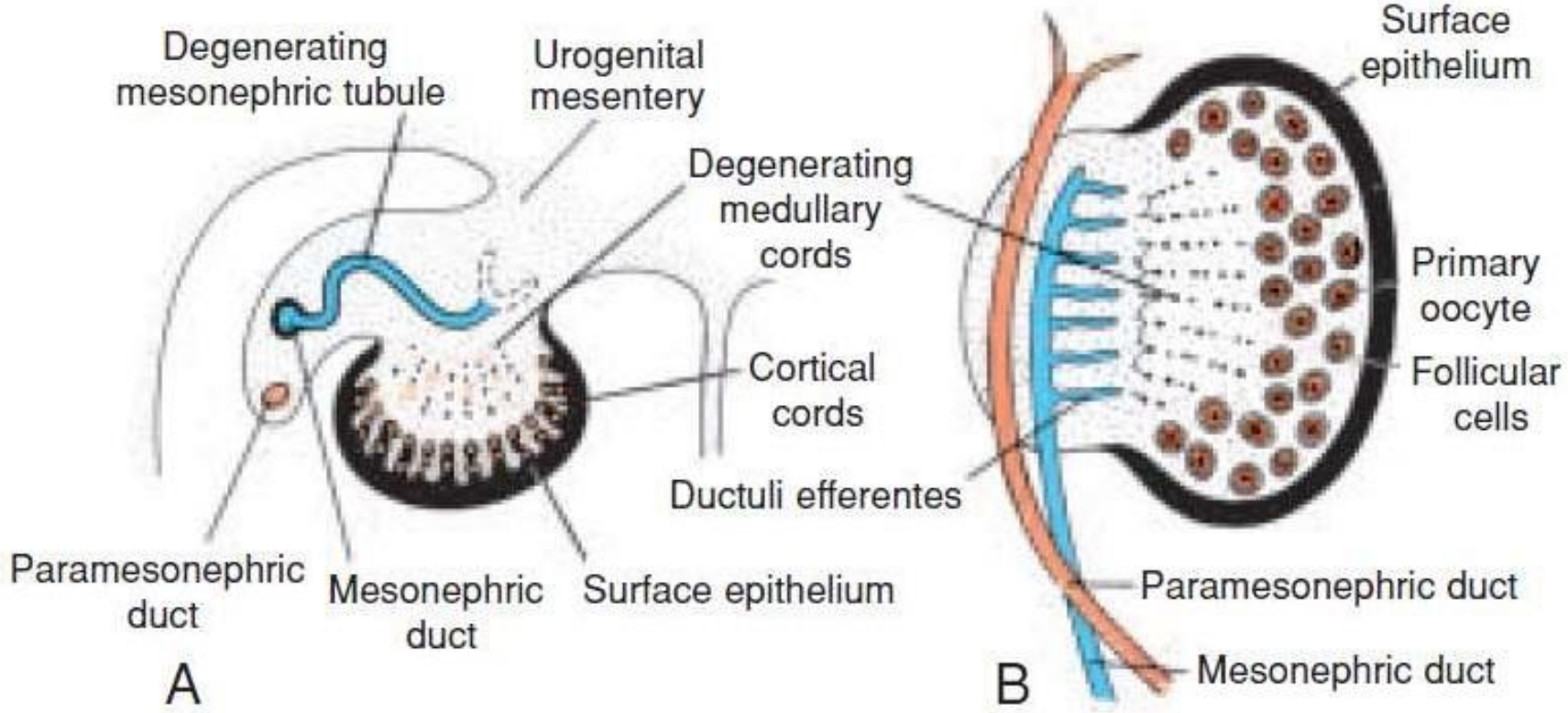
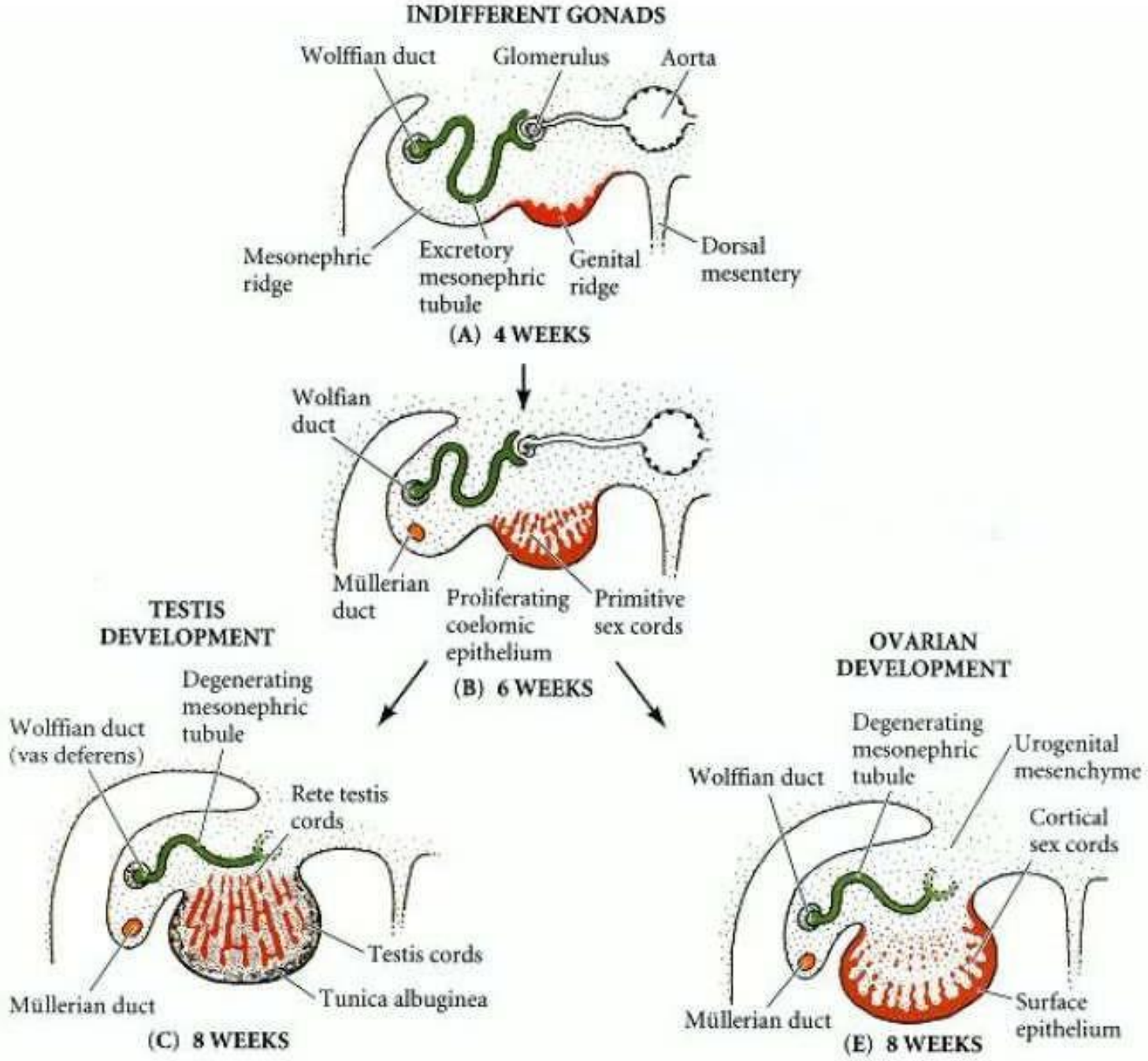
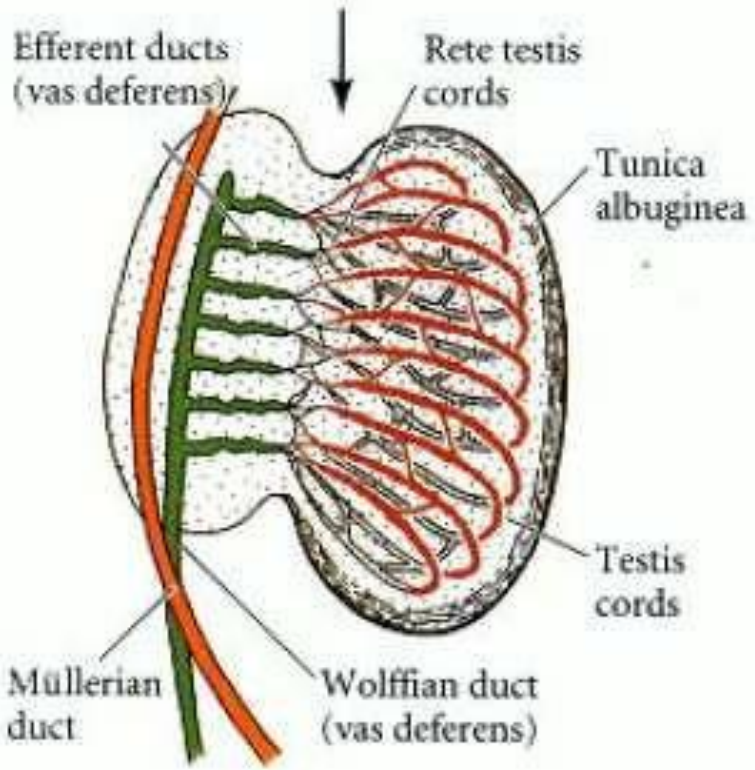


Figure 14.22 A. Transverse section of the ovary at the seventh week, showing degeneration of the primitive (medullary) sex cords and formation of the cortical cords. **B.** Ovary and genital ducts in the fifth month. Note degeneration of the medullary cords. The excretory mesonephric tubules (efferent ductules) do not communicate with the rete. The cortical zone of the ovary contains groups of oogonia surrounded by follicular cells.

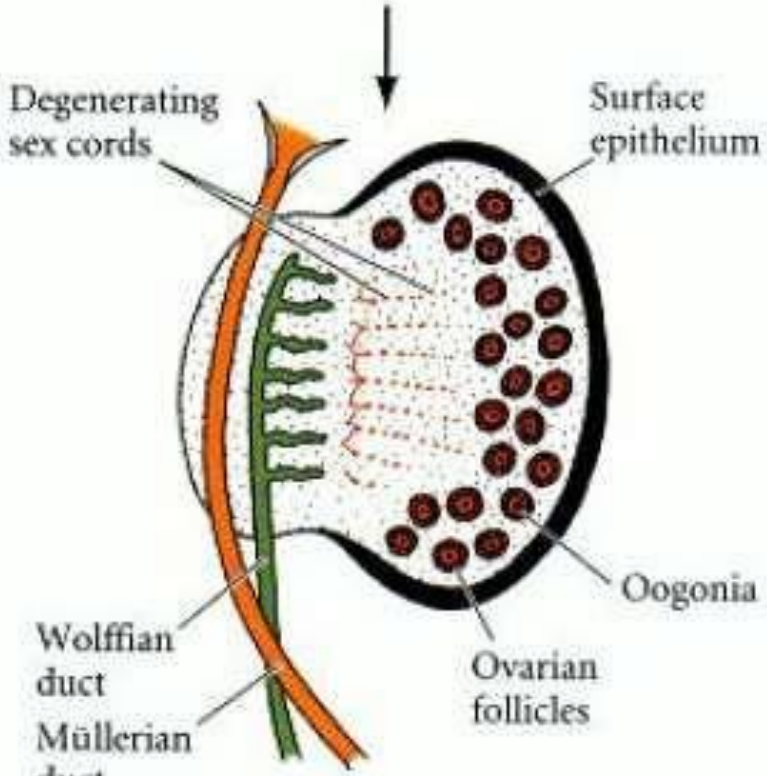
- The surface epithelium of the female gonad, unlike that of the male, continues to proliferate. In the seventh week, it gives rise to a second generation of cords, **cortical cords.**
- It penetrates underlying mesenchyme but close to the surface.
- In the fourth month, these cords split into isolated cell clusters, with each surrounding one or more primitive germ cells.
- Germ cells subsequently develop into oogonia, and the surrounding epithelial cells, descendants of the surface epithelium, form **follicular cells**

- It may thus be stated that the genetic sex of an embryo is determined at the time of fertilization, depending on whether the spermatocyte carries an X or a Y chromosome.
- In embryos with an XX sex chromosome configuration, medullary cords of the gonad regress, and a secondary generation of cortical cords develops
- In embryos with an XY sex chromosome complex, medullary cords develop into testis cords, and secondary cortical cords fail to develop.


INDIFFERENT GONADS
Wolffian duct
Glomerulus
Aorta
Mesonephric ridge
Excretory mesonephric tubule
Genital ridge
Dorsal mesentery
(A) 4 WEEKS
Wolfian duct
Müllerian duct
Proliferating coelomic epithelium
Primitive sex cords
(B) 6 WEEKS
TESTIS DEVELOPMENT
Degenerating mesonephric tubule
Wolffian duct (vas deferens)
Rete testis cords
Testis cords
Müllerian duct
Tunica albuginea
(C) 8 WEEKS
OVARIAN DEVELOPMENT
Degenerating mesonephric tubule
Urogenital mesenchyme
Wolffian duct
Cortical sex cords
Müllerian duct
Surface epithelium
(E) 8 WEEKS



(D) 16 WEEKS



(F) 20 WEEKS