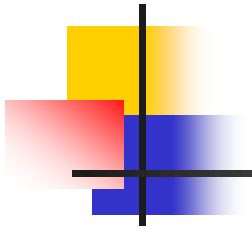
Urogenital Module

Dr. Gamal Taha Abdelhady
Assistant Professor of Anatomy & Embryology

Embryology of the UGS – Part 2



GENITAL SYSTEM

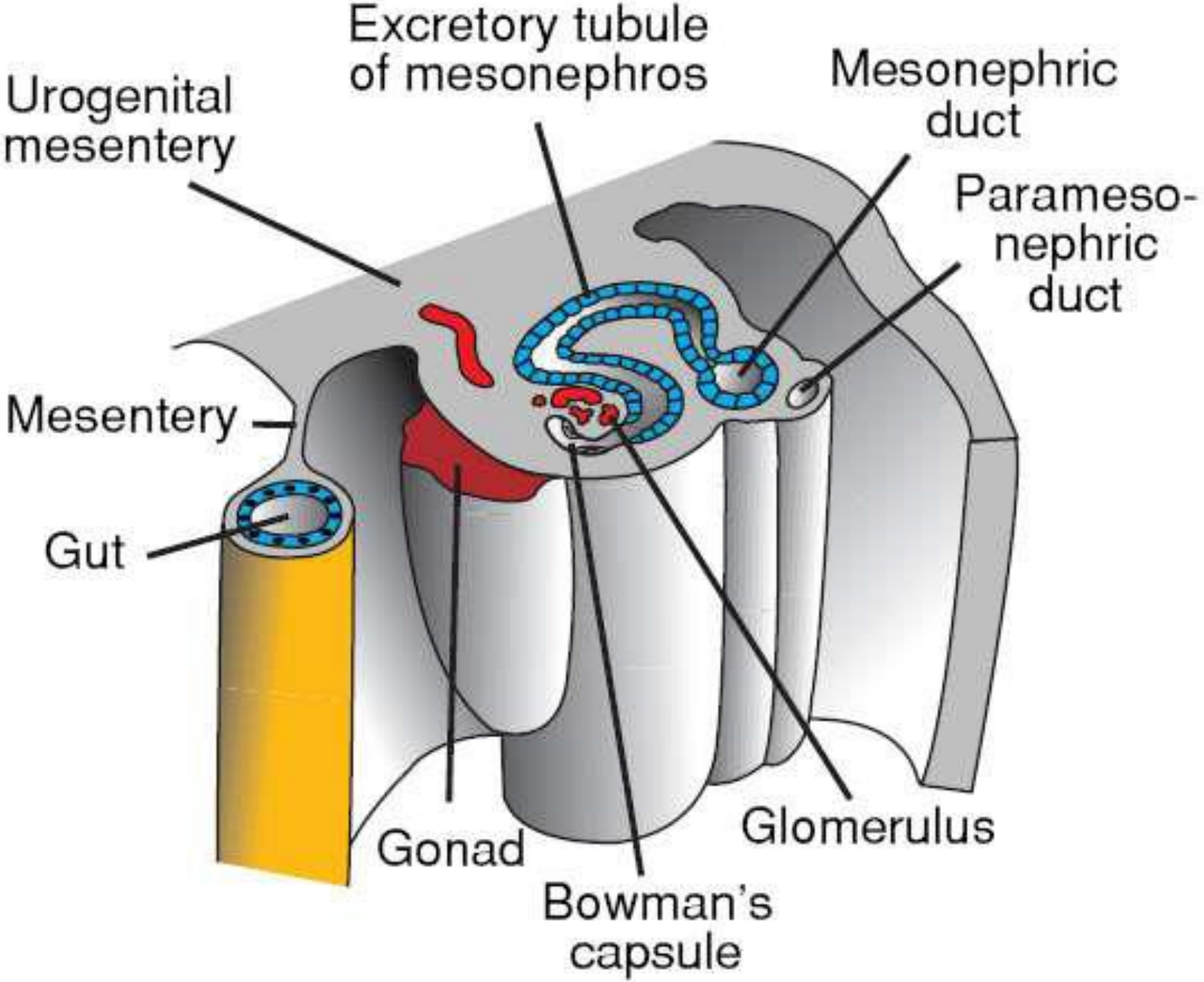
UGS Development

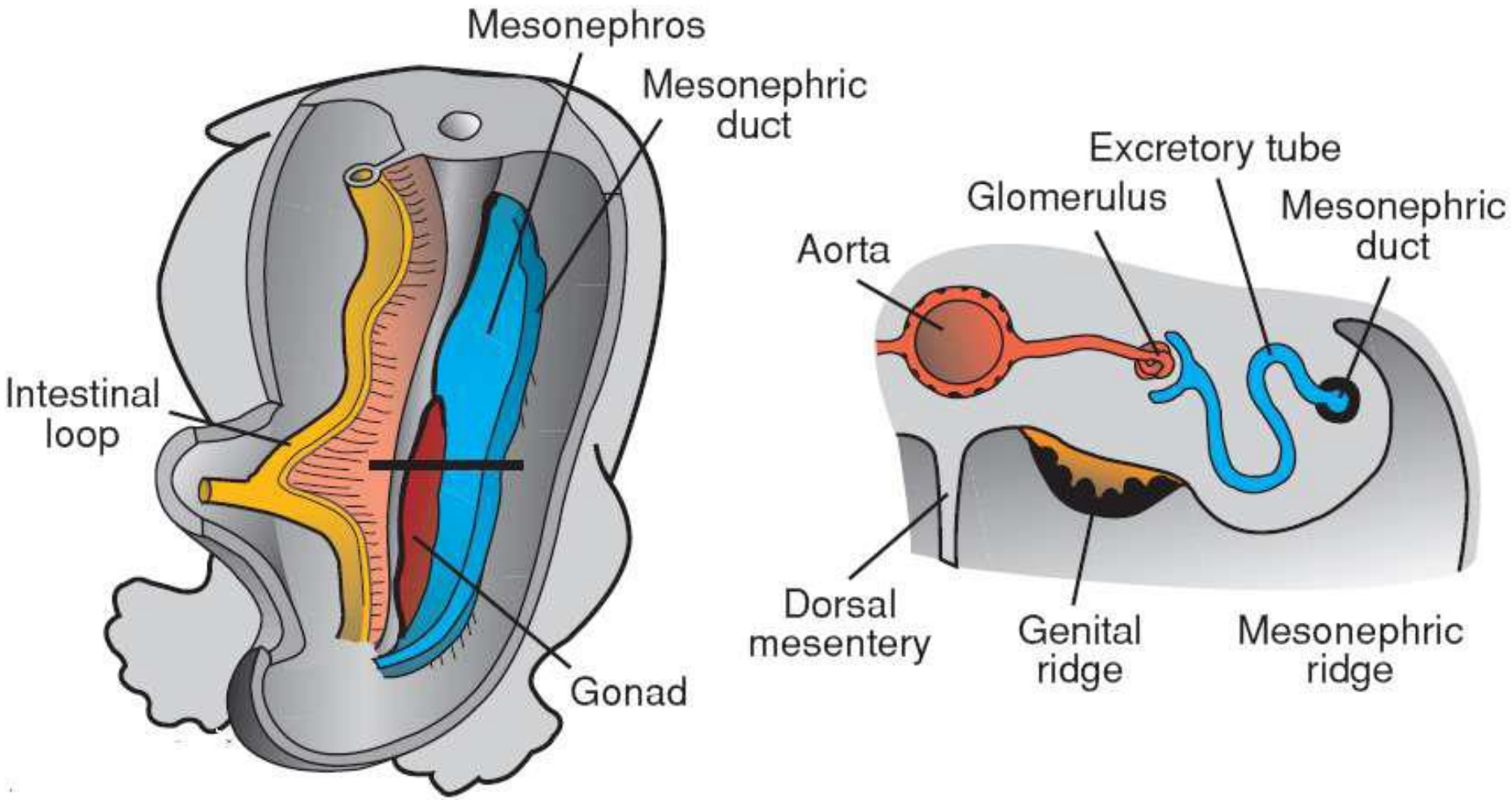
- **By the end of this session, you should be able to:**

1. Identify the different steps and components that will eventually lead to formation of the urogenital tract in both sexes

Gonads

- The sex of the embryo is determined at the time of fertilization
- The gonads acquire male or female morphology in **the seventh week** of development.
- Gonads appear initially as a pair of longitudinal ridges, the **genital or gonadal ridges (*Part of urogenital ridge*).**
- **Germ cells appear in** the genital ridges in the **sixth week** of development

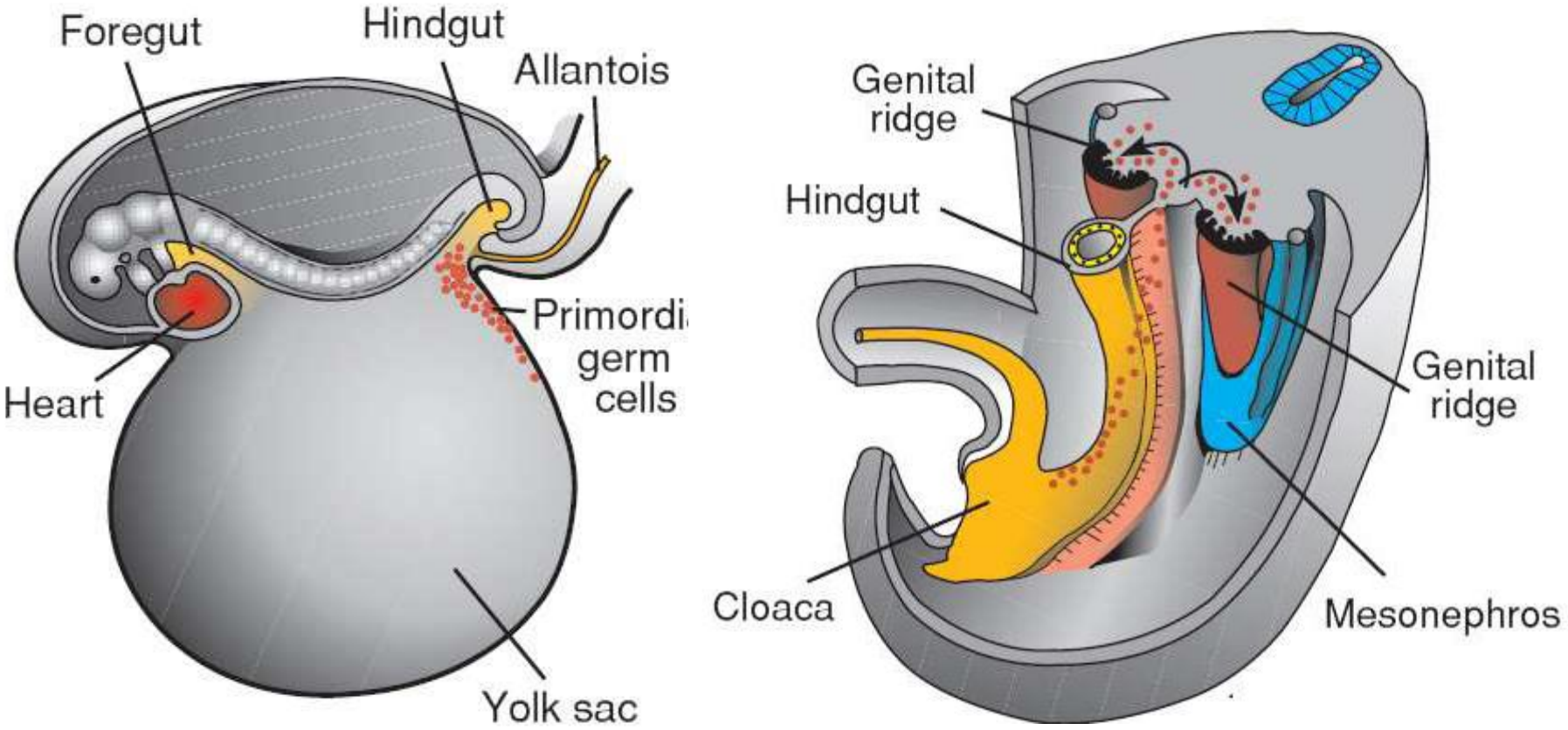

Excretory tubule
of mesonephros
Urogenital
mesentery
Mesonephric
duct
Parameso-
nephric
duct
Mesentery
Gut
Gonad
Glomerulus
Bowman's
capsule


Mesonephros
Mesonephric duct
Intestinal loop
Gonad
Excretory tube
Glomerulus
Mesonephric duct
Aorta
Dorsal mesentery
Genital ridge
Mesonephric ridge

Germ Cell Formation/Migration

- At 3-week-old embryo showing the ***primordial germ cells*** in the ***wall*** of the ***yolk sac close*** to the attachment of the ***allantois***

- ***Migration path*** of the primordial germ cells ***along*** the ***wall*** of the ***hindgut*** and the dorsal ***mesentery into*** the ***genital ridge***


Foregut
Hindgut
Allantois
Heart
Primordi
germ
cells
Yolk sac
Genital
ridge
Hindgut
Genital
ridge
Cloaca
Mesonephros

Development of the Gonads

- ***During 5th week:*** gonadal development occurs.
- ***Until 7th week:*** gonads are similar in both sexes.
- ***Gonads are derived from 3 sources:***

1. Mesothelium (mesodermal epithelium lining the coelomic cavity – ***Future Peritoneum***)
2. Underlying mesenchyme (***Future connective tissue***)
3. Primordial germ cells

Indifferent Gonads

Gonadal ridge:

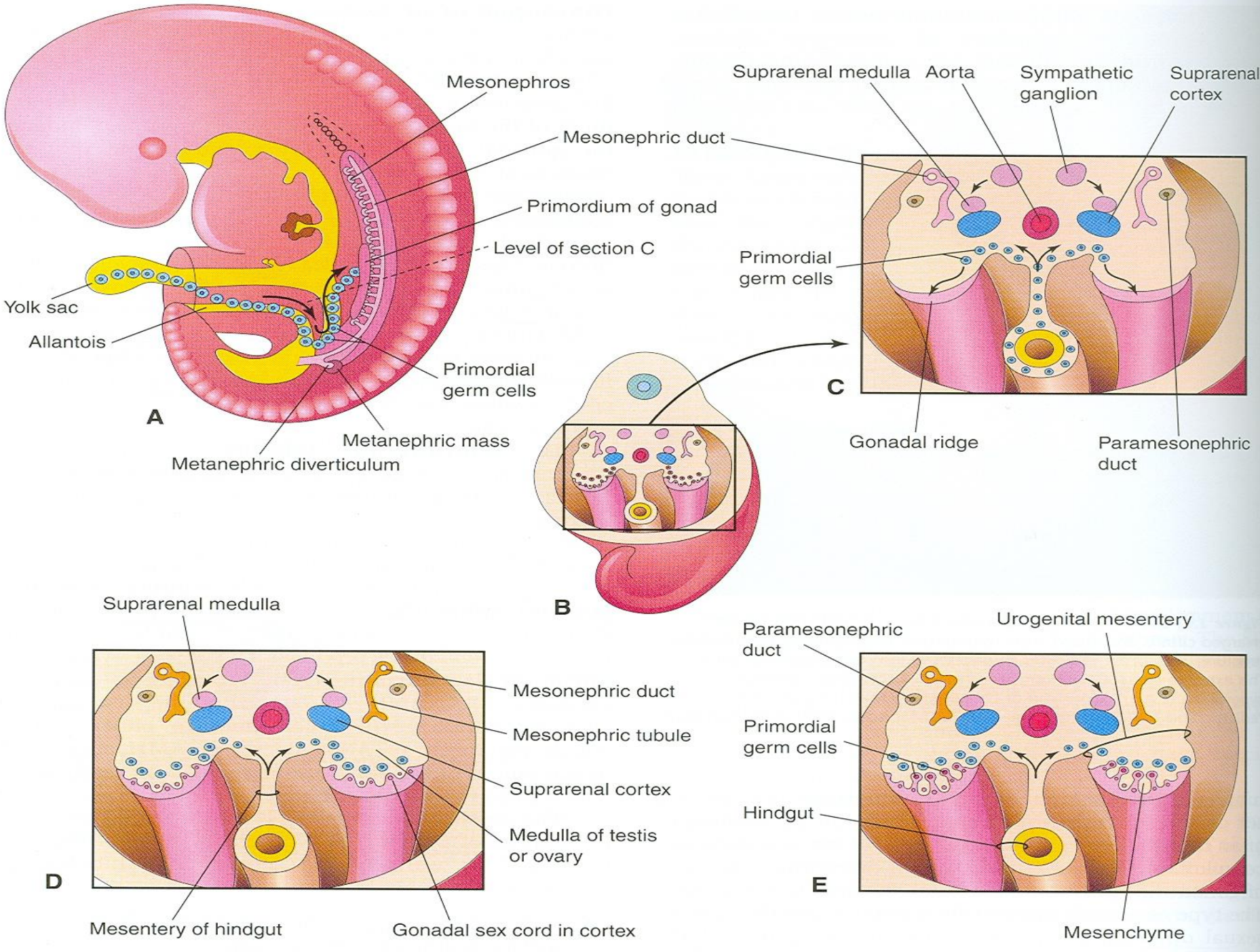
- **A bulge on the medial side of mesonephros produced by:**

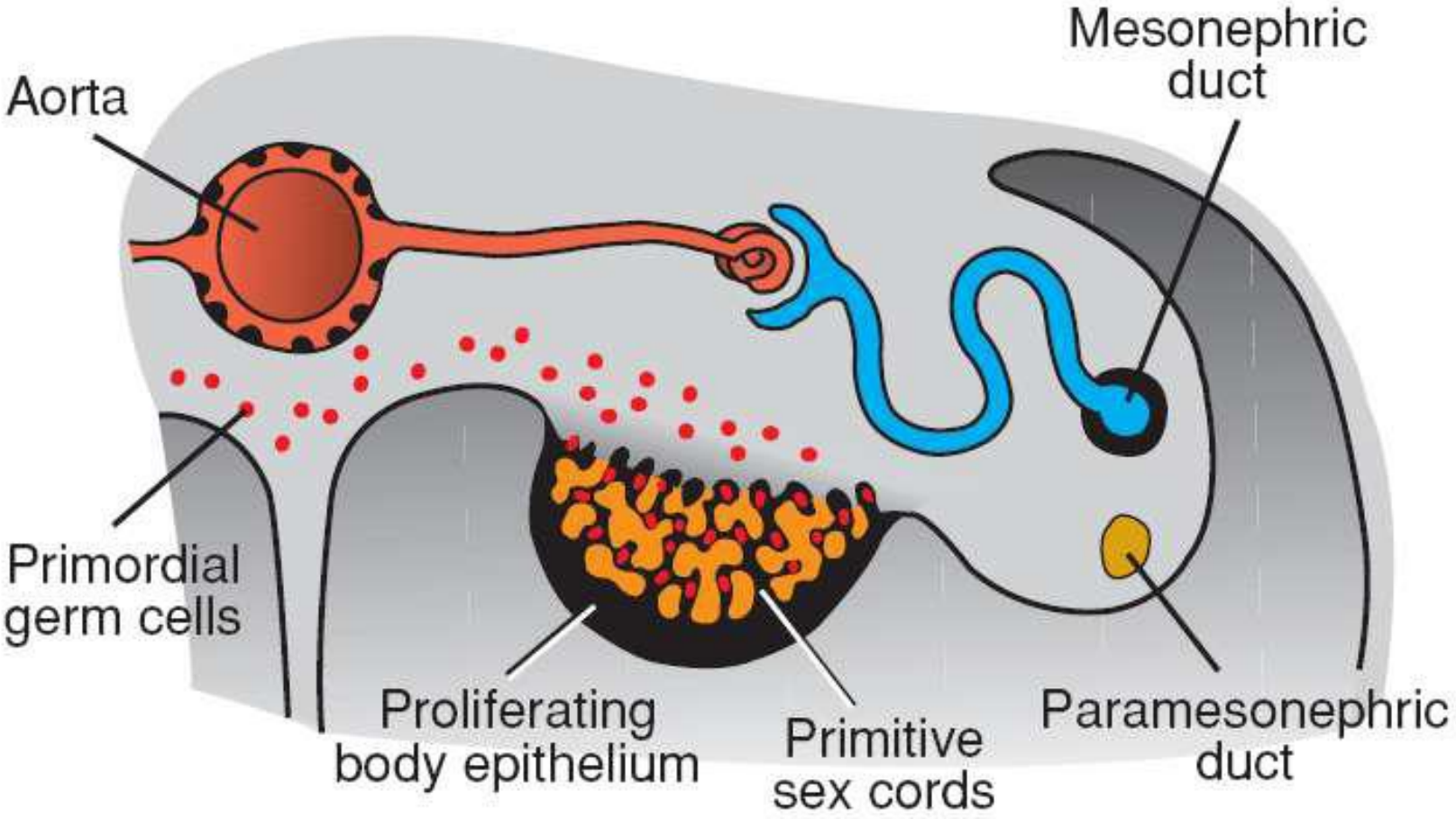
1. *Proliferation of mesothelium* (***cortex***)
2. *Proliferation of mesenchyme* (***medulla***)

Germ Cell Formation/Migration

- Shortly ***before*** and ***during arrival*** of ***primordial germ cells***, the epithelium of the ***genital ridge proliferates***, and ***epithelial*** cells ***penetrate*** the ***underlying mesenchyme (cortex invades the medulla)***

- They form the **primitive sex cords.**


Mesonephros
Mesonephric duct
Primordium of gonad
Level of section C
Yolk sac
Allantois
Primordial germ cells
A
Metanephric mass
Metanephric diverticulum
B
Suprarenal medulla
Aorta
Sympathetic ganglion
Suprarenal cortex
Primordial germ cells
C
Gonadal ridge
Paramesonephric duct
Suprarenal medulla
Mesonephric duct
Mesonephric tubule
Suprarenal cortex
Medulla of testis or ovary
D
Mesentery of hindgut
Gonadal sex cord in cortex
Paramesonephric duct
Urogenital mesentery
Primordial germ cells
Hindgut
E
Mesenchyme



- Transverse section through the lumbar region of a 6-week embryo showing the indifferent gonad with the primitive sex cords.

- Some of the primordial germ cells are surrounded by cells of the primitive sex cords.

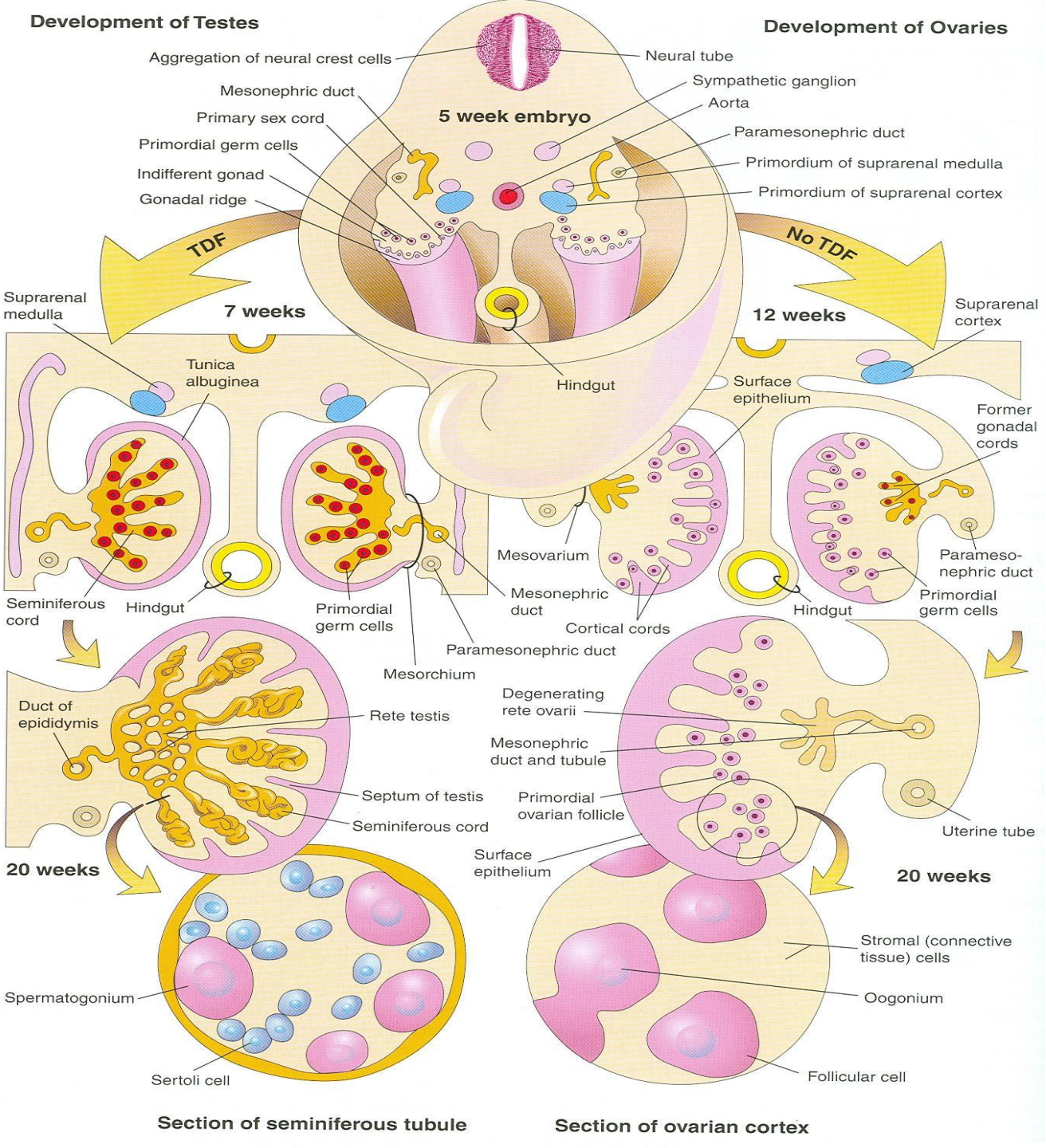
Indifferent Gonads

Gonadal (primary sex) cords:

- The proliferating mesothelial cells fuse to form cords.

Primordial germ cells:

- Endodermal cells of the yolk sac migrate along dorsal mesentery of hindgut to gonadal ridges & become incorporated into gonadal cords.


Development of Testes
Development of Ovaries
Aggregation of neural crest cells
Neural tube
Mesonephric duct
Sympathetic ganglion
Primary sex cord
Aorta
5 week embryo
Paramesonephric duct
Primordial germ cells
Primordium of suprarenal medulla
Indifferent gonad
Primordium of suprarenal cortex
Gonadal ridge
TDF
No TDF
7 weeks
12 weeks
Suprarenal medulla
Suprarenal cortex
Tunica albuginea
Hindgut
Surface epithelium
Former gonadal cords
Mesovarium
Seminiferous cord
Hindgut
Primordial germ cells
Mesonephric duct
Cortical cords
Hindgut
Paramesonephric duct
Primordial germ cells
Paramesonephric duct
Mesorchium
Duct of epididymis
Rete testis
Degenerating rete ovarii
Mesonephric duct and tubule
Septum of testis
Primordial ovarian follicle
Seminiferous cord
Uterine tube
Surface epithelium
20 weeks
20 weeks
Stromal (connective tissue) cells
Spermatogonium
Oogonium
Sertoli cell
Follicular cell
Section of seminiferous tubule
Section of ovarian cortex

Testicular Development

The Y chromosome has a ***testis-determining factor (TDS)*** that differentiates gonad into testis.

At 7th week:

1. ***Regression*** of ***cortex*** & ***differentiation*** of ***medulla*** into testis.
2. ***Gonadal sex cords*** condense & extend into medulla to form ***seminiferous cords***.
3. The characteristic feature is the development of a thick fibrous capsule (**tunica albuginea**) that separates the enlarging testis from mesonephros.

Testicular Development

- ***Seminiferous cords*** develop into: ***seminiferous tubules***

- Seminiferous tubules remain solid until puberty. Its walls are composed of:

1. ***Sertoli cells:*** derived from surface epithelium of testis *(Mesothelial cells - Cortex)*

2. ***Spermatogonia:*** derived from *primordial germ cells*

Testicular Development

- ***Sertoli cells***

Induces suppression of development of paramesonephric (***Müllerian***) duct by Müllerian inhibiting substance (***Anti-Müllerian hormone***) inhibiting formation of the female genital system (7th week)

Testicular Development

- ***Leydig's cells***

- **Derived from the original mesenchyme (medulla) of the** gonadal ridge, lie in-between the testis cords.

- Secretes testosterone (appear by the 8^{th} week)

Testicular Development

- ***They begin development shortly after onset of differentiation of these cords, inducing:***

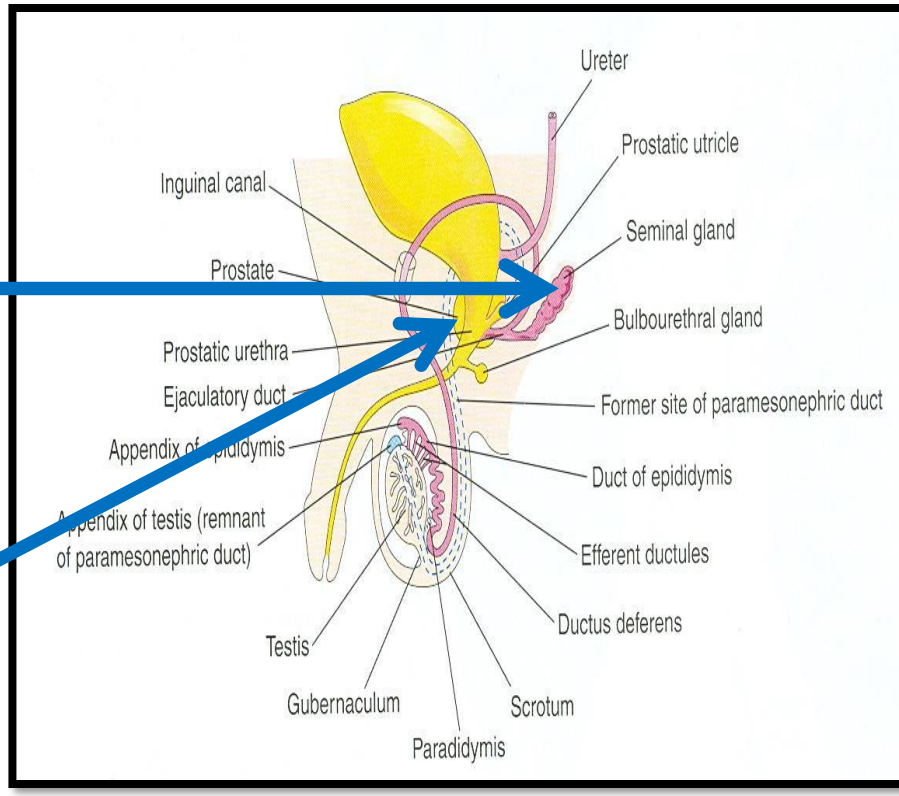
1. ***Masculine differentiation of mesonephric duct:*** epididymis, vas deferens, seminal glands, ejaculatory duct.

2. ***Masculine differentiation of external genitalia***

Testicular Development

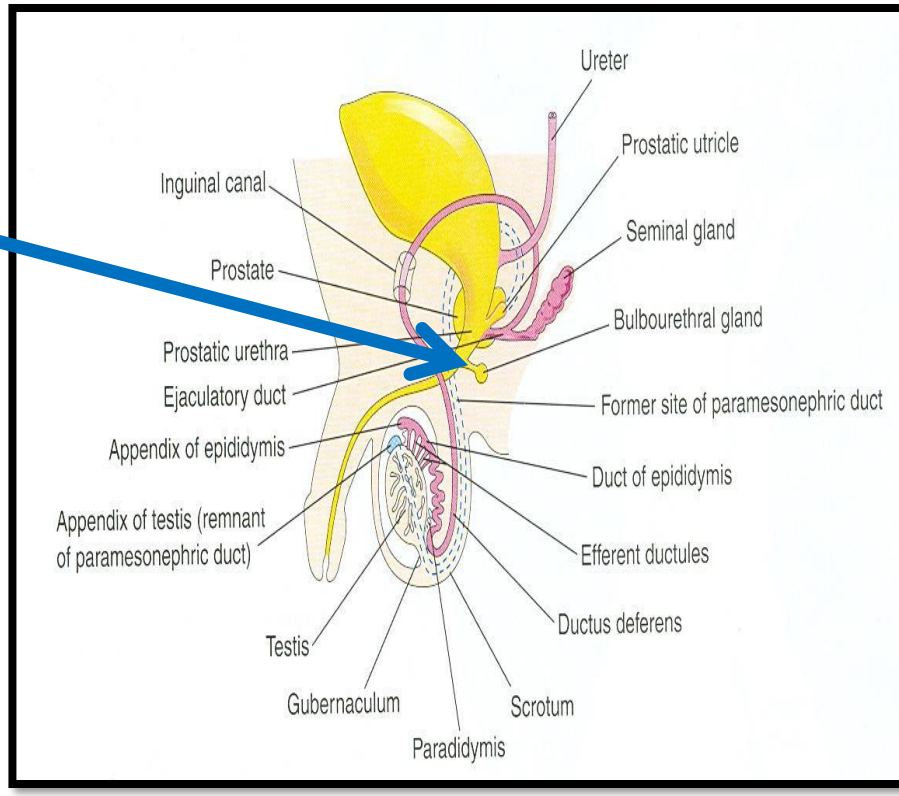
1. ***Seminal Vesicles:***
   Mesodermal outgrowth from mesonephric duct.

2. ***Prostate Gland:***
   Endodermal outgrowth from prostatic urethra.



Testicular Development

3. ***Bulbourethral Gland:*** Endodermal outgrowth from membranous urethra (***Pelvic part of Urogenital sinus***).



- Stroma & smooth muscles in 2 & 3 are derived from surrounding mesoderm

Testis

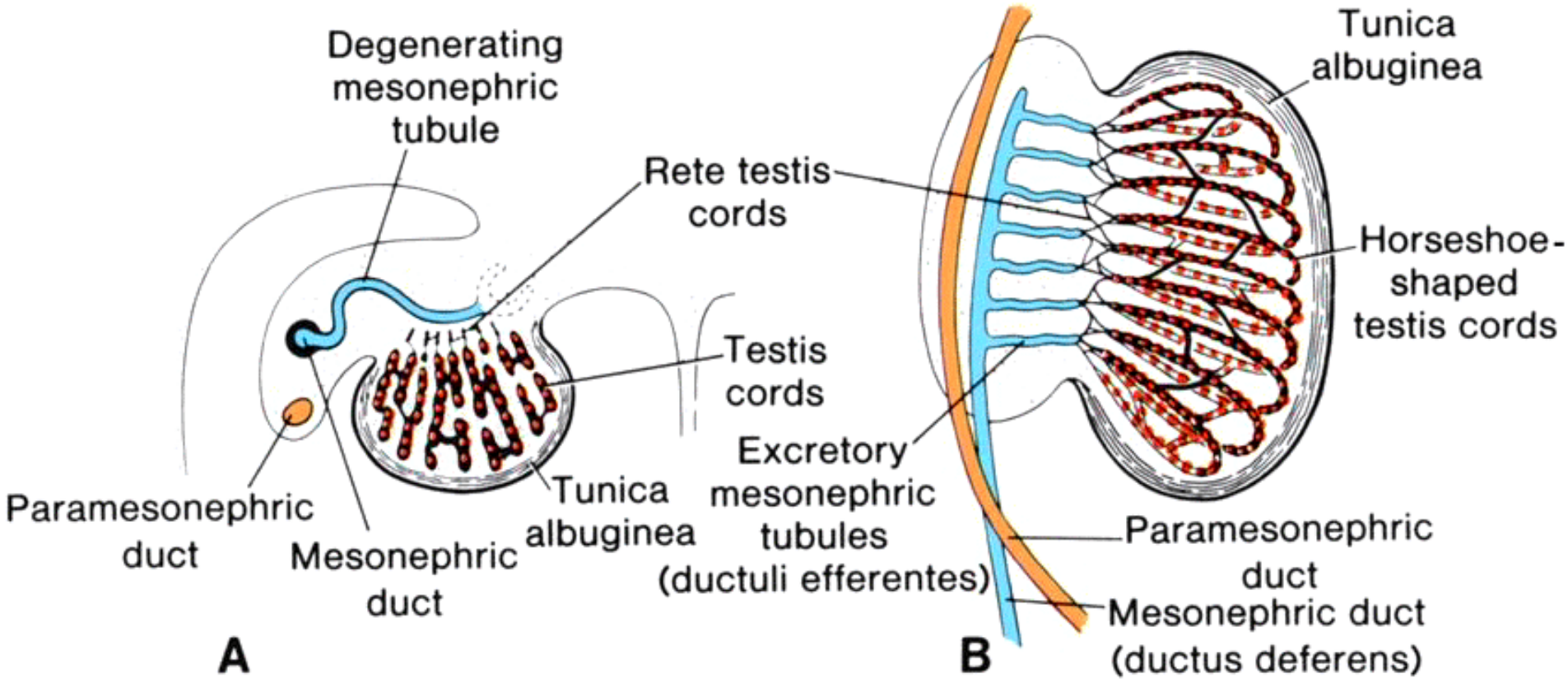
- **Toward the hilum of the gland, (distal part) break up and** become horseshoe shaped, and their extremities are continuous with network of tiny cell strands that later give rise to tubules of the **rete testis.**

Testis

- Testis cords (***proximal part***) remain solid until puberty, when they acquire a lumen, thus forming the **seminiferous tubules.**

- **Seminiferous tubules are** canalized, they join the rete testis tubules

- **Rete testis** in turn enter the **vasa efferentia**


Degenerating mesonephric tubule
Rete testis cords
Testis cords
Tunica albuginea
Paramesonephric duct
Mesonephric duct
A
Tunica albuginea
Horseshoe-shaped testis cords
Excretory mesonephric tubules (ductuli efferentes)
Paramesonephric duct
Mesonephric duct (ductus deferens)
B

Testis

- These vasa efferentia are the remaining parts of the excretory tubules of the ***mesonephric system***.

- They link the rete testis and **the mesonephric or wolffian duct**, which becomes the ***ductus deferens.***

Summary of Development

1. ***Testis:*** from medulla of genital ridge
2. ***Semineferous tubules:*** from sex cords of ridge from cortex
3. ***Sertoli cells:*** from mesothelial cells of ridge
4. ***Leydig's cells:*** from mesenchyme surrounding the tubules
5. ***Epididymis, vas deferens, seminal glands, ejaculatory duct:*** from mesonephric duct

Summary of Development

ENDODERMAL STRUCTURES

1. ***Spermotogonia:*** from primordial germ cells of yolk sac

2. ***Prostate gland:*** from prostatic urethra (**endodermal**)

3. ***Bulbourethral glands:*** from membranous urethra

Genital Ducts in Males

- As the mesonephros regresses, a few excretory tubules, the **epigenital tubules,** establish contact with cords of the rete testis and finally form the **efferent ductules of the testis.**

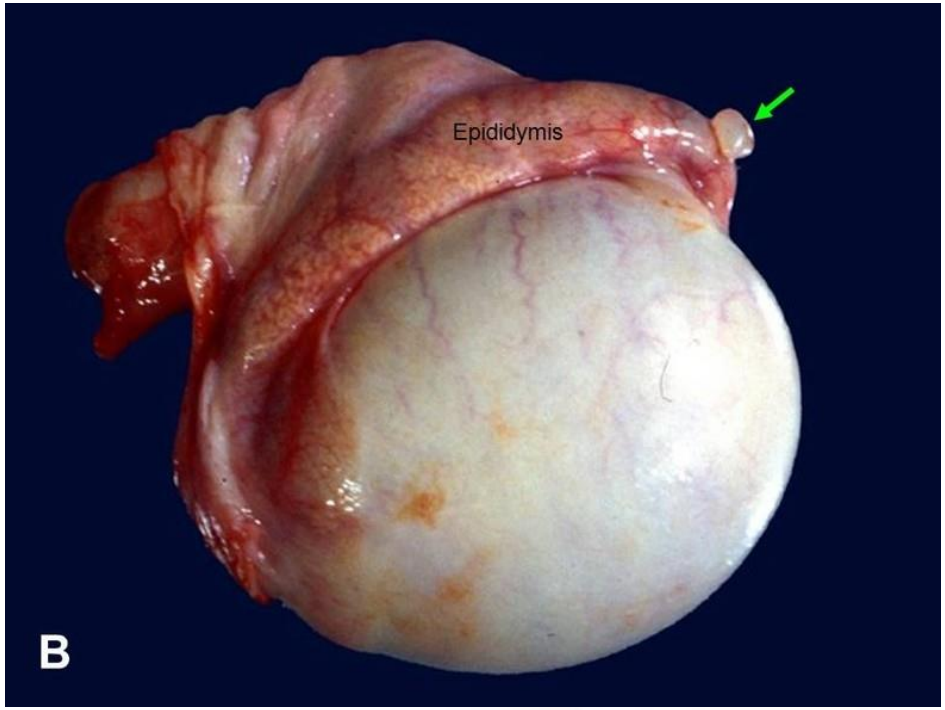
- **Excretory tubules along the caudal pole** of the testis, the **paragenital tubules, do not join the cords of the rete testis**.

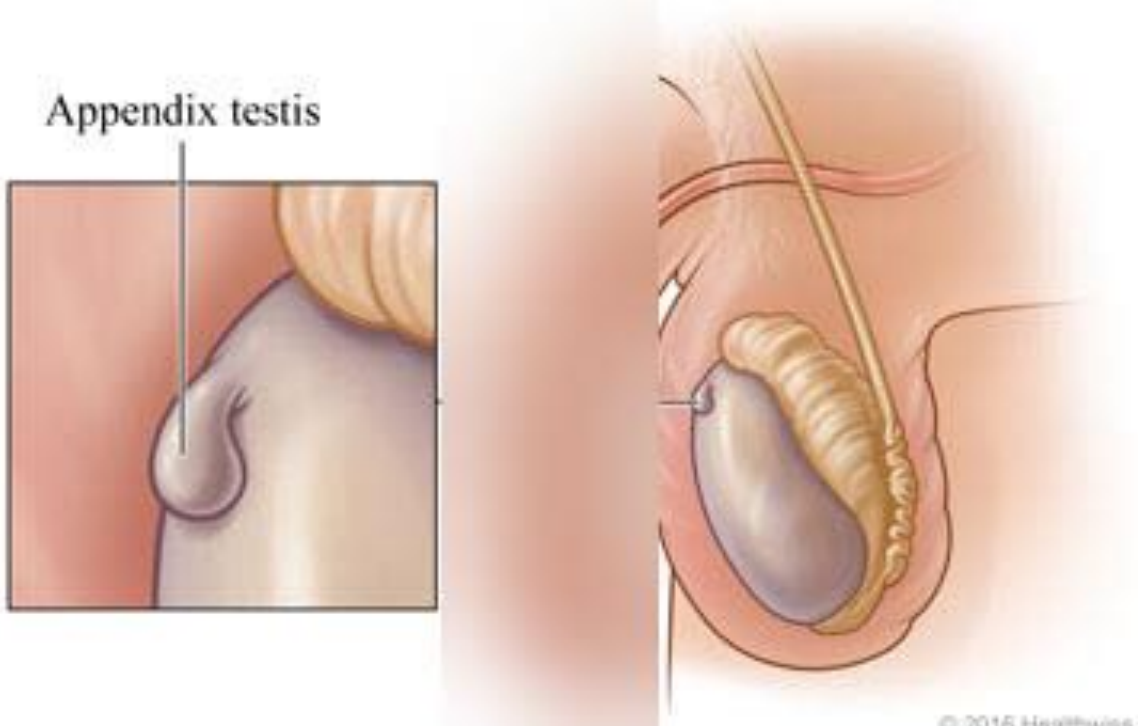
Genital Ducts in Males

- Except for the most cranial portion, **the** mesonephric ducts persist and form the main genital ducts

1. The **epididymis**
2. The **ductus deferens (Vas)**
3. **Ejaculatory duct**

- ***The paramesonephric ducts*** in the male degenerate except for a small portion at their cranial ends, the **appendix testis.**


Epididymis
B


Appendix testis

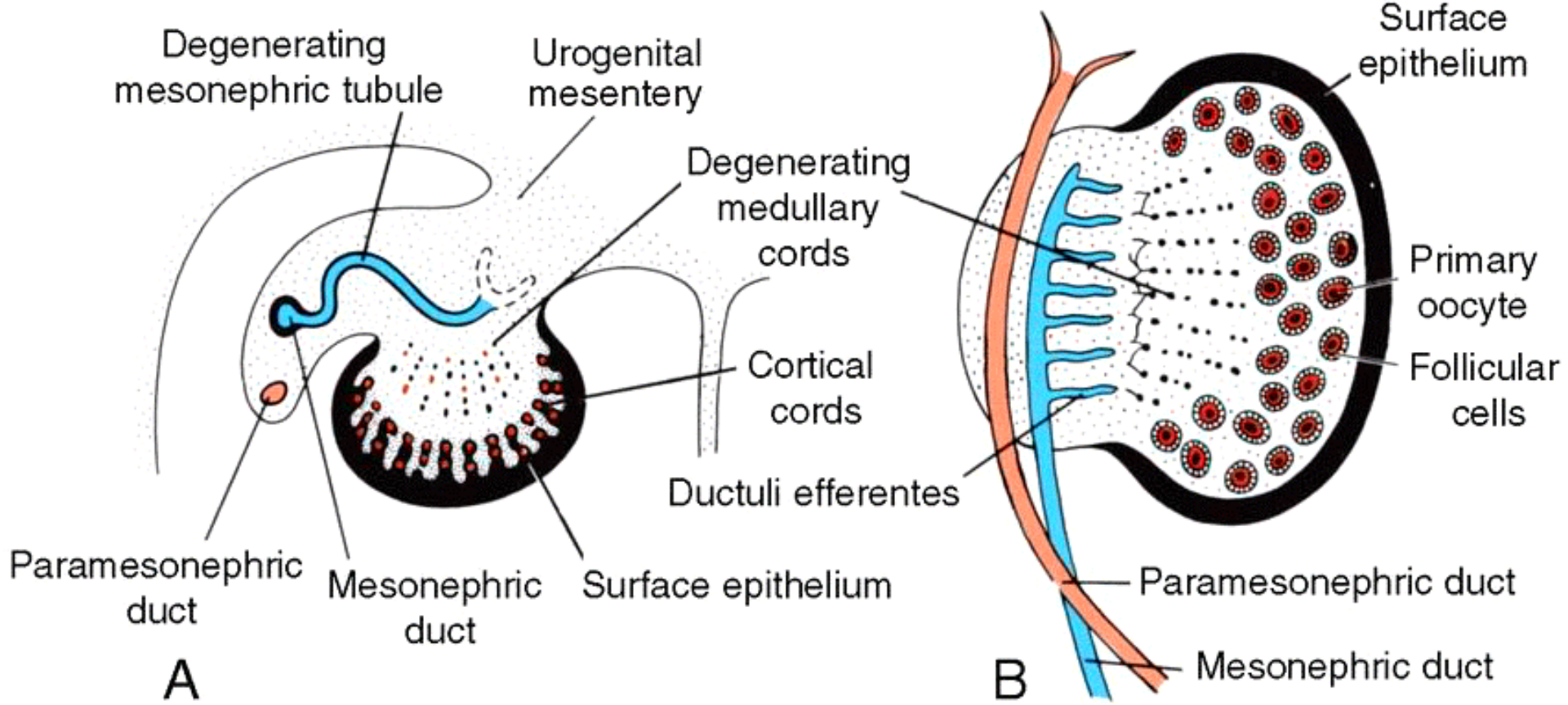
Ovary

- Development of the ovary is slower than the testis.
- The ***primitive sex cords*** break into irregular cell clusters called ***1ry or medullary cords***.
- These clusters, containing some germ cells, form a rudimentary rete ovarii, which ***disappears later*** and is ***replaced*** by a vascular stroma forming the ***ovarian medulla***.

Ovary

- The ***surface epithelium*** of the female gonad, ***unlike that of the male***, continues proliferation giving a second generation of cords, the ***2ry or cortical cords***, which remain close to the surface.

- In the fourth month these cords ***split*** into ***isolated cell clusters***, the primordial germ cells develop into ***'oogonia'***, each surrounded by cell clusters leading to a ***primordial follicle***


Degenerating mesonephric tubule
Urogenital mesentery
Degenerating medullary cords
Cortical cords
Ductuli efferentes
Paramesonephric duct
Mesonephric duct
Surface epithelium
A
Surface epithelium
Primary oocyte
Follicular cells
Paramesonephric duct
Mesonephric duct
B

Ovary

- The endodermal primordial germ cells → oogonia.
- Active mitosis → daughter oogonia (all oogonia are formed prenatally however, many degenerate before birth).
- The two million or so that remain enlarge primary oocytes.

1.Mesonephric duct (Wolff) atrophying

2.Primordial follicle in the ovarian cortex containing primary Oocyte

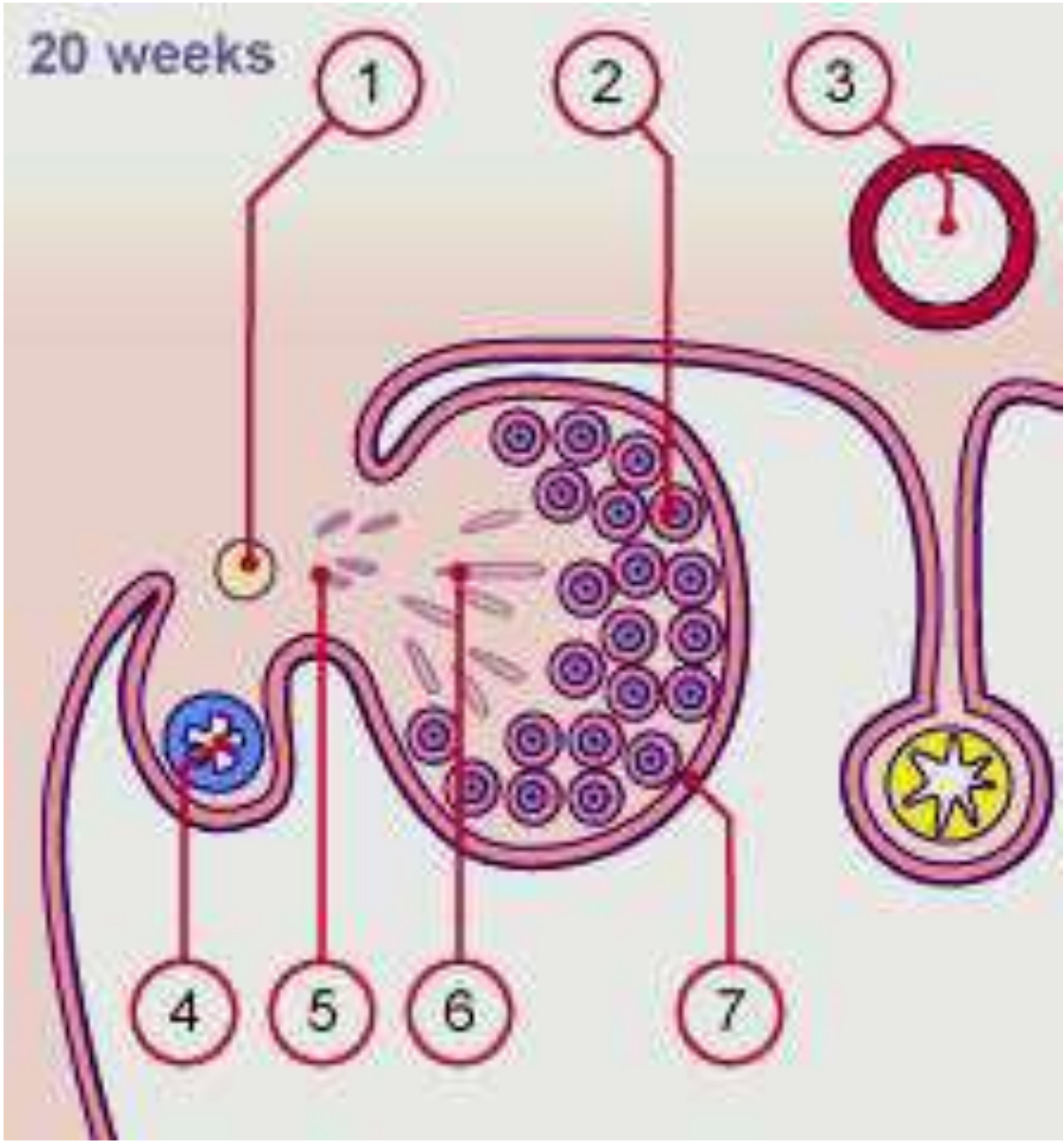
3.Aorta

4.Paramesonephric duct (Müller)

5.Mesonephric tubules atrophying

6.Degenerated Gonadal cords (ovarian medulla)

7.Mesothelium of the ovary



Ovary

- The surrounding mesodermal cells, derived from the surface epithelium → gives off the follicular cells.

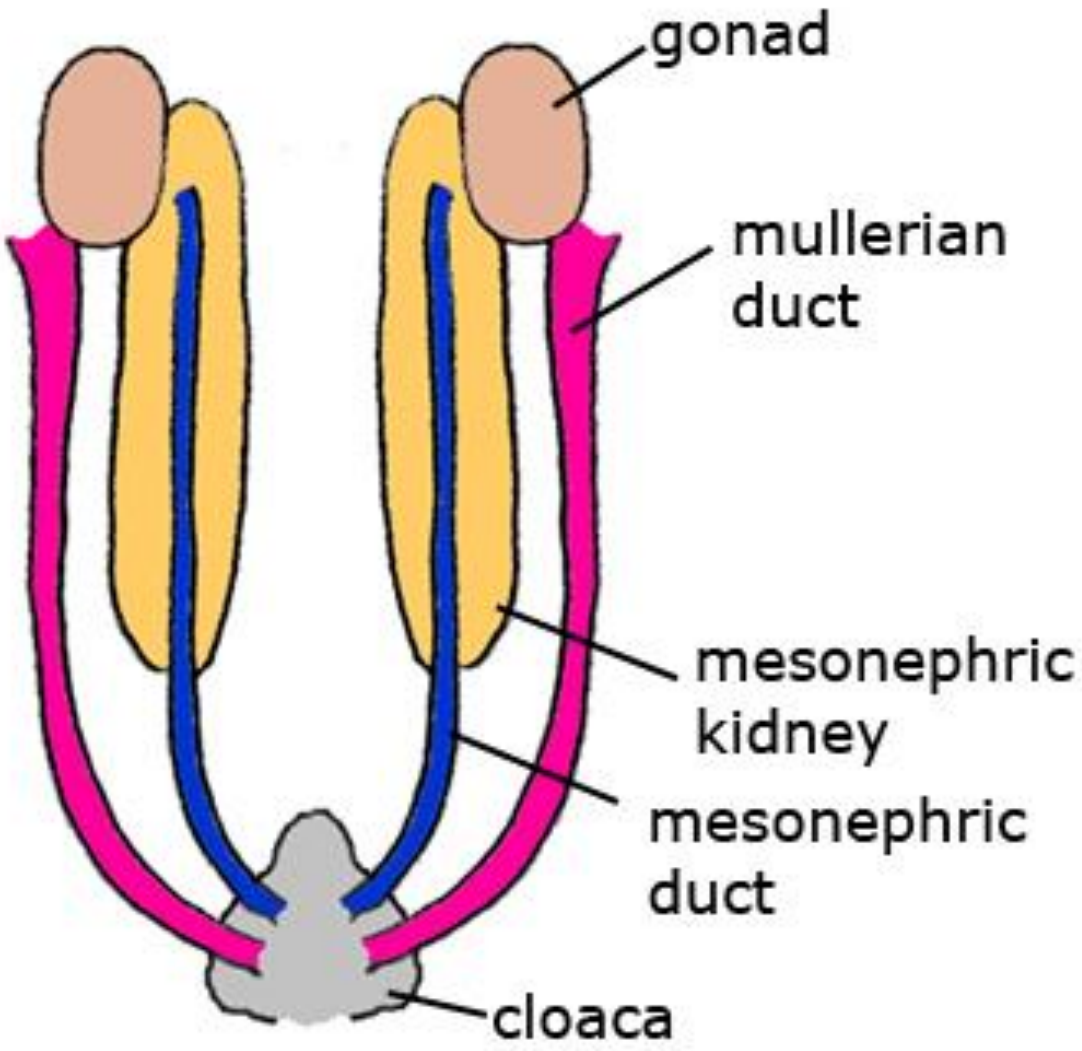
- After birth, the surface epithelium flattens to a single layer of cells → the "germinal epithelium", forming a thin, fibrous capsule, the tunica albuginea & separates the surface

Development of the Uterus & Fallopian tubes

- ***PARAMESONEPHRIC / MULLERIAN DUCTS leads to the formation of:***

1. Fallopian tubes
2. Uterus
3. Fundus
4. Body
5. Cervix
6. Vaginal fornixes

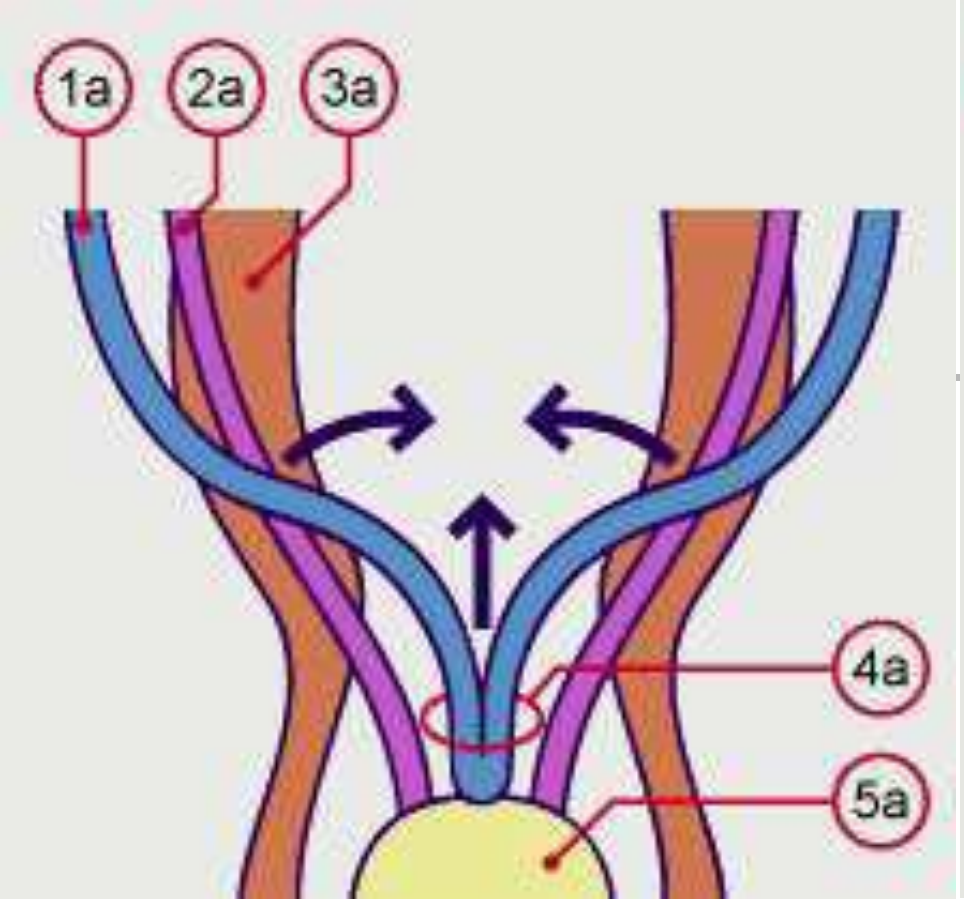
Basic embryonic urogenital system

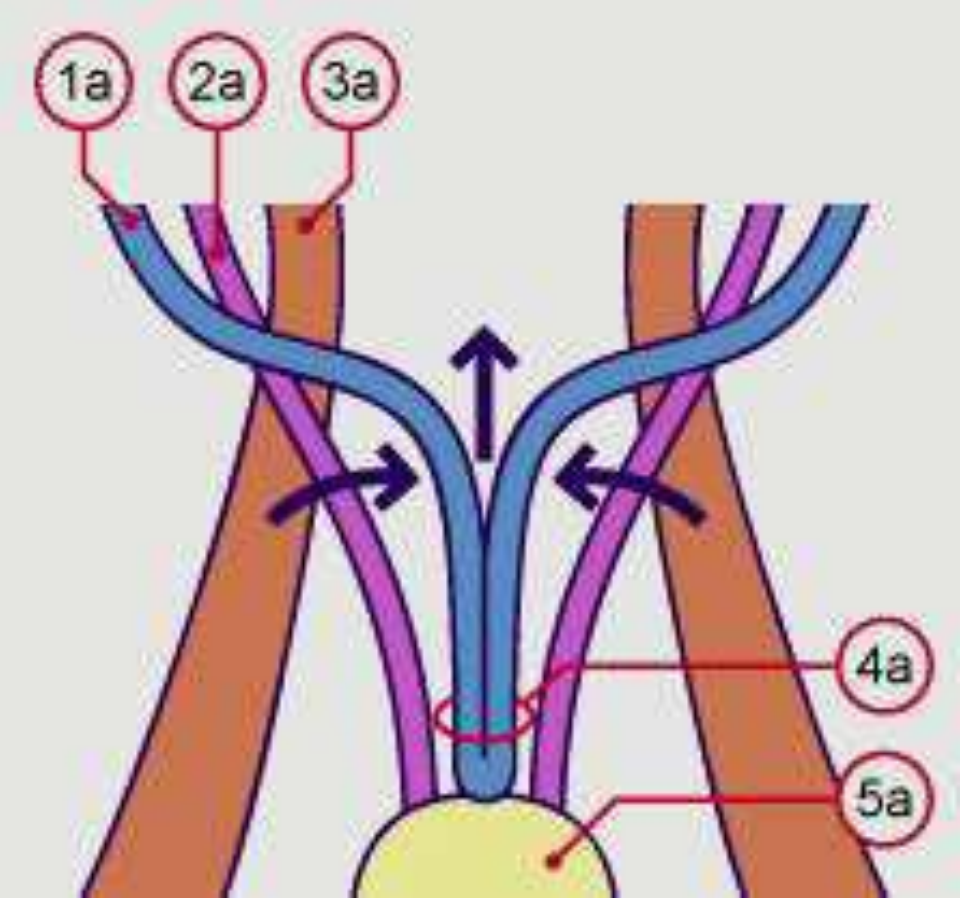


Development of the Uterus & Fallopian tubes

- ***Initially three parts of the Paramesonephric duct are recognizable:***

1. ***Cranial vertical*** part which ***opens*** with in the ***coelomic cavity***.
2. ***Mid horizontal*** part which ***crosses*** the ***mesonephric duct***.
3. ***Caudal vertical*** part which ***fuses*** in the ***midline*** with its partner from the opposite side.





- **1a. Paramesonephric duct (Müller)**
- **2a. Mesonephric duct (Wolff)**
- **3a. Lower gubernaculum,**
- **4a. Utero-vaginal canal,**
- **5a. Urogenital sinus**

Formation of the Fallopian Tubes & Uterus

- With the descent of ovaries into the pelvic inlet, the ***first two parts*** of the ***duct*** on each side will develop into the ***Fallopian/Uterine tube.***

- The ***caudal fused parts*** will become the ***Uterine canal***.

Formation of the Fallopian Tubes & Uterus

- The ***fused paramesonephric*** ducts will give rise to the ***fundus***, ***body***, and ***cervix*** of the uterus as well as the ***upper part*** of the ***vagina***.

- The surrounding mesenchyme will form the ***'myometrium' & 'perimetrium'***.

1b. Fallopian tube

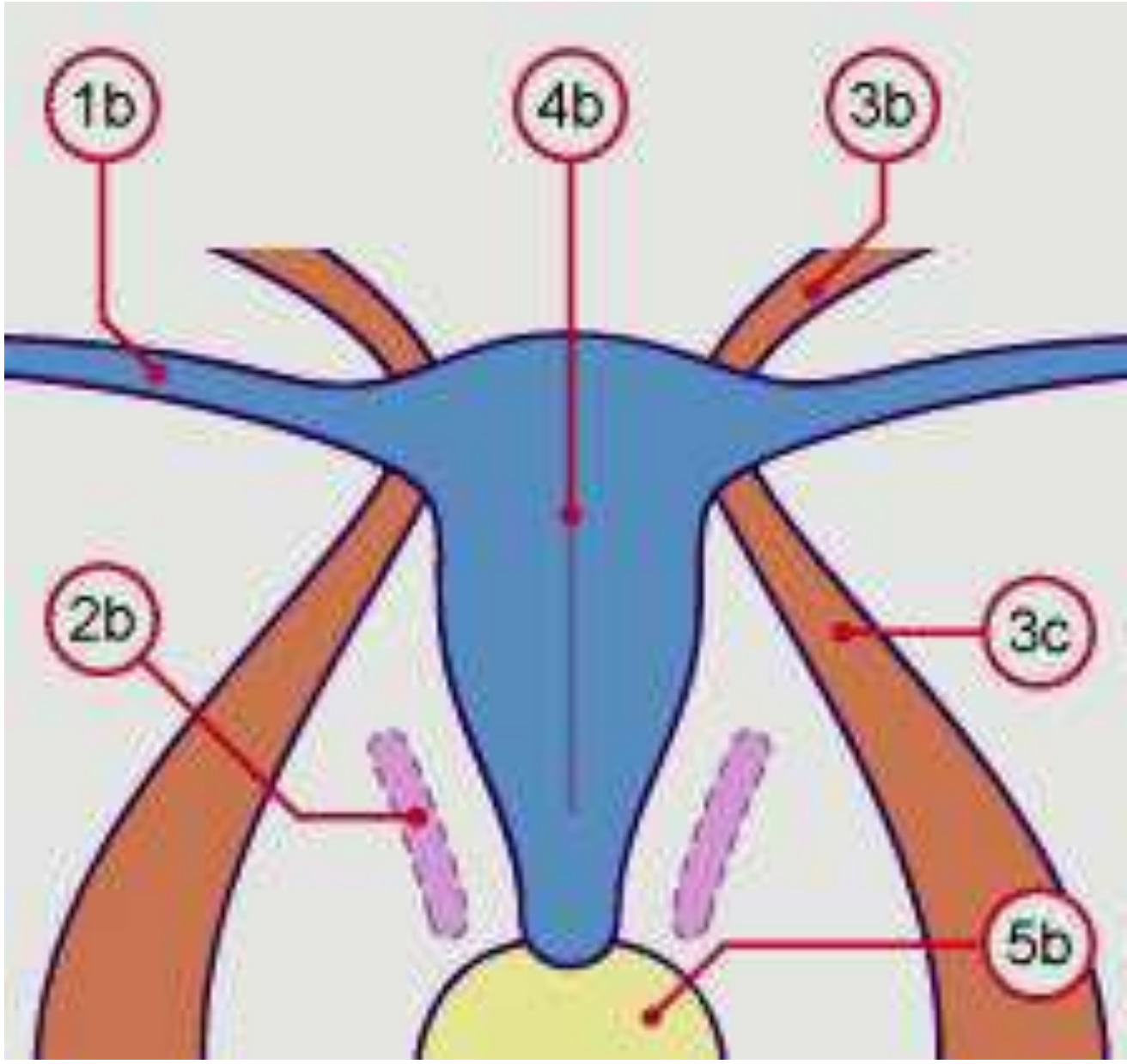
2b. Atrophied mesonephric duct

3b. Ovarian ligament

3c. Round ligament of uterus

4b. Uterus

5b. Vagina

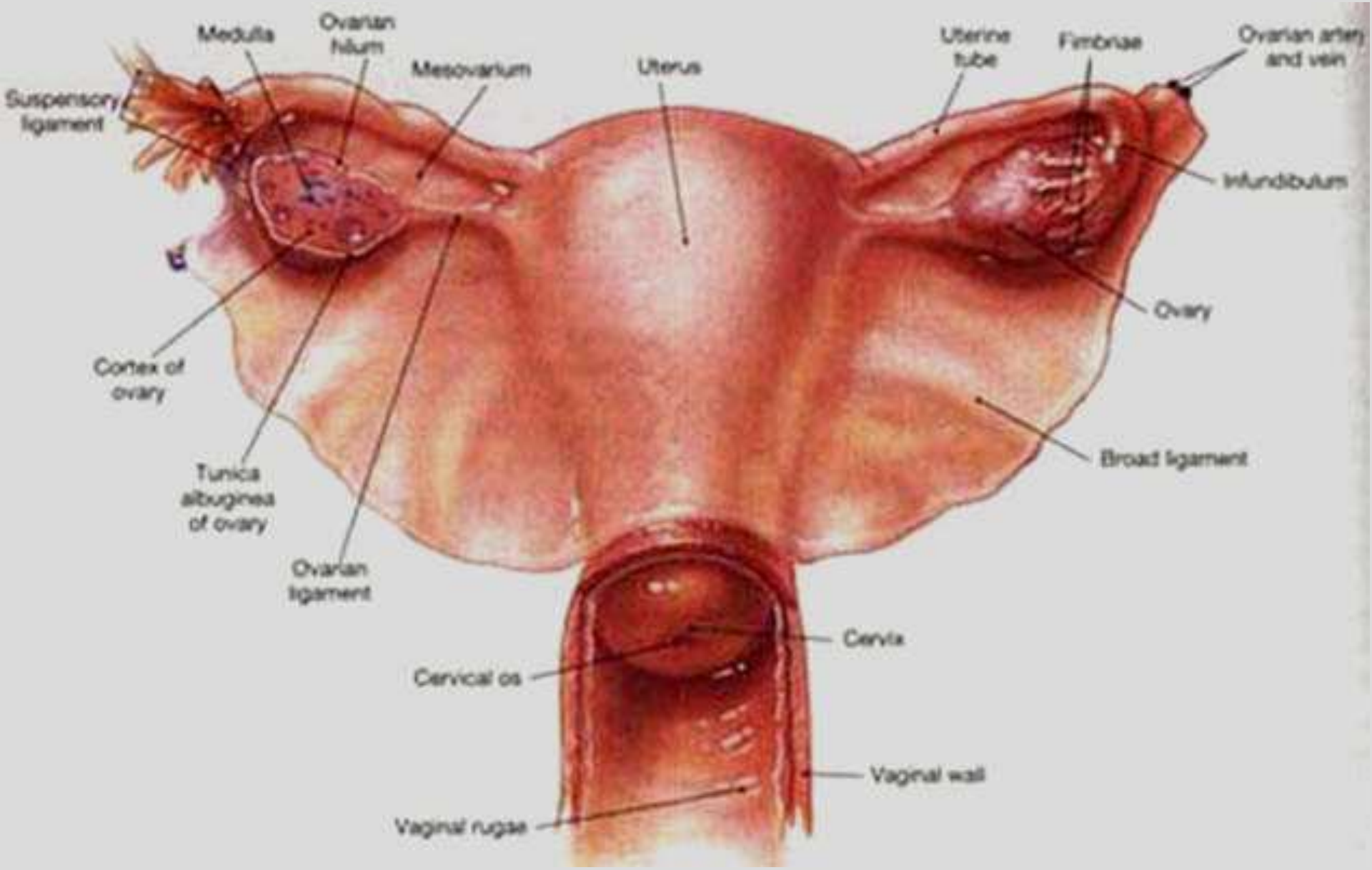


Formation of Broad Ligament of Uterus

- As the 2 paramesonephric ducts fuse in the midline, a broad transverse peritoneal fold establishes on each side, ***the Broad Ligament***.

- Each ligament extends from the side of the uterus towards Pelvic walls .

- The Fallopian tubes are located in the upper border of each ligament & the ovary lies behind it.


Medulla
Ovarian hilum
Mesovarium
Uterus
Uterine tube
Fimbriae
Ovarian artery and vein
Suspensory ligament
Infundibulum
Ovary
Cortex of ovary
Broad ligament
Tunica albuginea of ovary
Ovarian ligament
Cervix
Cervical os
Vaginal wall
Vaginal rugae

Congenital Malformations of the Uterus

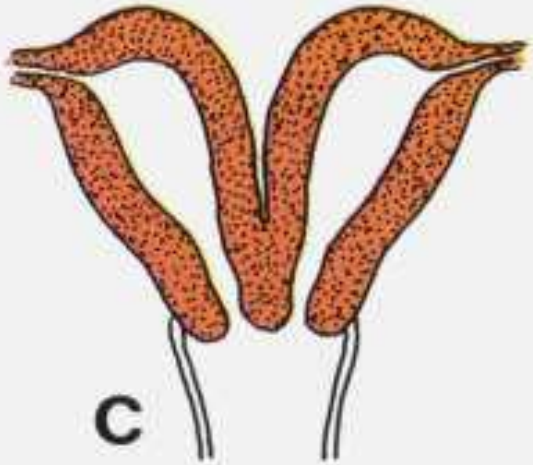
Lack of fusion of Paramesonephric ducts in a localized area or throughout the length results in different types of ***duplication of uterus.***

1. ***Uterus didelphys*** results from failure of fusion of the inferior parts of paramesonephric ducts. The uterus is entirely double and each one enters a separate vagina .

Congenital Malformations of the Uterus

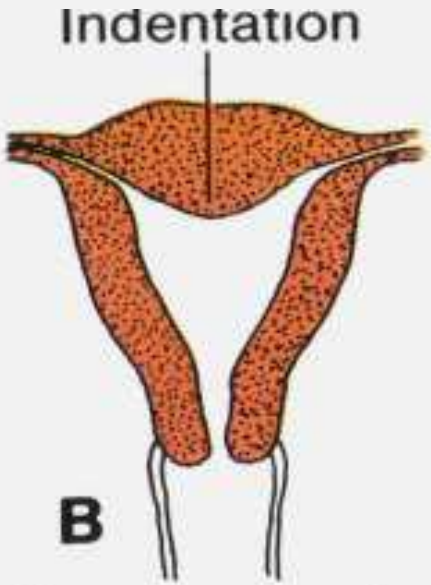
2. ***Uterus arcuatus*** is the least severe form in which there is malfusion in the upper region of the vertical parts of paramesonephric ducts & is represented by a slight indentation in the middle of the fundus of uterus.

3. ***Uterus bicornis*** is one of the more common anomalies in which the malfusion involves only the superior part of the paramesonephric ducts resulting in a double-horned uterus entering a single vagina



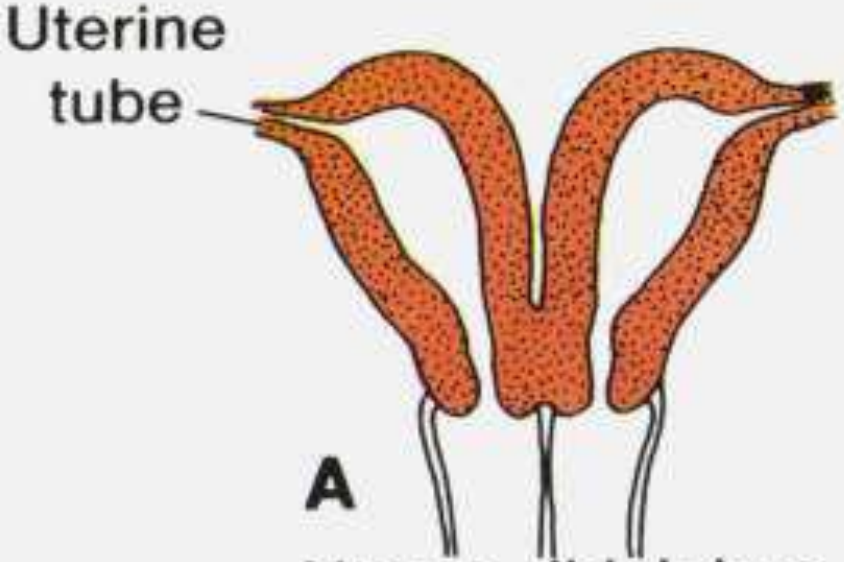
C

Uterus bicornis



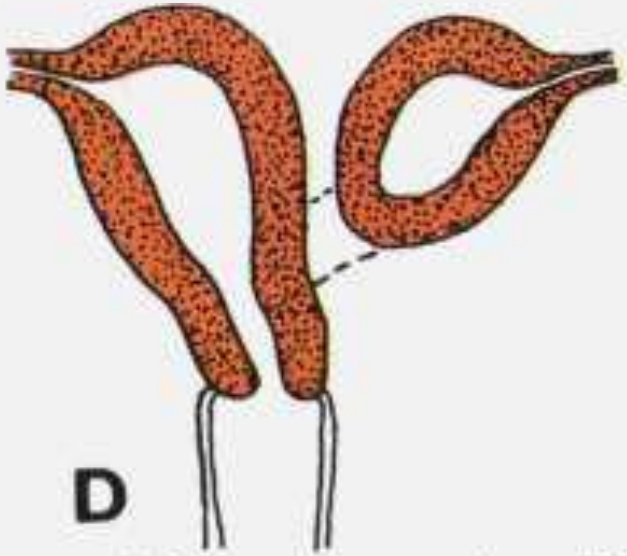
B

Uterus arcuatus



A

Uterus didelphys
with double vagina



D

Uterus bicornis unicollis
1 rudimentary horn

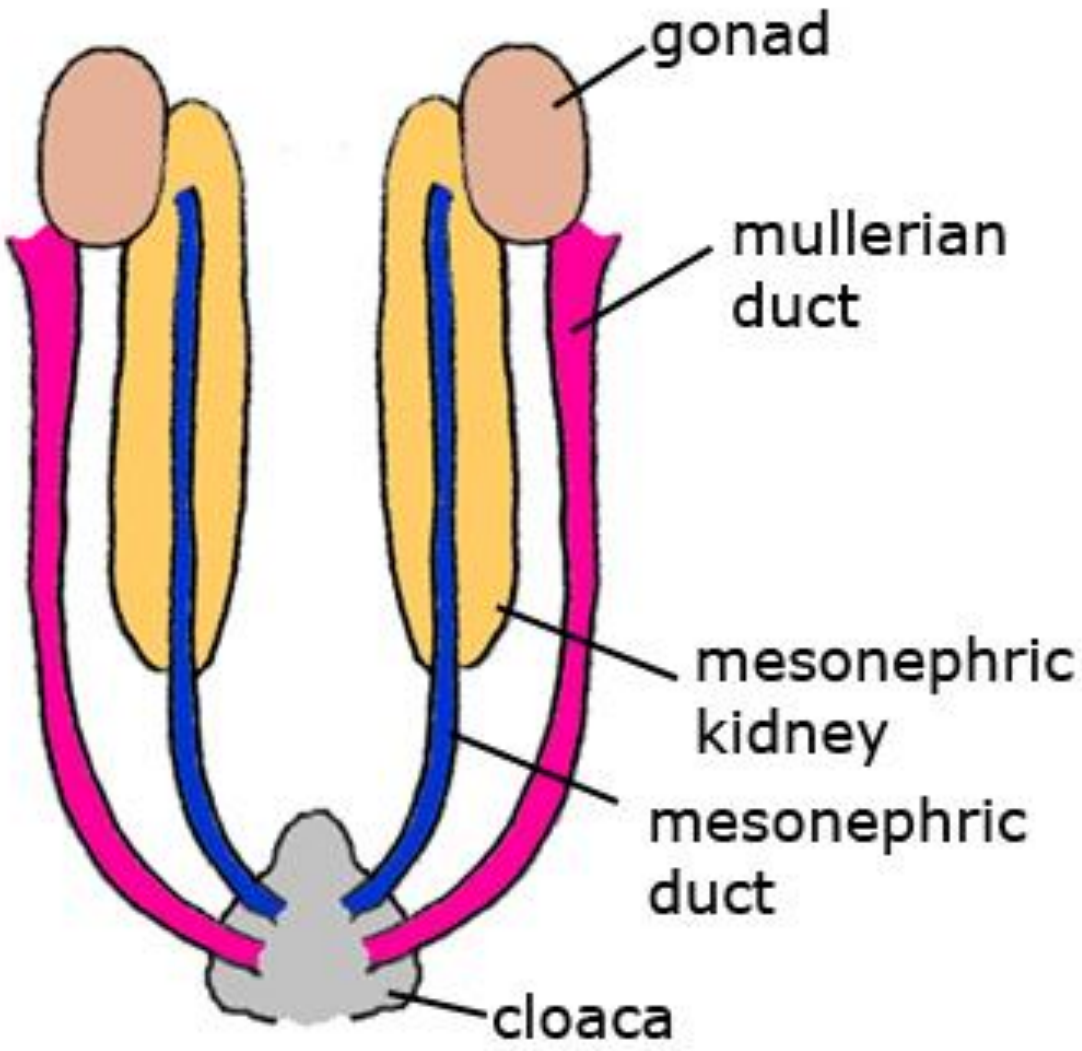
Development of the Vagina

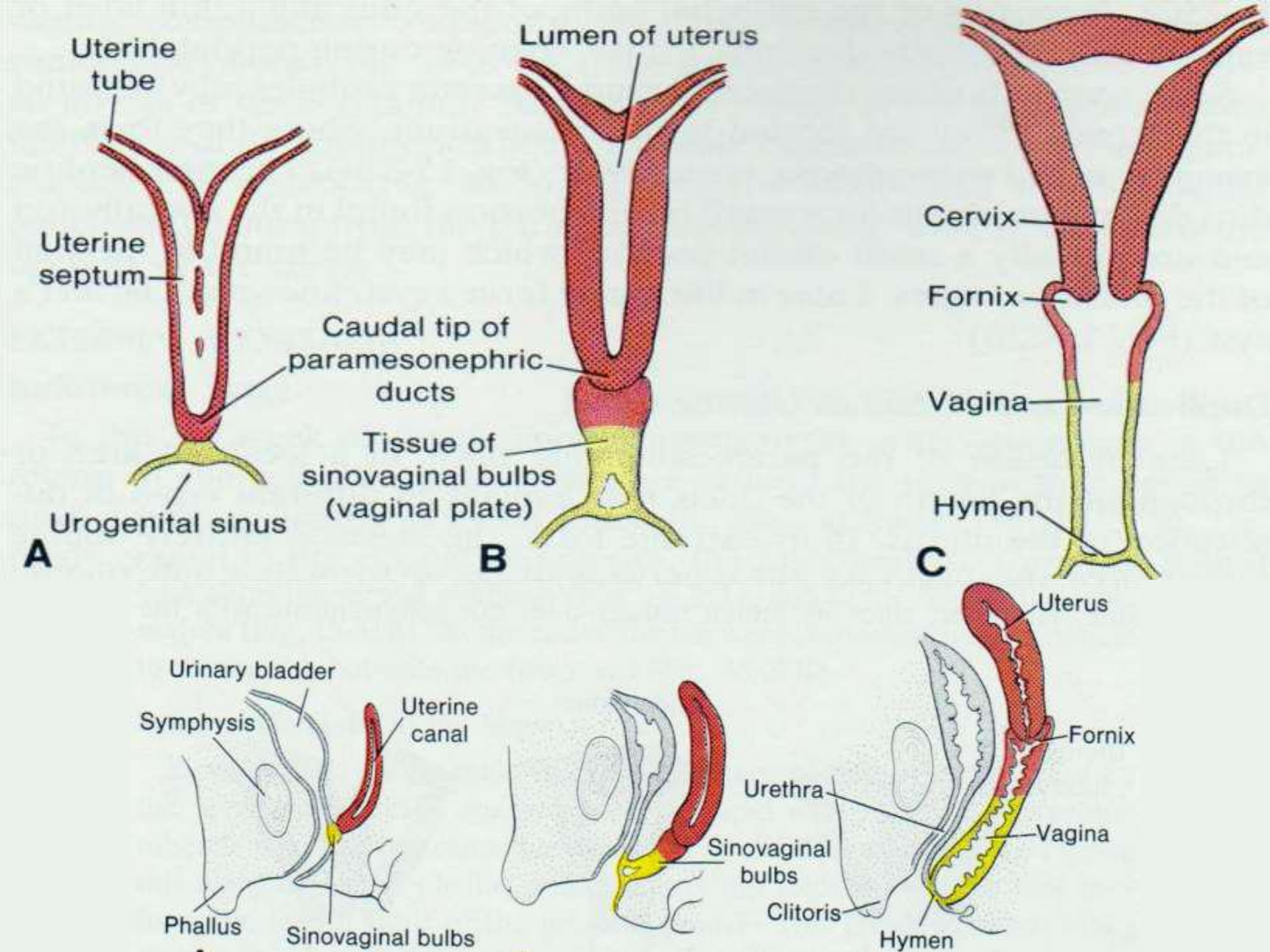
- ***(during 7th wk of IUL)***

- The solid tip of fused ***paramesonephric*** ducts reaches the dilated pelvic part of ***UG sinus.*** Thus, the vagina has a ***dual origin***,

- This solid part of UG sinus is known as "***sinovaginal bulb***" or ***vaginal plate***

Basic embryonic urogenital system

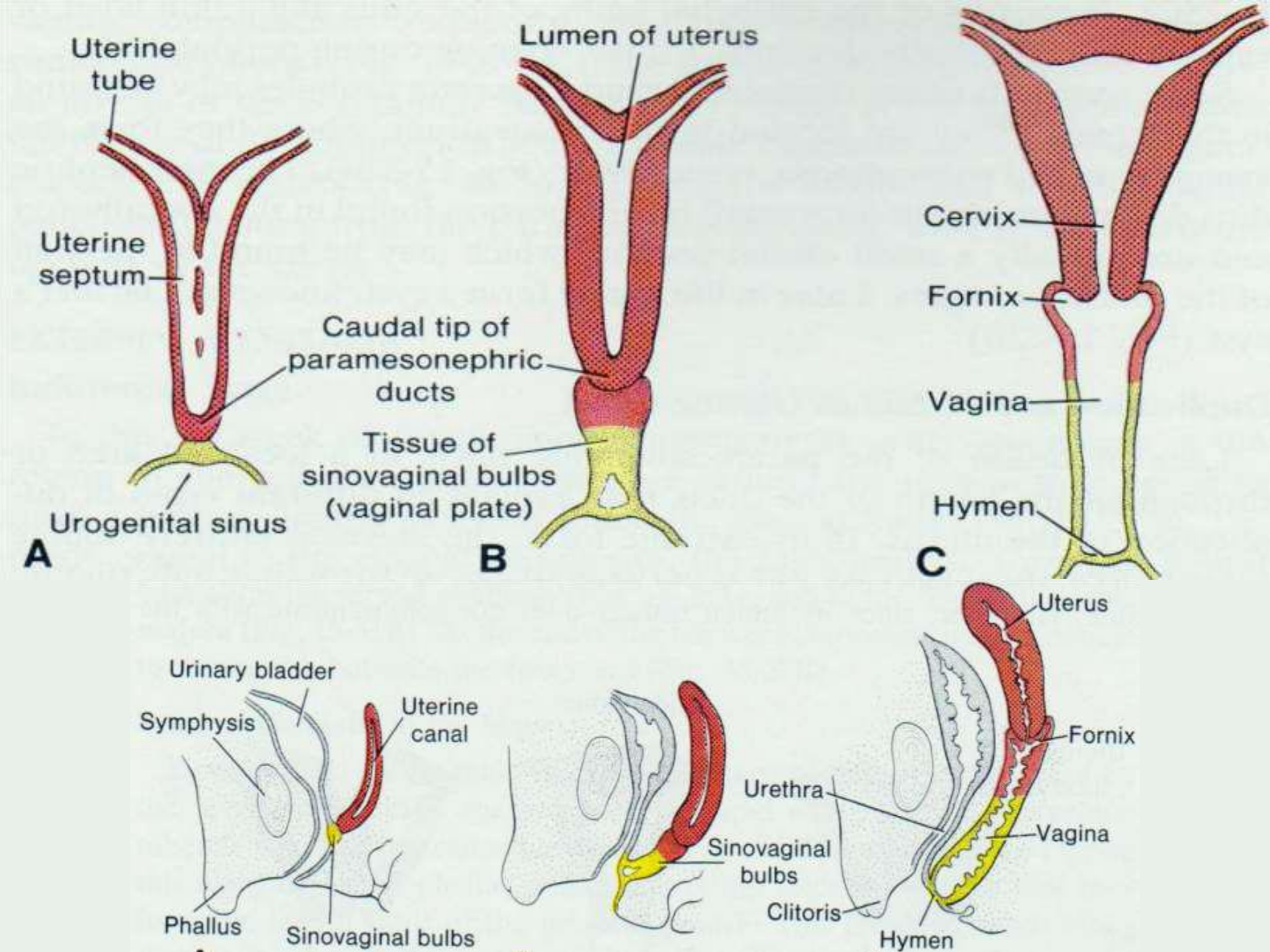



Uterine tube
Uterine septum
Urogenital sinus
A
Lumen of uterus
Caudal tip of paramesonephric ducts
Tissue of sinovaginal bulbs (vaginal plate)
B
Cervix
Fornix
Vagina
Hymen
C
Urinary bladder
Symphysis
Uterine canal
Phallus
Sinovaginal bulbs
Sinovaginal bulbs
Uterus
Fornix
Urethra
Vagina
Clitoris
Hymen

Development of the Vagina

- The plate keeps on proliferating (thus increasing the distance between the uterus & UG sinus).

- Four wing-like expansions of the fused paramesonephric duct will encircle the cranial part of the vaginal plate. They will become the "***vaginal fornixes***".

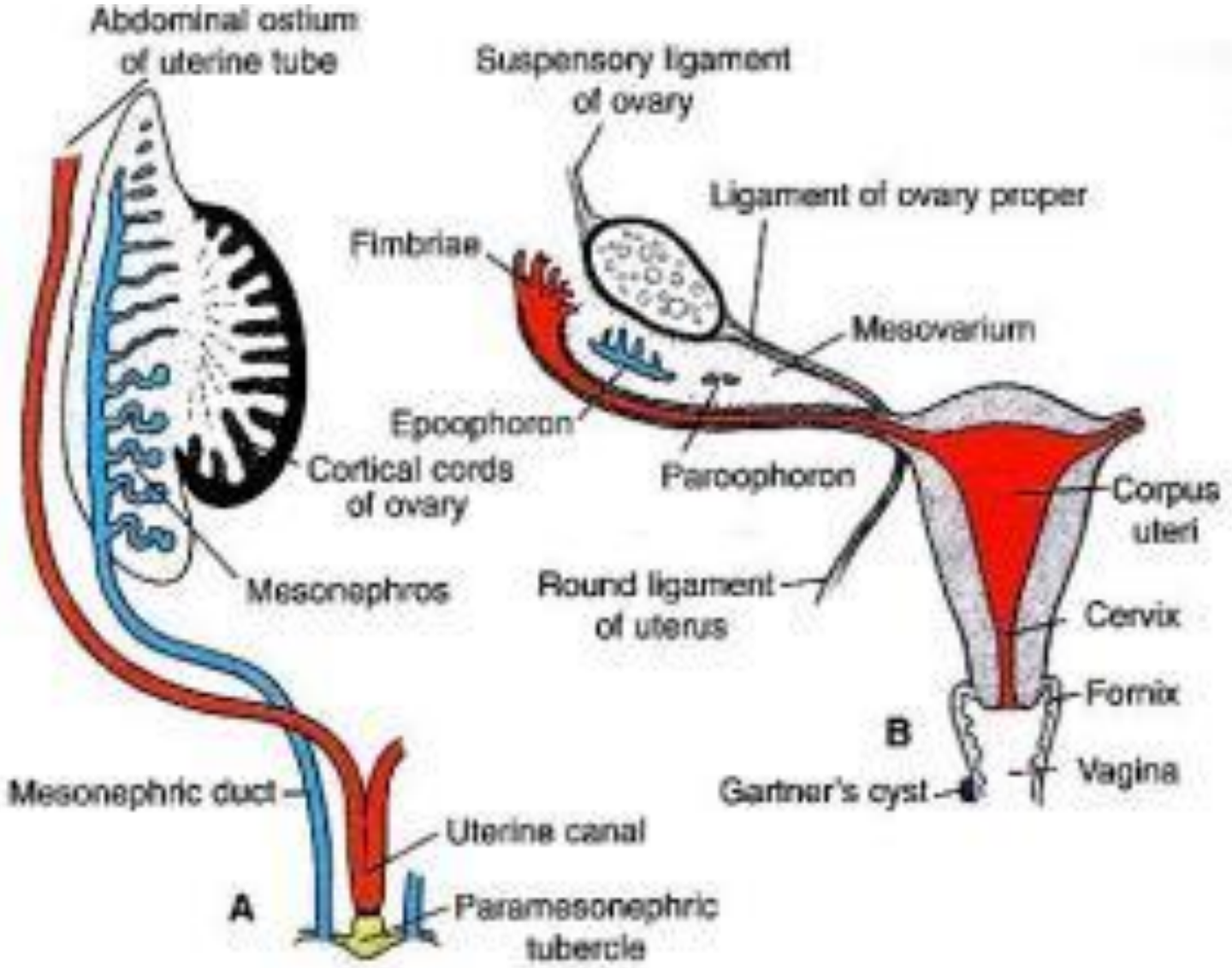

Uterine tube
Uterine septum
Urogenital sinus
A
Lumen of uterus
Caudal tip of paramesonephric ducts
Tissue of sinovaginal bulbs (vaginal plate)
B
Cervix
Fornix
Vagina
Hymen
C
Urinary bladder
Symphysis
Uterine canal
Phallus
Sinovaginal bulbs
Sinovaginal bulbs
Uterus
Fornix
Urethra
Vagina
Clitoris
Hymen

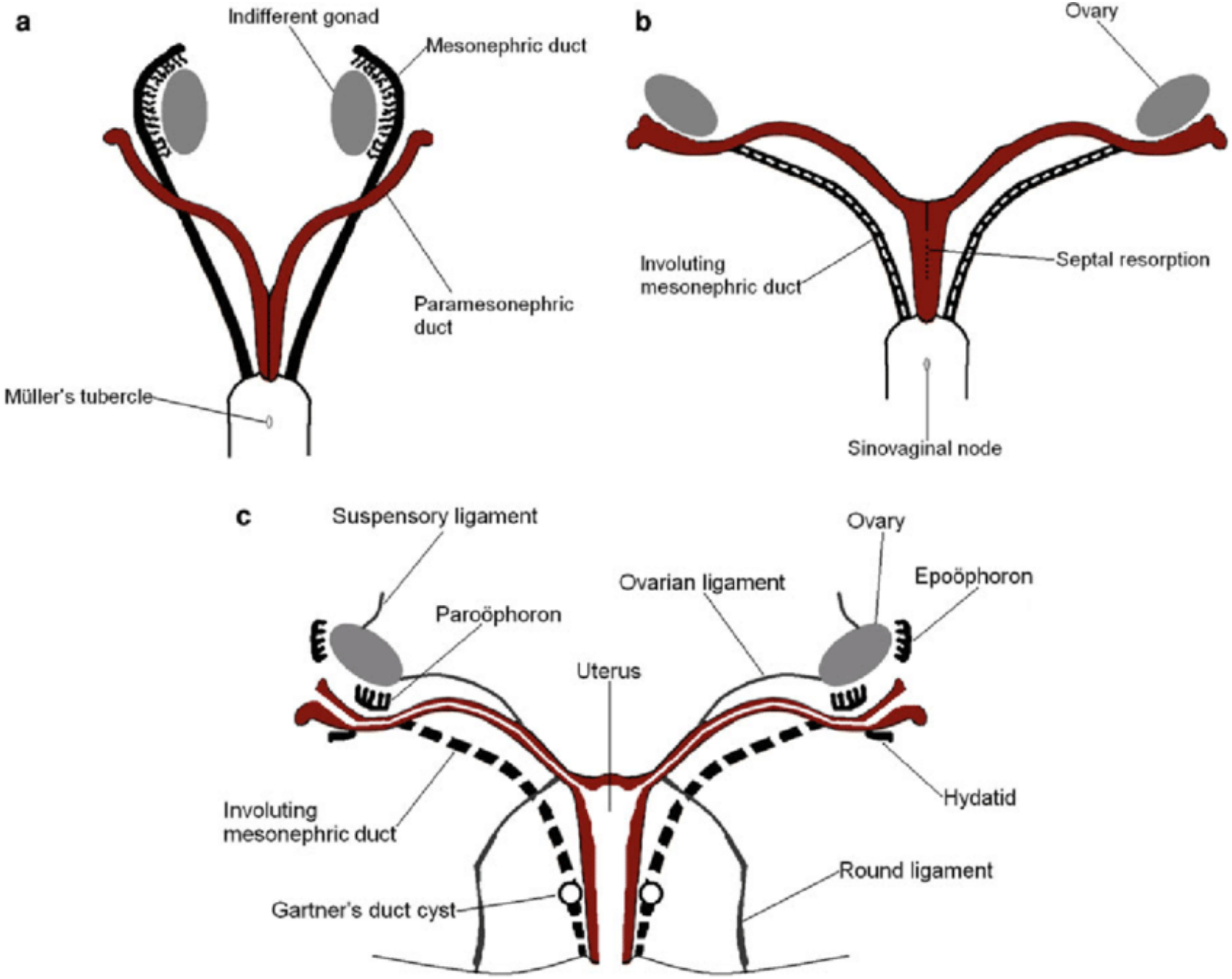
Canalization of the Vagina & formation of Hymen

- The ***central cells*** of the vaginal plate break down (by the process of ***apoptosis***) and a canal is formed which is ***continuous cranially*** with the uterine canal and complete canalization occurs by 5th month IU

- *The* ***mesonephric duct gives rise to Gartner's cyst*****.**

- ***Epoophoron*** **and** ***Paroophoron*** **are** ***remnant*** **of** ***excretory tubule*** **in the mesovarium.**


Abdominal ostium of uterine tube
Suspensory ligament of ovary
Ligament of ovary proper
Fimbriae
Mesovarium
Epoophoron
Paroophoron
Cortical cords of ovary
Mesonephros
Round ligament of uterus
Corpus uteri
Cervix
Fornix
Vagina
Gartner's cyst
B
Mesonephric duct
Uterine canal
A
Paramesonephric tubercle


a
Indifferent gonad
Mesonephric duct
Paramesonephric duct
Müller's tubercle
b
Ovary
Involuting mesonephric duct
Septal resorption
Sinovaginal node
c
Suspensory ligament
Ovary
Ovarian ligament
Epoöphoron
Paroöphoron
Uterus
Hydatid
Involuting mesonephric duct
Round ligament
Gartner's duct cyst

Canalization of the Vagina & formation of Hymen

- ***Caudally,*** the vagina is ***separated*** from the cavity of the ***UG sinus*** by a transverse membrane, the '***hymen'***.

- At the time of birth (perinatal period), this hymen usually ruptures in the middle & remains as a thin fold of mucous membrane just within the vaginal orifice.

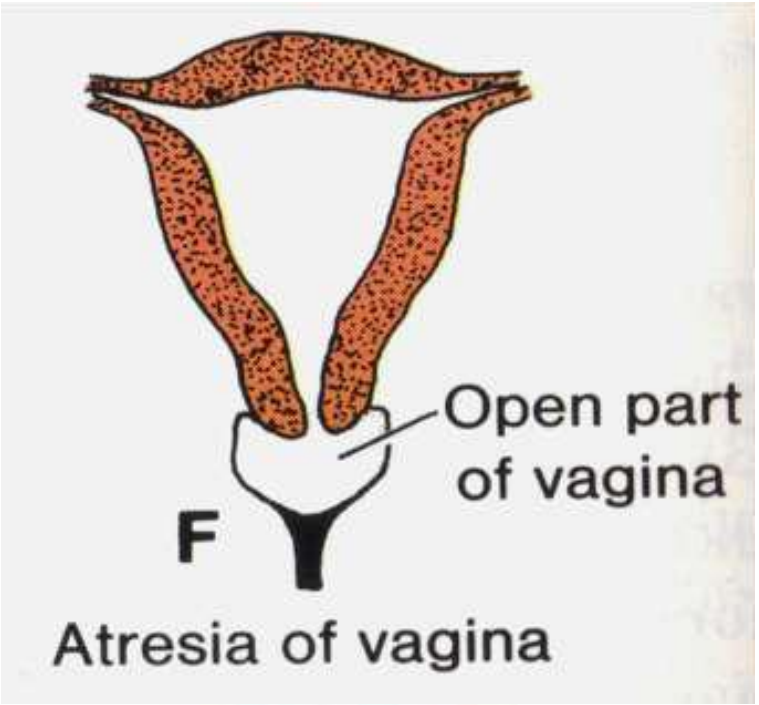
Anomalies of the Vagina

Vaginal Atresia:

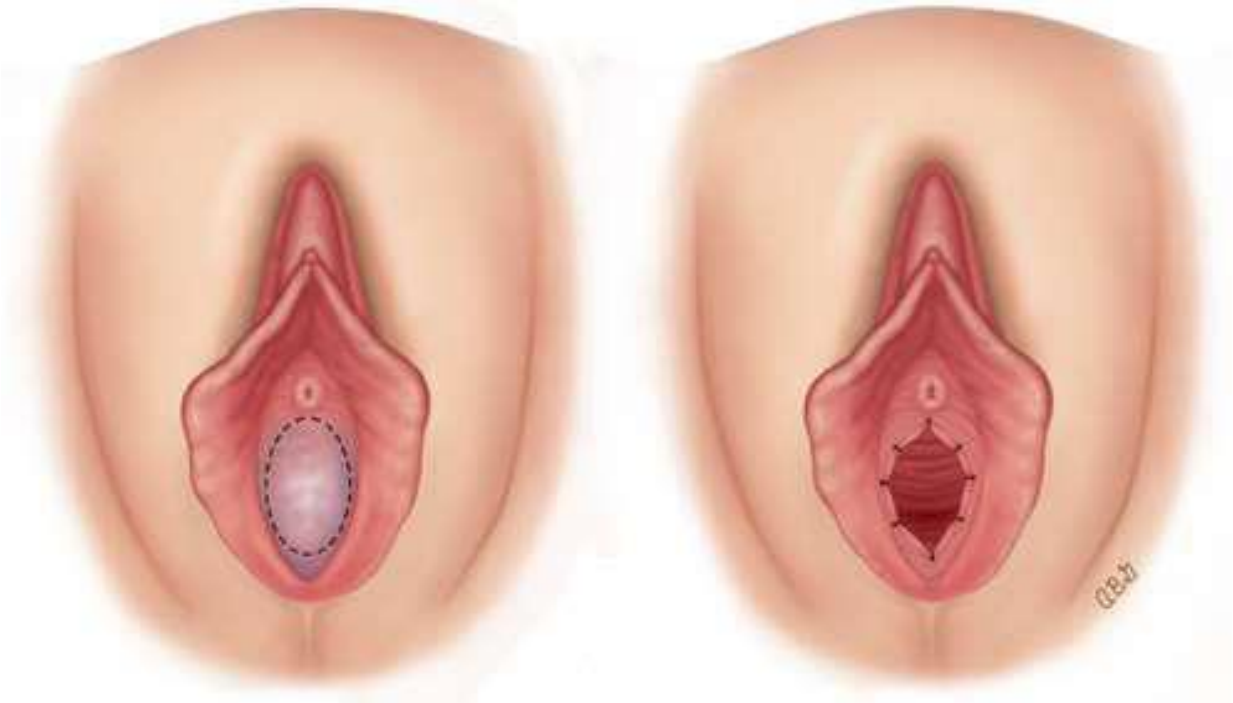
- Failure of canalization of the vaginal plate will lead to vaginal atresia.

Imperforated hymen:

- If the middle portion of the hymen fails to get thin down during the last weeks of IUL, there would be failure of rupture of hymen during the time of birth resulting in an imperforate hymen



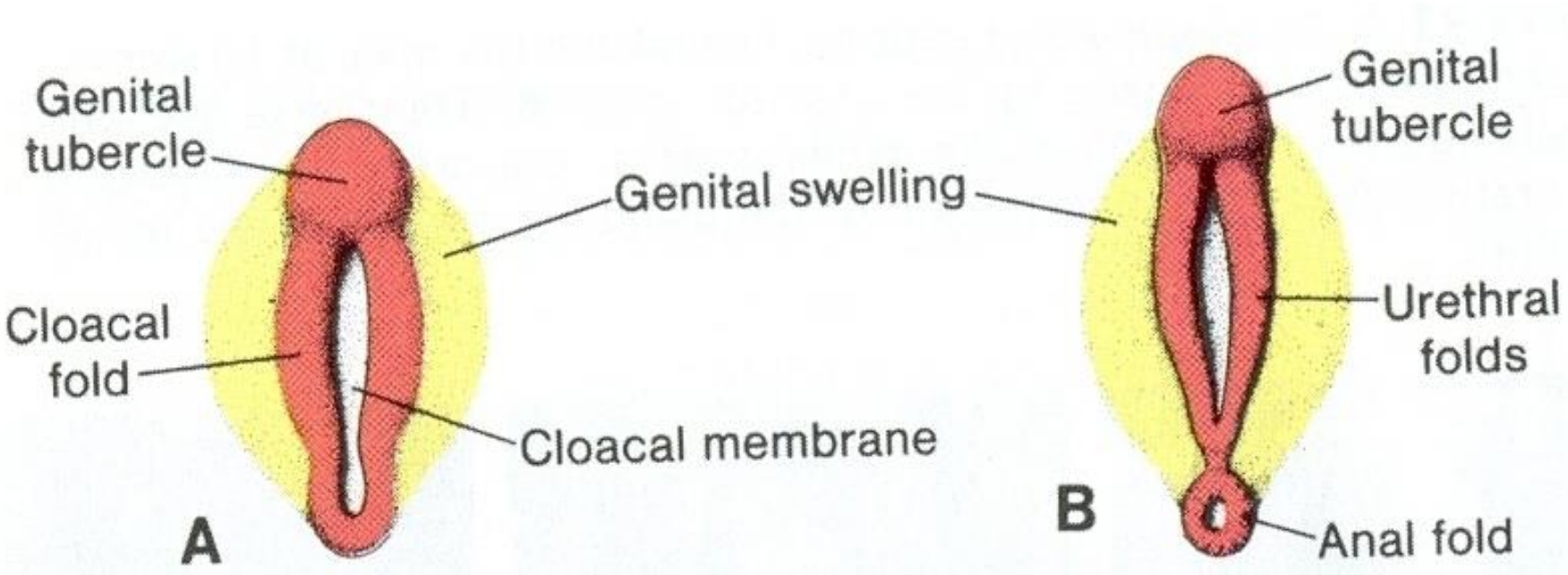
Imperforated hymen



Development of External Genitalia

- The cloacal membrane is surrounded by the cloacal fold which meet anteriorly to form the **genital tubercle**.

- The cloacal membrane is divided by the urorectal septum into urogenital & anal membrane. Likewise, the cloacal fold is divided into **genital (urethral) & anal folds**.


Genital tubercle
Genital swelling
Cloacal fold
Cloacal membrane
A
Genital tubercle
Urethral folds
B
Anal fold

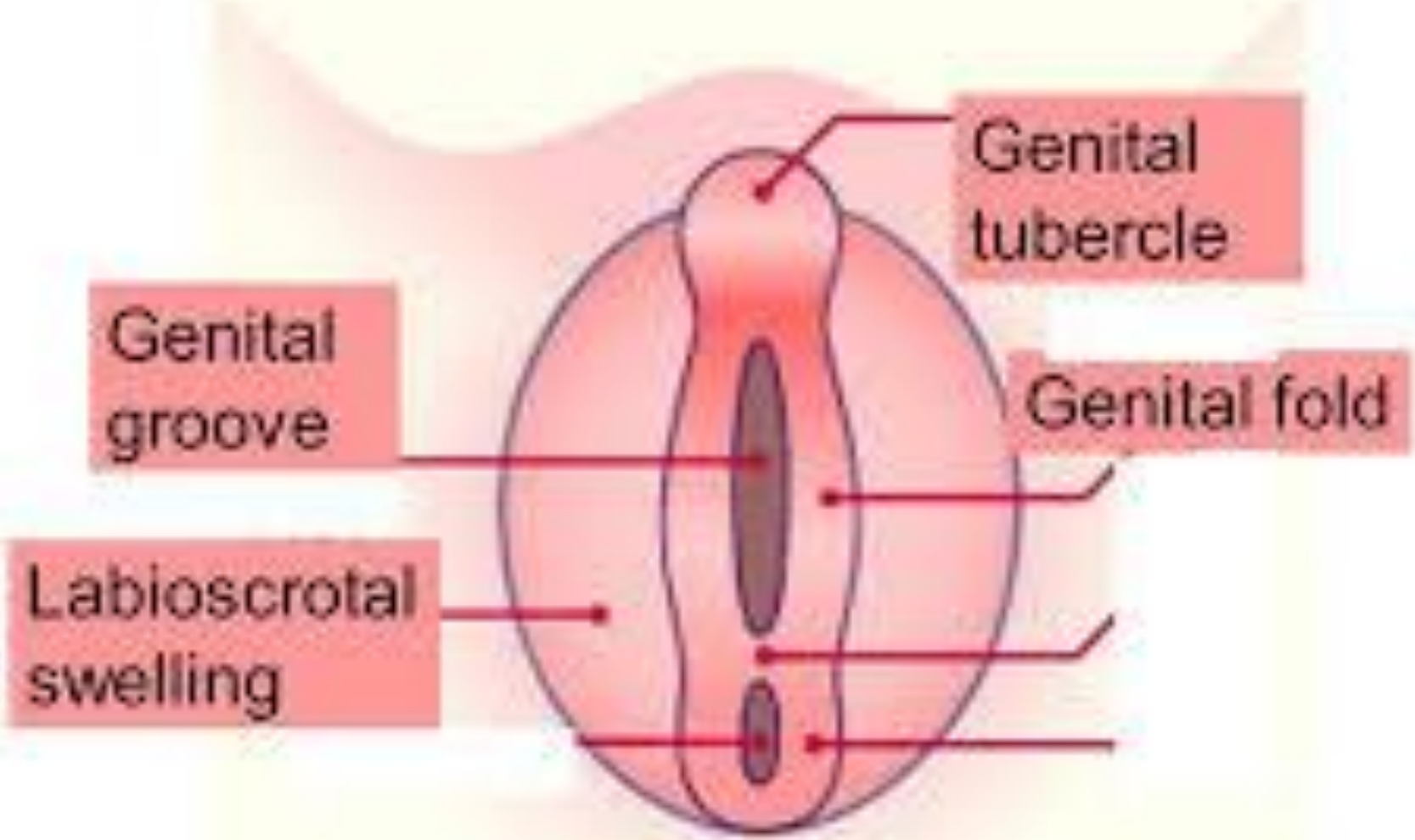
External Genitalia

Genital tubercle: produced from mesenchyme at the cranial end of cloacal membrane. It elongates to form a primordial phallus/clitoris

Urogenital folds: develop on each side of cloacal membrane

Labioscrotal swellings: develop on each side of urogenital folds

Undifferentiated external



Development of External Genitalia

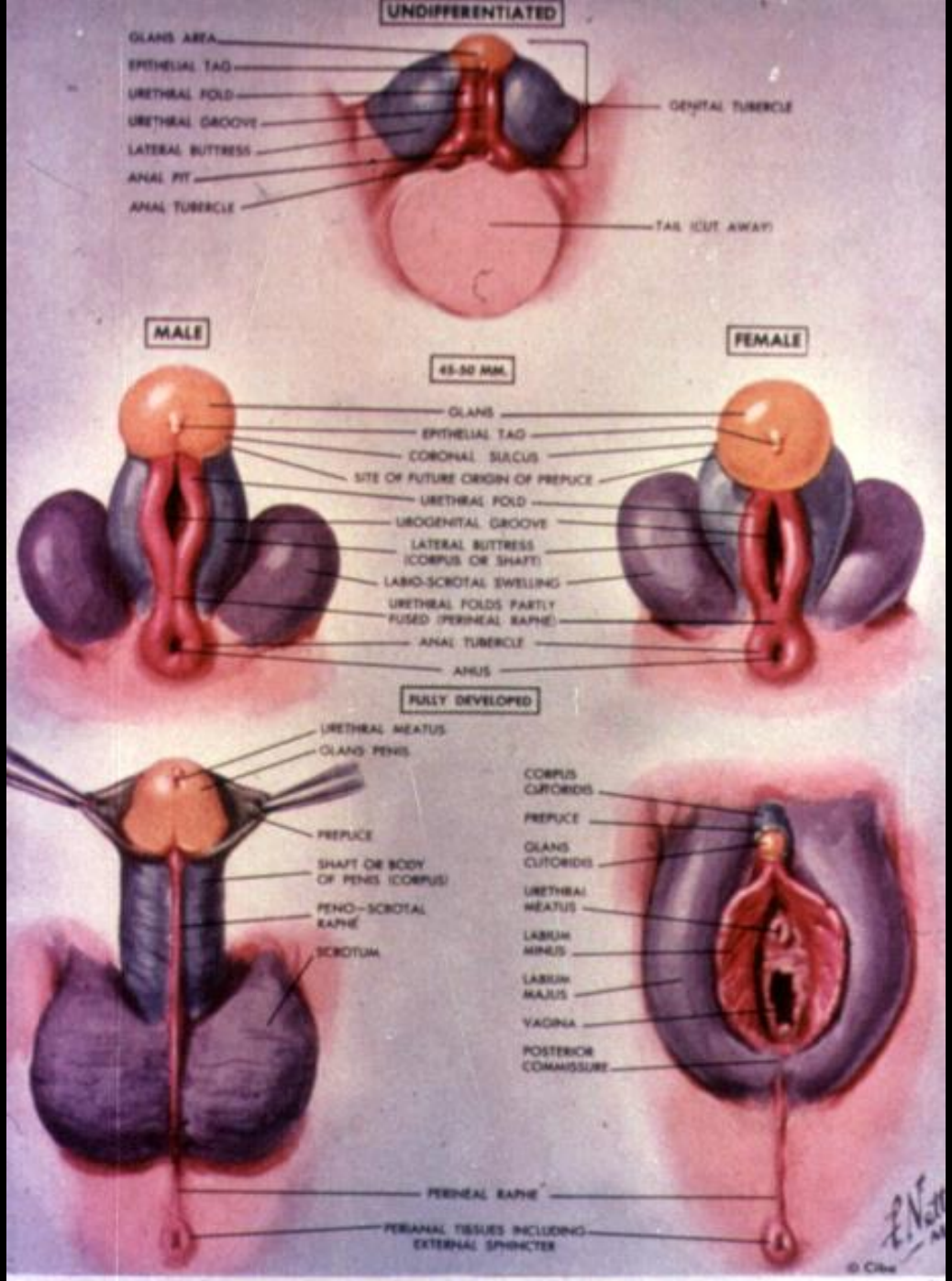
- The genital tubercle, the genital fold & the genital swelling form together the ***indifferent stage*** because male & female genitalia cannot be differentiated at this stage

- A genital swelling is formed lateral to the urethral (genital) fold.

- Later these swellings form the scrotal swellings in male, labia majora in female

Female Embryo

- The **genital tubercle** enlarges slightly to form the **clitoris**.
- The **genital swellings** form **labia majora**.
- The **urethral (genital) folds** form **labia minora**.
- The **definitive urogenital sinus** forms the **vestibule of the vagina**.

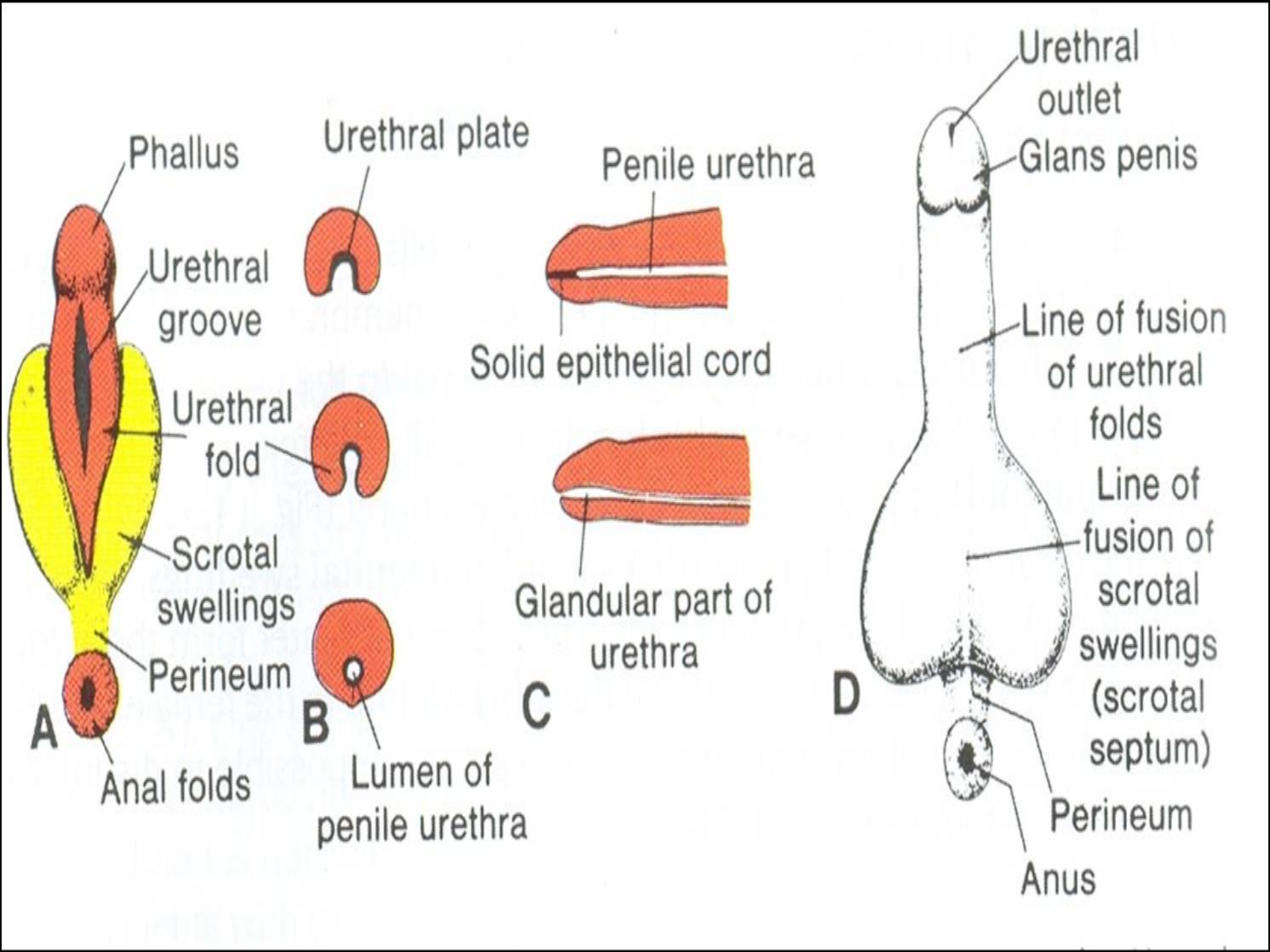


HOMOLOGUES OF EXTERNAL GENITALIA

Male Embryo

- The **genital tubercle** enlarges to form the **phallus (penis).**

- The **urethral (genital) folds** form the lateral boundary of urethral groove. The endoderm of the groove proliferates to form **urethral plate** (floor of the groove) .

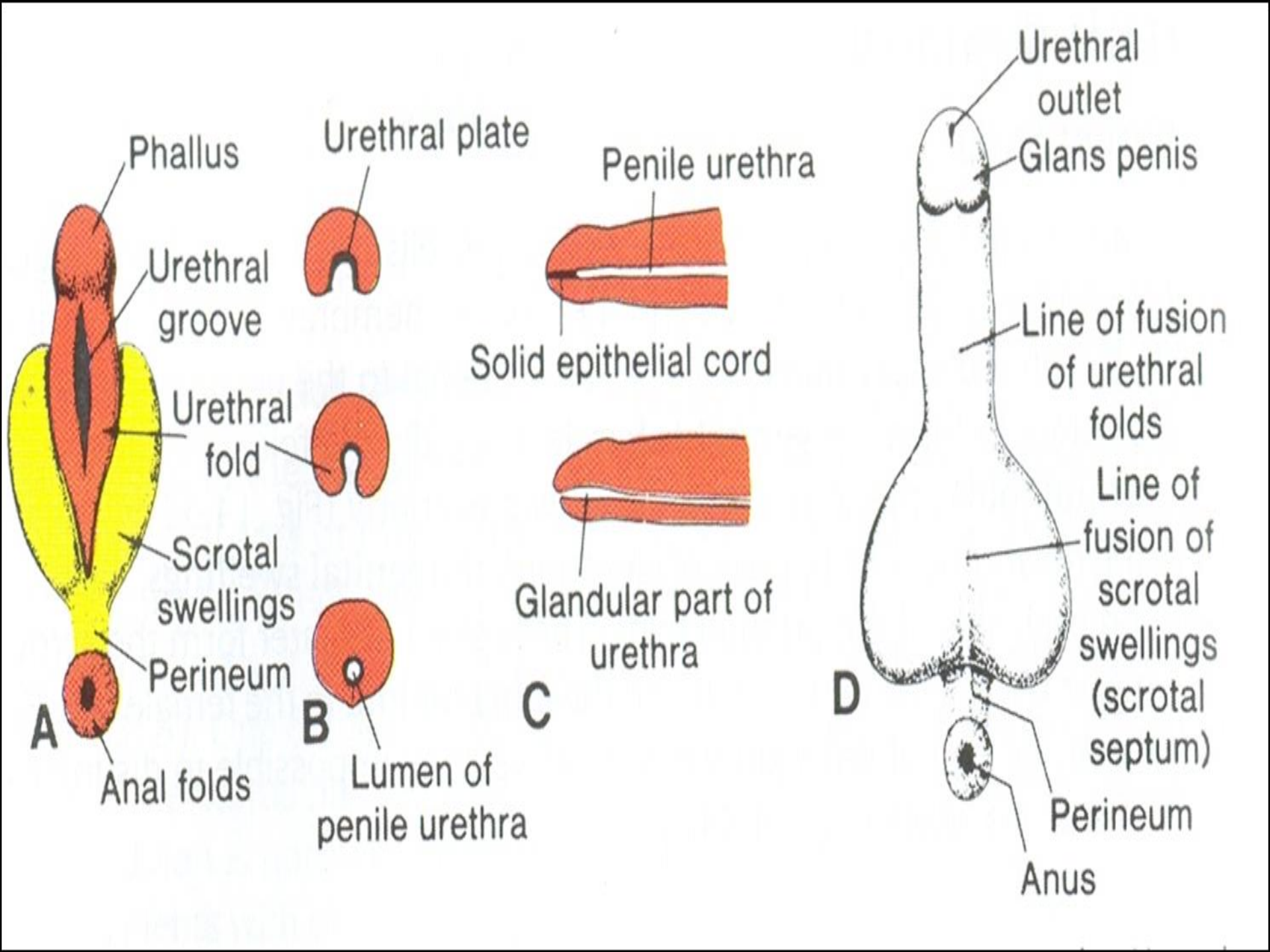

Phallus
Urethral groove
Urethral fold
Scrotal swellings
Perineum
Anal folds
A
Urethral plate
Lumen of penile urethra
B
Penile urethra
Solid epithelial cord
Glandular part of urethra
C
Urethral outlet
Glans penis
Line of fusion of urethral folds
Line of fusion of scrotal swellings (scrotal septum)
Perineum
Anus
D

Male Embryo

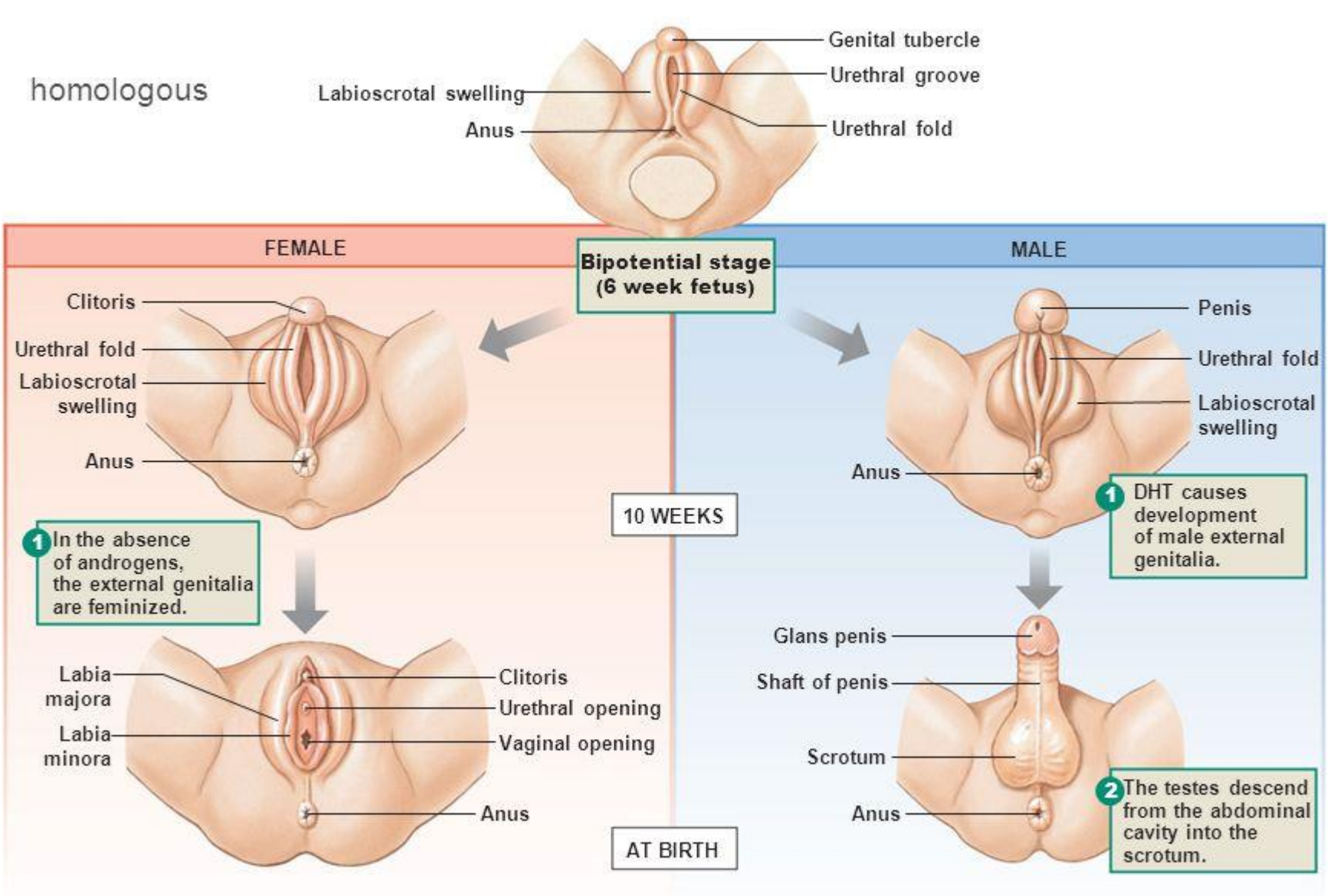
- Stimulated by ***testosterone***, the urethral folds close over the urethral plate forming the **penile urethra** **in** a **posteroanterior direction**.

- A solid cord of ectoderm is formed in the glans then becomes canalized at the tip of the penis

- The **genital swellings** form the **scrotum**.


Phallus
Urethral groove
Urethral fold
Scrotal swellings
Perineum
Anal folds
A
Urethral plate
Lumen of penile urethra
B
Penile urethra
Solid epithelial cord
Glandular part of urethra
C
Urethral outlet
Glans penis
Line of fusion of urethral folds
Line of fusion of scrotal swellings (scrotal septum)
Perineum
Anus
D

Development of External Genitalia



(b) DEVELOPMENT OF EXTERNAL GENITALIA

Figure 26-3b

Internal Descent of Testis

- ***Definition:*** Descent of testis from posterior abdominal wall to deep inguinal ring.

- ***Time:*** During 12th week

- The testis descends till it reaches the deep inguinal ring in the 3rd month.

Internal Descent of Testis

Cause:

- This stage of descent is caused by ***relative elongation*** of the ***posterior abdominal wall*** in an ***upward direction***, without corresponding elongation of the gubernaculum. Thus, it is a growth displacement rather than active migration.

Descent of Testis

Gubernaculum:

- A mesenchymal band extending from inferior pole of gonad to labioscrotal fold.

Inguinal canal:

- A pathway formed by gubernaculum through layers of anterior abdominal wall.

Processus vaginalis:

- A peritoneal fold passing through inguinal canal before testis to facilitate its descent.

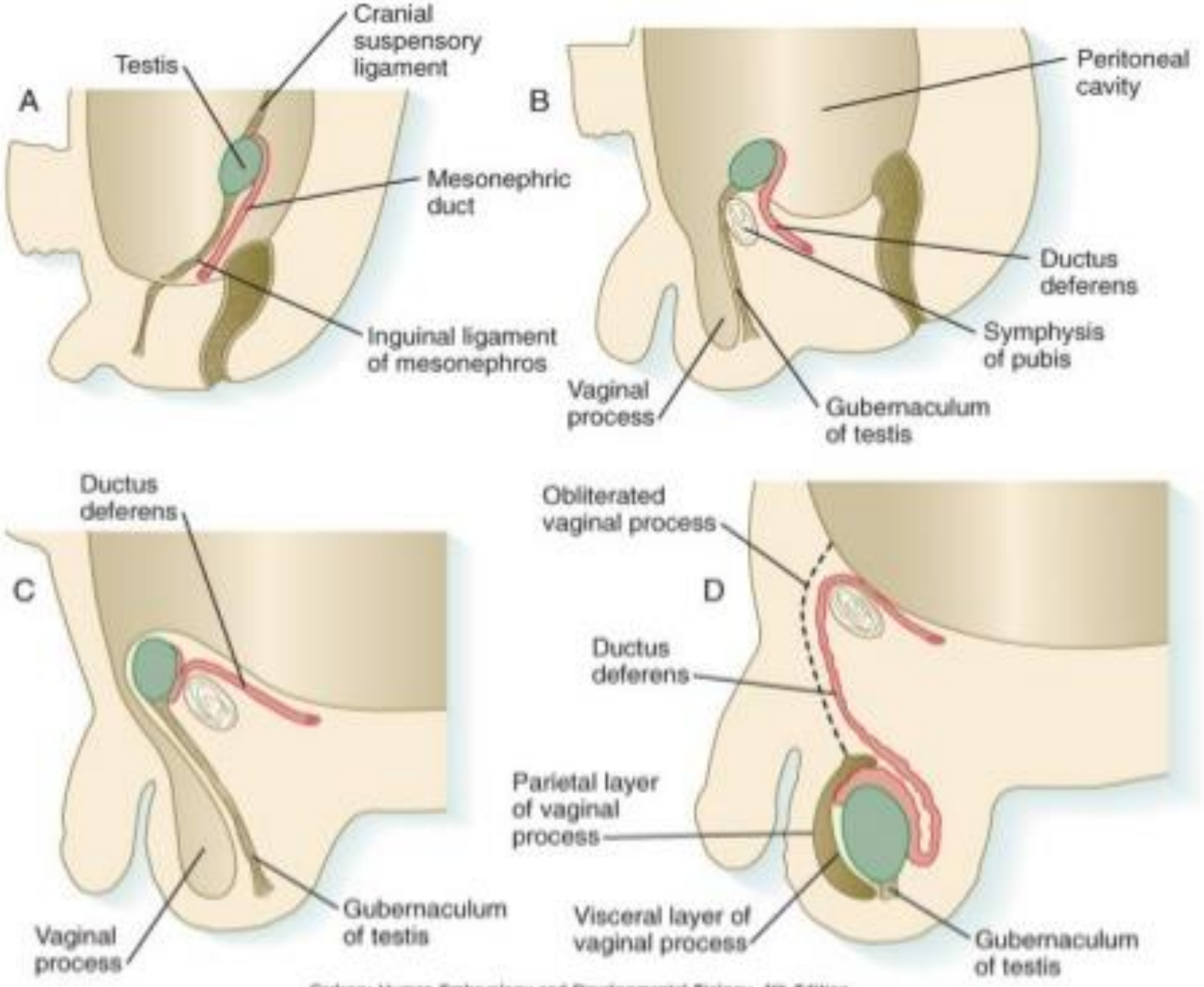
External Descent of Testis

- ***Definition:*** Descent of testis from deep inguinal ring, through inguinal canal, to scrotum

- ***Time:*** Begins in 7th month and takes 2 to 3 months

- ***Causes:***

1. Controlled by androgens.
2. Guided by gubernaculum.
3. Facilitated by processus vaginalis.
4. Helped by increased intra-abdominal pressure resulting from growth of abdominal viscera.



External Descent of Testis

- More than 97% of full-term newborn males have both testis in scrotum.
- During first 3 months after birth, most undescended testes descend into scrotum.
- No spontaneous descent occurs after the age of 1 year.

External Descent of Testis

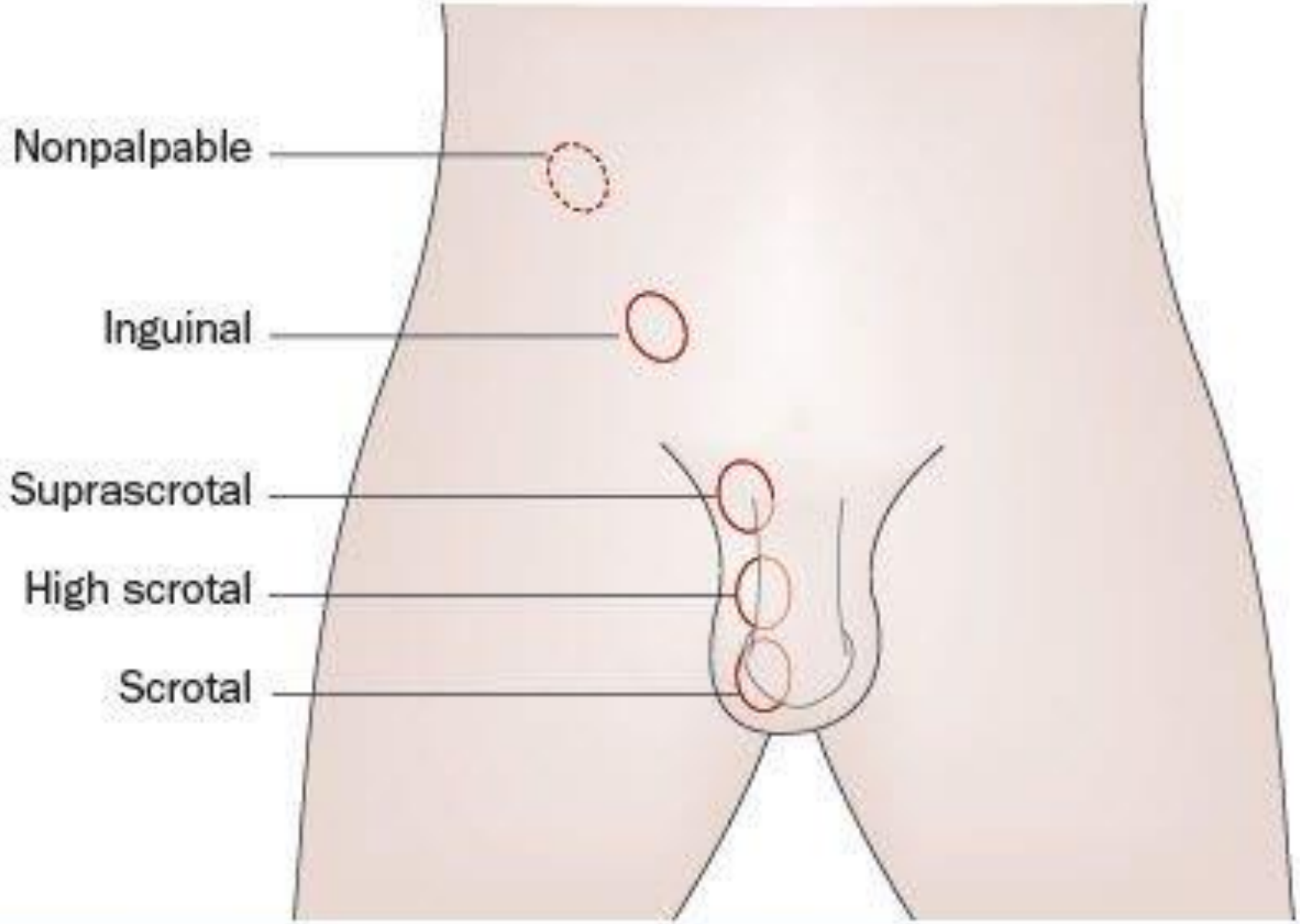
- ***Complete descent of testis is associated with:***

1. Degeneration of gubernaculum
2. Obliteration of stalk of processus vaginalis
3. Persistence of part of processus vaginalis surrounding the testis in the scrotum to form "tunica vaginalis"

Cryptorchidism (Undescended Testis)

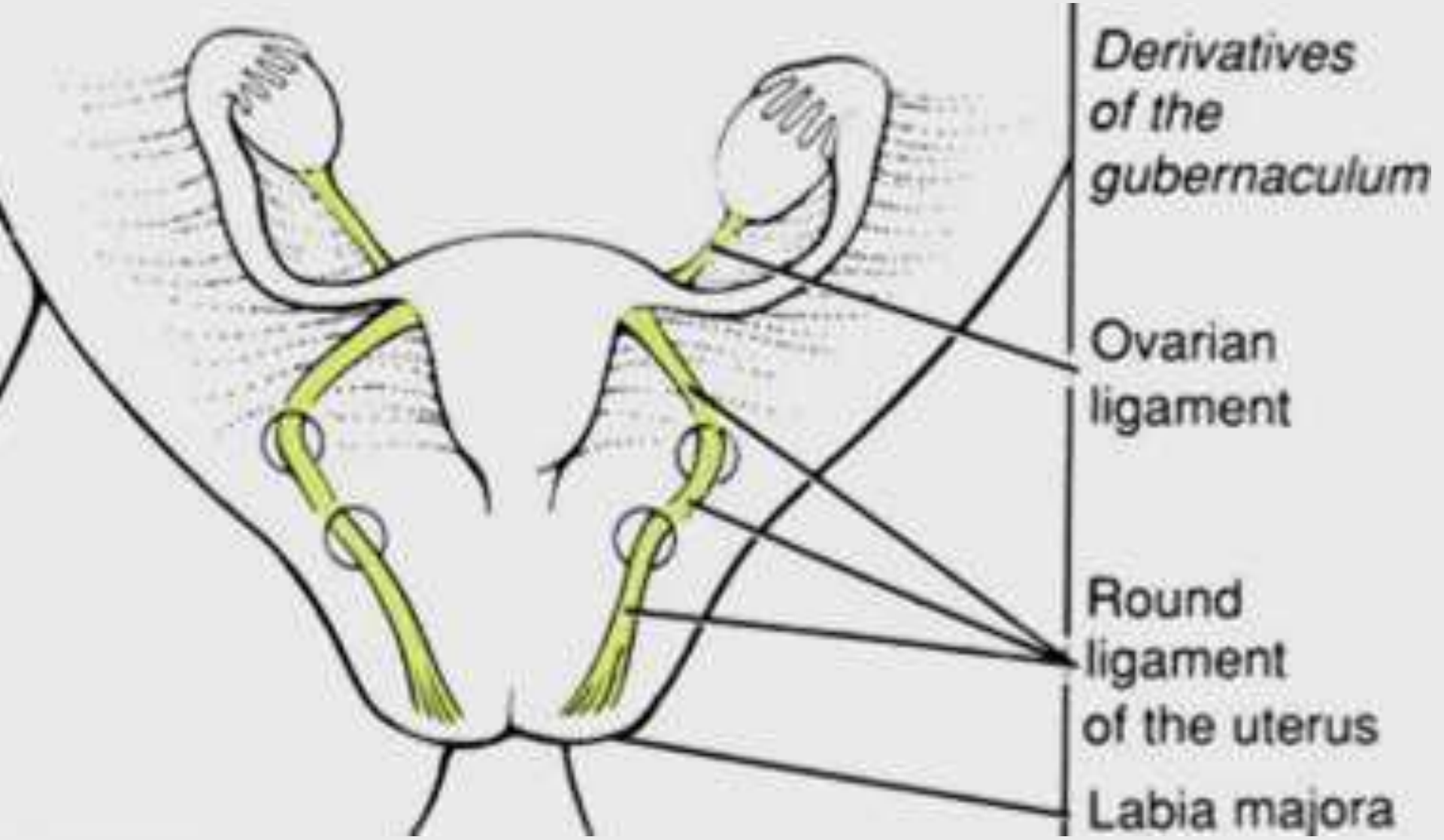
- ***Incidence:*** in up to 30% of premature & 3-4% of full term males
- ***Cause:*** deficiency of androgens.
- ***Common sites:*** look to figure
- ***Complications:***

1. Sterility, if bilateral.
2. Testicular cancer (20-44%).



Descent of Ovaries & the Fate of Gubernaculum

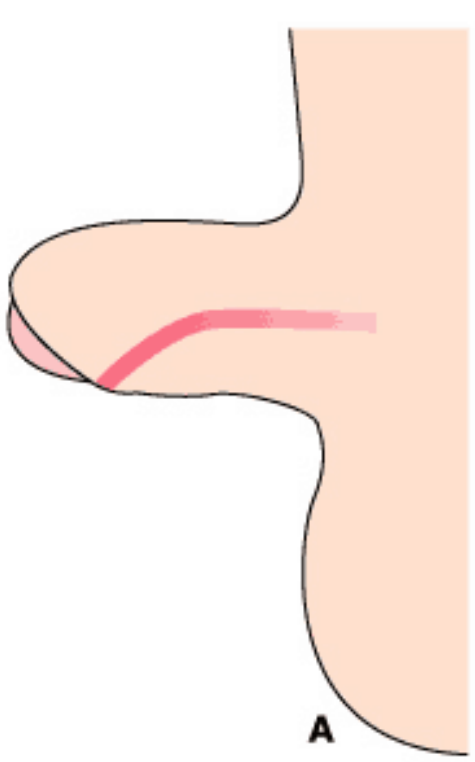
- The ovaries are also pulled down from the lumbar region to the Pelvic cavity.
- They settle down slightly below the level of pelvic brim.
- Cranial end of Gubernaculum attached between the lower pole of ovary & side of uterus becomes the '***round ligament of ovary***'.
- While, the portion crossing the sides of uterus till the caudal end attached on the Labia majora becomes the '***round ligament of uterus***'


Derivatives of the gubernaculum
Ovarian ligament
Round ligament of the uterus
Labia majora

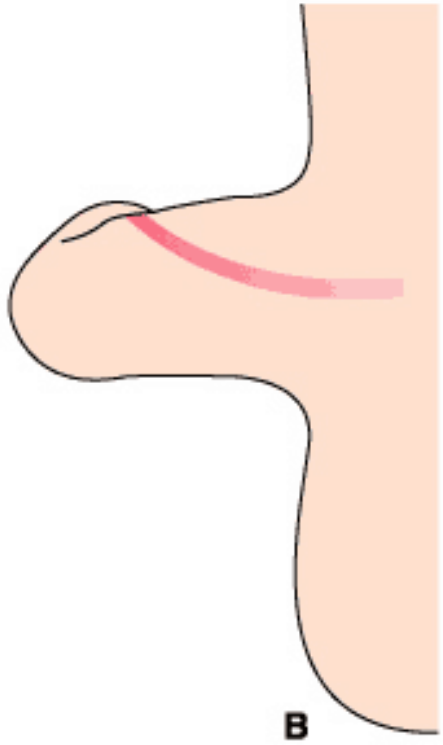
Congenital Anomalies

- ***Hypospadias:*** most common anomaly of the penis. The external urethral orifice is on the ventral surface of the glans penis (***penile hypospadias***)

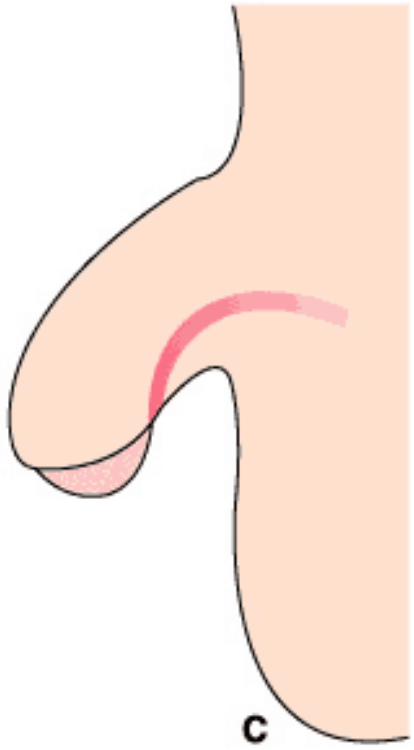
- ***Epispadias:*** The urethra opens on the dorsal surface of the penis; often associated with exstrophy of the bladder; resulting from inadequate ectodermal-mesodermal interactions during development of genital tubercle



Hipospadias

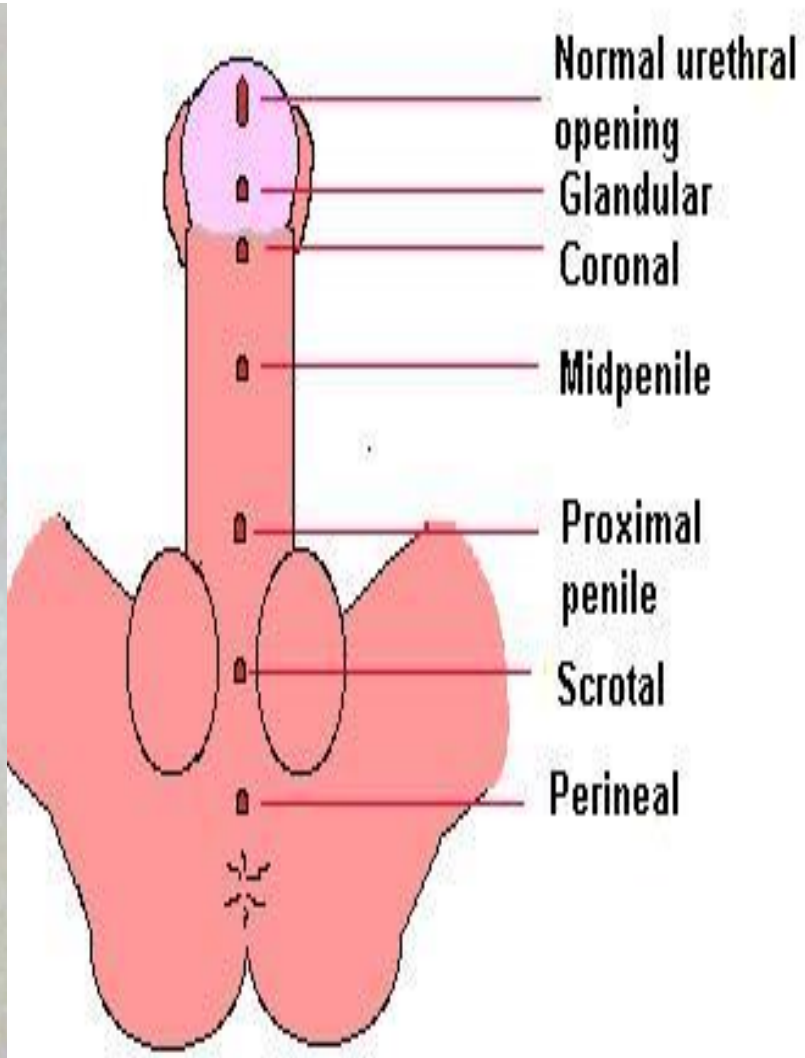


Epispadias

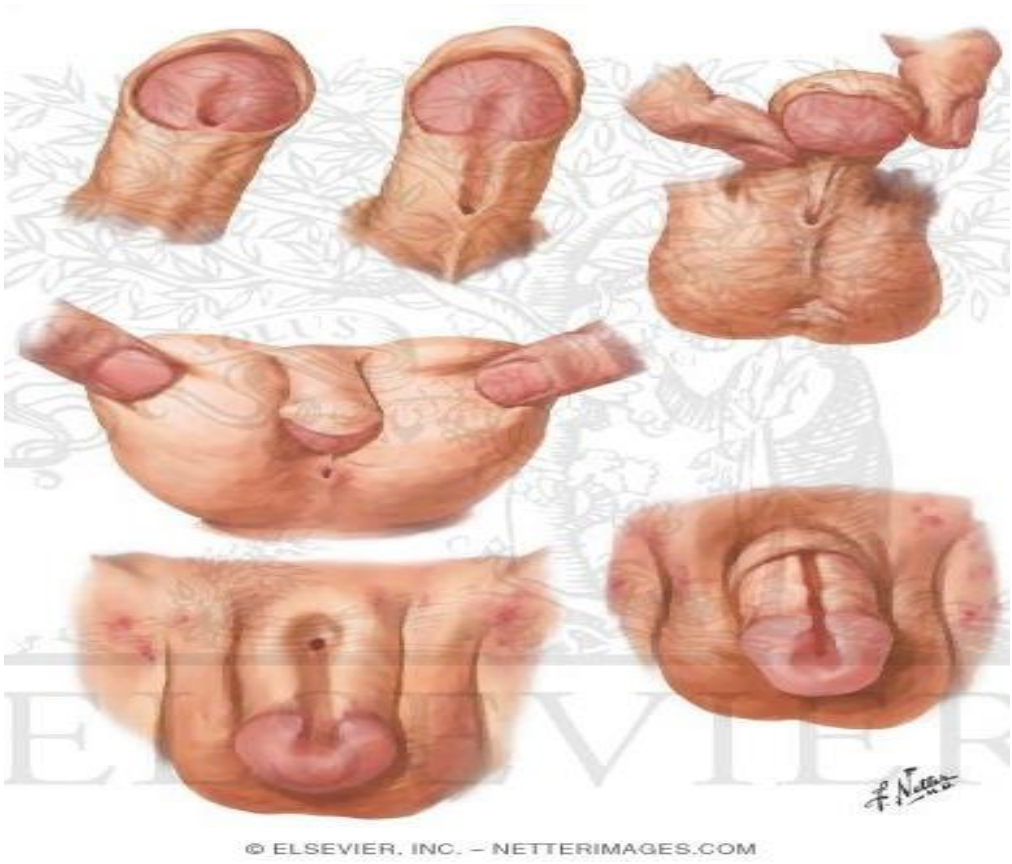


Hipospadias

Hypospadias



Epispadias



Congenital Anomalies

- ***Agenesis of external genitalia:*** Absence of penis or clitoris; resulting from the failure of development of genital tubercle.

- ***Bifid penis and double penis:*** vary rare, often associated with exstrophy of the bladder or urinary anomalies; results when two genital tubercles develop.

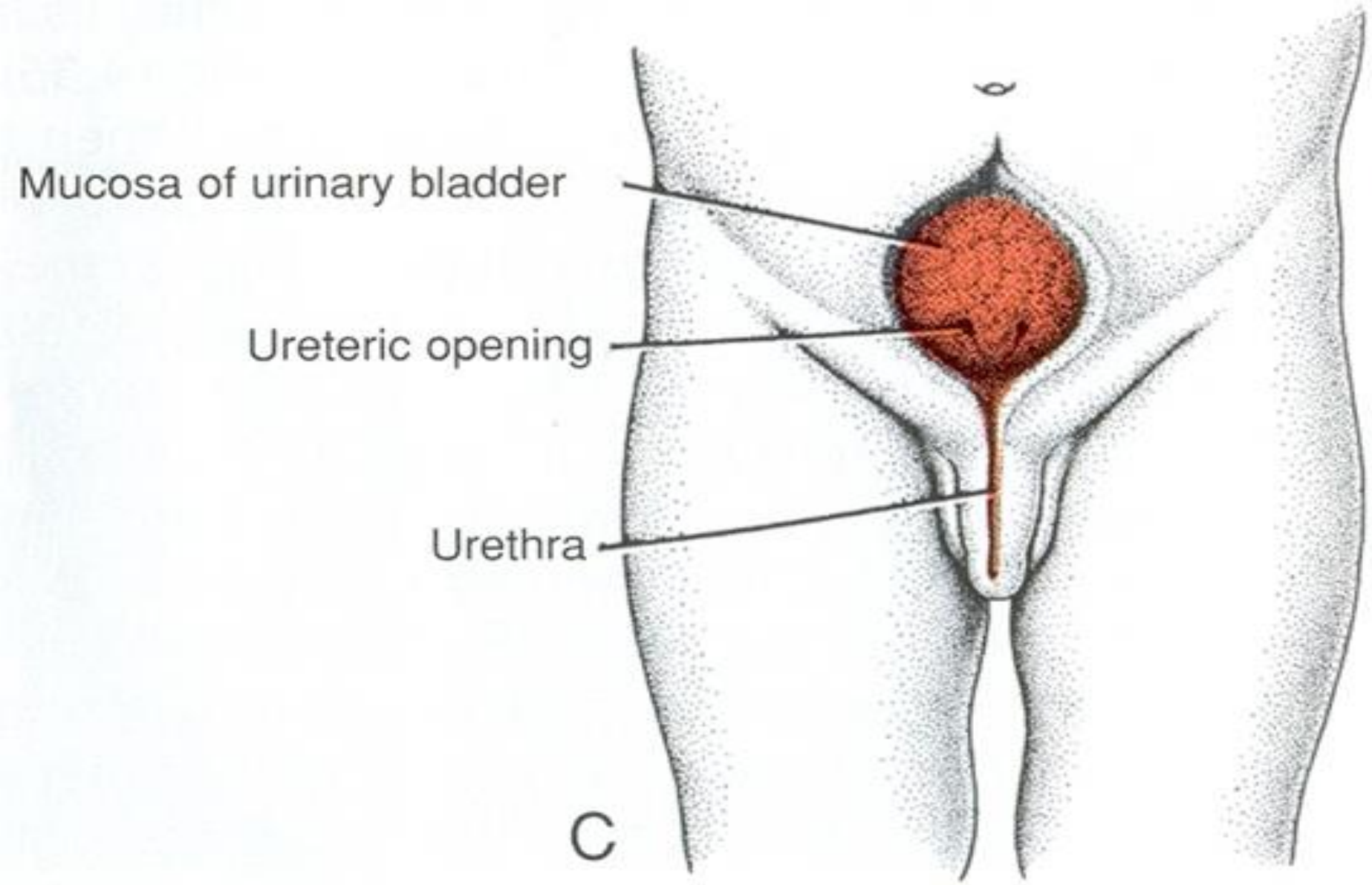
Agenesis of External Genitalia

Double penis

Congenital Anomalies

- ***Micropenis:*** The penis is so small that it is almost hidden by the suprapubic pad of fat. It results from a fetal testicular failure.

- ***Exstrophy of bladder with epispadias***

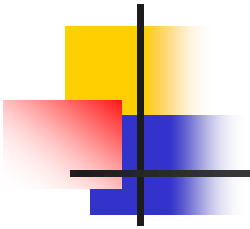


- **Exstrophy of bladder with epispadias**

- For further inquiries ***PLZ*** feel free to contact at any time through email

gamal.abdelhady@yu.edu.jo

gamaltaha@med.asu.edu.eg



Thank You