ANA214: Systemic Embryology

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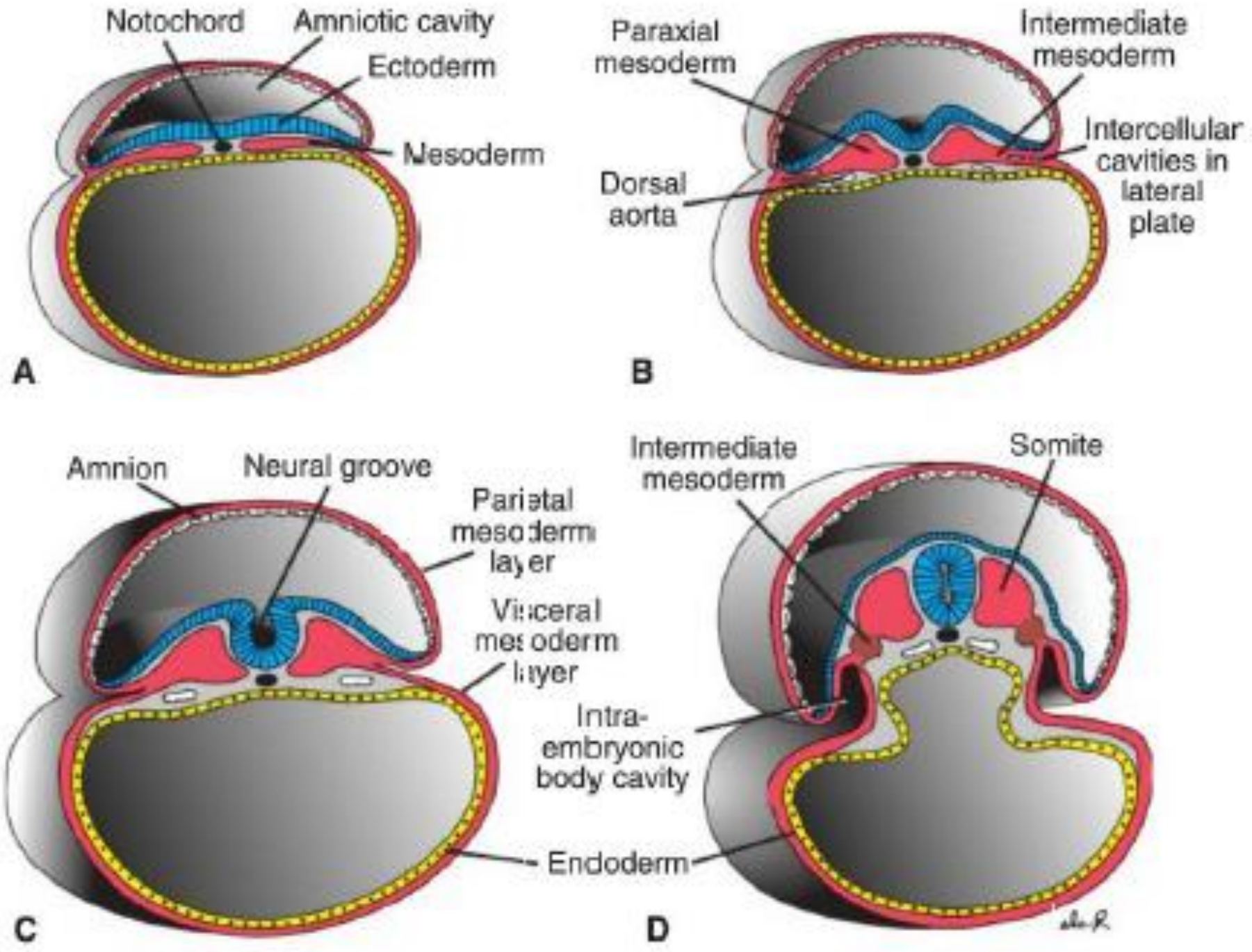
Outline

- Organogenesis foundation
- Respiratory System
  - Larynx
  - Trachea & Bronchi
  - Lungs
- Cardiovascular System
  - Heart
  - Blood vessels
  - Fetal Circulation
  - Changes in Circulation at Birth
- Gastrointestinal System
  - Mouth
  - Pharynx
  - GI Tract
  - Liver, Spleen, Pancreas
- Urogenital system
  - Kidney
  - Ureter
  - Urinary bladder
  - Male urethra
  - Female urethra
  - Prostate
  - Uterus and uterine tubes
  - Vagina
  - External genitalia
  - Testes
  - Ovary
- Nervous System
  - Neurulation
  - Neural crests

Segmentation of Mesoderm

- Start by 17th day
- Under the influence of notochord
- Cells close to midline proliferate – PARAXIAL MESODERM
- Lateral cells remain thin – LATERAL PLATE MESODERM
  - Somatic/Parietal mesoderm – close to amnion
  - Visceral/Splanchnic mesoderm – close to yolk sac
- Intermediate mesoderm connects paraxial and lateral mesoderm


Notochord
Amniotic cavity
Ectoderm
Mesoderm
A
Paraxial mesoderm
Intermediate mesoderm
Intercellular cavities in lateral plate
Dorsal aorta
B
Amnion
Neural groove
Parietal mesoderm layer
Visceral mesoderm layer
Endoderm
C
Intermediate mesoderm
Somite
Intra-embryonic body cavity
D

Paraxial Mesoderm

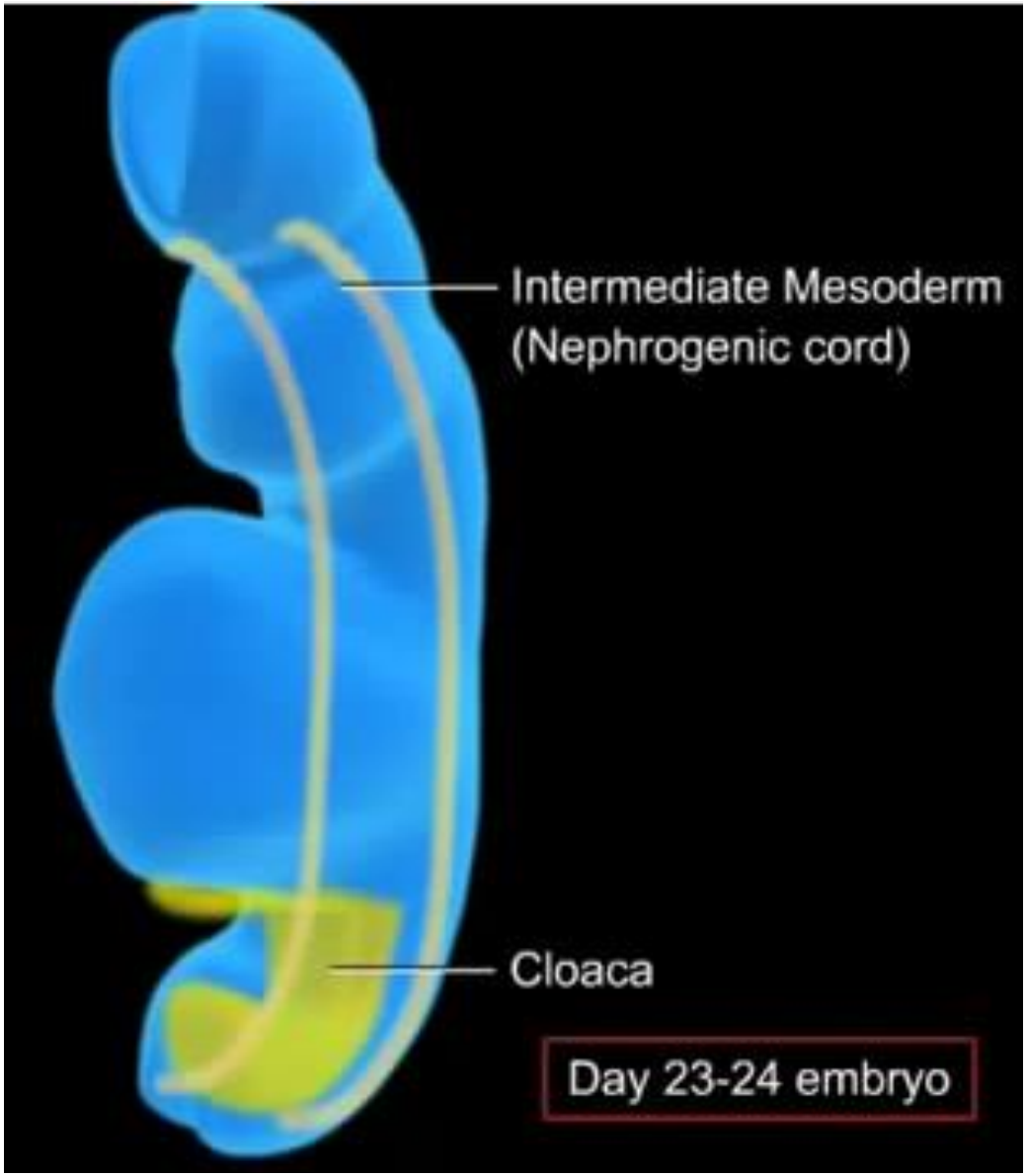
- Paraxial mesoderm organized into segments – **SOMITOMERES**
- Occurs in craniocaudal sequence and start from occipital region
- 1st developed by day 20 (3 pairs per day) – 5th week
- Gives axial skeleton

TABLE 6.2 Number of Somites Correlated to Approximate Age in Days

Approximate Age (d)	Number of Somites
20	1-4
21	4-7
22	7-10
23	10-13
24	13-17
25	17-20
26	20-23
27	23-26
28	26-29
30	34-35

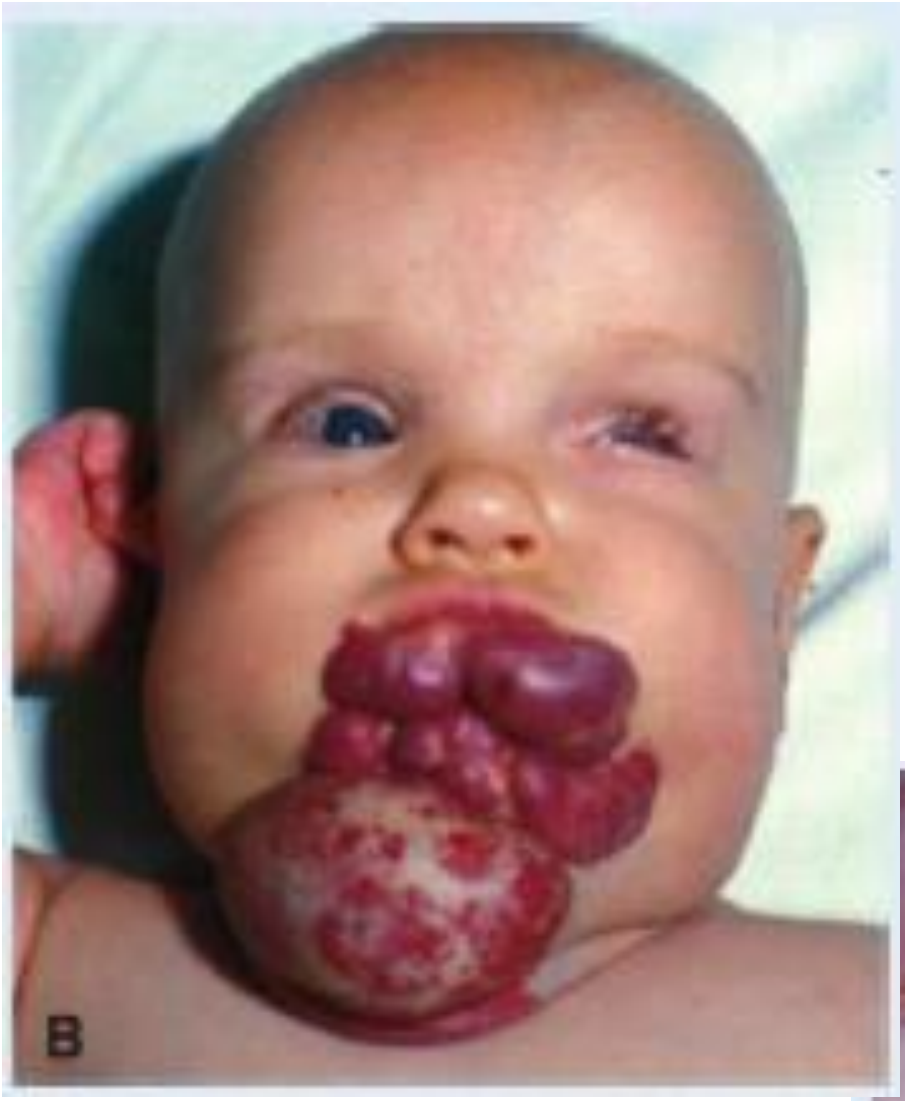
Intermediate Mesoderm

- Differentiate into Urogenital structures
  - Pronephros, mesonephros



Lateral Plate Mesoderm

- Parietal mesoderm + ectoderm = lateral body wall folds
  - Dermis of skin
  - Bones + CT of limb + sternum
- Visceral Mesoderm + endoderm = wall of gut tube
- Parietal mesoderm surrounding cavity = pleura, peritoneal and pericardial cavity
- Blood & Blood Vessels
  - Mesoderm – blood islands
  - Vasculogenesis & angiogenesis


B


A

Neurulation

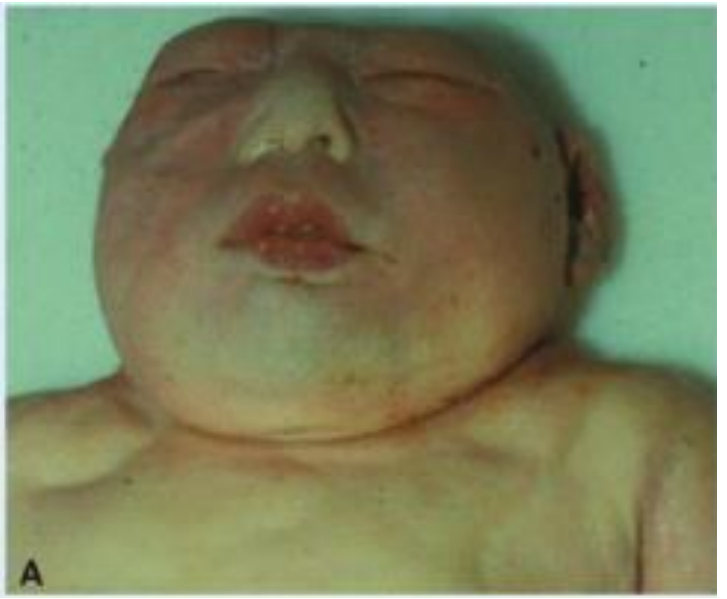
- Under the influence of notochord;
  - Surface ectoderm proliferates – NEURAL PLATE
  - This signal beginning of neurulation
- Lengthening of neural plate
- Lateral edges elevate to form NEURAL FOLD
- The depression is called NEURAL GROOVE
- The folds approach each other at the midline
- Fusion starts at cervical region and proceeds craniocaudally
- This gives NEURAL TUBE
- Cranial (25 day) & Caudal (28) NEUROPORES

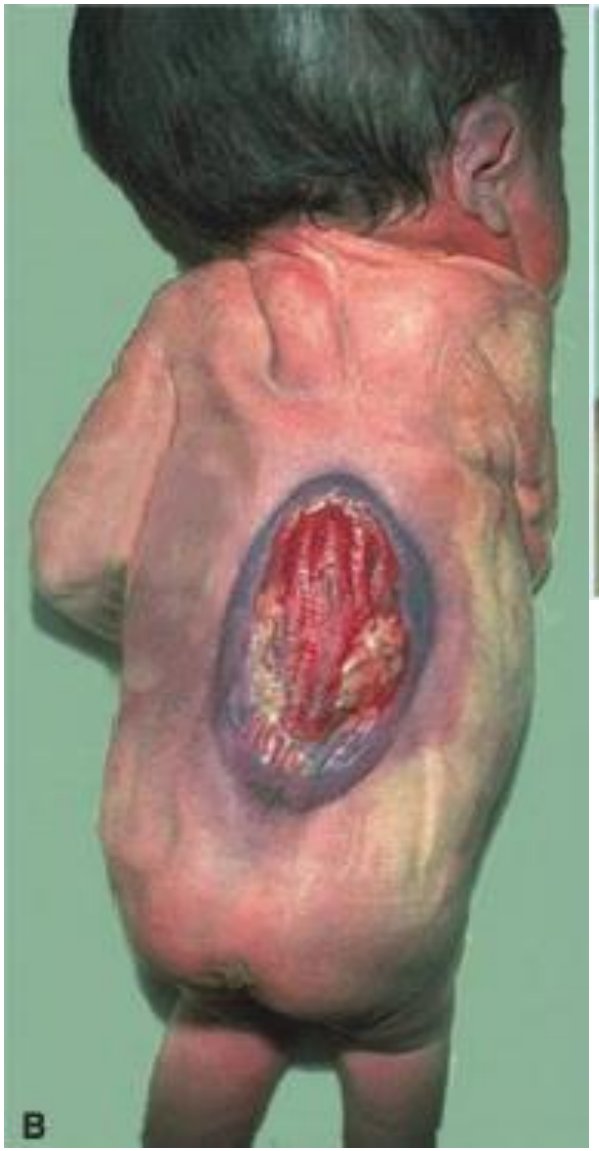
Neurulation

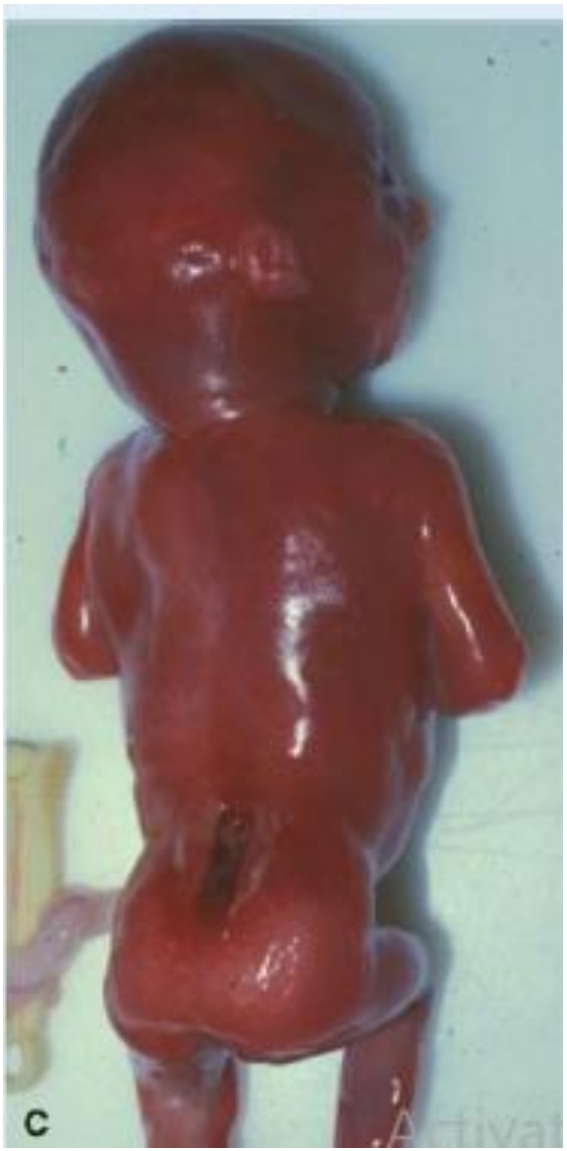
Neurulation marks the beginning of the formation of the central nervous system and is the process whereby the neural plate forms into a neural tube.

Neural Crest Cells

- Cells at the lateral border of neuroectoderm dissociates
- They give rise to NEURAL CREST CELLS
- They form;
  - Melanocytes & Hair follicle
  - Sensory ganglia
  - Sympathetic & enteric neurons
  - Schwann cells
  - Adrenal medulla
  - Craniofacial skeleton


A


B

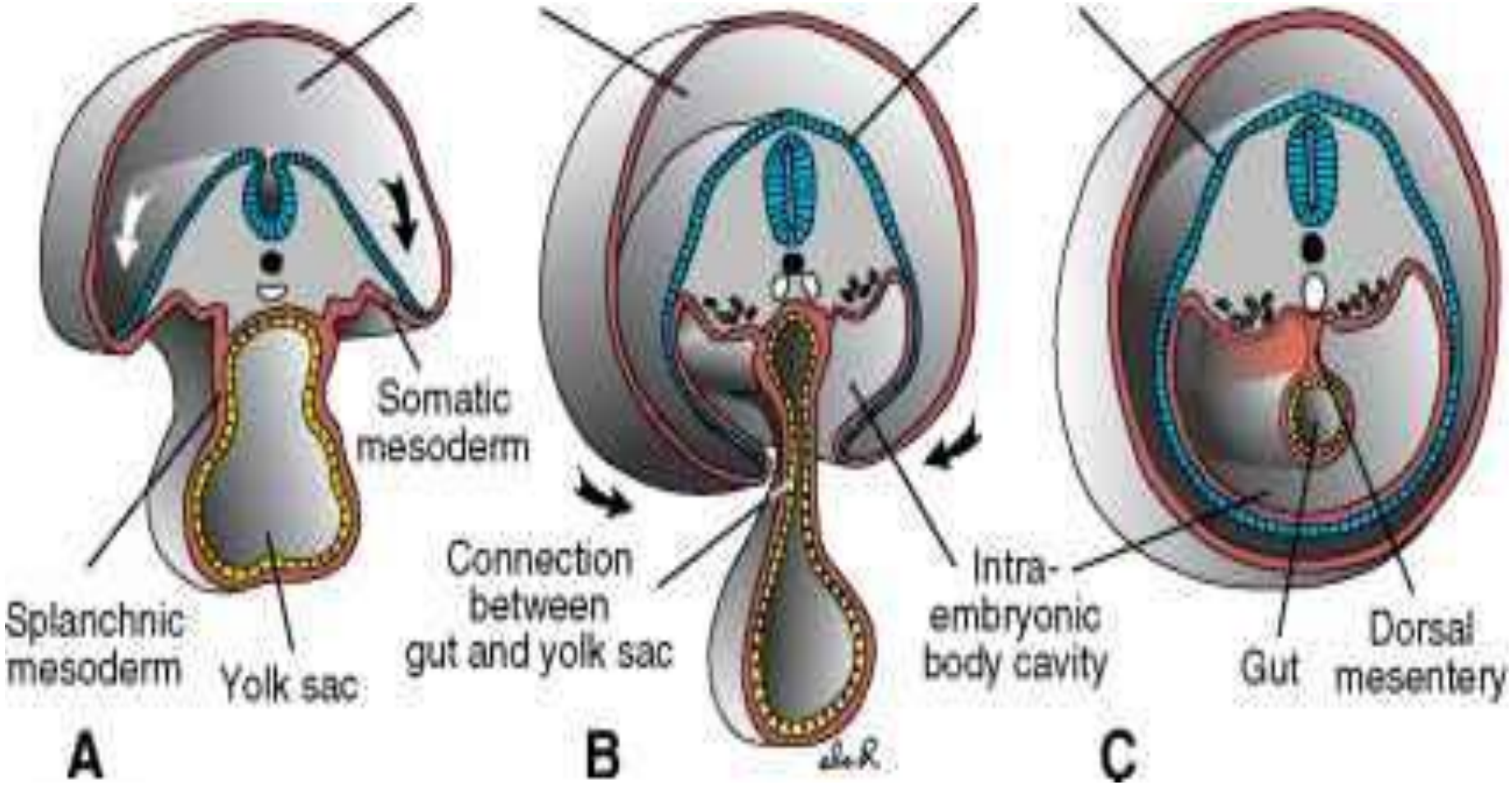

C

Embryonic Folding

- With the development & growth of brain vesicles
  - Embryonic disc bugles into amniotic cavity
  - Lengthening of Neural tube make the embryo to curve into fetal position
  - Head and tail regions move ventrally
- Simultaneously, two lateral body wall folds form and move ventrally
- The amnion is pulled with the fold making the embryo to be surrounded by amniotic cavity
- Ventral body closure is deficient at umbilical region
  - Yolk sac + connecting stalk
- Folding made the endoderm into tube which is divided into 3 by yolk sac

Embryonic folding

From the fourth week of development, the embryo undergoes a rapid development in size and shape.
The trilaminar disc undergoes a process called embryonic folding
to create a basic three dimensional human body plan.


Somatic mesoderm
Splanchnic mesoderm
Yolk sac
A
Connection between gut and yolk sac
B
Intra-embryonic body cavity
Gut
Dorsal mesentery
C

Germ Layers	Derivatives
Ectoderm	CNS, PNS, Sensory part of eye, ear & nose, epidermis & its appendages Mammary glands, pituitary gland, subcutaneous glands, enamel of teeth, Neural crest cells – spinal, cranial (V, VII, IX & X) & autonomic ganglia, Schwann cells, pigment cells of dermis, pharyngeal arch muscles, bones & CT, meninges and adrenal medulla
Mesoderm	CT, cartilage, bone, muscle, heart, blood & lymphatic vessels, kidneys, ovaries, testes, genital ducts, serous membranes of body cavities, spleen, adrenal cortex
Endoderm	Epithelial lining of GIT & Respiratory, tonsils, thyroid & parathyroid glands, thymus, liver, pancreas, epithelial lining of urinary bladder & most of urethra, & auditory tube

TABLE 6.4 Summary of Key Events during the Embryonic Period

Days	Somites	Length (mm)	Figure	Characteristic Features
14–15	0	0.2	6.1*A*	Appearance of primitive streak
16–18	0	0.4	6.1*B*	Notochordal process appears; hemopoietic cells in yolk sac
19–20	0	1.0–2.0	6.2*A*	Intraembryonic mesoderm spread under cranial ectoderm; primitive streak continues; umbilical vessels and cranial neural folds begin to form
20–21	1–4	2.0–3.0	6.2*B,C*	Cranial neural folds elevated and deep neural groove established; embryo begins to bend
22–23	5–12	3.0–3.5	6.3*B,C*	Fusion of neural folds begins in cervical region; cranial and caudal neuropores open widely; visceral arches 1 and 2 present; heart tube begins to fold
24–25	13–20	3.0–4.5	6.4	Cephalocaudal folding under way; cranial neuropore closing or closed; optic vesicles formed; otic placodes appear
26–27	21–29	3.5–5.0	6.4*B*	Caudal neuropore closing or closed; upper limb buds appear; three pairs of visceral arches
28–30	30–35	4.0–6.0	6.21*A*	Fourth visceral arch formed; hind limb buds appear; otic vesicle and lens placode
31–35		7.0–10.0	6.22	Forelimbs paddle-shaped; nasal pits formed; embryo tightly C-shaped
36–42		9.0–14.0	6.23	Digital rays in hand and foot plates; brain vesicles prominent; external auricle forms from auricular hillocks; umbilical herniation initiated
43–49		13.0–22.0	6.24	Pigmentation of retina visible; digital rays separate; nipples and eyelids formed; maxillary swellings fuse with medial nasal swellings as upper lip forms; prominent umbilical herniation
50–56		21.0–31.0	6.25	Limbs long, bent at elbows, knees; fingers, toes free; face more humanlike; tail disappears; umbilical herniation persists to end of third month

Respiratory System

- Develops from median diverticulum of the foregut
- Appears first as ***Tracheobronchial Groove***
- Distal part gets separated from the esophagus
- Free caudal end divides into **2**
- The free end forms bud called ***Lung Bud***

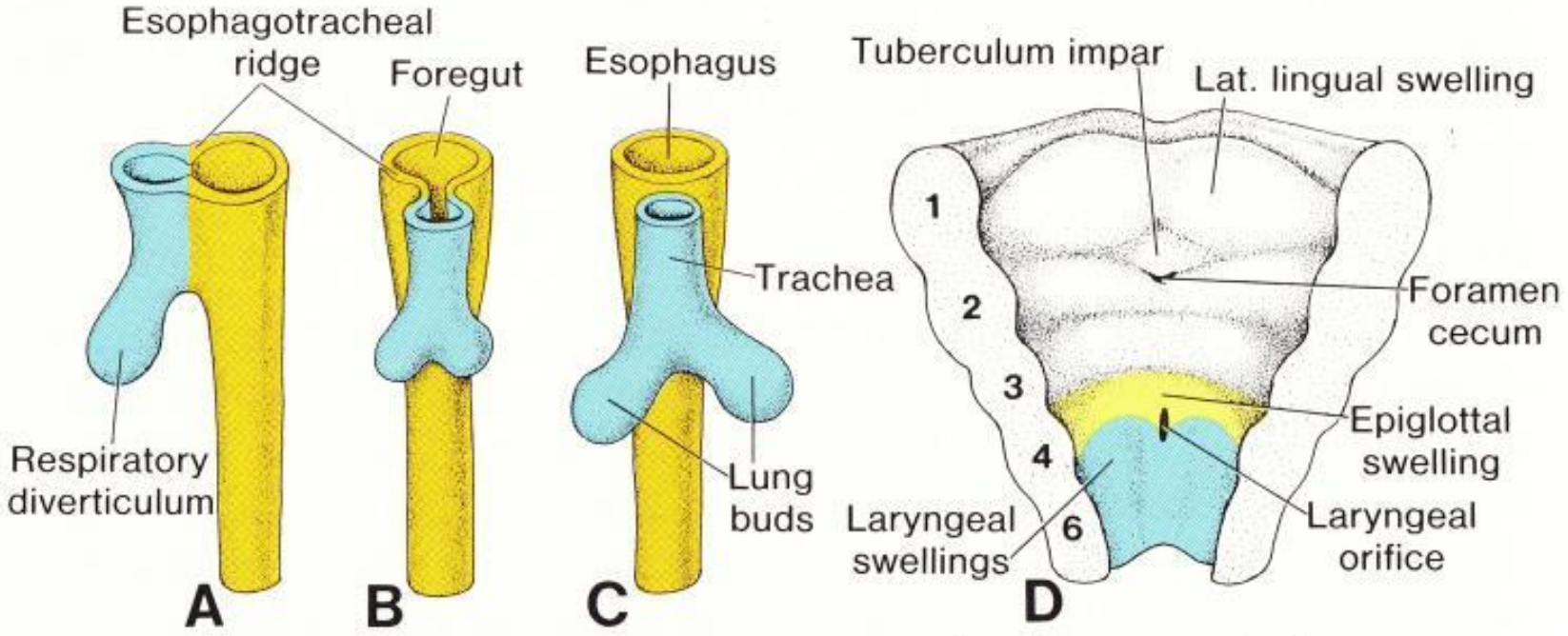


Figure 13-2. (*A–C*) Successive stages in the development of the respiratory diverticulum. Note the esophagotracheal ridges and the formation of the septum, splitting the foregut into the esophagus and trachea with lung buds. (*D*) The ventral portion of the pharynx seen from above. Note the laryngeal orifice and the surrounding swellings.

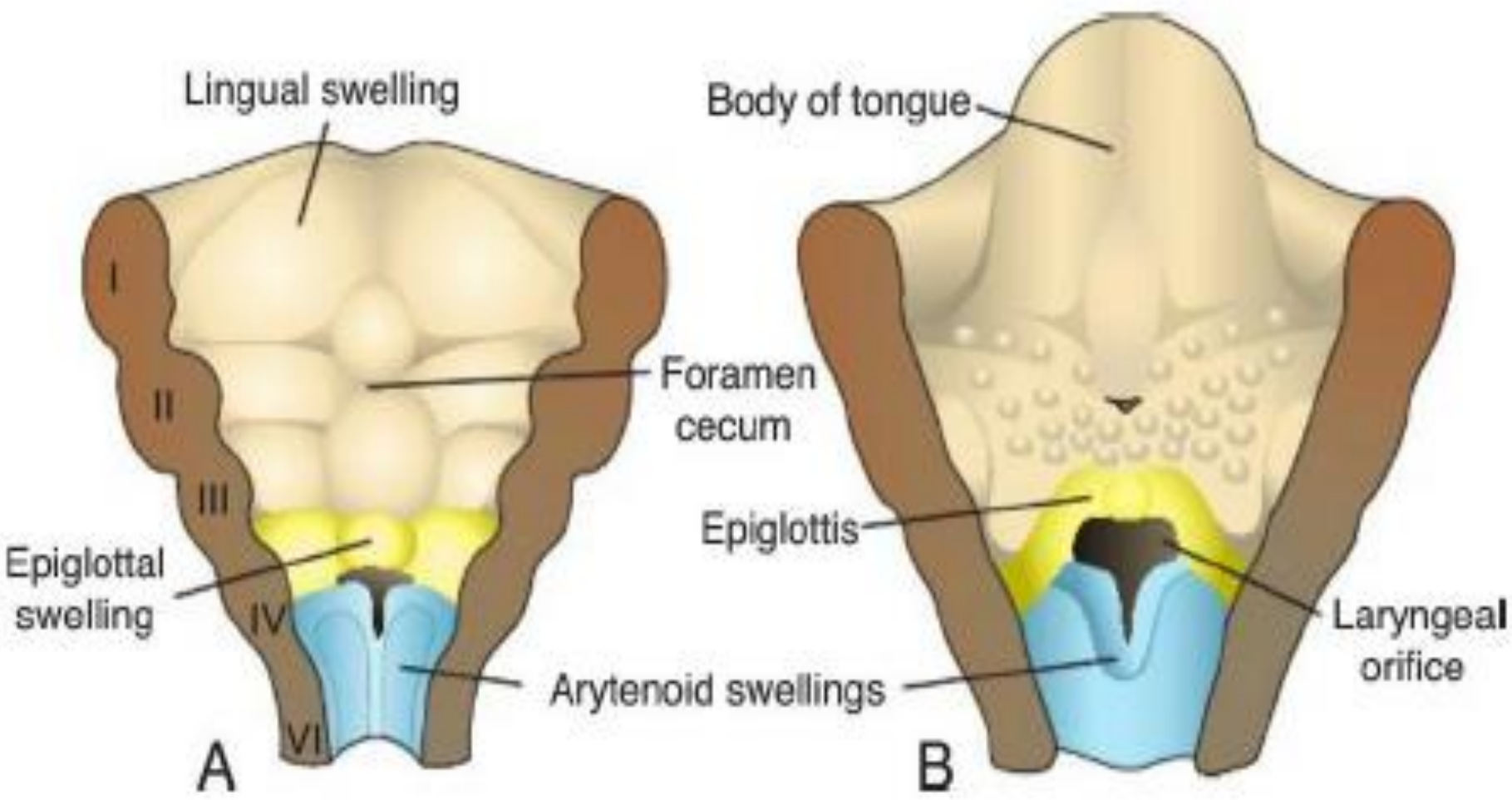
Respiratory System

LARYNX

- **Develops from the cranial most part of respiratory diverticulum**
- **The caudal part of hypochrondial eminence forms *Epiglottis***
- ***Thyroid, Cricoid and Arytenoid* cartilages are from 4th, 5th, and 6th pharyngeal arches**

Congenital Anomalies

- Laryngocoele: swelling
- Congenital stenosis/atresia: blockage
- Laryngoptosis: abnormal location
- Absence of laryngeal cartilage
- Duplication of parts or all of larynx


Lingual swelling
I
II
III
IV
VI
Epiglottal swelling
Foramen cecum
A
Body of tongue
Epiglottis
Laryngeal orifice
Arytenoid swellings
B

Respiratory System

Trachea and Bronchi

- Develops from part between point of bifurcation and larynx
- The division forms the **Right and Left Principal Bronchi**
- The main bronchi gives the **Lobar (2 in left, 3 in right) bronchi**
- The left is more transverse than the right
- The main bronchi further subdivides into **Lobar Bronchi (2L, 3R)**

Respiratory System

Lungs

- Formed by further subdivisions of lobar bronchi (17 b4 birth)
- Alveoli are formed by the expansion of the terminal parts of the tree
- Each segments of the tree is lined by mesoderm which gives fissures
- Pulmonary circulation is adequate by 7^{th} month
- **NB:**
  - **Respiratory passages are full of fluid**
  - **When breathing commences, the fluid is absorbed and some expelled**

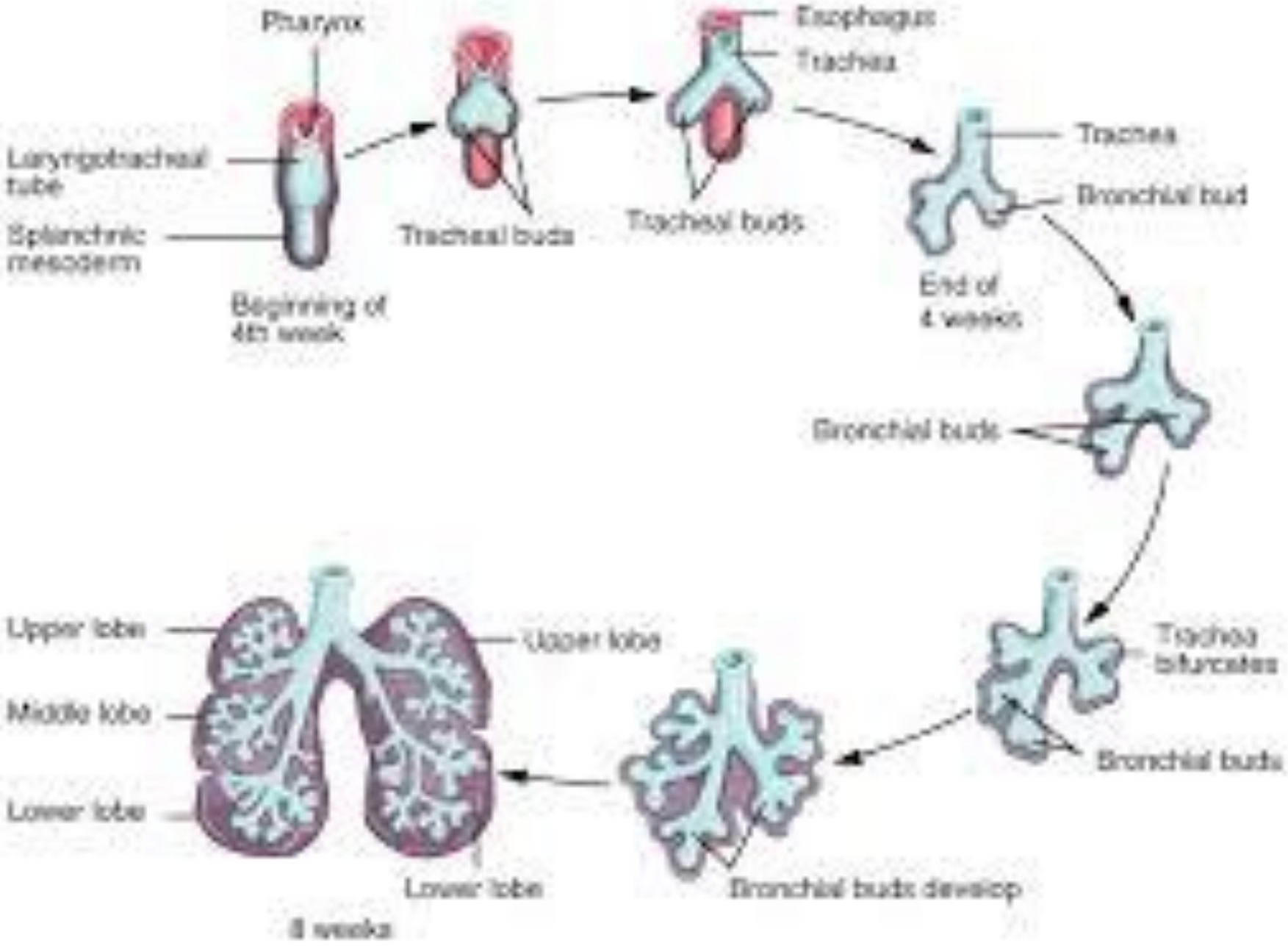

Pharynx
Laryngotracheal tube
Splanchnic mesoderm
Beginning of 4th week
Tracheal buds
Esophagus
Trachea
Tracheal buds
Trachea
Bronchial bud
End of 4 weeks
Bronchial buds
Trachea bifurcates
Bronchial buds
Bronchial buds develop
Upper lobe
Middle lobe
Lower lobe
Upper lobe
Lower lobe
8 weeks

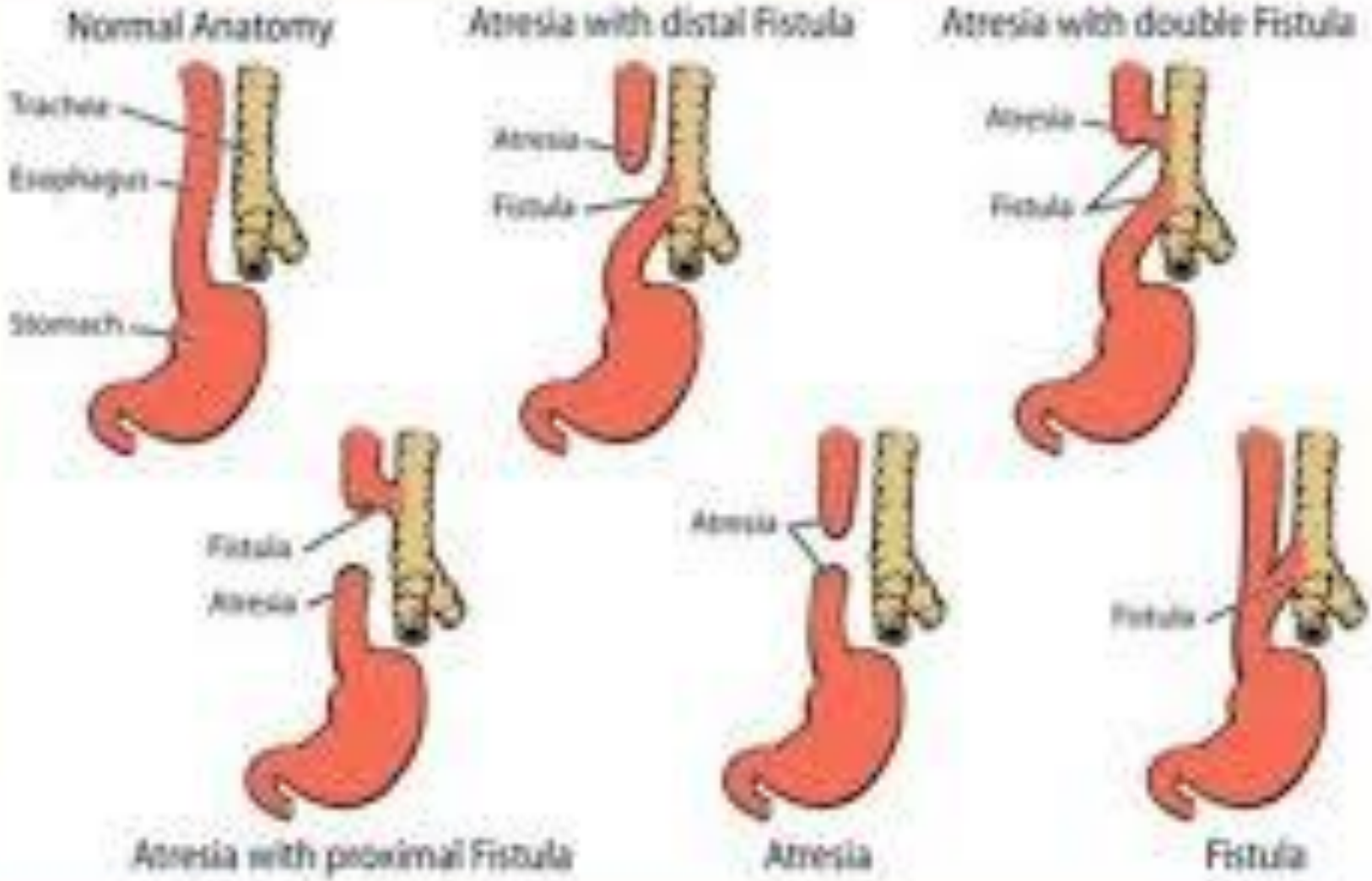
TABLE 14.1 Maturation of the Lungs

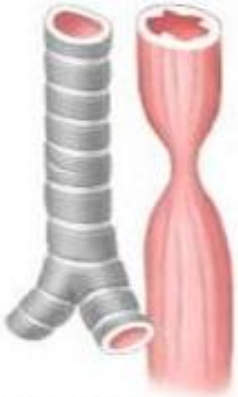
Pseudoglandular period	5–16 wk	Branching has continued to form terminal bronchioles. No respiratory bronchioles or alveoli are present.
Canalicular period	16–26 wk	Each terminal bronchiole divides into two or more respiratory bronchioles, which in turn divide into three to six alveolar ducts.
Terminal sac period	26 wk to birth	Terminal sacs (primitive alveoli) form, and capillaries establish close contact.
Alveolar period	8 mo to childhood	Mature alveoli have well-developed epithelial endothelial (capillary) contacts.

Congenital Anomalies

- Trachea
  - Tracheo-oesophageal fistulae
  - Accessory bronchi
  - Absence of trachea
  - Trachea diverticulum
- Bronchi & Lungs
  - Agenesis/hypoplasia
  - Absence of fissures
  - Presence of abnormal fissures
  - Accessory lobes
  - Lung sequestration
  - Lung hernia
  - Displaced bronchi
  - Respiratory distress syndrome (premature infant)

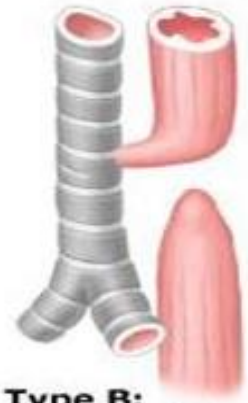
Types of TEF


Normal Anatomy
Trachea
Esophagus
Stomach
Atresia with distal Fistula
Atresia
Fistula
Atresia with double Fistula
Fistula
Fistula
Atresia
Atresia with proximal Fistula
Atresia
Fistula

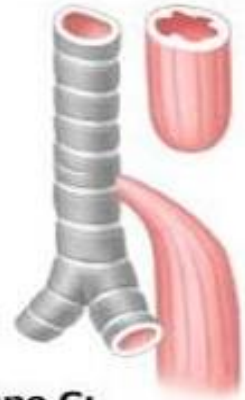


Type: A
Esophageal atresia without tracheoesophageal fistula (8% of cases)

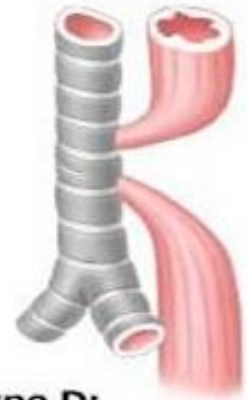
Esophageal atresia with tracheoesophageal fistula (88% of cases)



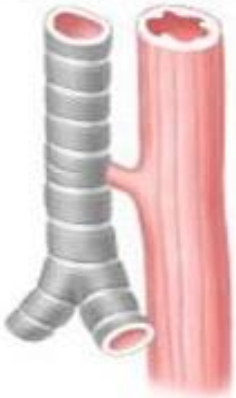
Type B:
Esophageal atresia with proximal tracheoesophageal fistula (1% of cases)



Type C:
Esophageal atresia with distal tracheoesophageal fistula (84% of cases)



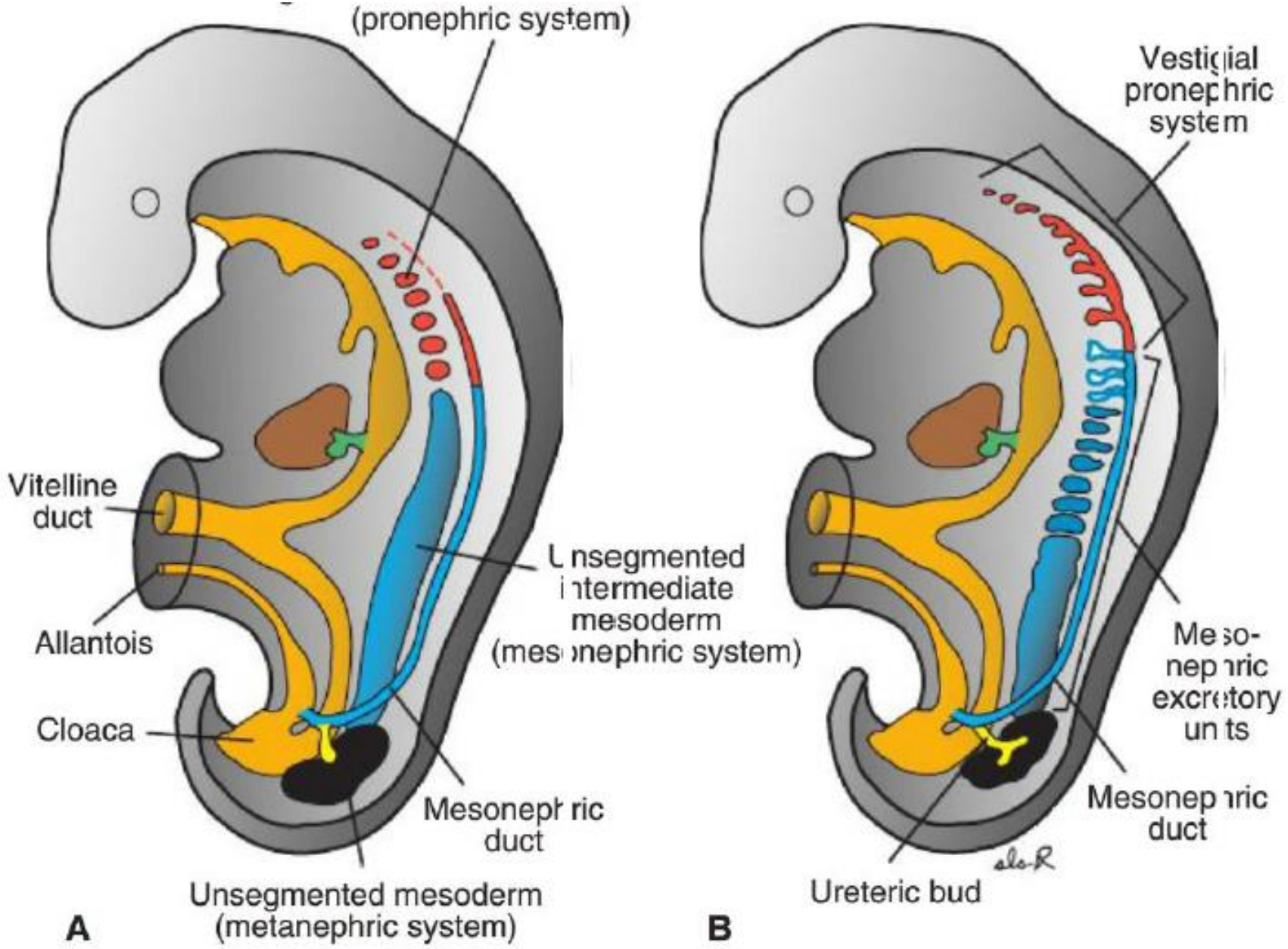
Type D:
Esophageal atresia wit proximal and distal tracheoesophageal fistula (3% of cases)



Type E:
Tracheoesophageal fistula without esophageal atresia (H-type) (4% of cases)

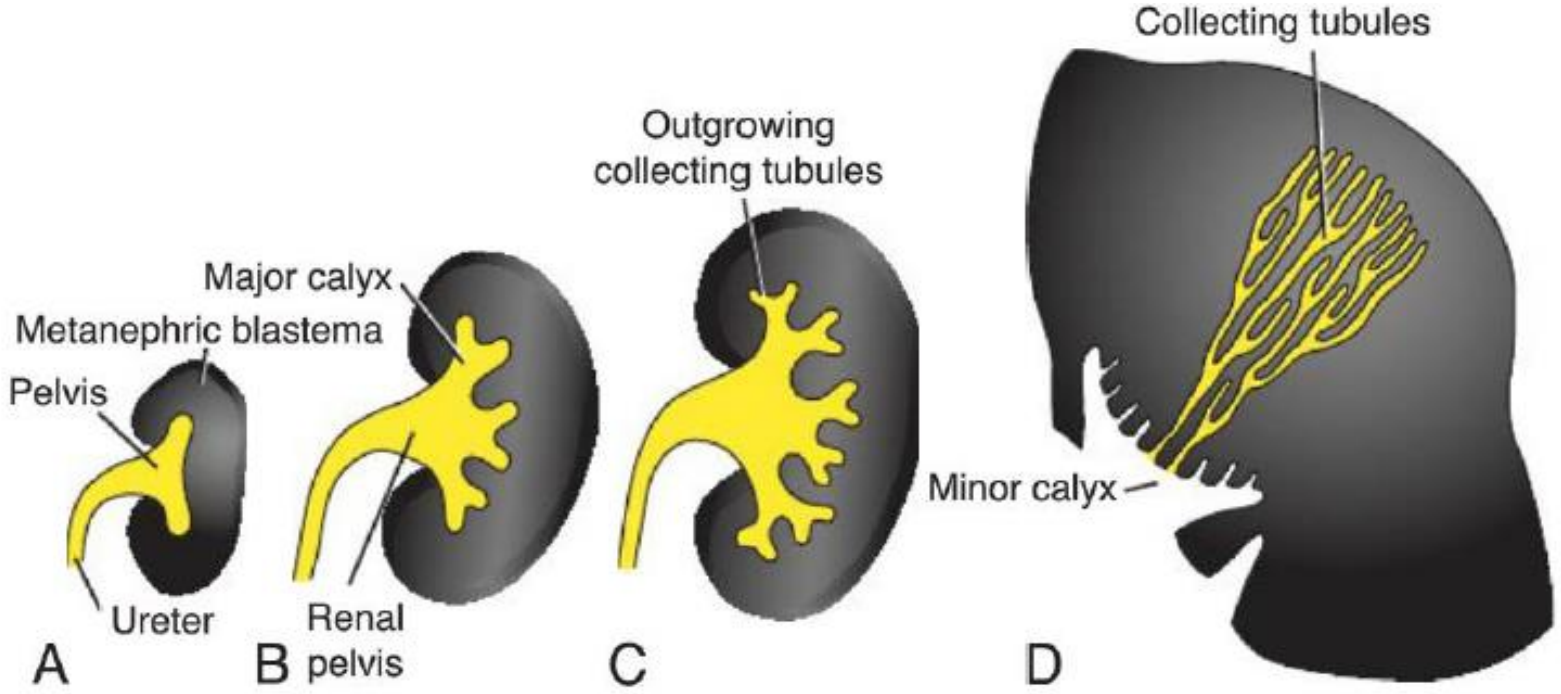
Development Urinary System

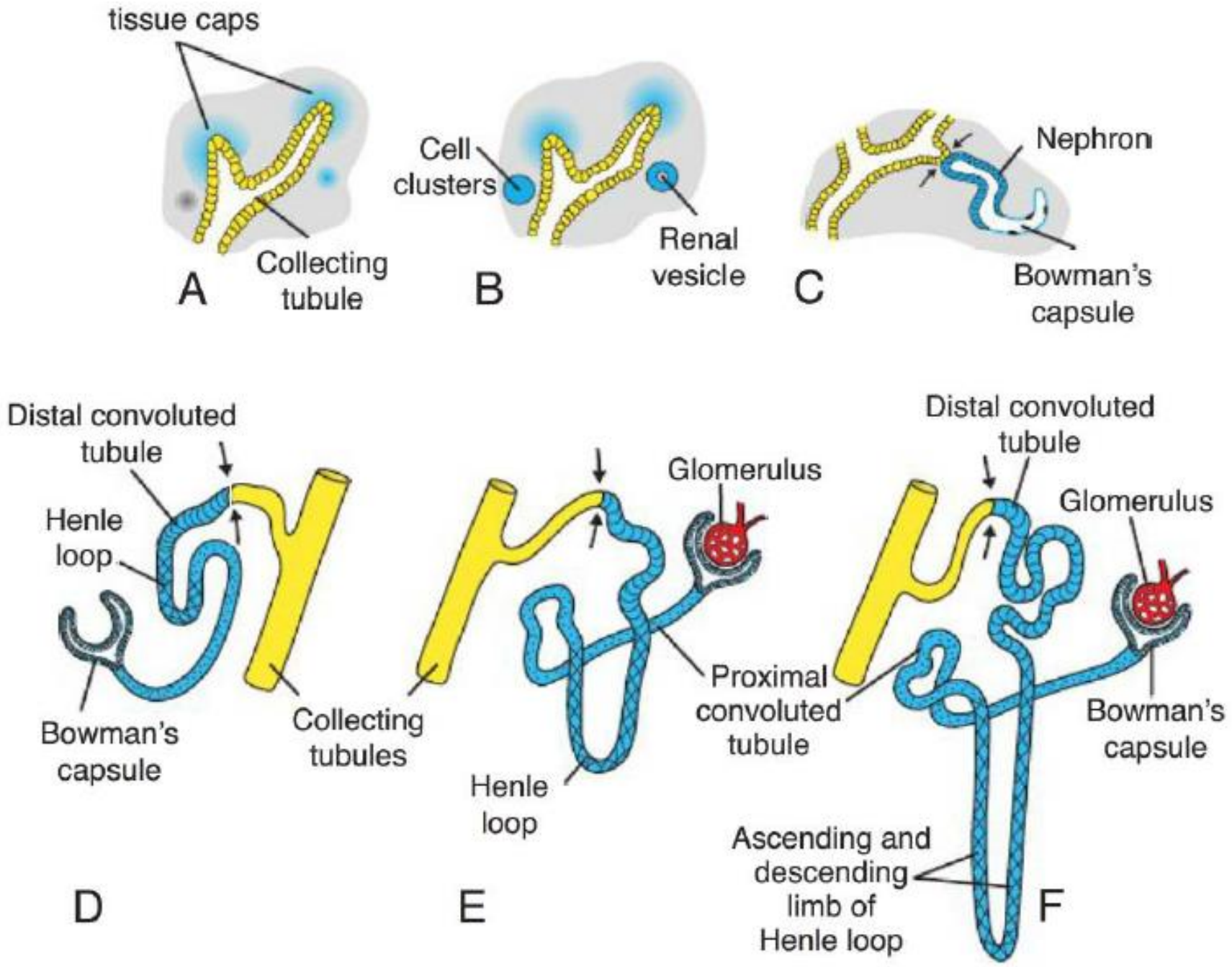
- Pronephros
  - 4th week
  - 7-10 solid cell in cervical region
  - Vestigial excretory units (nephrotomes)
  - Regresses by the end of 4th week
- Mesonephros
  - Develop in the upper thoracic to lumbar (L3) region
  - Excretory tubules appear in the early 4th week
  - Increased in length to form S-shaped loop
  - Forms primitive nephrons
  - Laterally the tubules joins mesonephric/Wolffian duct
  - Middle of 2nd month, urogenital ridge appears
  - Majority of tubules degenerate by end of 2nd month


(pronephric system)
Vestigial pronephric system
Vitelline duct
Allantois
Cloaca
Unsegmented intermediate mesoderm (mesonephric system)
Mesonephric duct
Unsegmented mesoderm (metanephric system)
Mesonephric excretory units
Mesonephric duct
Ureteric bud
A
B

Development Urinary System

- Metanephros (Definite Kidney)
  - Appears in 5th week
  - Excretory units develops from metanephric mesoderm
- Collecting System
  - Develops from ureteric bud
  - Bud penetrates metanephric tissue
  - Give rise to; ureter, renal pelvis, major & minor calyces, 1-3 million collecting tubules
- Excretory System
  - The collecting tubule isw covered by metanephric tissue cap
  - Cap – vesicles – S-shaped tubules
  - Glomerulus grows into one-end of the S and later forms Bowman's capsule
  - The continuous elongation of the other part give rise to PCT, Loop of Henle, DCT
  - Urine production start around 10th week


Collecting tubules
Outgrowing collecting tubules
Major calyx
Metanephric blastema
Pelvis
Minor calyx
Ureter
Renal pelvis
A
B
C
D


tissue caps
Collecting tubule
A
Cell clusters
Renal vesicle
B
Nephron
Bowman's capsule
C
Distal convoluted tubule
Henle loop
Bowman's capsule
Collecting tubules
D
Glomerulus
Proximal convoluted tubule
Henle loop
E
Distal convoluted tubule
Glomerulus
Bowman's capsule
Ascending and descending limb of Henle loop
F

Clinical Correlates

- Wilms tumor: mutation
- Renal dysplasia and agenesis
  - Multicystic dysplastic kidney; undifferentiated metanephric tissue
  - Potter sequence
- Congenital polycystic kidney disease – cilia disorder
- Duplication of ureter
- Pelvic kidney
- Horseshoe kidney
- Acessory renal; arteries

Development Urinary System

- Bladder & Urethra
  - In 4^{th}-7^{th} weeks, cloaca divides to urogenital sinus & anal canal
  - Urorectal septum separates the two (tip give rise to perineal body)
  - Urogenital sinus divides to three;
    - Upper part (largest) – urinary bladder
    - Pelvic part – in male give prostatic and membranous urethra
    - Phallic part – flattened & grows with genital tubercle
  - Caudal portion of mesonephric ducts are absorbed into bladder
  - Mesonephric duct gives the ejaculatory duct
  - At the end of 3^{rd} month, epithelium of prostatic urethra proliferates to give prostate gland (male), urethral & paraurethral glands (female)

Development Urinary System

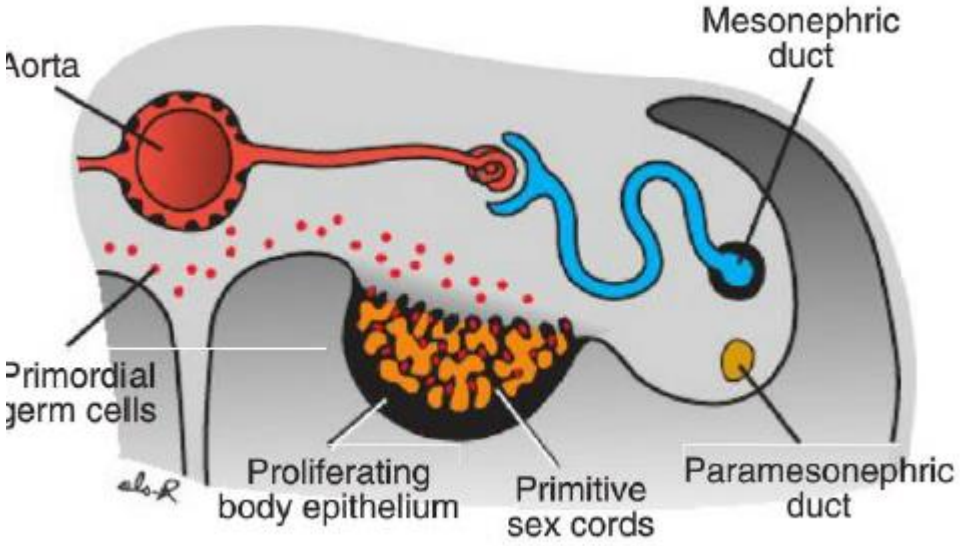
- Congenital Anomalies
  - Urachal fistula
  - Urachal cyst
  - Urachal sinus
  - Exstrophy of bladder
  - Exstrophy of cloaca

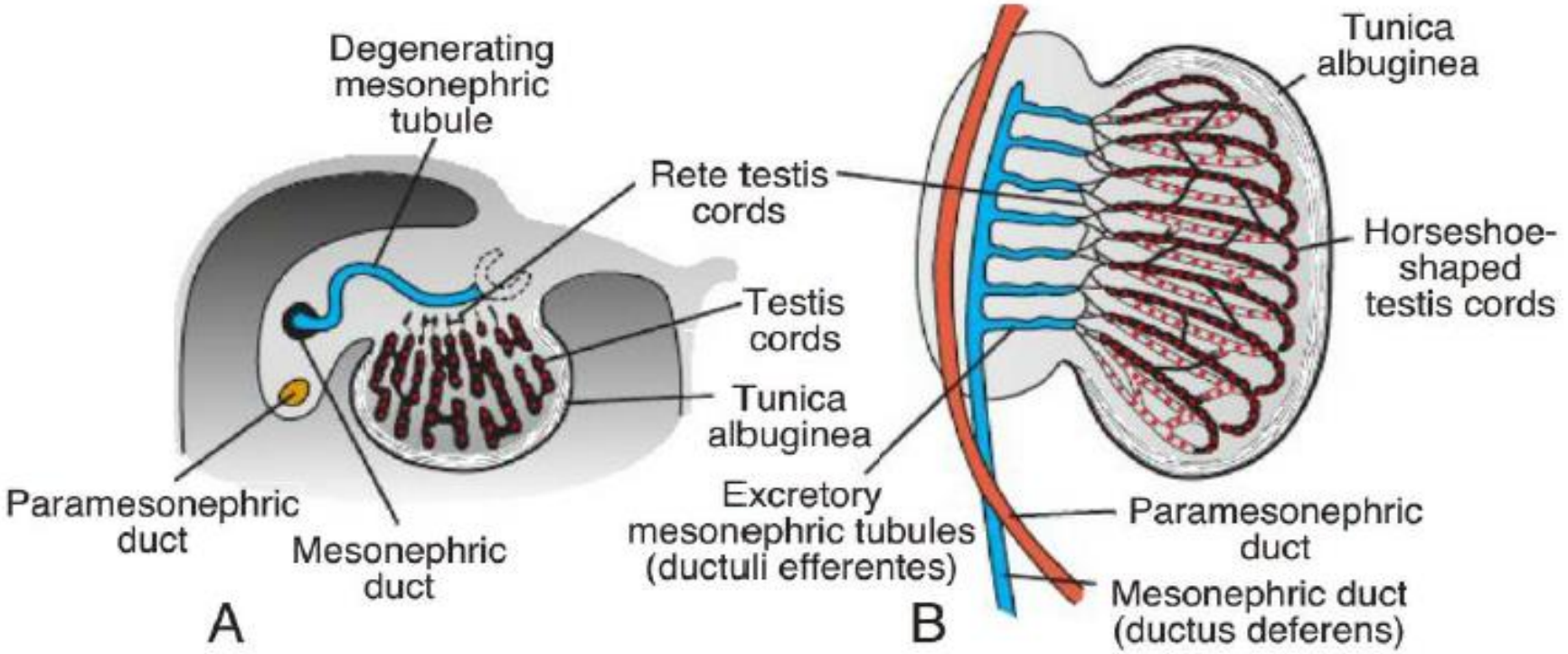
Development Genital System

- Gonads
  - Appear as pair of longitudinal ridges **GONADAL/GENITAL RIDGES**
  - Germ cells appear in the ridges by 6th week
  - Primordial germ cells originate in the epiblast
  - Migrate through primitive streak to wall of yolk sac close to allantois
  - By 4th week, move to primitive gonads by ameboid movement
  - Arrived by 5th week and invade the genital ridges in the 6th week
  - Shortly before arrival, epithelium of genital ridges proliferate
  - Epithelium penetrates underlying mesenchyme forming irregular shaped cords PRIMITIVE SEX CORDS

Development Genital System

- Testis
  - Due to Y chromosome, SRY gene encodes for testis-determining factor
  - Primitive sex cords continue to proliferate and penetrate deep to the medulla MEDULLARY CORDS
  - Towards the hilum, cords break up into network of tiny cell strands – **rete testis**
  - **Tunica albuginea** develops to separate testis cords from surface epithelium
  - By 4th month, testis cords become horseshoe-shaped, continuous with rete testis
  - Testis cords composed of primitive germ cells, supporting cells (epithelium)
  - Leydig cells (gonadal ridge mesenchyme), produce testosterone by 8th week


Aorta
Mesonephric duct
Primordial germ cells
Proliferating body epithelium
Primitive sex cords
Paramesonephric duct


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

Development Genital System

- Ovary
  - Due to absence of Y chromosome
  - Primitive sex cords dissociate into irregular clusters containing groups of primitive germ cells
  - They disappear and replaced by vascular stroma giving **ovarian medulla**
  - Surface epithelium proliferates to give **cortical cords** by 7^{th} week
  - In 3^{rd} month cortical cords split into cell clusters
  - The cell clusters proliferate and surround each oogonium forming primordial follicle

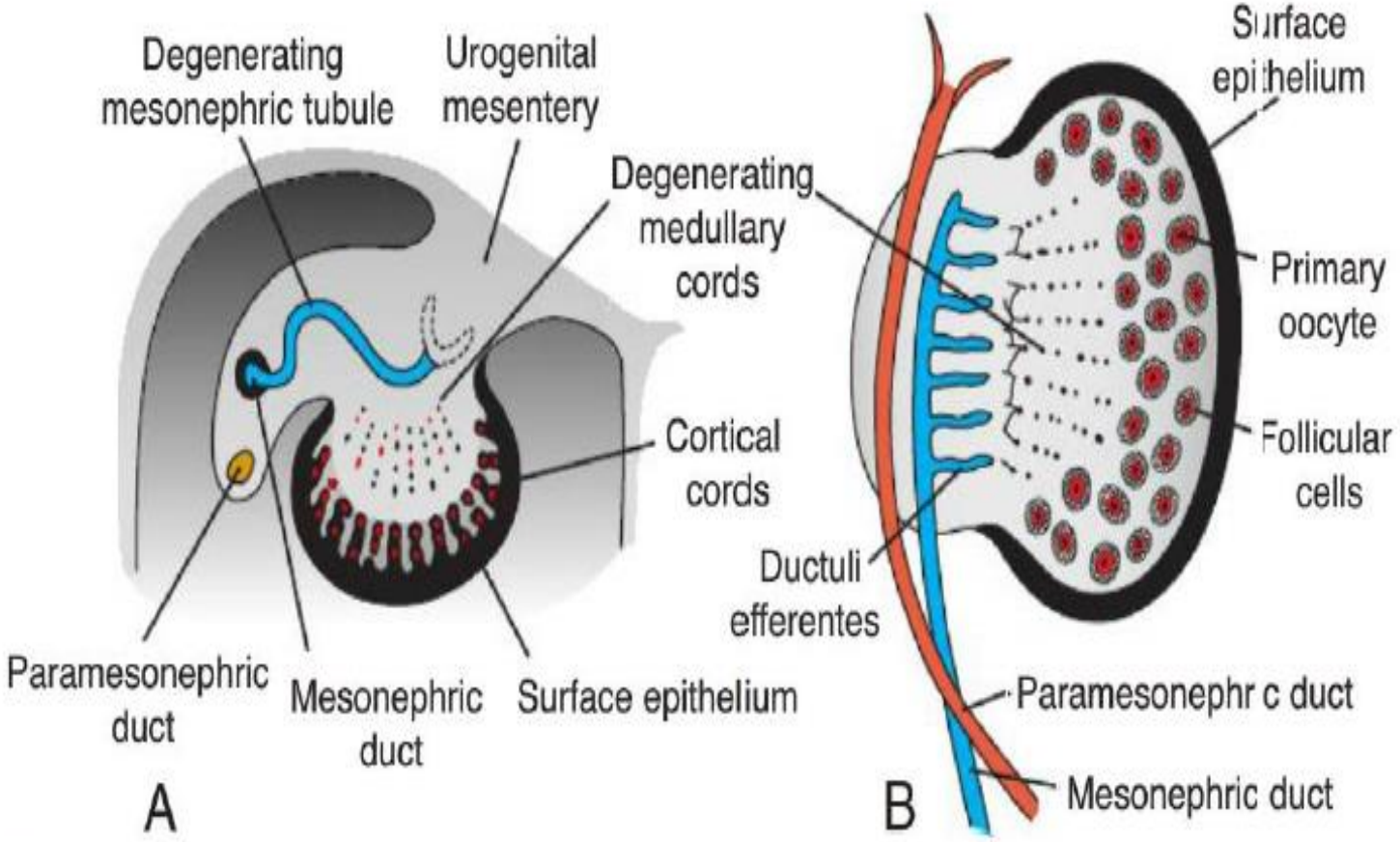
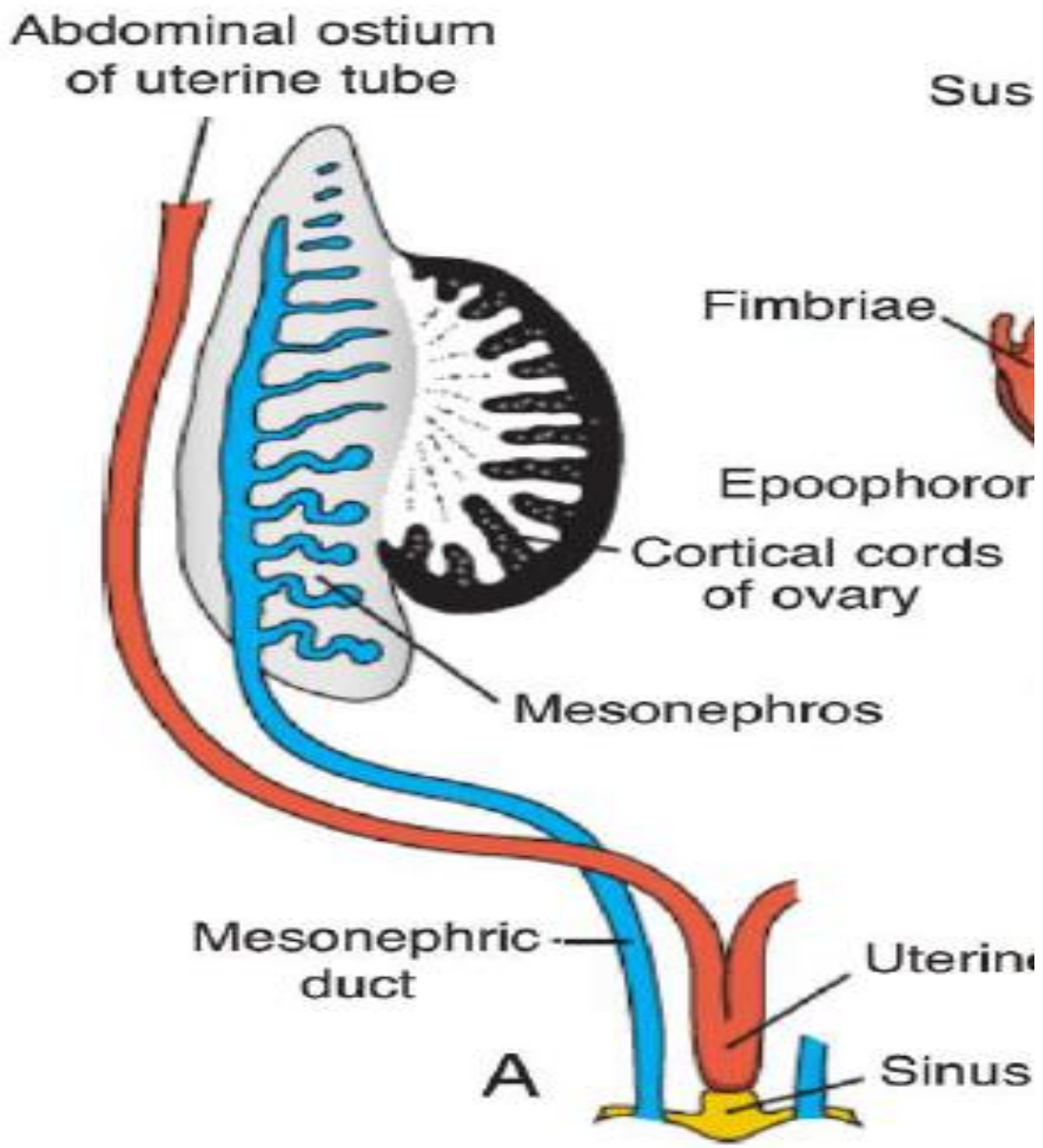


FIGURE 16.22 **A.** Transverse section of the ovary at the seventh week, showing degeneration of the primitive (medullary) sex cords and formation of the cortical cords. **B.** Ovary and genital ducts in the fifth month. Note degeneration of the medullary cords. The excretory mesonephric tubules (efferent ductules) do not communicate with the rete. The cortical zone of the ovary contains groups of oogonia surrounded by follicular cells.

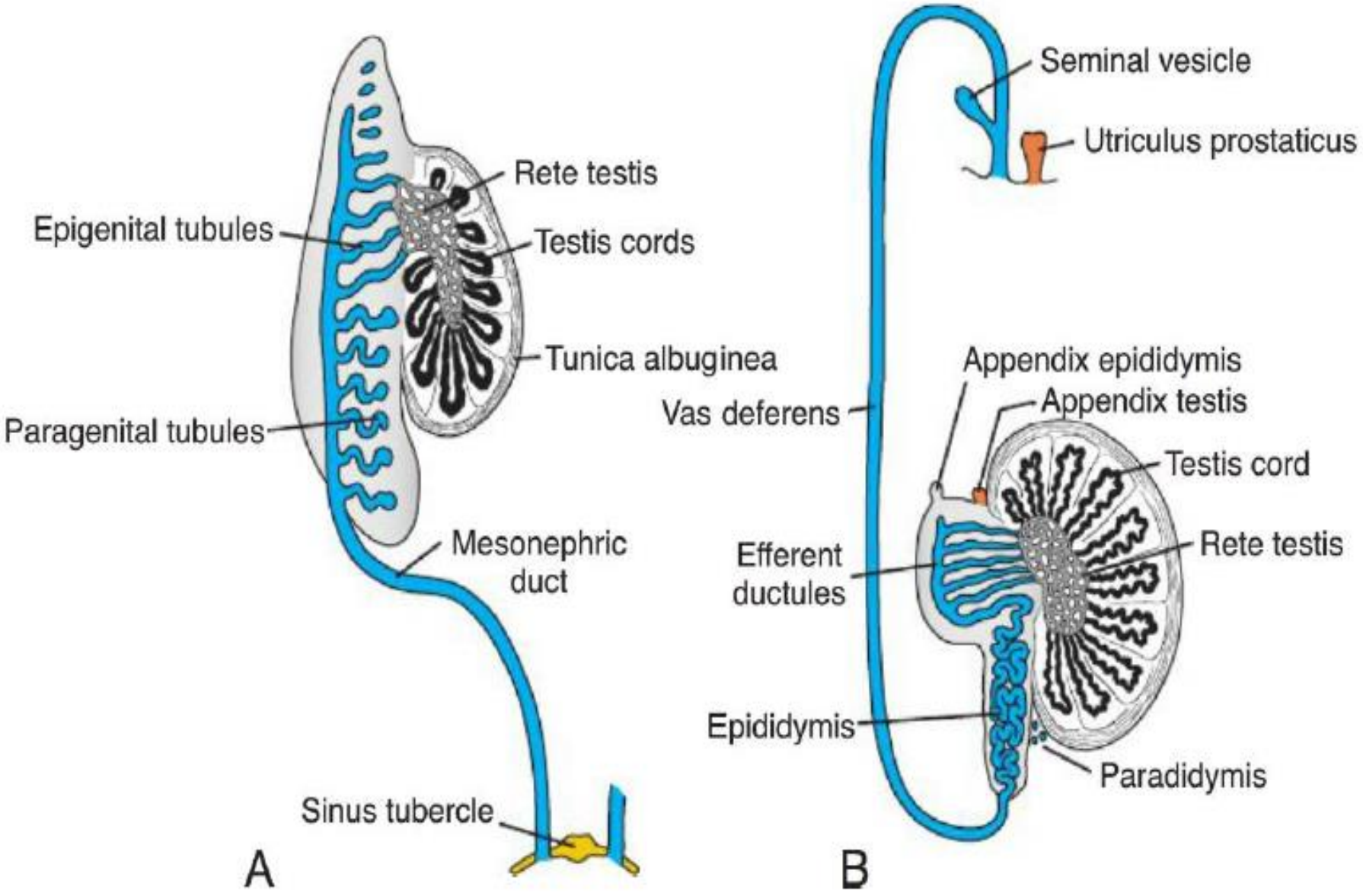
Development Genital System

- Genital duct
  - Mesonephric (Wolfian) ducts
  - Paramesonephric (Müllerian) ducts



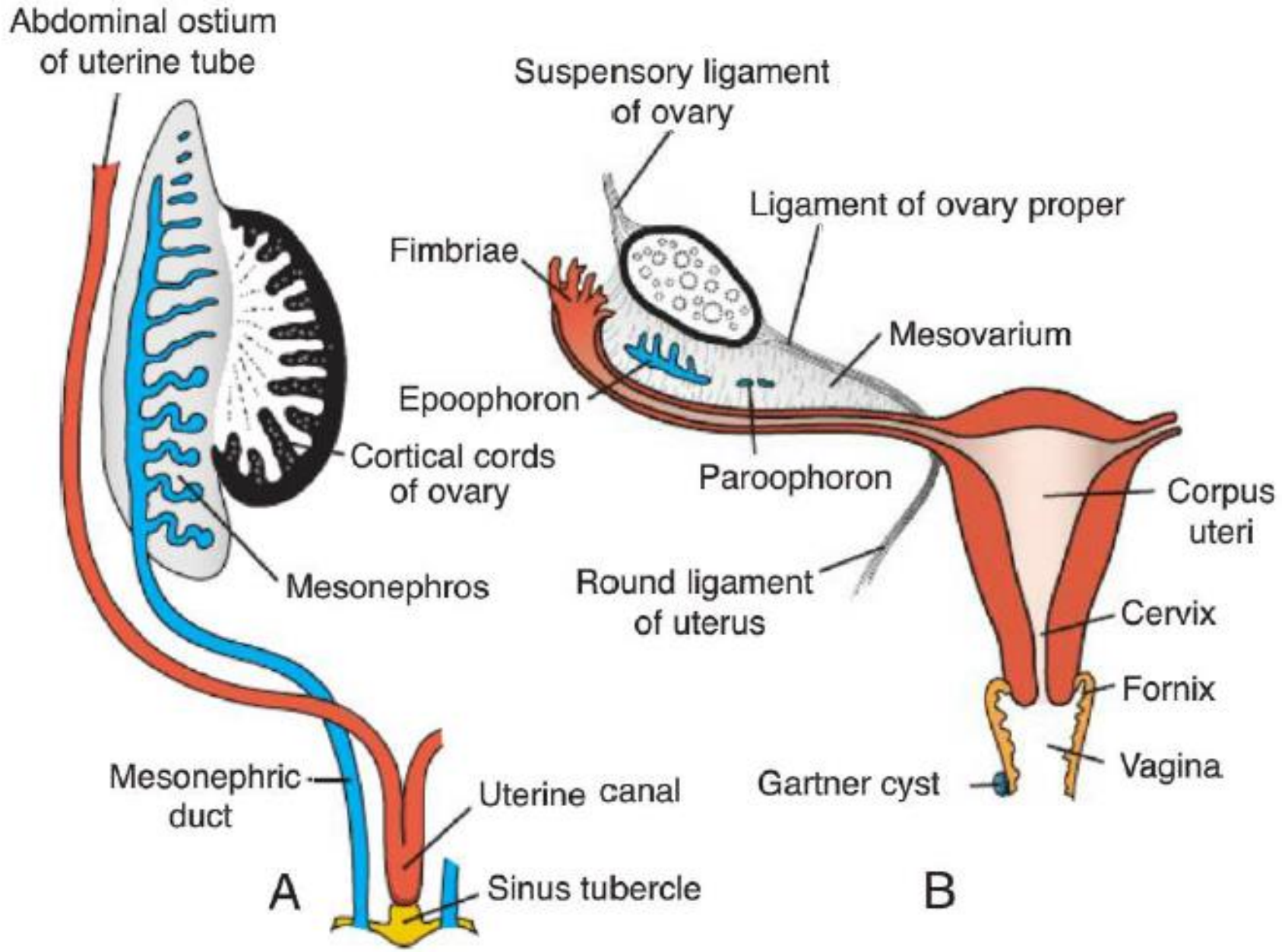
Development Genital System

- Genital ducts in male
  - Stimulated by testosterone
  - Some of the excretory tubules **(epigenital tubules)** contacts with rete testis to form **efferent ductules**
  - Those on the caudal pole do not join and form **paradidymis**
  - Cranial part of mesonephric duct forms appendix epididymis
  - The rest of mesonephric duct forms main genital ducts
  - Below efferent ductules, mesonephric duct elongate to form **ductus epididymis**
  - From tail of epididymis to seminal vesicles gives ductus deferens
  - Under the influence of MIS by Sertoli cells, paramesonephric ducts in male degenerates except at cranial portion which forms appendix testis


Rete testis
Epigenital tubules
Testis cords
Tunica albuginea
Paragenital tubules
Mesonephric duct
Sinus tubercle
A
Seminal vesicle
Utriculus prostaticus
Appendix epididymis
Appendix testis
Vas deferens
Testis cord
Rete testis
Efferent ductules
Epididymis
Paradidymis
B

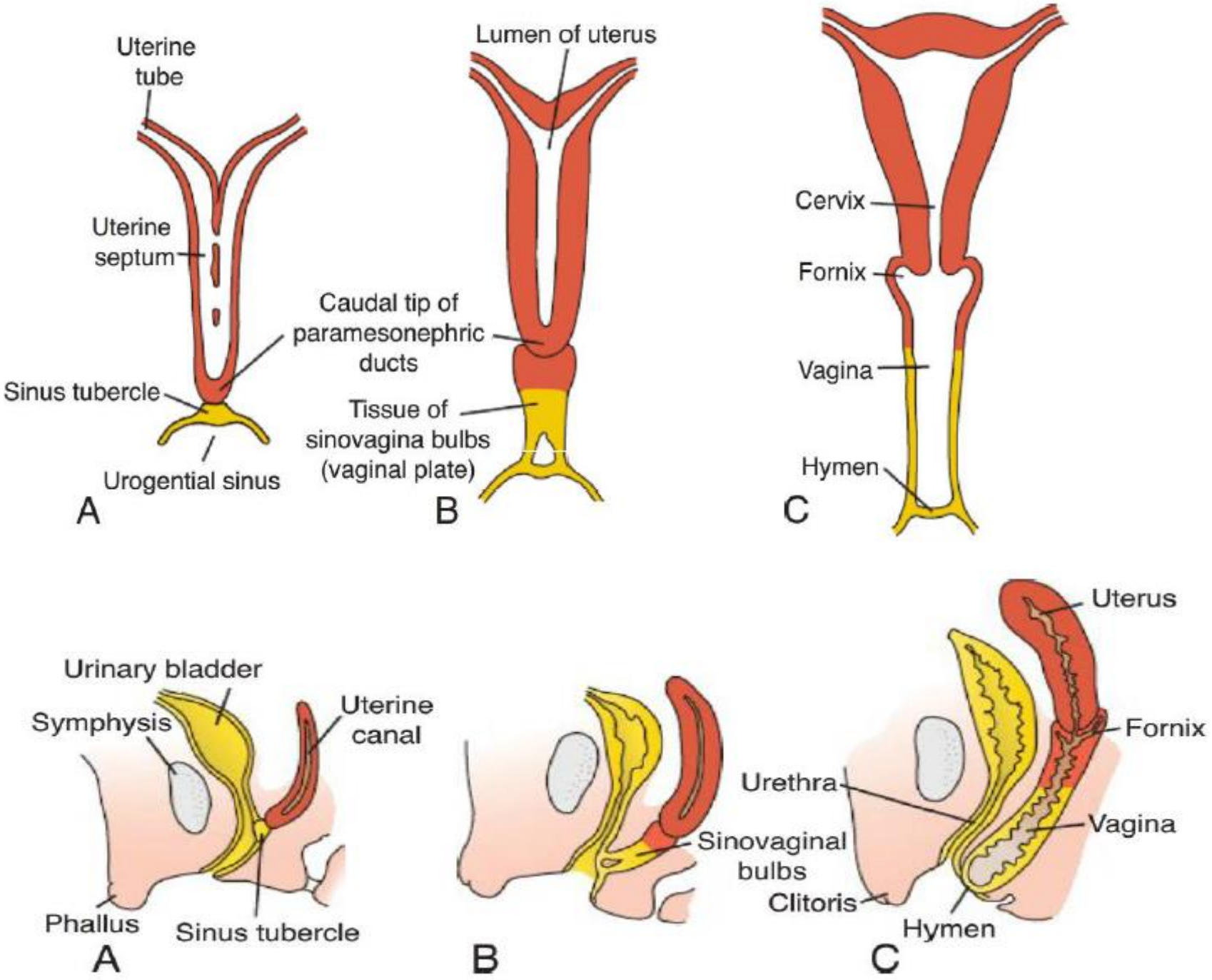
Development Genital System

- Genital ducts in female
  - Due to presence of estrogen, paramesonephric ducts develop into main genital ducts
  - Paramesonephric ducts divides into 3;
    - Cranial/vertical portion
    - Horizontal part
    - Caudal vertical part
  - First 2 parts give **uterine tube**
  - Caudal part fuse to form **uterine canal**
  - Uterine canal gives corpus, cervix of uterus and upper portion of vagina
  - In the absence of testosterone, mesonephric duct degenerate in female except cranial part found in **epoophoron**

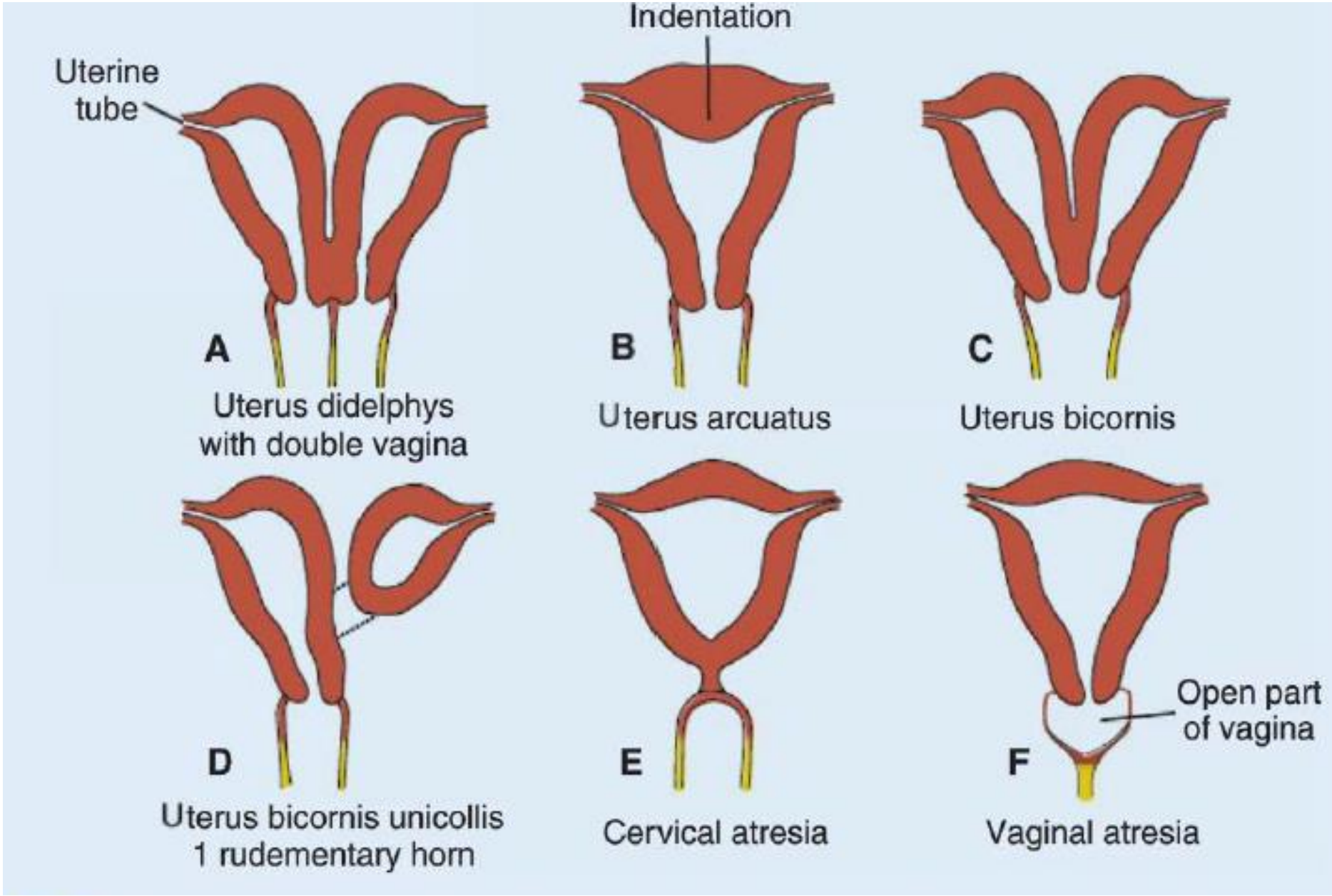

Abdominal ostium
of uterine tube
Suspensory ligament
of ovary
Ligament of ovary proper
Fimbriae
Mesovarium
Epoophoron
Cortical cords
of ovary
Paroophoron
Corpus
uteri
Mesonephros
Round ligament
of uterus
Cervix
Fornix
Vagina
Gartner cyst
Mesonephric
duct
Uterine canal
Sinus tubercle
A
B

Development Genital System

- Vagina
  - After contacts of paramesonephric duct with urogenital siuns
  - 2 evaginations grow from the pelvic part of the sinus **sinovaginal bulbs**
  - The bulbs form **vaginal plate**
  - The growth progresses cranially separating the sinus from the uterus
  - In the 5th month the vaginal outgrowth is canalized
  - Lumen of vagina is separated from urogenital sinus by **hymen**

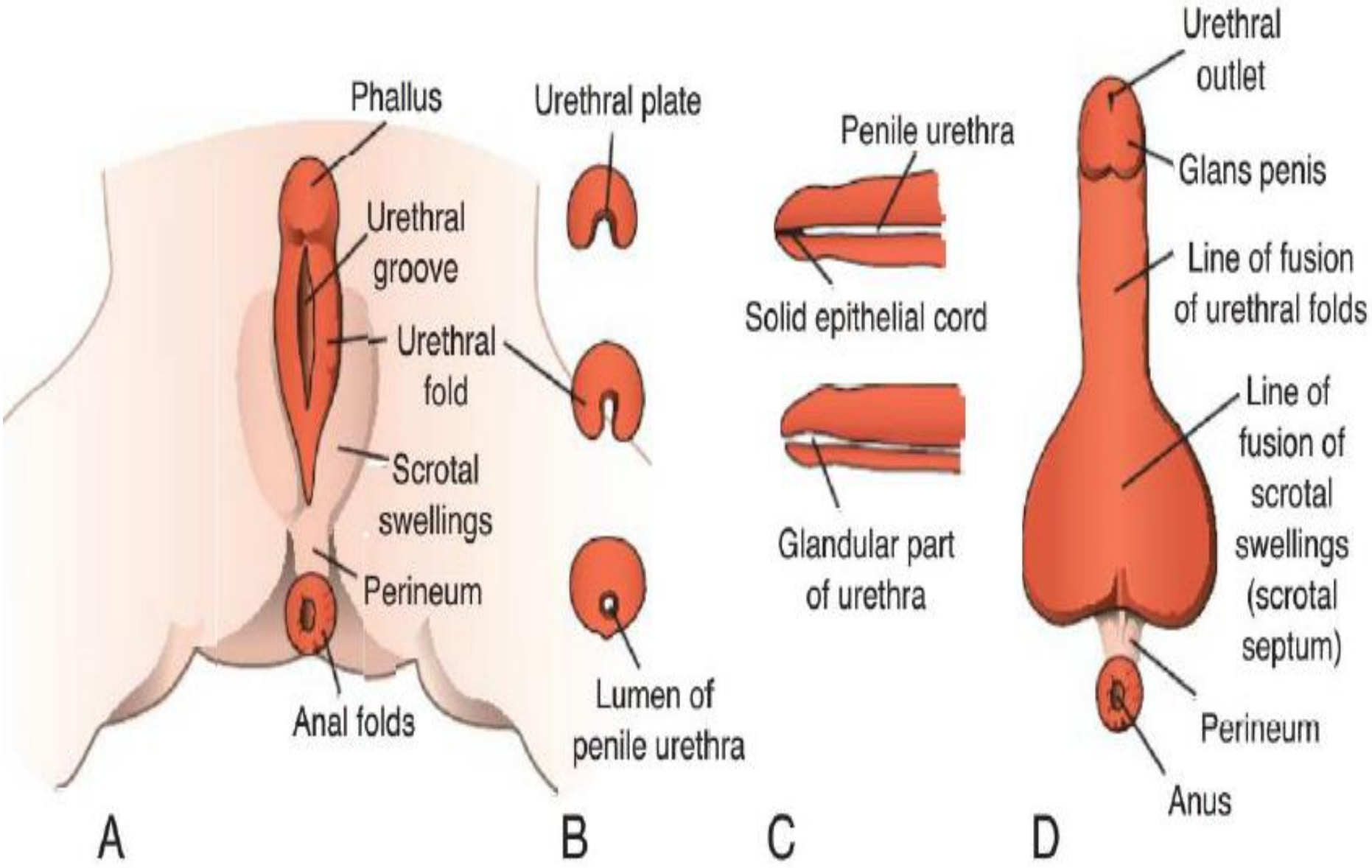

Uterine tube
Uterine septum
Sinus tubercle
Urogential sinus
A
Lumen of uterus
Caudal tip of paramesonephric ducts
Tissue of sinovagina bulbs (vaginal plate)
B
Cervix
Fornix
Vagina
Hymen
C
Urinary bladder
Symphysis
Uterine canal
Phallus
Sinus tubercle
A
Sinovaginal bulbs
B
Uterus
Fornix
Urethra
Vagina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

Development Genital System



Development Genital System

- External Genitalia
  - Cloaca folds – mesenchyme from primitive streak
    - Urethral folds – anteriorly
    - Anal folds – posteriorly
  - Cloaca folds unite anteriorly **genital tubercle**
  - **Genital swellings** appear lateral to urethral folds
- Male External Genitalia
  - Rapid elongation of genital tubercle – **phallus**
  - Phallus pulls urethral fold forming **urethral groove**
  - Epithelial cells in the groove forms **urethral plate**
  - Urethral folds close by end of 3rd month – **penile urethra**

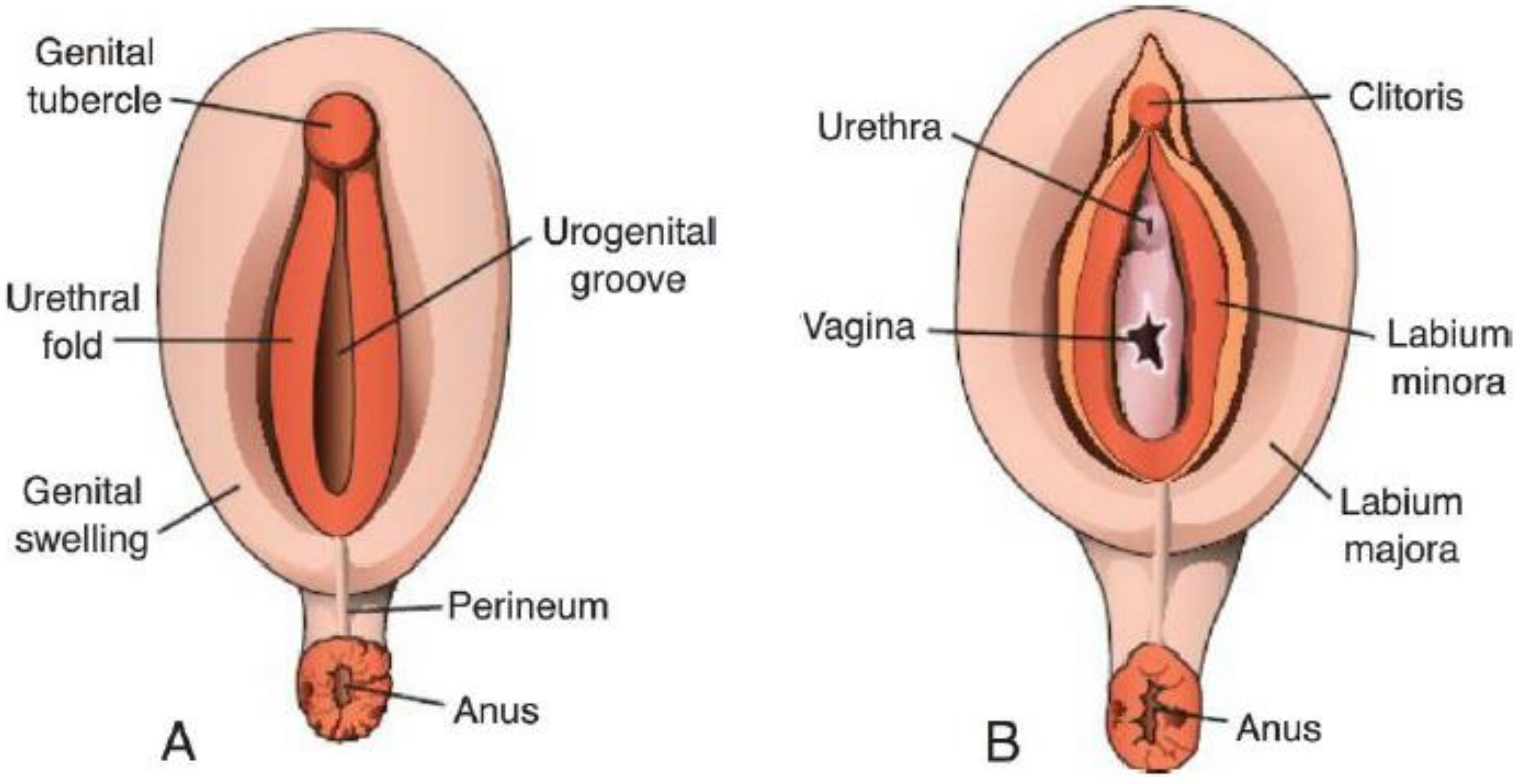

Phallus
Urethral groove
Urethral fold
Scrotal swellings
Perineum
Anal folds
A
Urethral plate
Lumen of penile urethra
B
Penile urethra
Solid epithelial cord
Glandular part of urethra
C
Urethral outlet
Glans penis
Line of fusion of urethral folds
Line of fusion of scrotal swellings (scrotal septum)
Perineum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

Development Genital System

- Congenital Anomalies
  - Hypospadias
  - Epispadias
  - Micropenis
  - Bifid penis

Development Genital System

- Female External Genitalia
  - Genital tubercle elongates slightly – **clitoris**
  - urethral folds do not fuse – **labia minora**
  - Genital swellings enlarge – **labia majora**
  - Urogenital groove is open – **vestibule**



Development Genital System

- Congenital Anomalies
  - Ambiguous genitalia
    - Enlarge clitoris
    - Small penis with hypospadias
    - Causes;
      - Congenital adrenal hyperplasia
      - Androgen insensitivity syndrome
  - Gonadal dysgenesis
  - Swyer syndrome (XY female gonadal dysgenesis)
  - Turner syndrome
  - Klinefelter syndrome