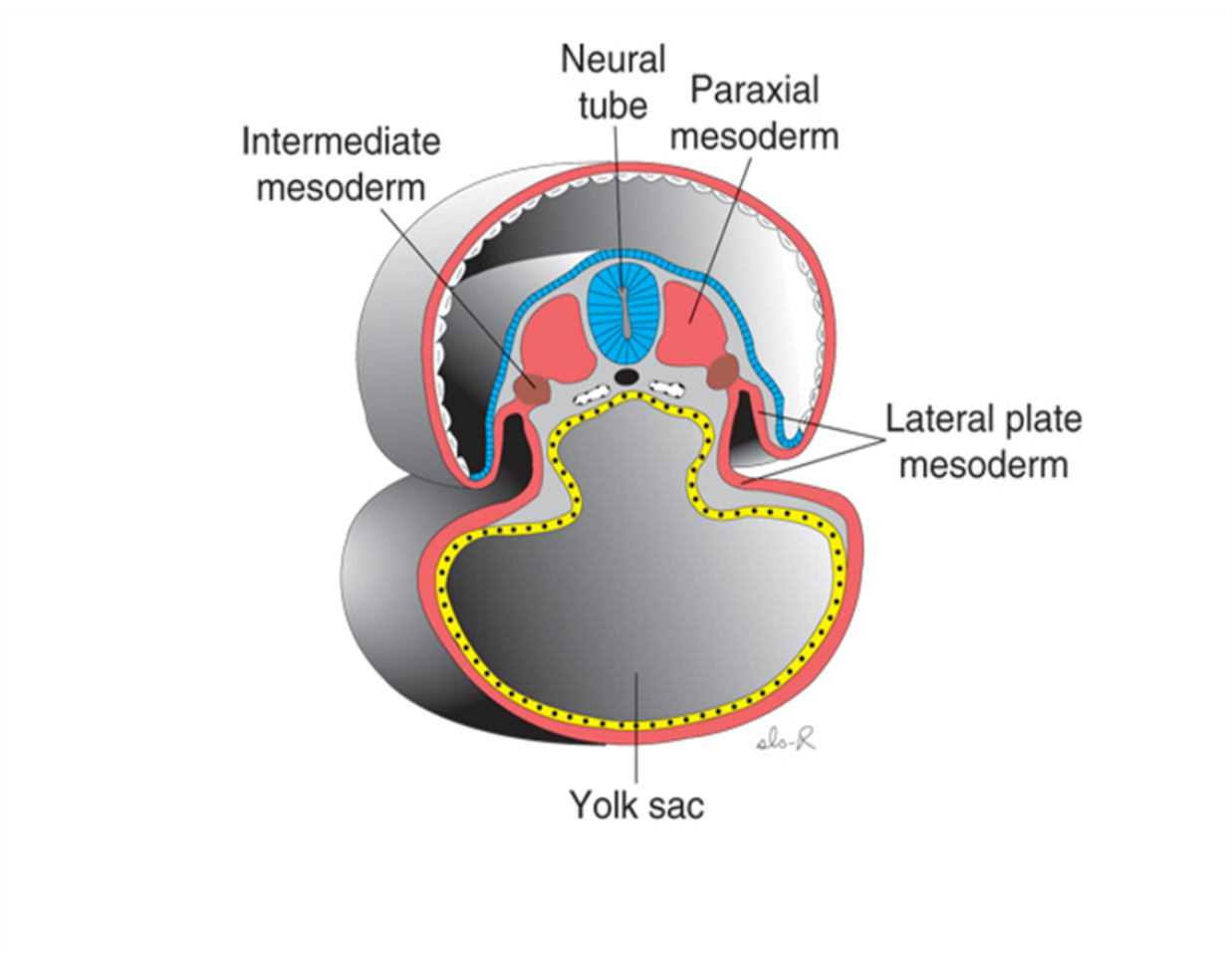
Urogenital System

- Functionally the urogenital system can be divided into two entirely different components:

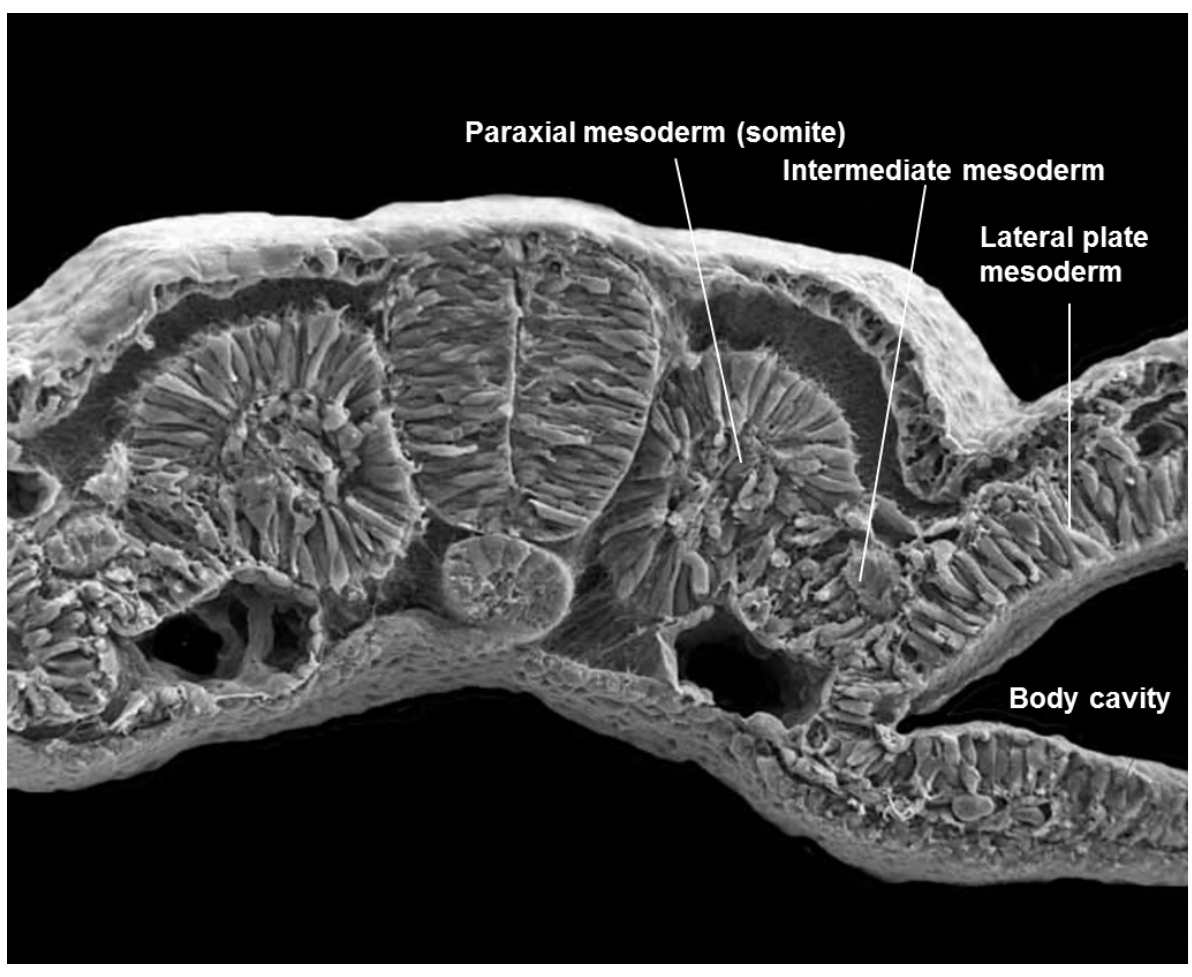
1. The **urinary system**
2. **The genital system.**

- **Embryologically and anatomically they are intimately interwoven.**
- **Both develop from** a common mesodermal ridge **(intermediate mesoderm)** **along** the posterior wall of the abdominal cavity,
- Initially the excretory ducts of both systems enter a common cavity, **the cloaca.**

Intermediate Mesoderm Forms Much of the Urogenital System



Mesoderm in the Chick Embryo



Lateral Rotation

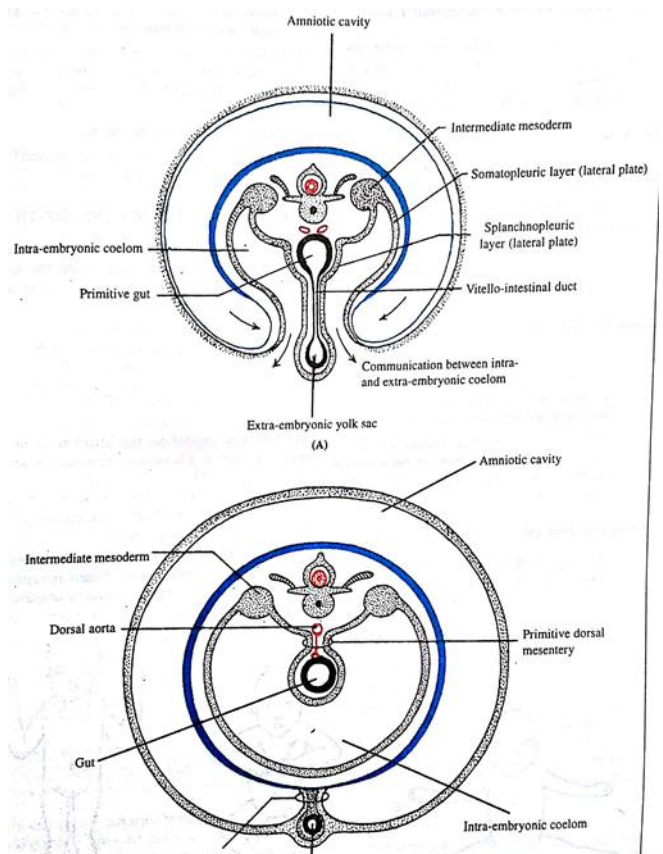
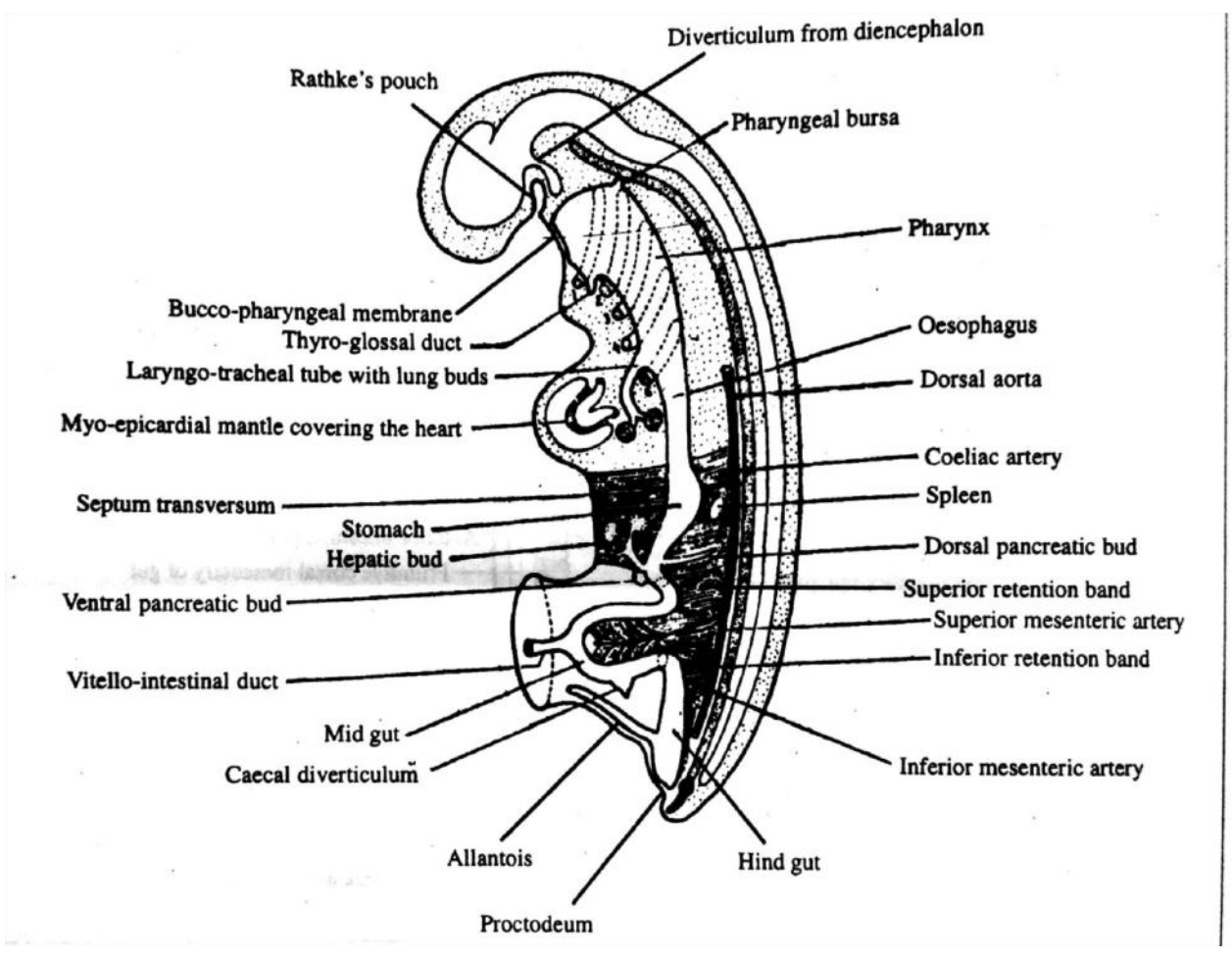


Fig. 7.15. *Lateral folds of the embryo.*

Hindgut with allantois



Hind Gut-Cloaca

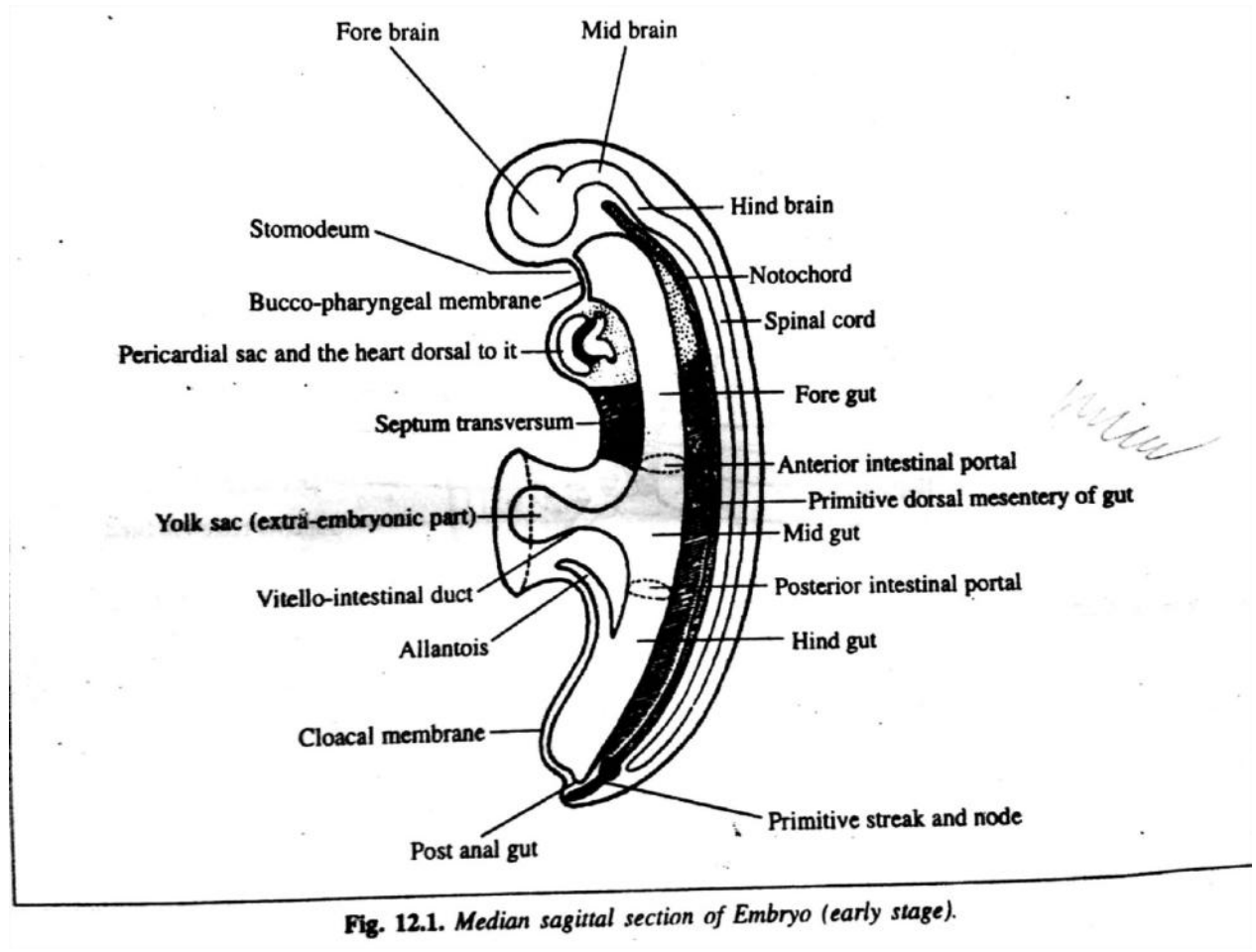


Fig. 12.1. *Median sagittal section of Embryo (early stage).*

Urorectal Septum

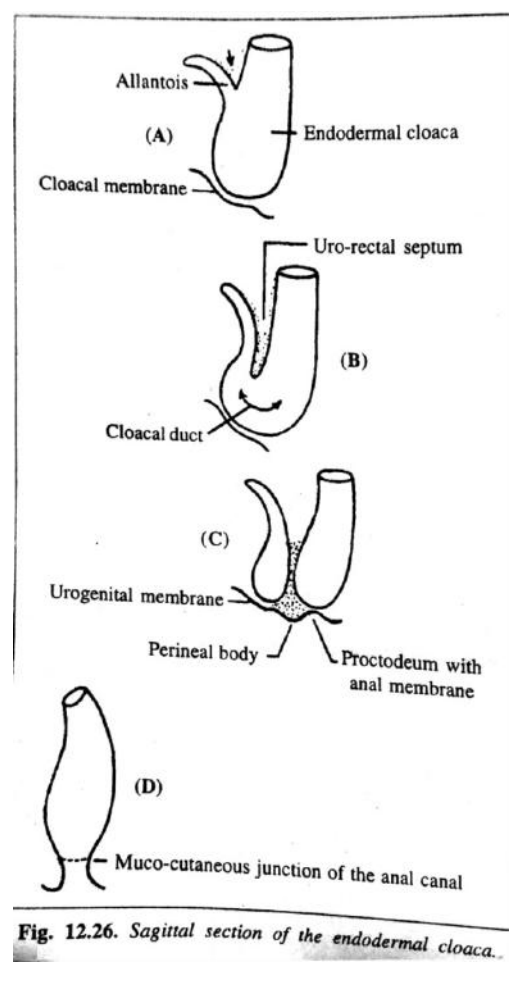


Fig. 12.26. *Sagittal section of the endodermal cloaca.*

Urorectal Septum

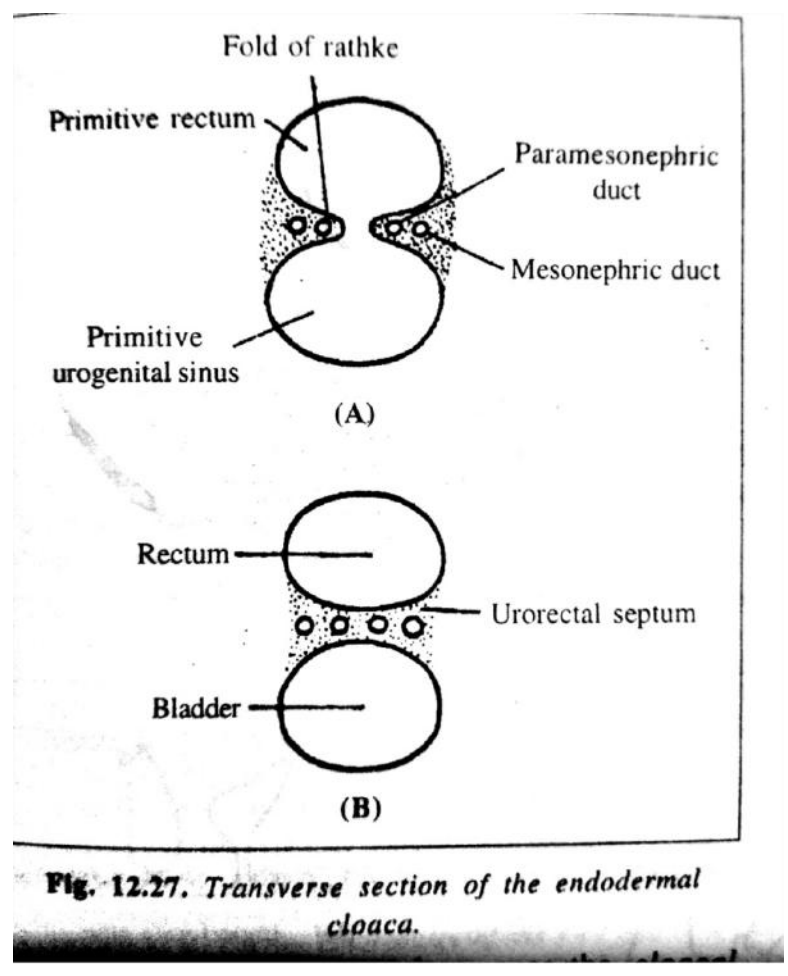
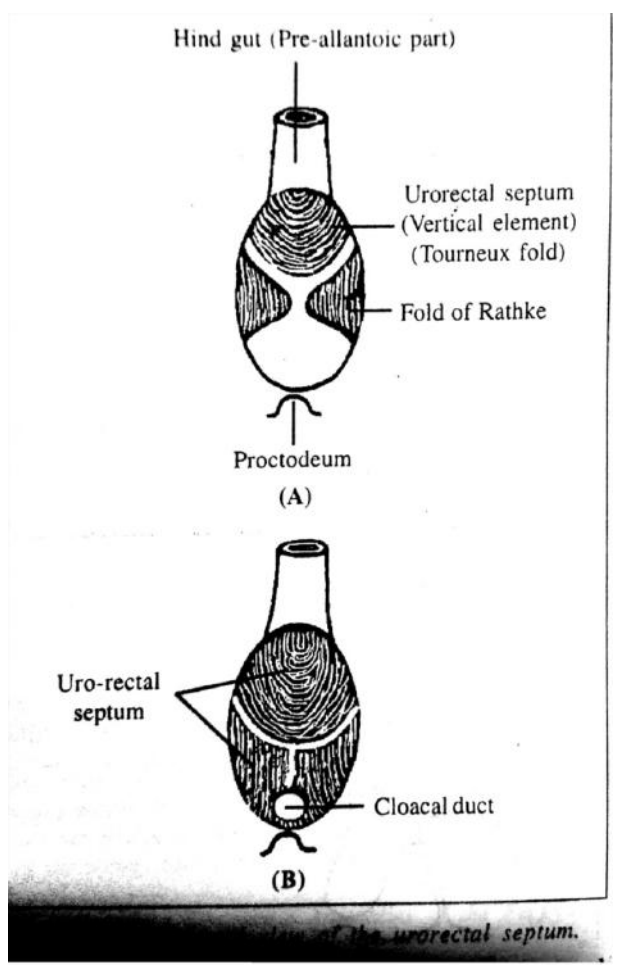
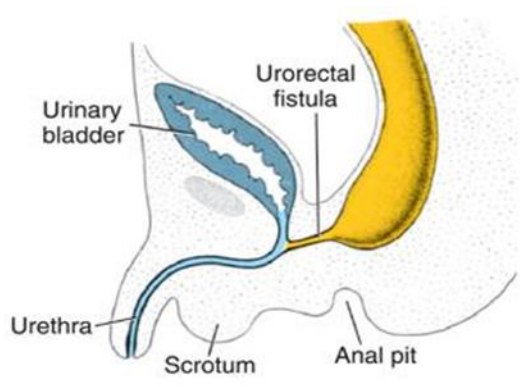


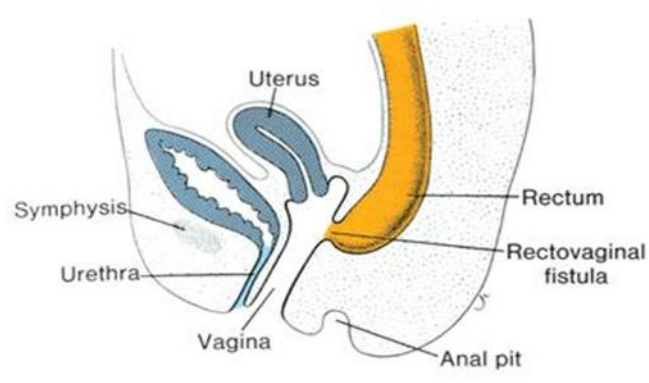
Fig. 12.27. *Transverse section of the endodermal cloaca.*

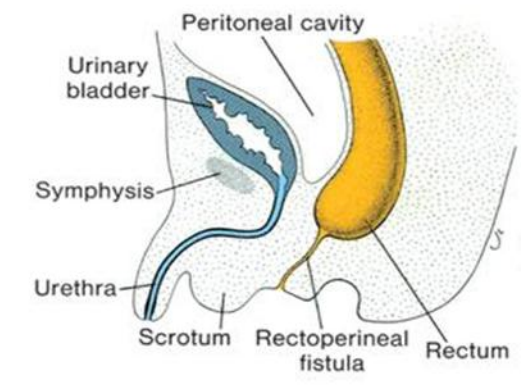
Urorectal Septum

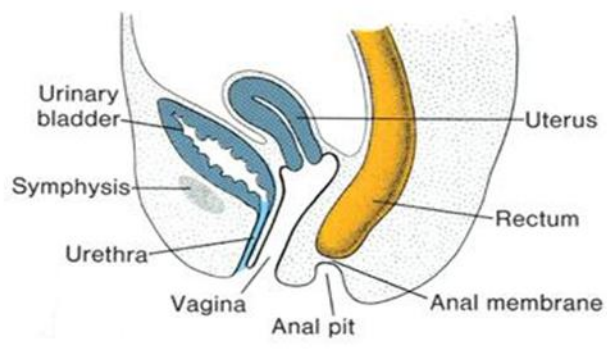


Urorectal Septal Defects and Imperforate Anus

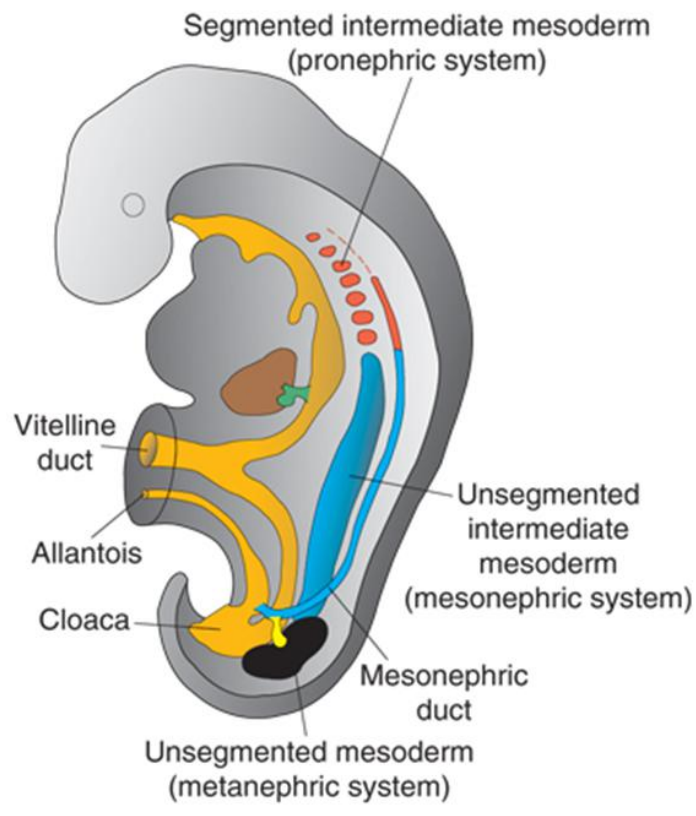








Kidney Systems



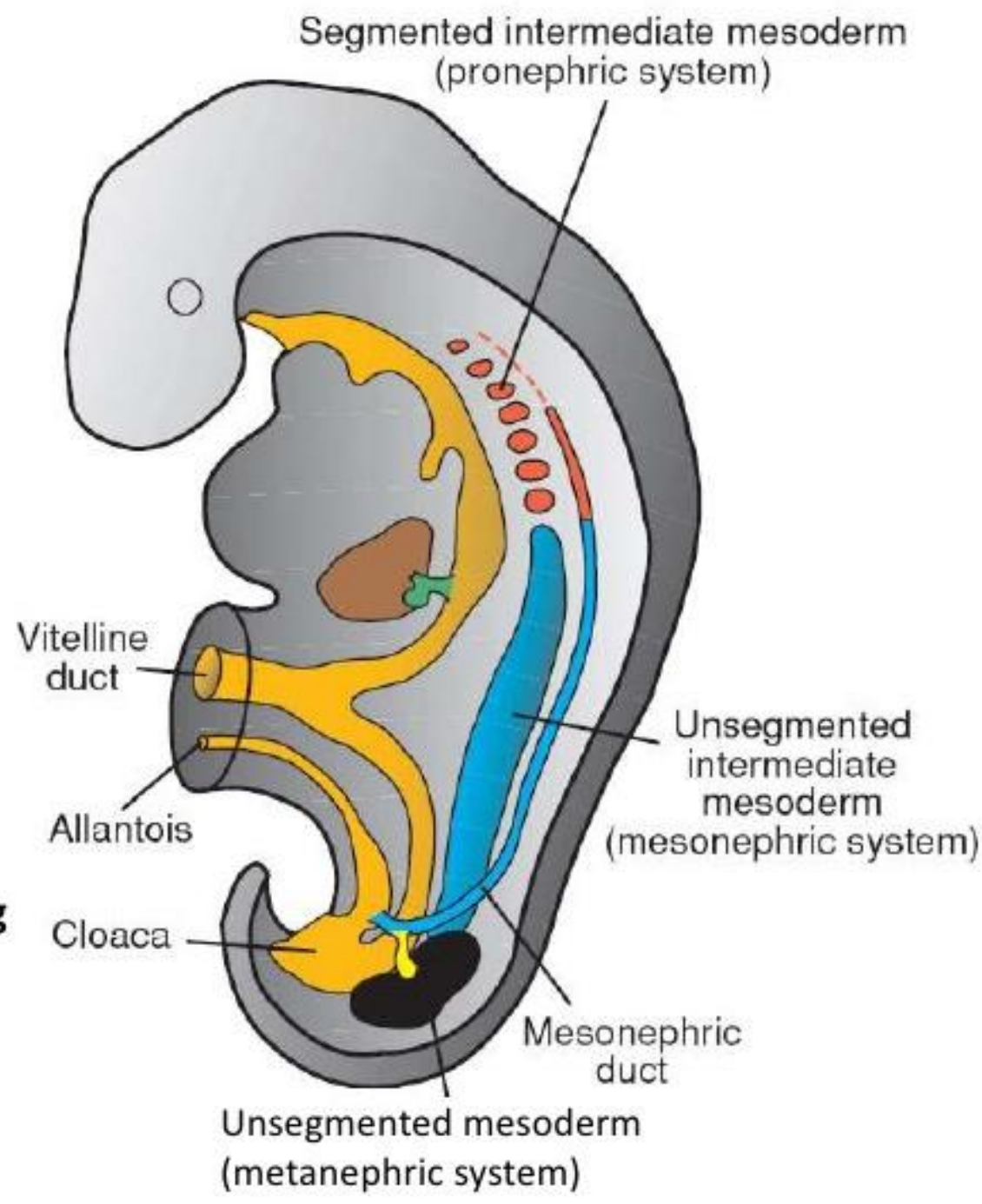
Pronephric Kidney

Fig. 16.1. *A transverse section showing pronephric kidney.*

Pronephros

- **At the beginning** of the **fourth week**, the pronephros is represented by **7 to 10 solid cell groups** in the cervical region.
- These groups form vestigial excretory units, **nephrotomes**, that regress before more caudal ones are formed.
- **By the end** of the **fourth week**, all indications of the pronephric system have **disappeared**.

Relationship of the intermediate mesoderm of the pronephric, mesonephric, and metanephric systems.
In cervical and upper thoracic regions intermediate mesoderm is segmented; in lower thoracic, lumbar, and sacral regions it forms a solid, unsegmented mass of tissue, the nephrogenic cord.

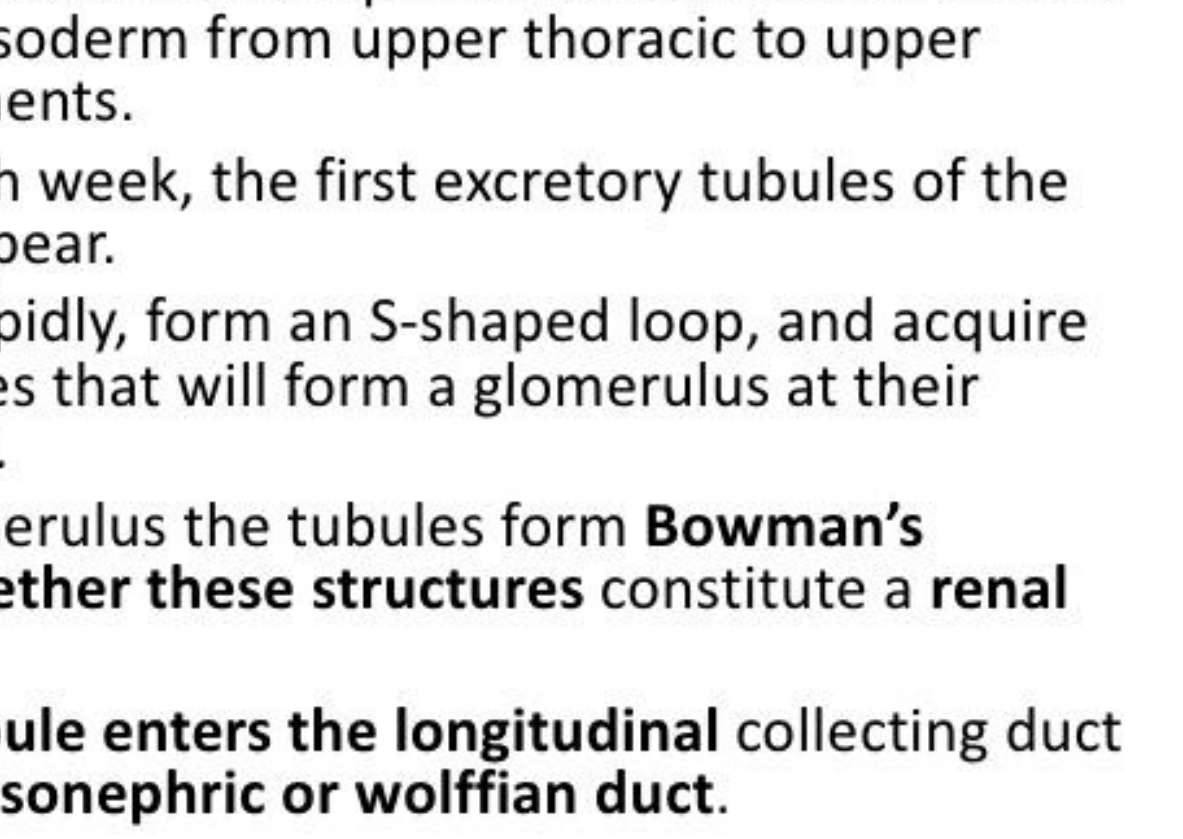


Note the longitudinal collecting duct, formed initially by the pronephros but later by the mesonephros

Mesonephros

- The mesonephros and mesonephric ducts are derived from intermediate mesoderm from upper thoracic to upper lumbar (L3) segments.
- Early in the fourth week, the first excretory tubules of the mesonephros appear.
- They lengthen rapidly, form an S-shaped loop, and acquire a tuft of capillaries that will form a glomerulus at their medial extremity.
- *Around the* glomerulus the tubules form **Bowman's capsule, and together these structures** constitute a **renal corpuscle.**
- **Laterally the tubule enters the longitudinal** collecting duct known as the **mesonephric or wolffian duct**.

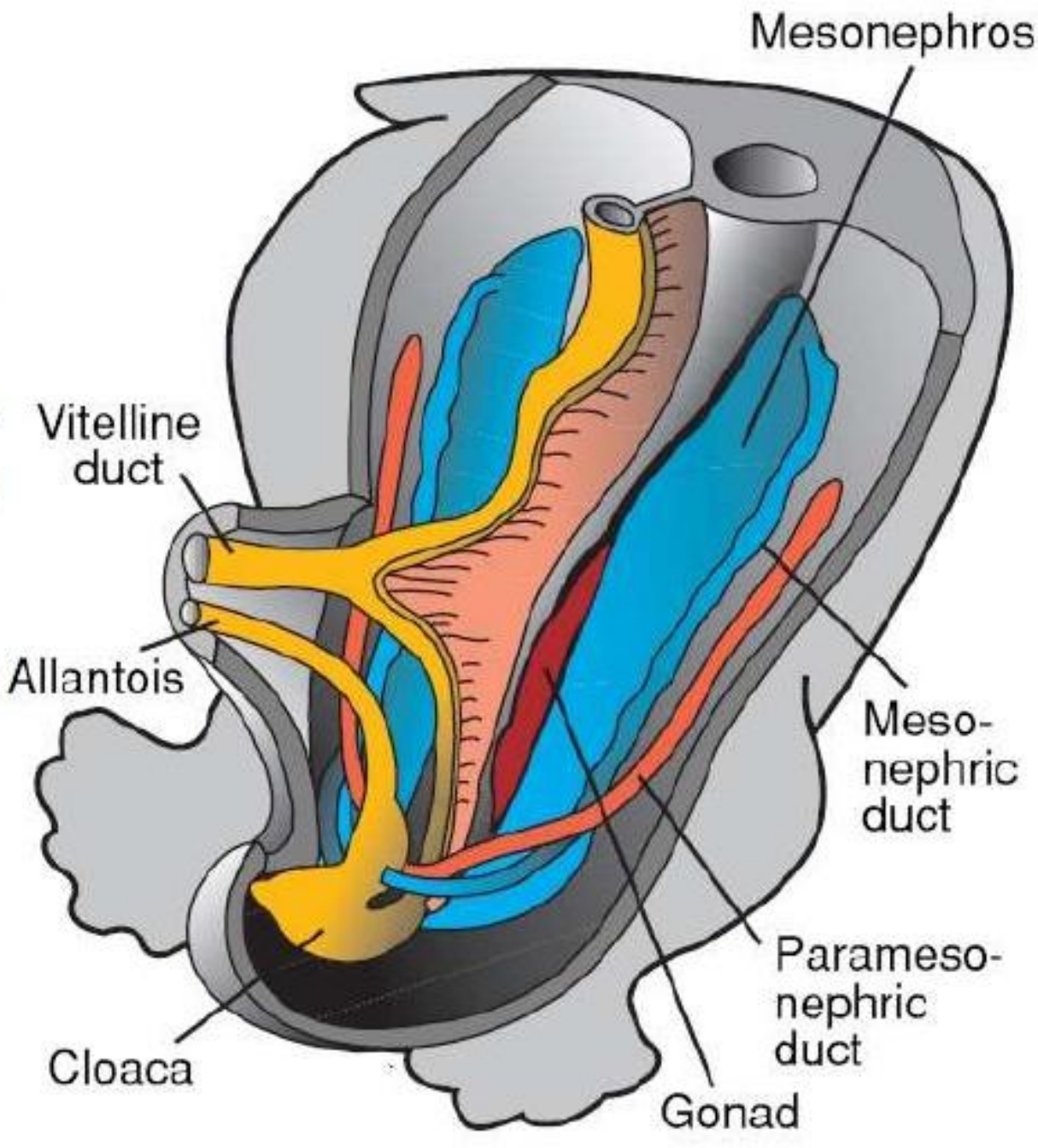
Transverse section through the urogenital ridge in the lower thoracic region of a 5-week embryo showing formation of an excretory tubule of the mesonephric system.



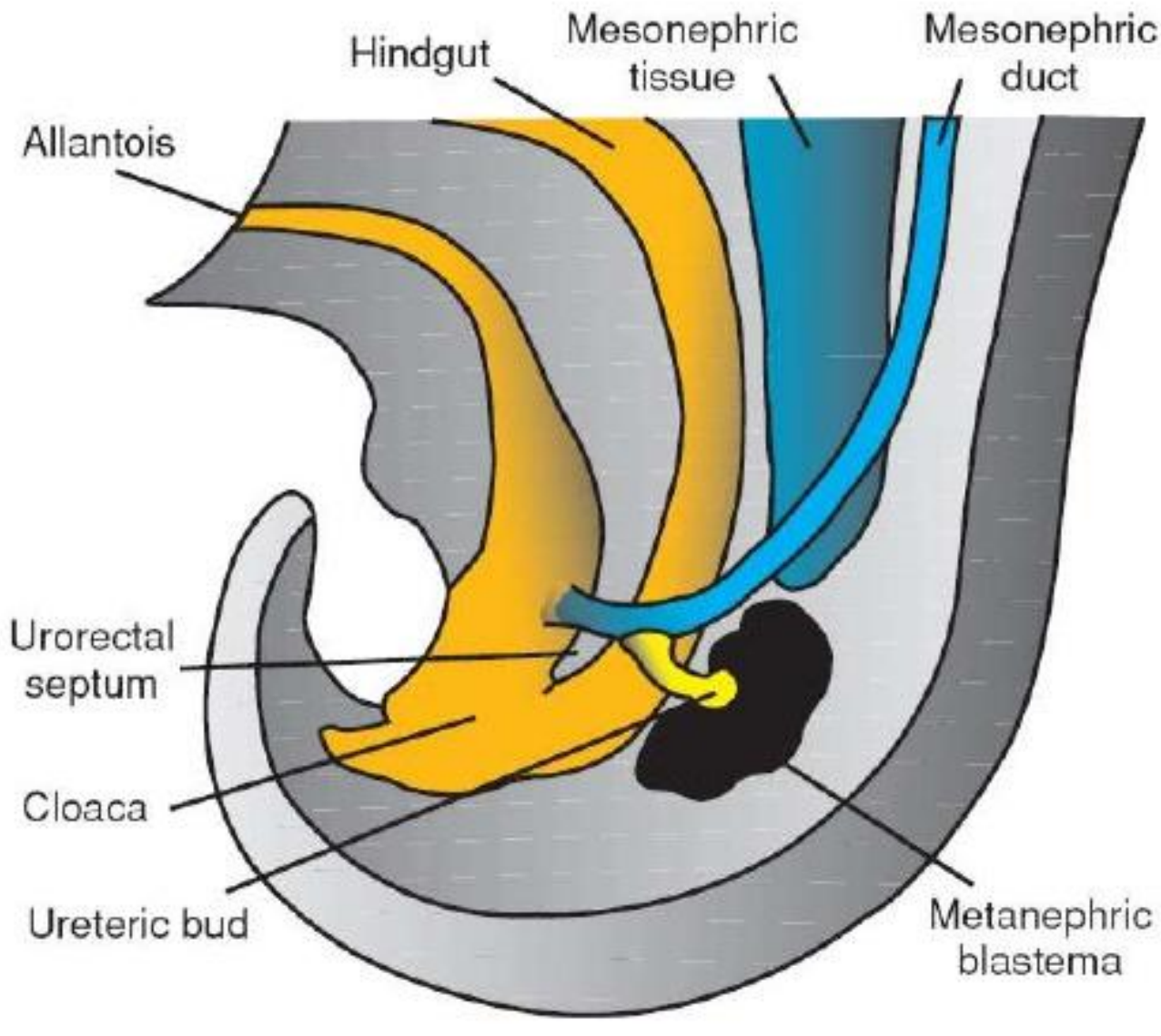
Note the appearance of Bowman's capsule and the gonadal ridge.
The mesonephros and gonad are attached to the posterior abdominal wall by a broad urogenital mesentery.

Relation of the gonad and the mesonephros

Note the size of the mesonephros. The mesonephric duct (wolffian duct) runs along the lateral side of the mesonephros



Relation of the hindgut and cloaca at the end of the 5th week.

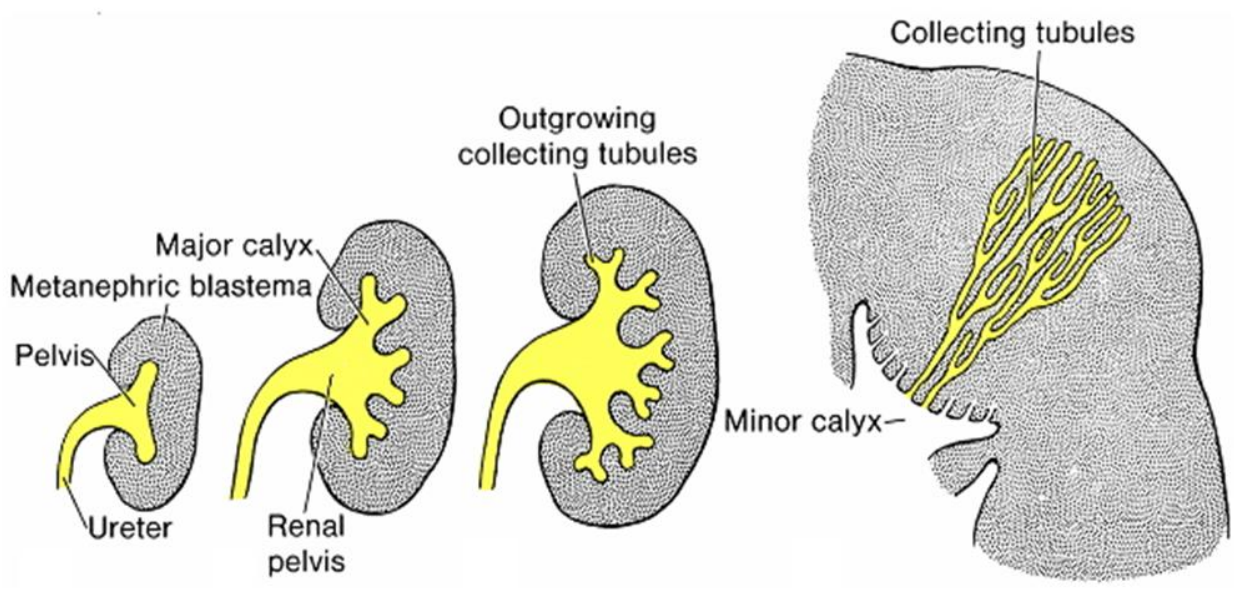


The ureteric bud penetrates the metanephric mesoderm (blastema).

Collecting System

- The tubules of **the second order enlarge and absorb those of the third and fourth generations**, forming the **minor calyces of the renal pelvis**.
- Collecting tubules of the fifth and successive generations form the **renal pyramid.**
- ***The ureteric bud gives rise to the;***
  - **ureter,**
  - **renal pelvis,**
  - **major and minor calyces,**
  - **1 million to 3 million collecting tubules.**

Collecting System Forms from the Ureteric Bud

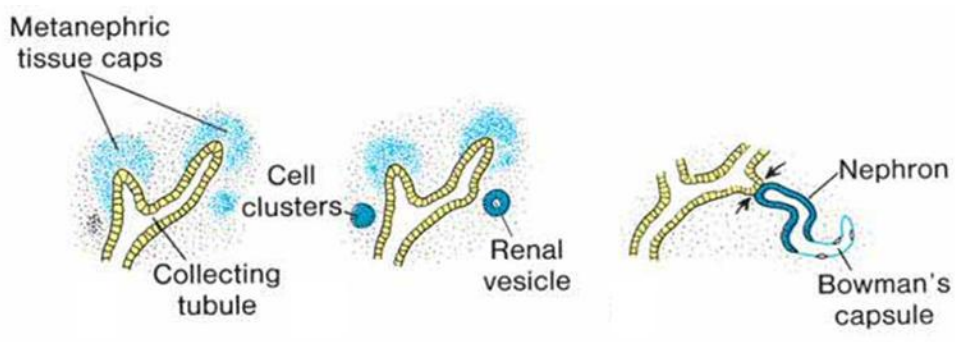


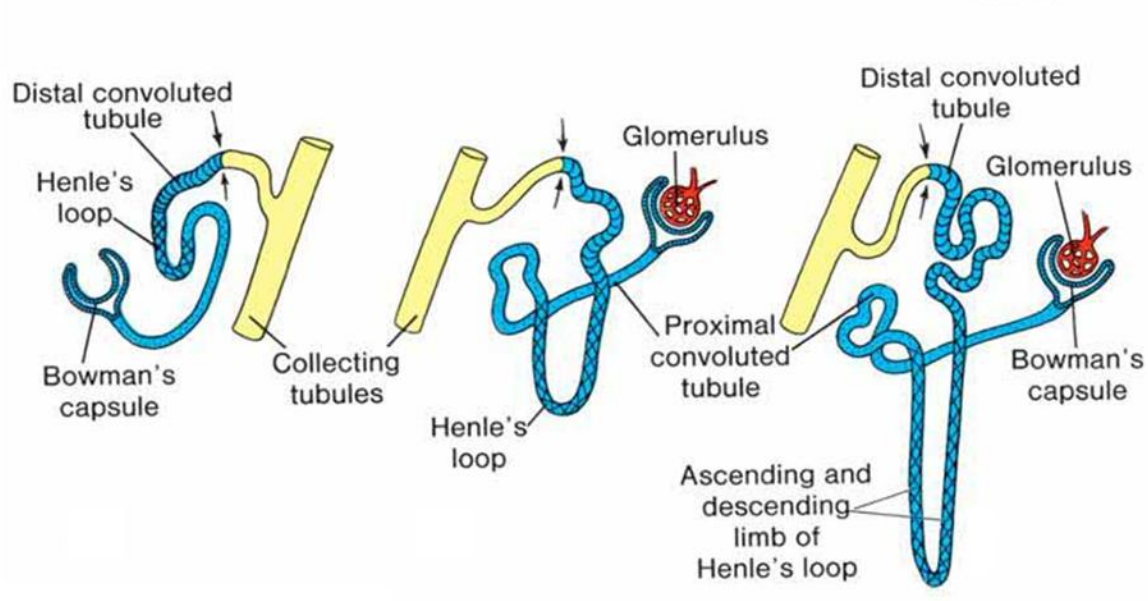
6-7 Weeks

Collecting System

- The tubules of **the second order** **enlarge and absorb those of the third and fourth generations**, forming the **minor calyces of the renal pelvis**.
- Collecting tubules of the fifth and successive generations form the **renal pyramid.**
- ***The ureteric bud gives rise to the;***
  - **ureter,**
  - **renal pelvis,**
  - **major and minor calyces,**
  - **1 million to 3 million collecting tubules.**

The Ureteric Bud Induces the Metanephric Blastema to Form Filtration Units





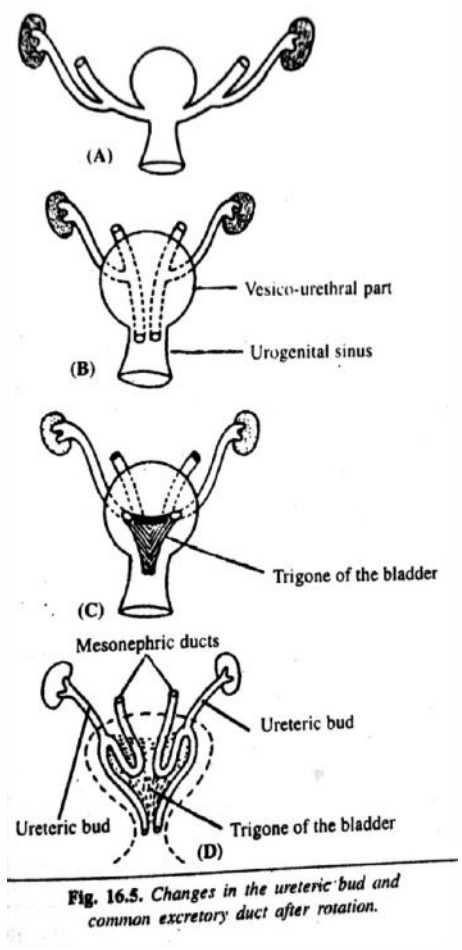


Fig. 16.5. *Changes in the ureteric bud and common excretory duct after rotation.*

Function of the Kidney

- The definitive kidney formed from the metanephros becomes functional near the 12th week. Urine is passed into the amniotic cavity and mixes with the amniotic fluid. The fluid is swallowed by the fetus and recycles through the kidneys. During fetal life, the kidneys are not responsible for excretion of waste products, since the placenta serves this function.

MCQ

When does the metanephros become functional?

(A) At week 3 of development

(B) At week 4 of development

(C) At week 10 of development

(D) Just before birth

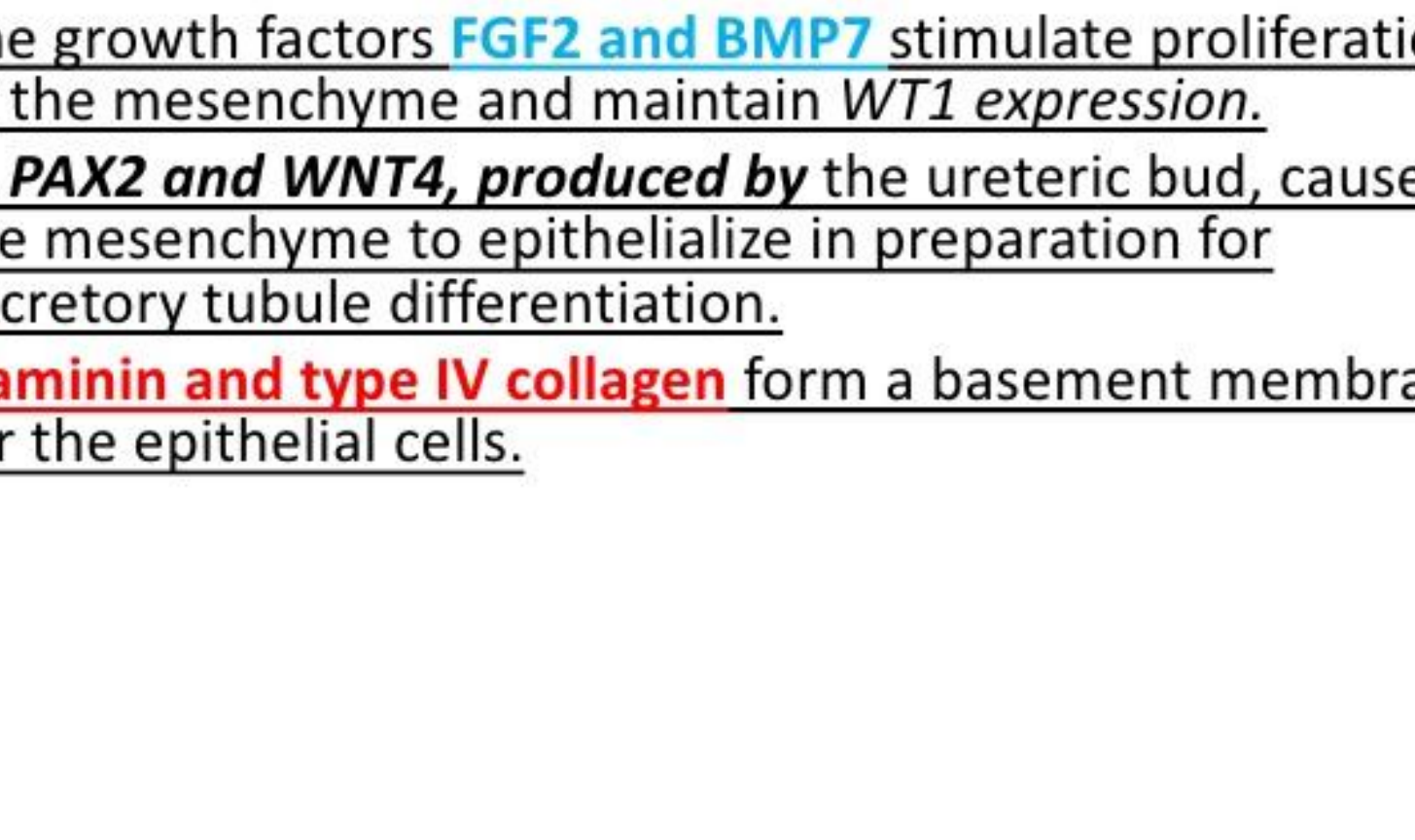
(E) Just after birth

Genes involved in differentiation of the kidney

(explanation of the figure in the previous slide)

- **A. *WT1, expressed by the*** mesenchyme, enables this tissue to respond to induction by the ureteric bud.
- **GDNF and HGF interact** through their receptors, RET and MET, respectively, to stimulate growth of the bud and maintain the interactions.
- The growth factors **FGF2 and BMP7** stimulate proliferation of the mesenchyme and maintain *WT1 expression.*
- ***B. PAX2 and WNT4, produced by*** the ureteric bud, cause the mesenchyme to epithelialize in preparation for excretory tubule differentiation.
- **Laminin and type IV collagen** form a basement membrane for the epithelial cells.

Molecular Regulation of Kidney Development



MOLECULAR REGULATION OF KIDNEY DEVELOPMENT

- Differentiation of the kidney involves epithelial mesenchymal interactions.
- Epithelium of the ureteric bud from the mesonephros interacts with mesenchyme of the metanephric blastema.
- The mesenchyme expresses ***WT1,*** a transcription factor that
  - **MAKES** this tissue competent to respond to induction by the ureteric bud,
  - **REGULATES** production of **glial-derived neurotrophic factor (GDNF) and hepatocyte growth factor (HGF) by the mesenchyme.**
  - **and these proteins** stimulate growth of the ureteric buds.
- The **tyrosine kinase receptors RET, for GDNF, and MET, for HGF, are synthesized by the epithelium of** the ureteric buds, establishing signaling pathways between the two tissues.
- In turn, the buds induce the mesenchyme via **fibroblast growth factor-2 (FGF-2)** and **bone morphogenetic protein-7 (BMP-7).**

MOLECULAR REGULATION OF KIDNEY DEVELOPMENT

- ***Both of these*** growth factors block apoptosis and stimulate proliferation in the metanephric mesenchyme while maintaining production of *WT1*.
- *Conversion of the* mesenchyme to an epithelium for nephron formation is also mediated by the ureteric buds, in part through modification of the extracellular matrix.
- Thus **fibronectin, collagen I, and collagen III** are replaced with **laminin and type IV collagen**, characteristic of an epithelial basal lamina.
- ***In addition,*** the cell adhesion molecules **syndecan and E-cadherin, which are essential for** condensation of the mesenchyme into an epithelium, are synthesized. Regulatory genes for conversion of the mesenchyme into an epithelium appear to involve ***PAX2 and WNT4.***

Renal Tumors and Defects

- Wilms' tumor is a cancer of the kidneys that usually affects children by 5 years of age but may also occur in the fetus.
- Wilms' tumor is due to mutations in the WT1 gene on 11p13, and it may be associated with other abnormalities and syndromes.
- For example, WAGR syndrome is characterized by aniridia, Genitourinary abnormalities, and Wilms' tumor and mental retardation
- Denys-Drash syndrome consists of renal failure, pseudohermaphrodism, and Wilms' tumor.

Renal dysplasias and agenesis

- **Multicystic dysplastic kidney** in which numerous ducts are surrounded by undifferentiated cells.
- Nephrons fail to develop
- ureteric bud fails to branch,
- the collecting ducts never form.

In some cases, these defects cause involution of the kidneys and **renal agenesis**

Position of the Kidney

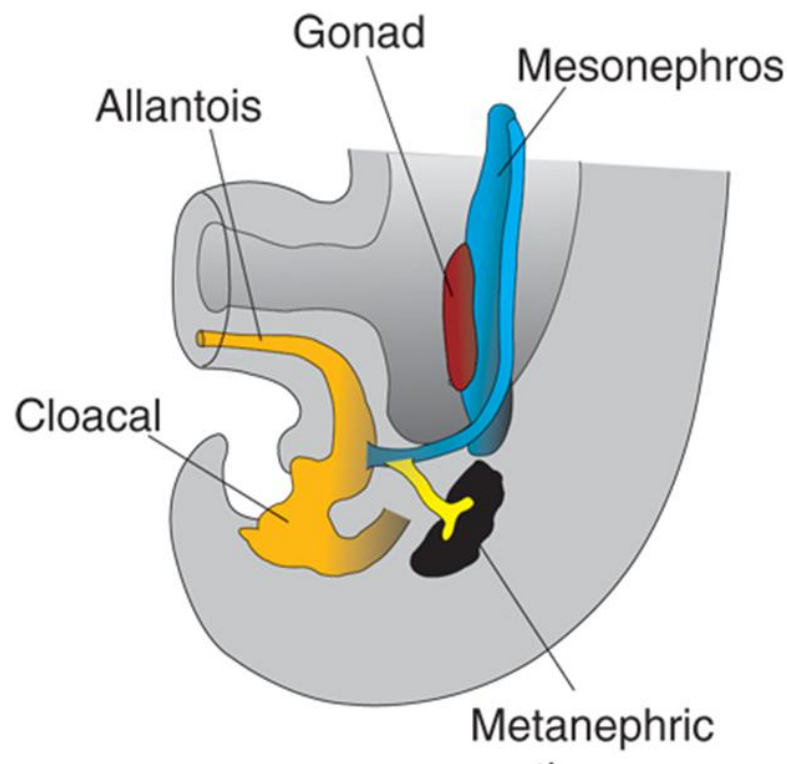
- The kidney, initially in the pelvic region, later shifts to a more cranial position in the ab-domen.

This ascent of the kidney is caused by

- diminution of body curvature
- by growth of the body in the lumbar and sacral regions

In the pelvis, the metanephros re-ceives its arterial supply from a pelvic branch of the aorta. During its ascent to the abdominal level, it is vascularized by arteries that originate from the aorta at continuously higher levels. The lower vessels usually degenerate, but some may remain.

Kidneys Develop in the Pelvic Region



Ascent of the Kidneys

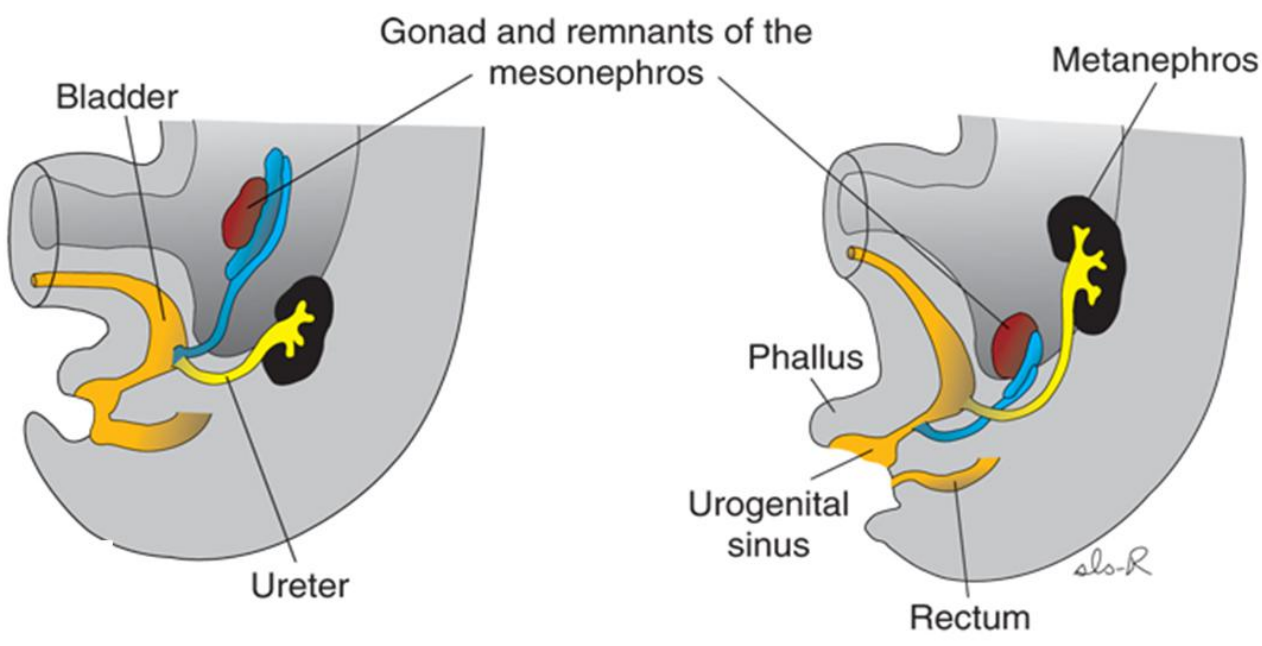


Fig. 16.8. *Ascent of the kidney.*

Rotation Of Kidney

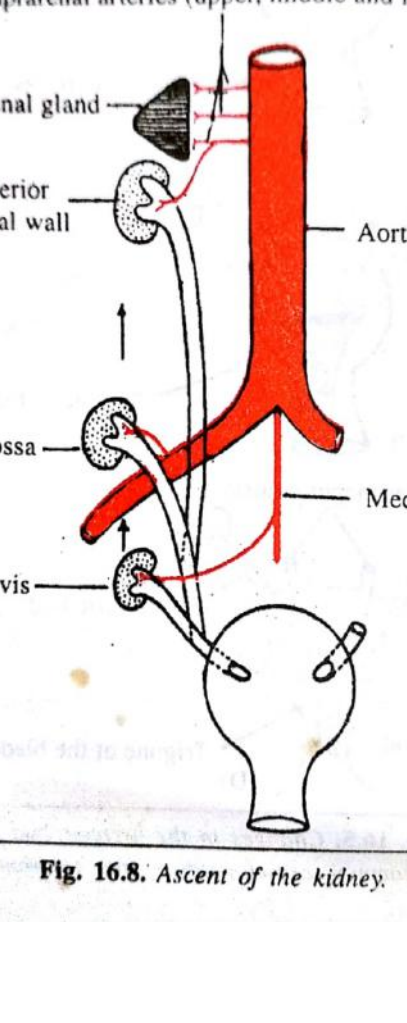


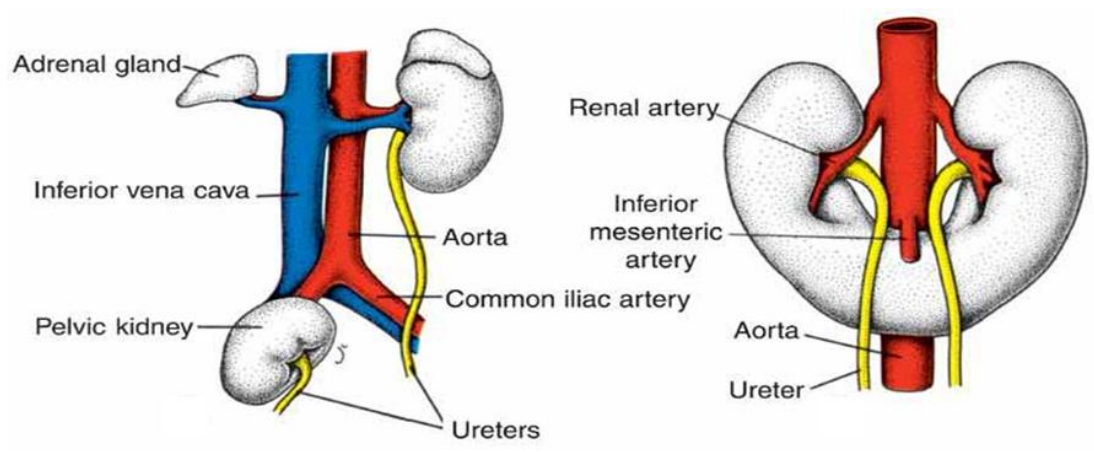
Fig. 16.9. *Rotation of the kidney (normal and abnormal).*

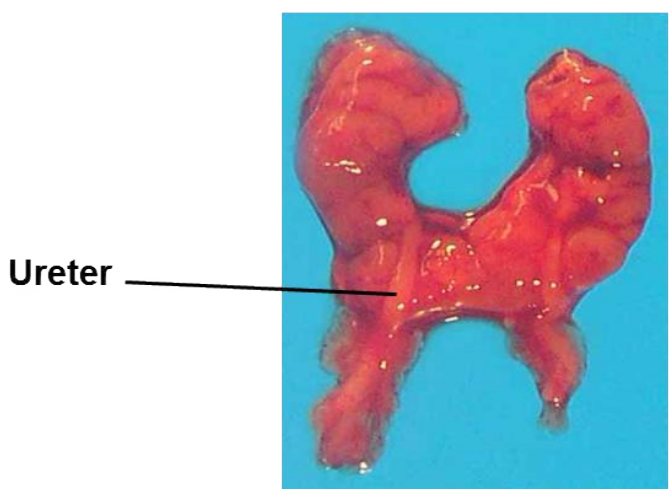
Developmental anomalies of the kidney

A. Renal agenesis :

- Failure of one or both kidneys to develop
- Bilateral: rare, associated with other congenital anomalies, incompatible with life
- Unilateral: common (one in 4,000 infants, more boys than girls) , asymptomatic;
- Other kidney enlarges to compensate#Absent ipsilateral renal artery

Pelvic and Horseshoe Kidneys





Developmental Anamoly- Fused Kidneys

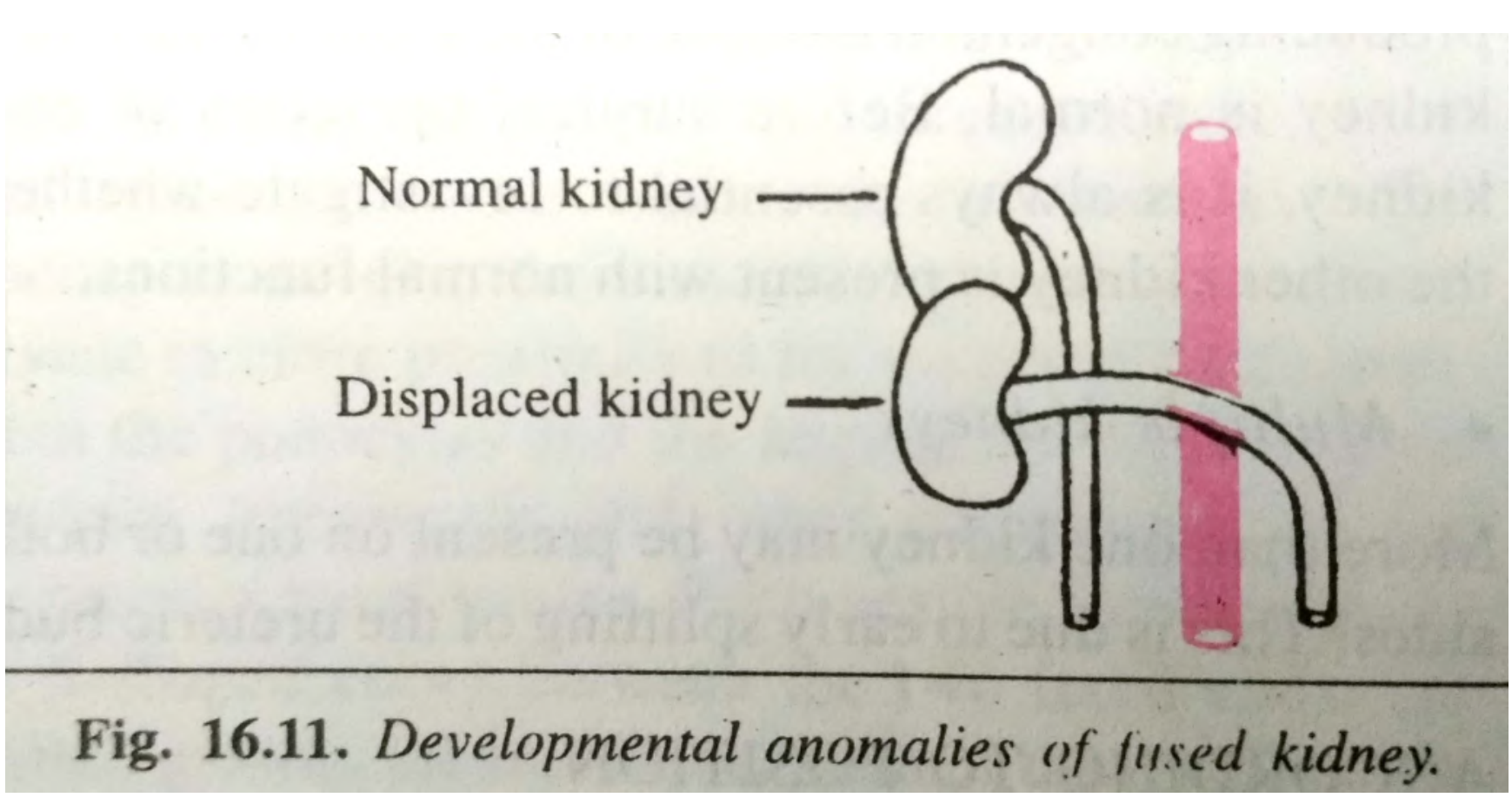


Fig. 16.11. *Developmental anomalies of fused kidney.*

Developmental Anamoly- Disc Kidney

In congenital polycystic kidney disease

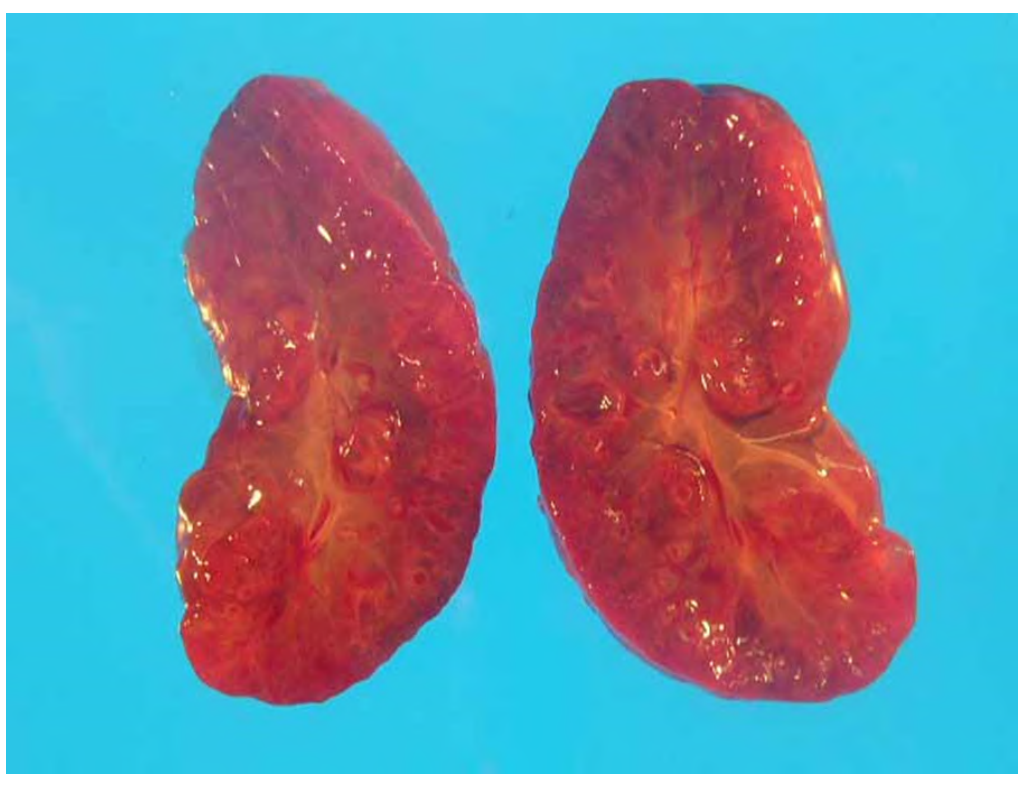
- It may be inherited as an autosomal recessive or autosomal dominant disorder or may be caused by other factors.

Autosomal recessive polycystic kidney disease

- which occurs in 1/5,000 births, is a pro-gressive disorder in which cysts form from collecting ducts. The kidneys become very large, and renal failure occurs in infancy or childhood.

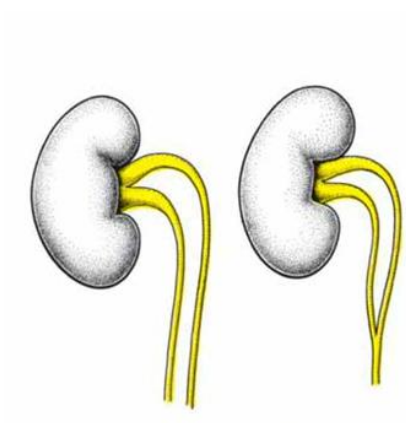
In autosomal dominant poly-cystic kidney disease, cysts form from all segments of the nephron and usually do not cause renal failure until adulthood. The autosomal dominant disease is more common (1/500 to 1/1,000 births) but less progressive than the autosomal recessive disease.

Polycystic Kidney

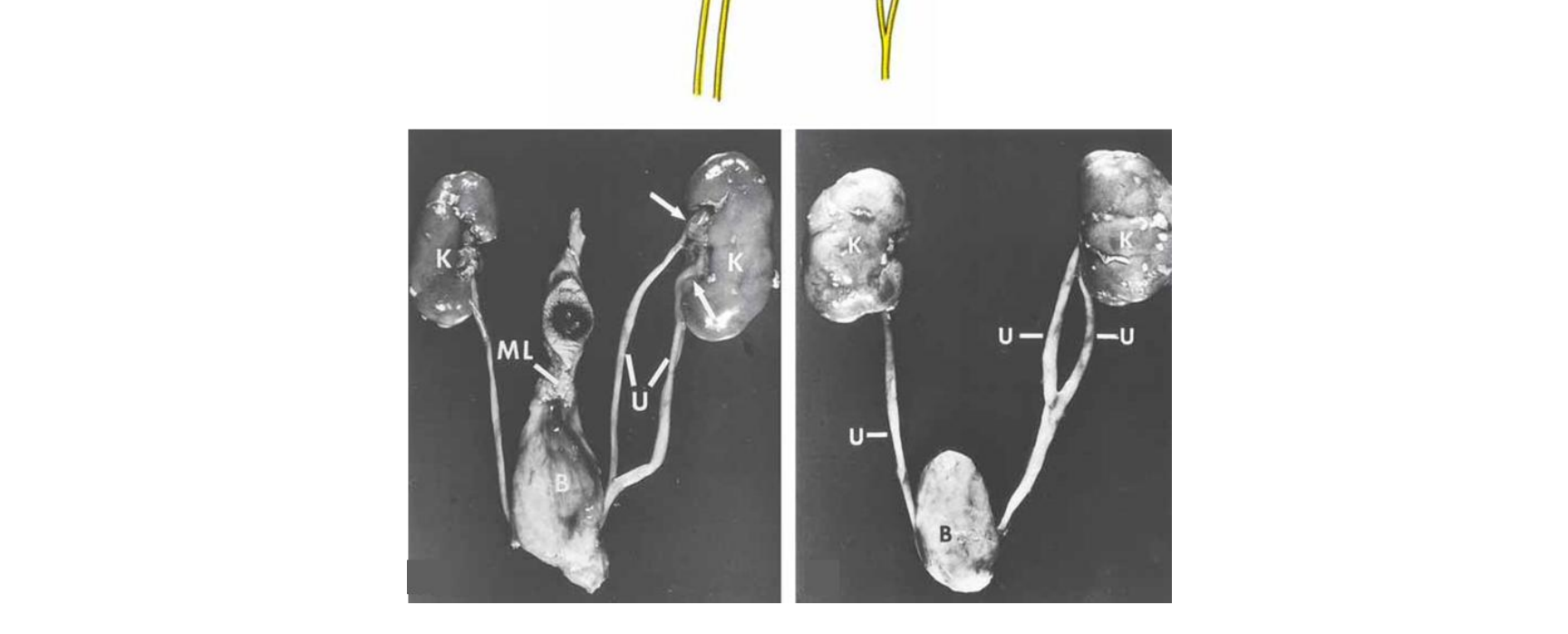


Recessive form: 1:5000; cysts from collecting tubules; renal failure in infancy
Dominant form: 1:500-1000: cysts from anywhere; renal failure in adulthood

Duplications of the Ureters



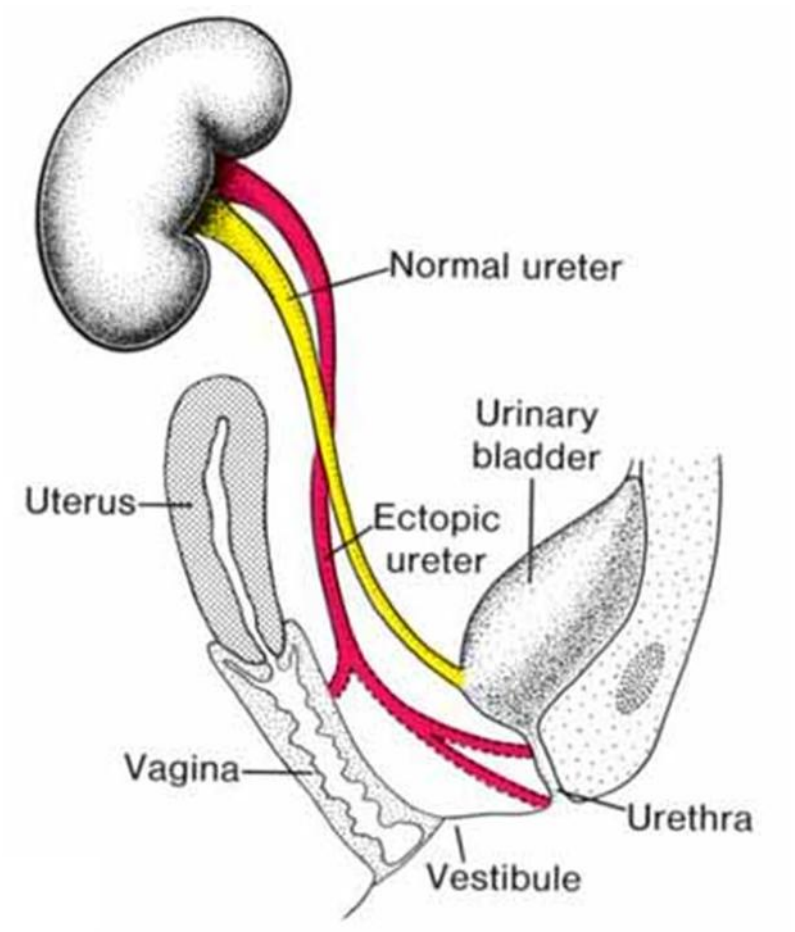
Kidneys With Double Ureter

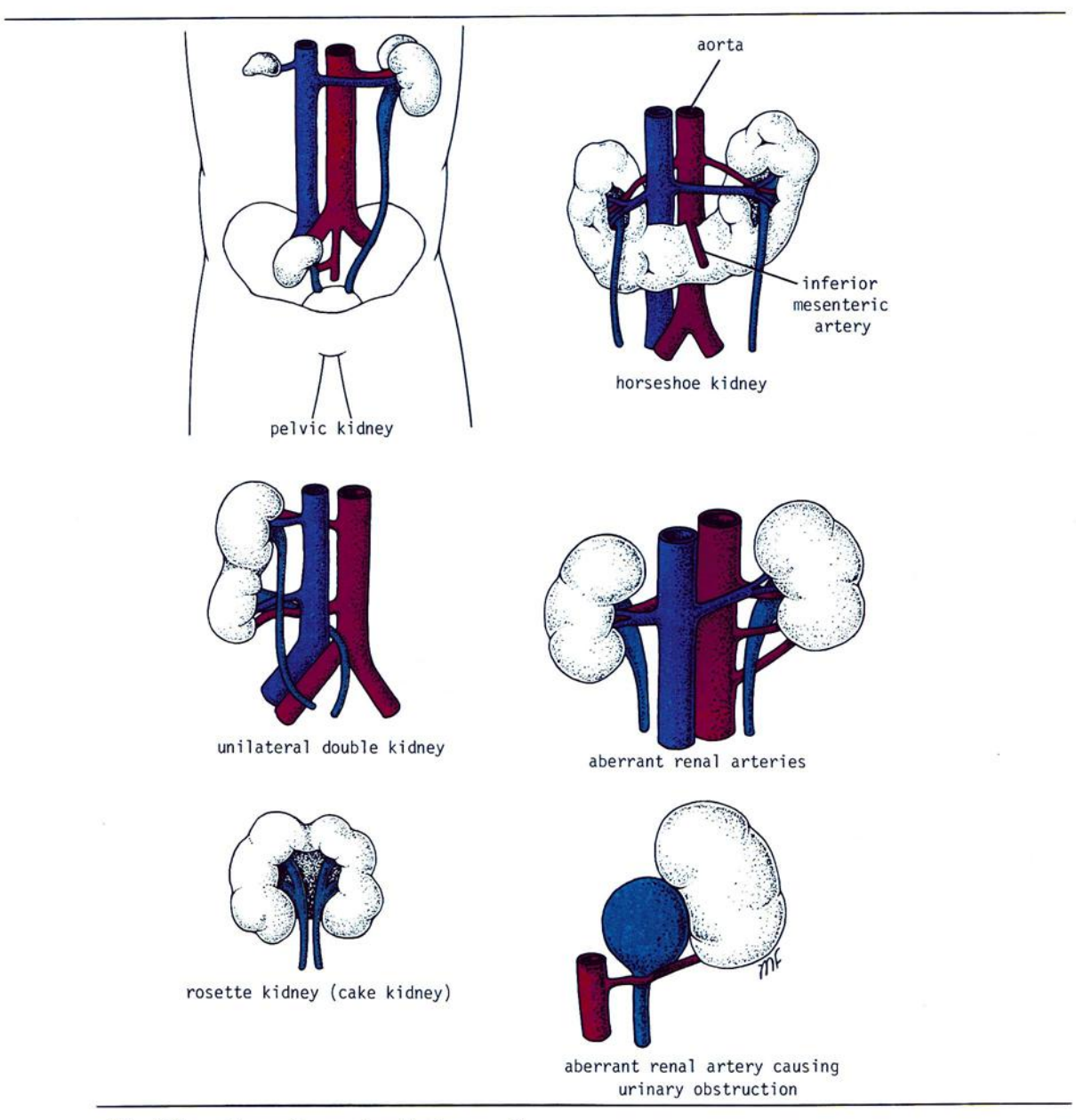


Duplication of the ureter

- results from early splitting of the ureteric bud
- Splitting may be partial or complete, and metanephric tissue may be divided into two parts, each with its own renal pelvis and ureter. More frequently, however, the two parts have a number of lobes in common as a result of intermingling of collecting tubules.
- In rare cases, one ureter opens into the blad-der, and the other is ectopic, entering the vagina, urethra, or vestibule . This abnormality results from development of two ureteric buds. One of the buds usually has a normal position, whereas the abnormal bud moves down together with the mesonephric duct. Thus it has a low, abnor-mal entrance in the bladder, urethra, vagina, or epididymal region.

Possible Positions for Ectopic Ureters





The different forms of anomalous development of the kidney.

MCQ

During surgery for a benign cyst on the kidney, the surgeon notes that the patient's right kidney has two ureters and two renal pelves. This malformation is

- (A) an abnormal division of the pronephros
- (B) an abnormal division of the mesonephros
- (C) formation of an extra mass of intermediate mesoderm
- (D) a premature division of the metanephric blastema
- (E) a premature division of the ureteric bud

MCQ

- The transitional epithelium lining the urinary bladder is derived from
- (A) ectoderm
- (B) endoderm
- (C) mesoderm
- (D) endoderm and mesoderm
- (E) neural crest cells

MCQ

The transitional epithelium lining the ureter is derived from

- (A) ectoderm
- (B) endoderm
- (C) mesoderm
- (D) endoderm and mesoderm
- (E) neural crest cells

MCQ

The podocytes of Bowman's capsule are derived from

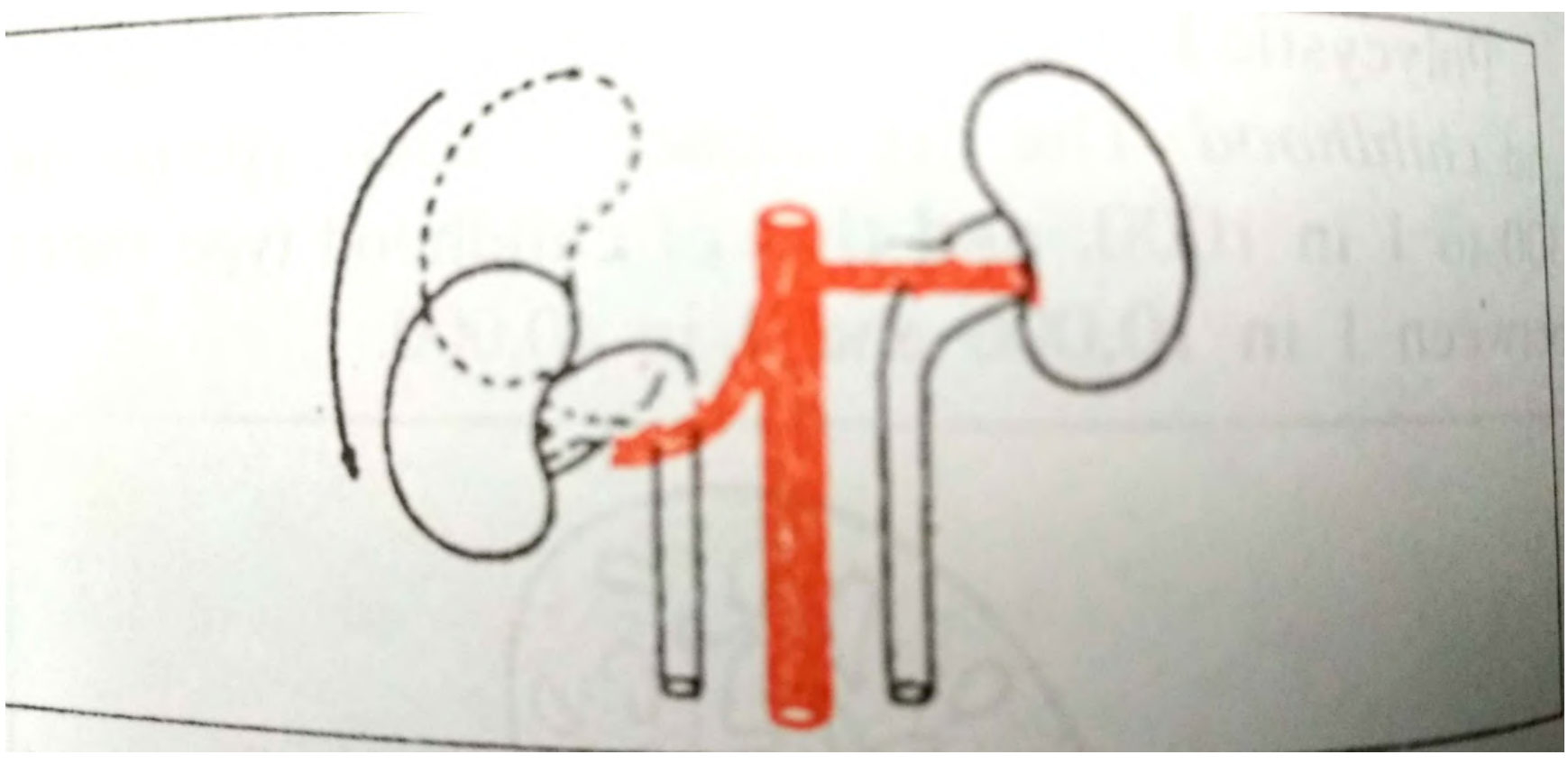
- (A) ectoderm
- (B) endoderm
- (C) mesoderm
- (D) endoderm and mesoderm
- (E) neural crest cells

MCQ

The proximal convoluted tubules of the definitive adult kidney are derived from the

- (A) ureteric bud
- (B) metanephric vesicle
- (C) mesonephric duct
- (D) mesonephric tubules
- (E) pronephric tubules

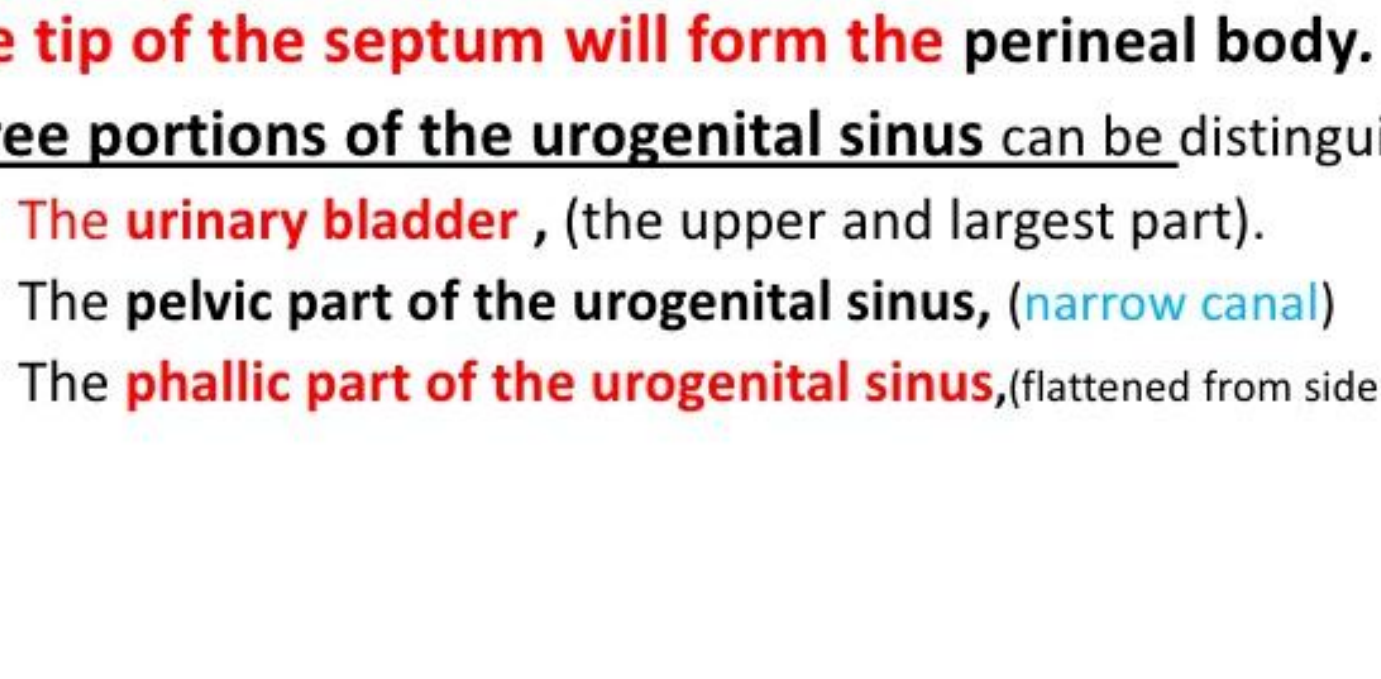
Floating kidney- Dietl's Crisis



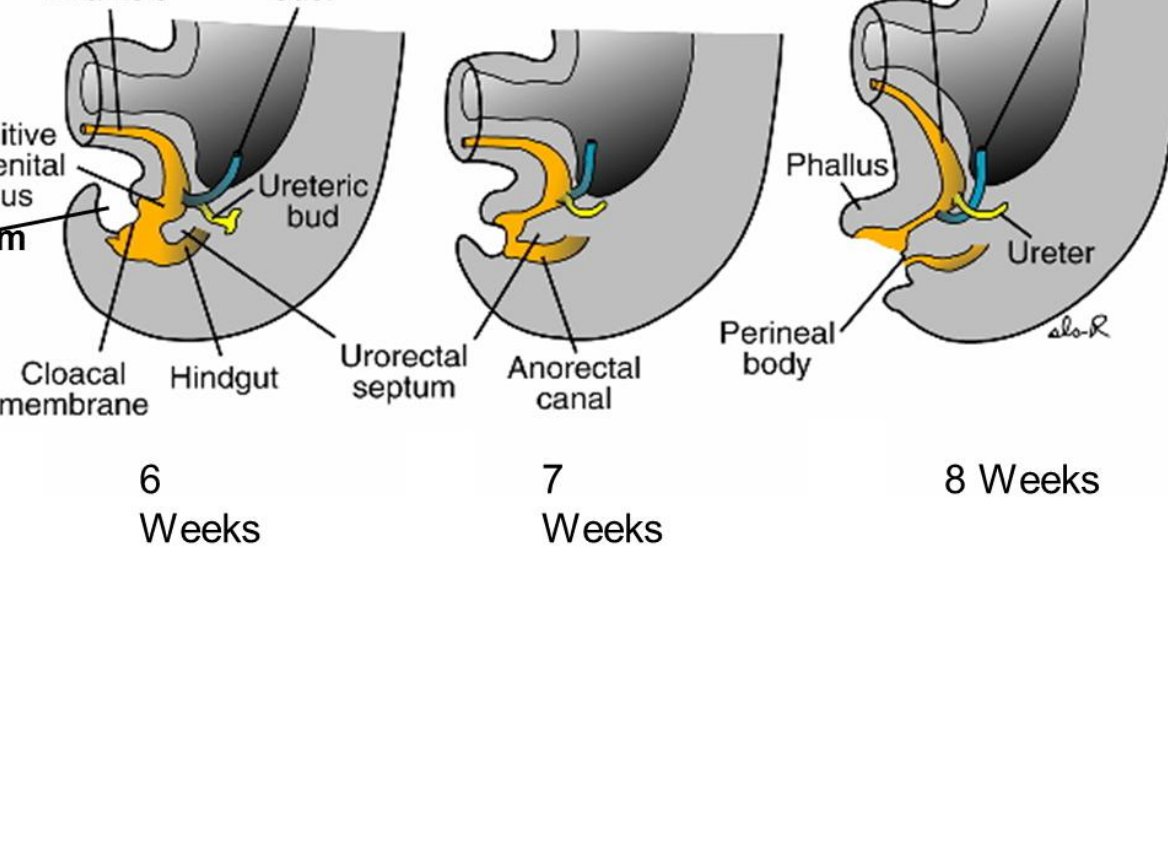
BLADDER AND URETHRA 1/2

- During **the fourth to seventh weeks** of development the **cloaca divides into** the **urogenital sinus anteriorly and the anal canal posteriorly**.
- The **urorectal septum is a layer of mesoderm between the** primitive anal canal and the urogenital sinus.
- **The tip of the septum will form the perineal body.**
- **Three portions of the urogenital sinus** can be distinguished:
  1. The **urinary bladder** , (the upper and largest part).
  2. The **pelvic part of the urogenital sinus,** (narrow canal)
  3. The **phallic part of the urogenital sinus,**(flattened from side to side).

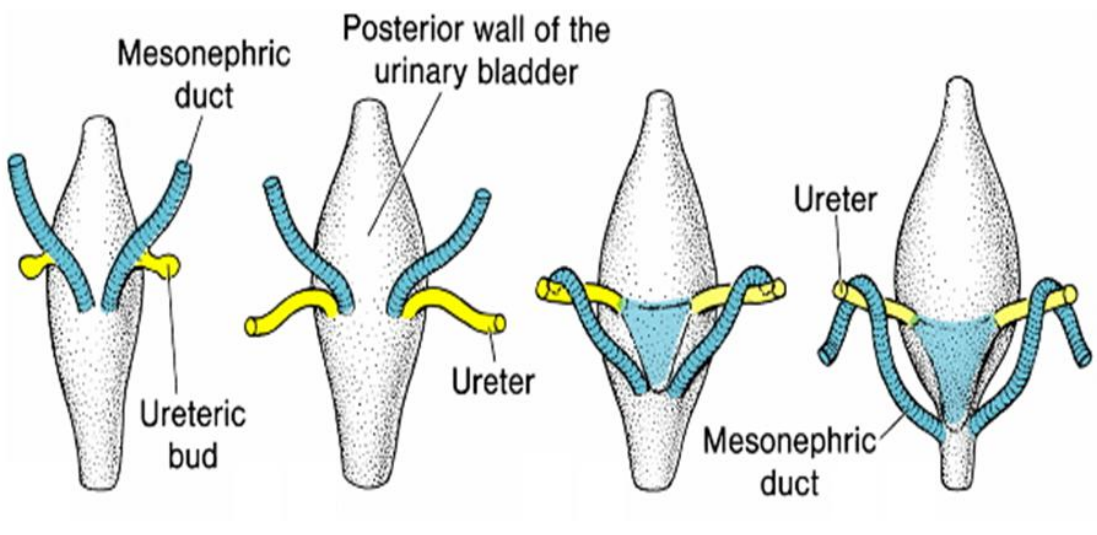
Bladder Development



Final Position of the Ureters and Mesonephric Duct (Vas Deferens)



Bladder Development: Incorporation of the Mesonephric Duct



BLADDER AND URETHRA 2/2

- ❑ Initially the bladder is continuous with the allantois,
- **but** when the lumen of the allantois is obliterated, the **urachus, remains and connects** the apex of the bladder with the umbilicus.
- **In the adult**, it is known as the **median umbilical ligament.**

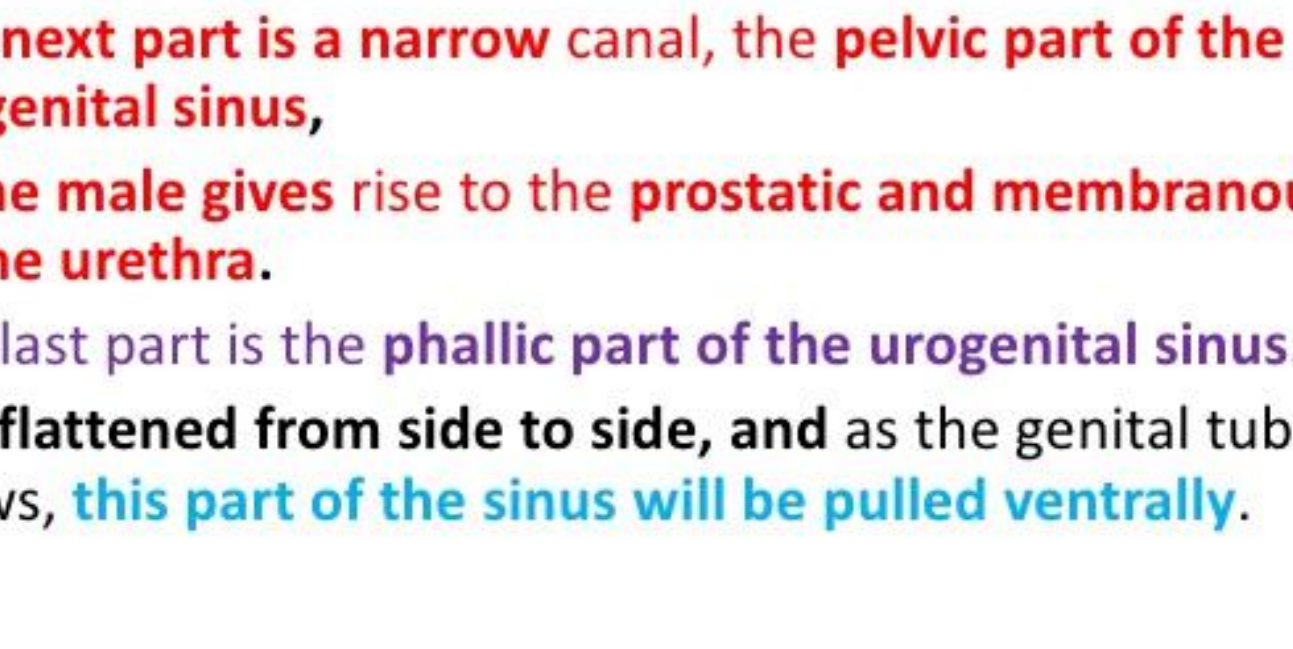
❑ **The next part is a narrow** canal, the **pelvic part of the urogenital sinus,**

➢ **In the male gives** rise to the **prostatic and membranous parts of the urethra.**

❑ The last part is the **phallic part of the urogenital sinus.**

❖ **It is flattened from side to side, and** as the genital tubercle grows, **this part of the sinus will be pulled ventrally.**

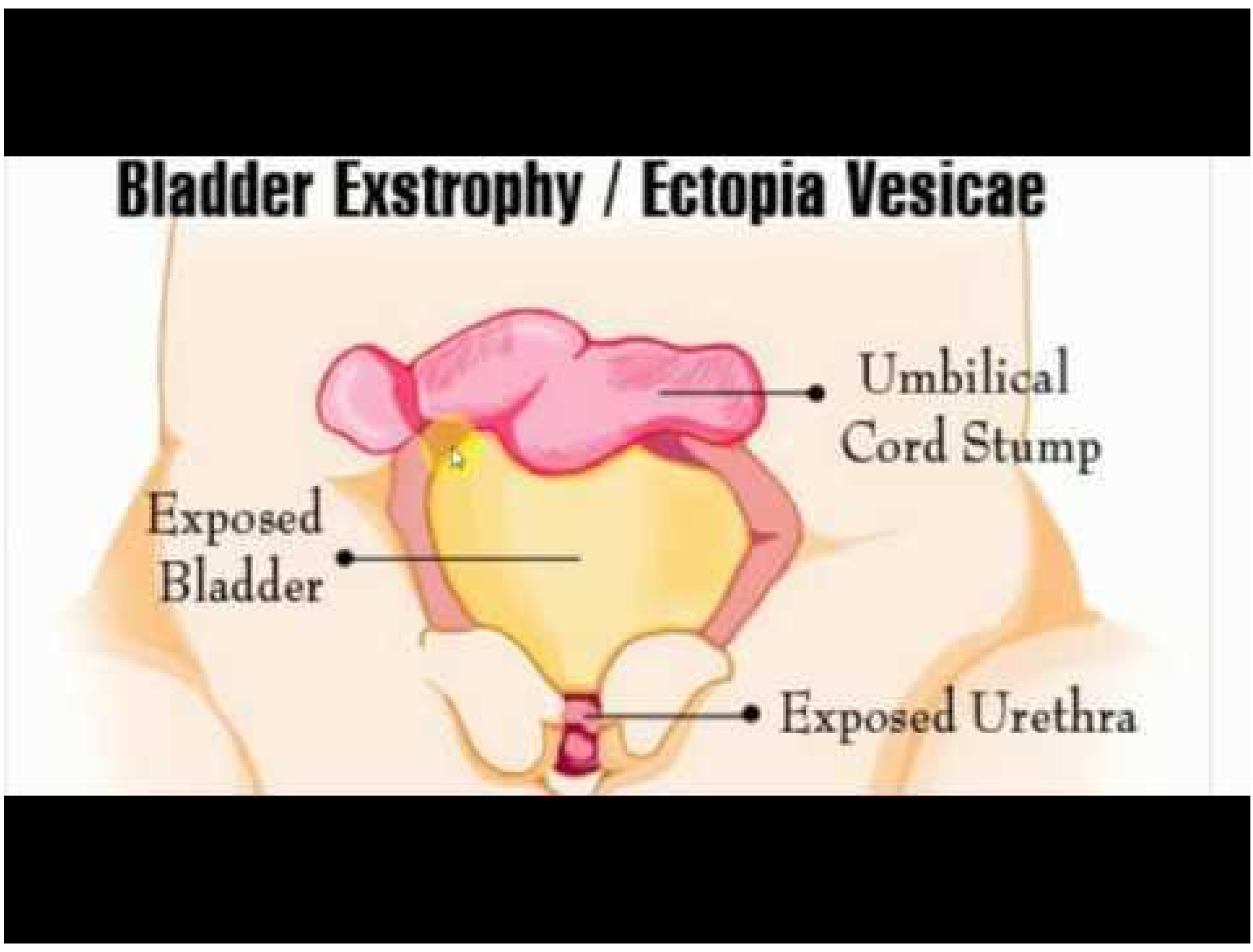
Urachal Abnormalities



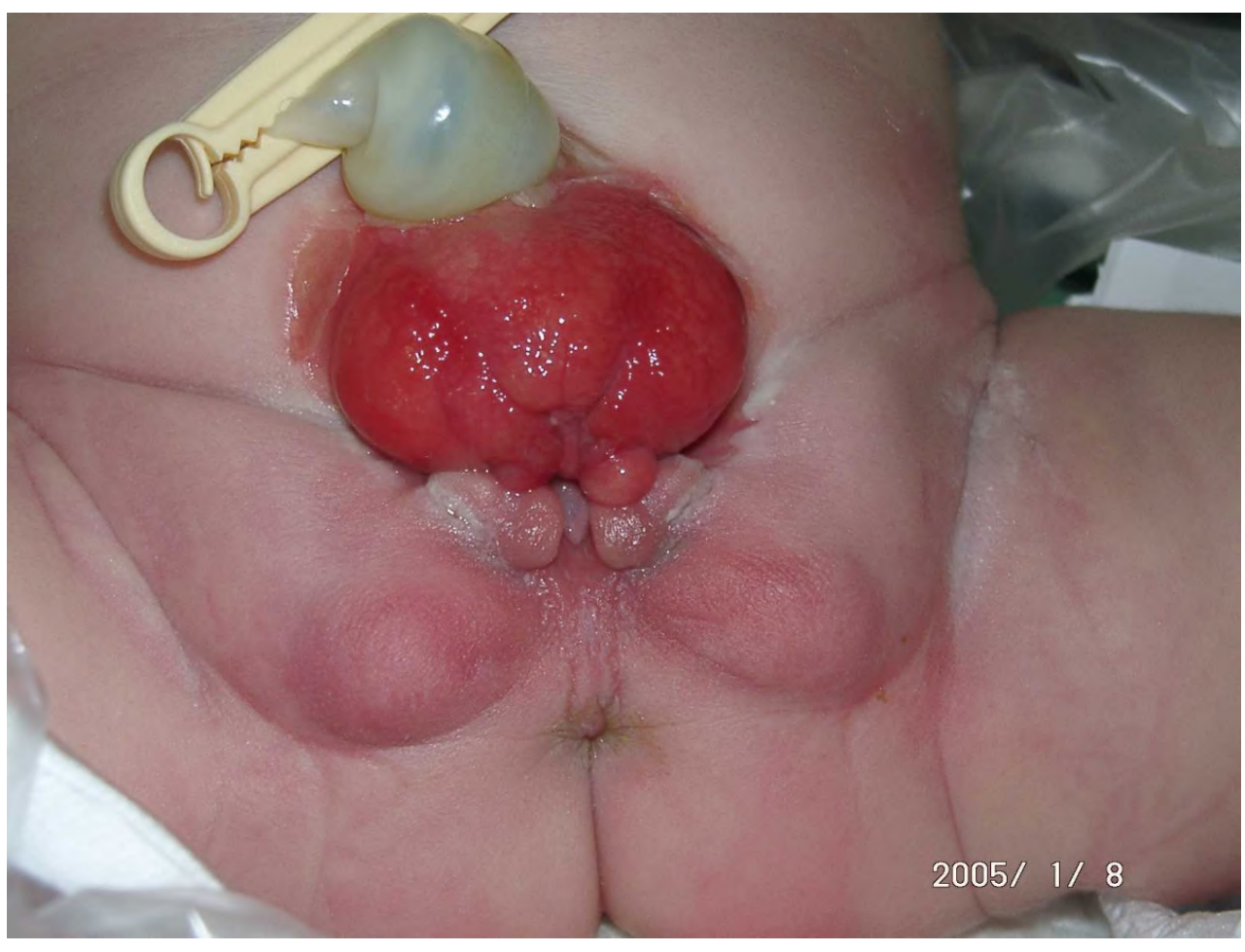
MCQ

The trigone on the posterior wall of the urinary bladder is formed by the

- (A) incorporation of the lower end of the mesonephric ducts
- (B) incorporation of the lower end of the pronephric ducts
- (C) incorporation of the metanephric blastema
- (D) incorporation of the mesonephric tubules
- (E) incorporation of the pronephric tubules



Ectopic Vesicae



- **Exstrophy of the bladder**
- **is a ventral body wall defect** in which the bladder mucosa is exposed outside.
- This anomaly is rare, occurring in 2/100,000 live births.
- **Exstrophy of the Cloaca**
- **is a more severe ventral body wall** defect in which migration of mesoderm to the midline is inhibited and the tail (caudal) fold fails to progress.
- Occurrence is rare (1/30,000),
- defect is associated with early amniotic rupture.
- **The defect includes** exstrophy of the bladder, spinal defects with or without meningomyelocele, imperforate anus, and usually omphalocele.

During Differentiation of the Cloaca

- The caudal portions of the mesonephric ducts are absorbed into the wall of the urinary bladder.
- **The ureters enter the bladder separately.**
- *As a result of ascent of the kidneys, the* orifices of the ureters move farther cranially;
- **those of the mesonephric ducts move close together to enter the prostatic urethra and in the male become the ejaculatory ducts.**
- The mucosa of the bladder formed by incorporation of the ducts (the **trigone of the bladder) is also mesodermal.**
- **With time** the mesodermal lining of the trigone is replaced by endodermal epithelium, **so that finally the inside of the bladder is completely lined with endodermal epithelium.**

MCQ

Immediately after birth of a boy, a moist, red protrusion of tissue is noted just superior to his pubic symphysis. After observation, urine drainage is noted from the upper lateral corners of this tissue mass. What is the diagnosis?

- **(A)** Pelvic kidney
- **(B)** Horseshoe kidney
- **(C)** Polycystic disease of the kidney
- **(D)** Urachal cyst
- **(E)** Exstrophy of the bladder

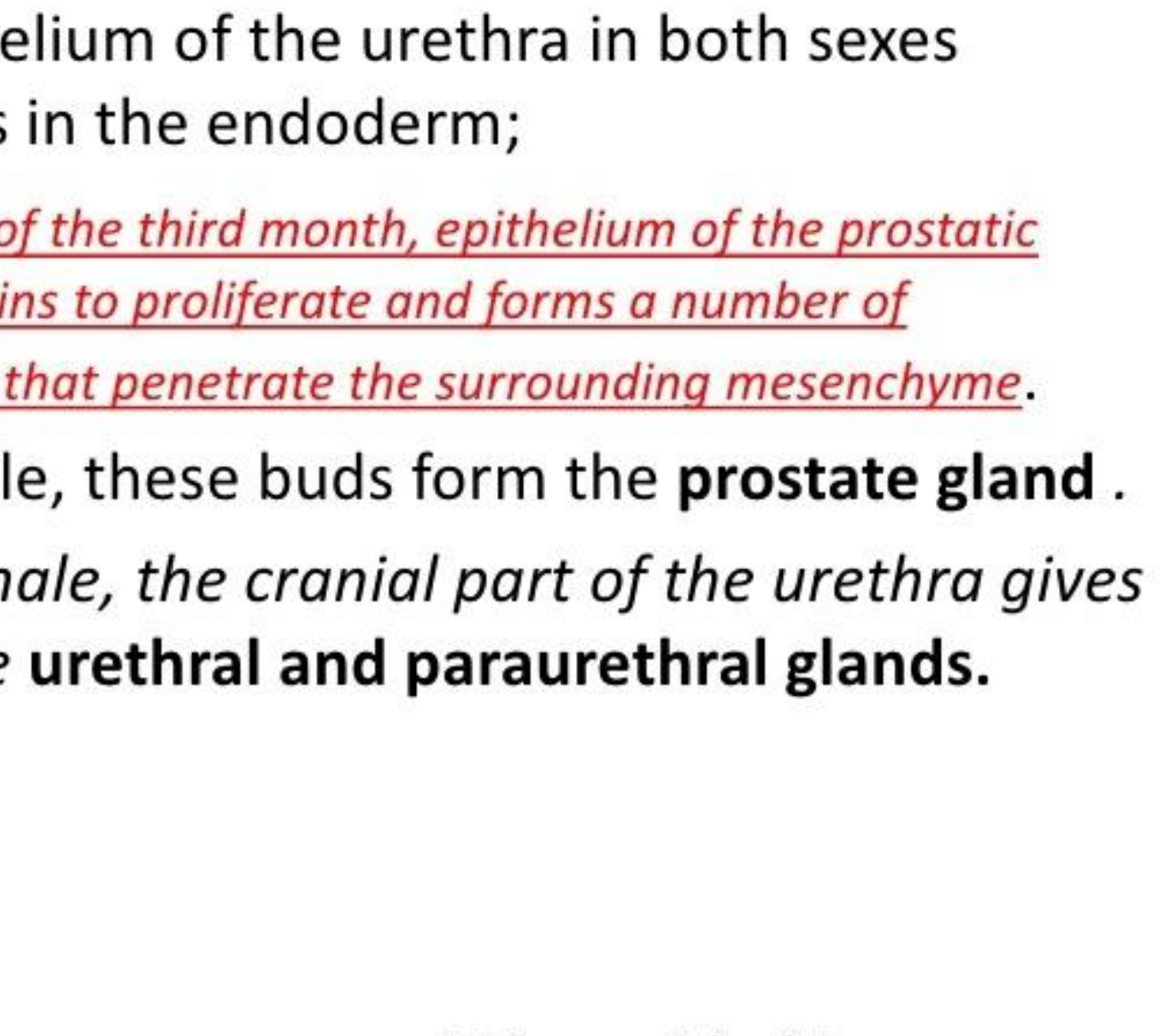
MCQ

A urachal cyst is a remnant of the

- (A) urogenital sinus
- (B) urogenital ridge
- (C) cloaca
- (D) allantois
- (E) mesonephric duc

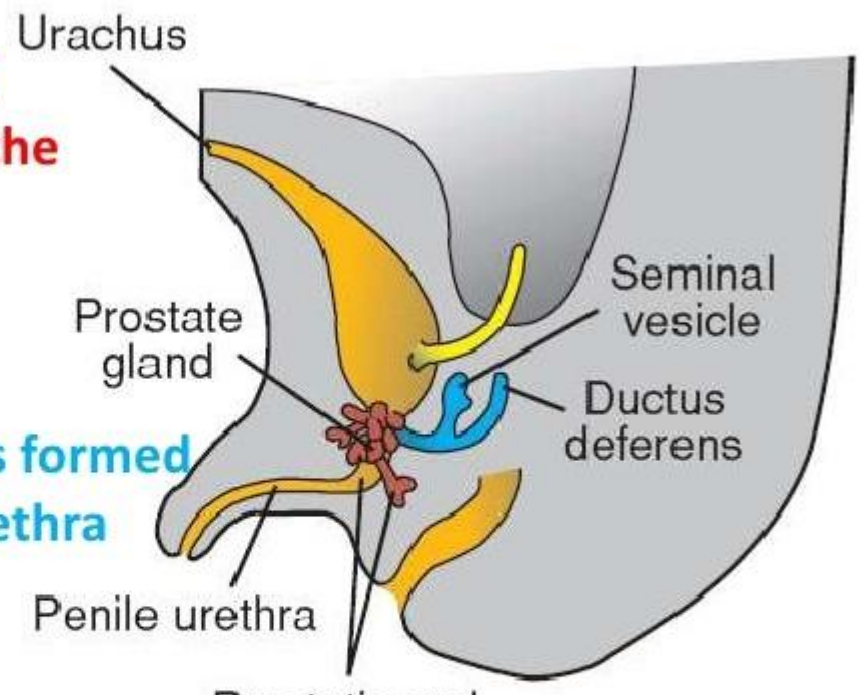
URETHRA

- The epithelium of the urethra in both sexes originates in the endoderm;
- *At the end of the third month, epithelium of the prostatic urethra begins to proliferate and forms a number of outgrowths that penetrate the surrounding mesenchyme*.
- In the male, these buds form the **prostate gland** .
- *In the female, the cranial part of the urethra gives rise to the* **urethral and paraurethral glands.**



Development of the urogenital sinus into the urinary bladder and definitive urogenital sinus.

In the male the definitive urogenital sinus develops into the penile urethra.,



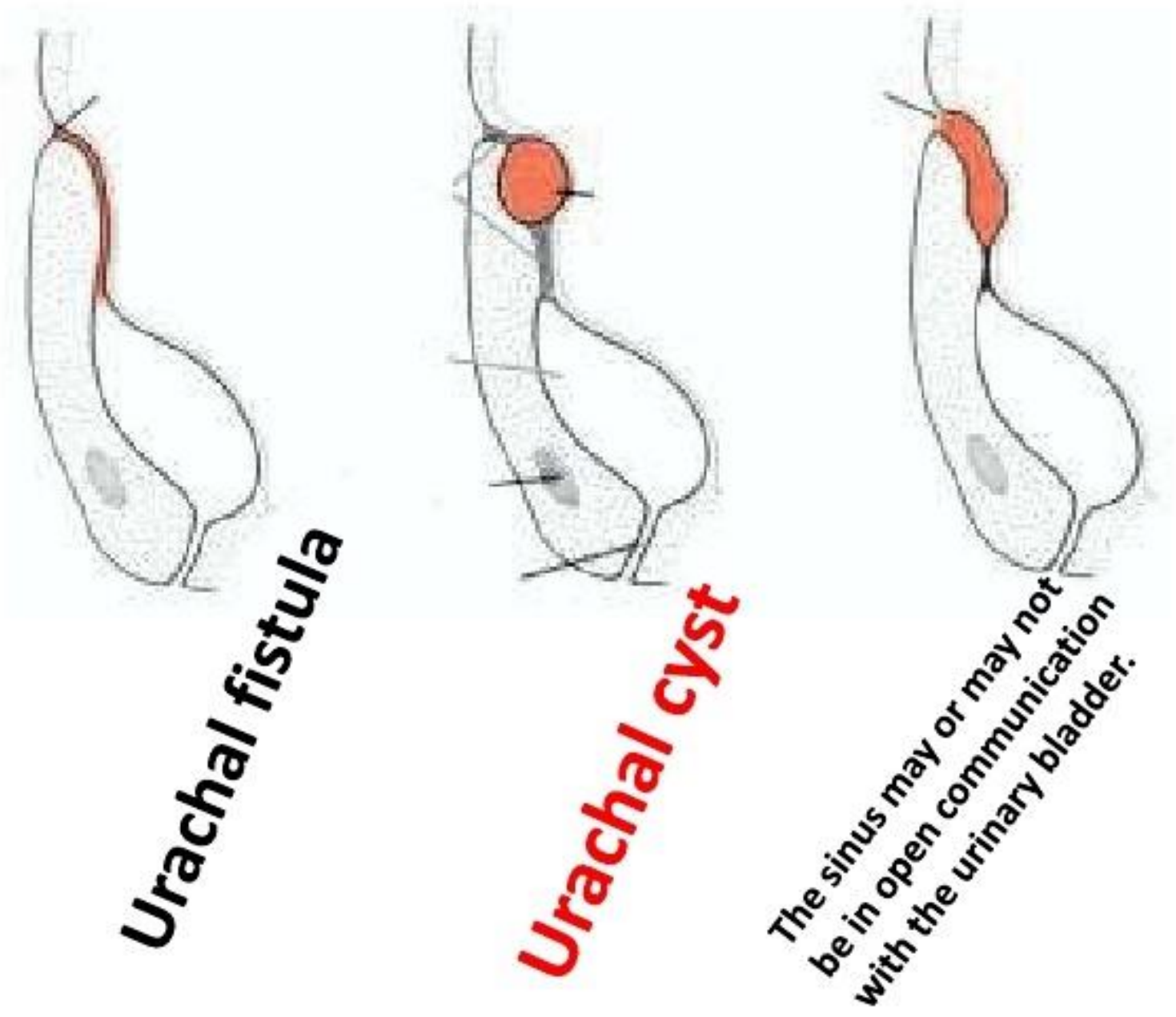
The prostate gland is formed by buds from the urethra

Seminal vesicles are formed by budding from the ductus deferens.

CLINICAL CORRELATES

Bladder Defects

- **Urachal fistula** **(may cause urine to drain from the umbilicus).**
- **Urachal cyst** *(If* only a local area of the allantois persists, results in a cystic dilation).
- **Urachal sinus** *(When the lumen in the upper* part persists).
- **This sinus is usually continuous with** the urinary bladder.



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