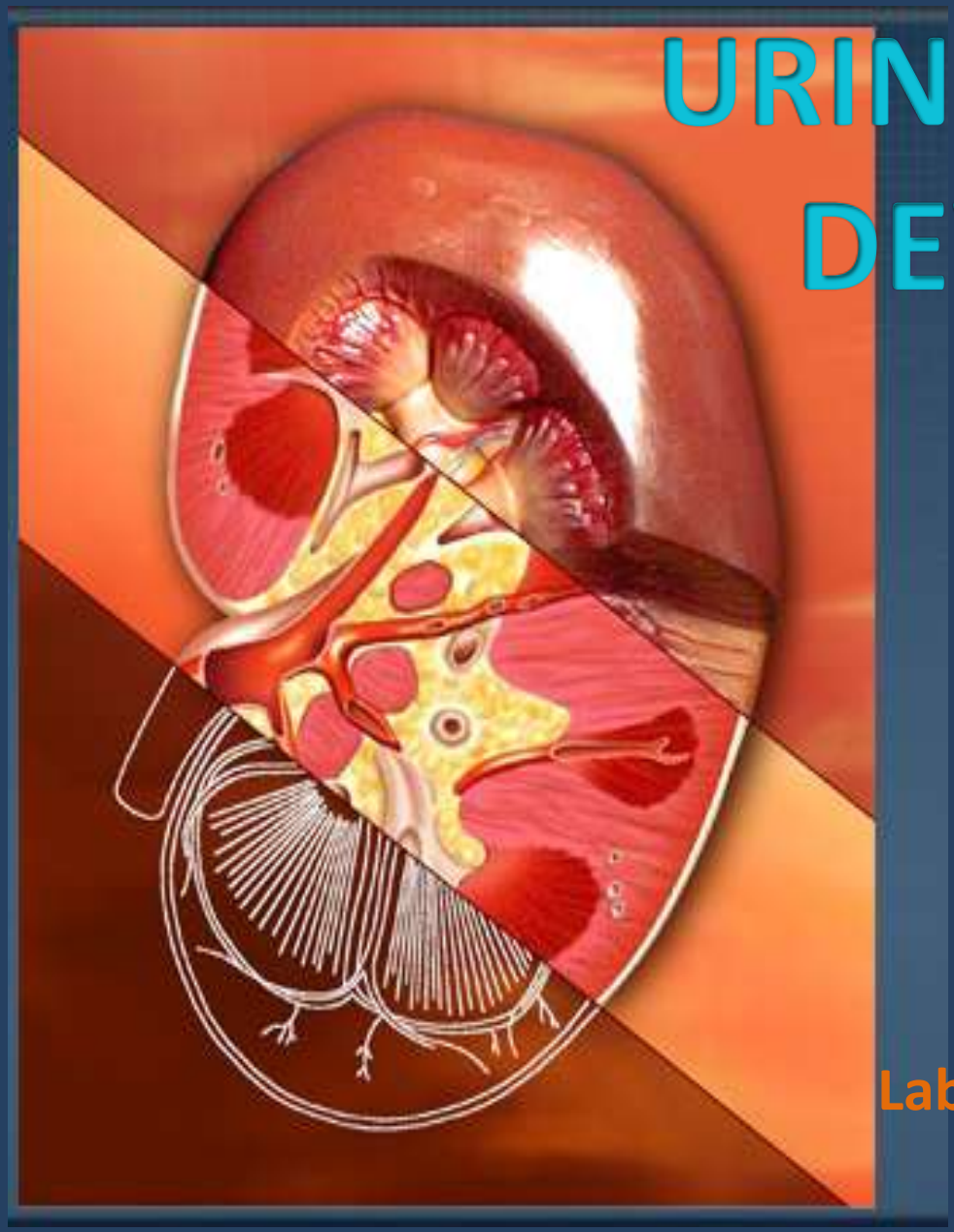
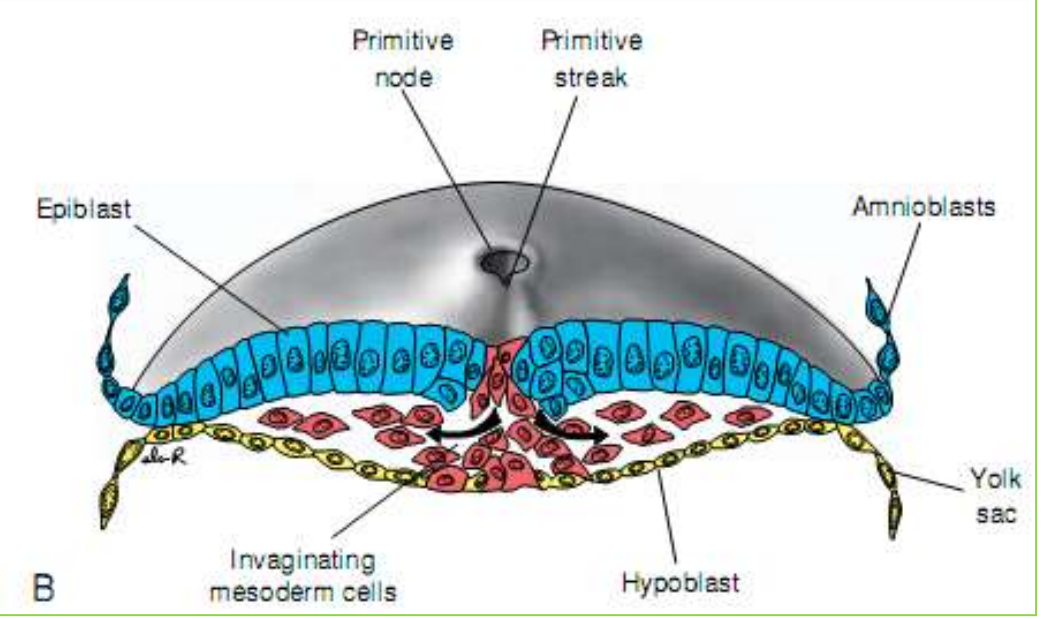


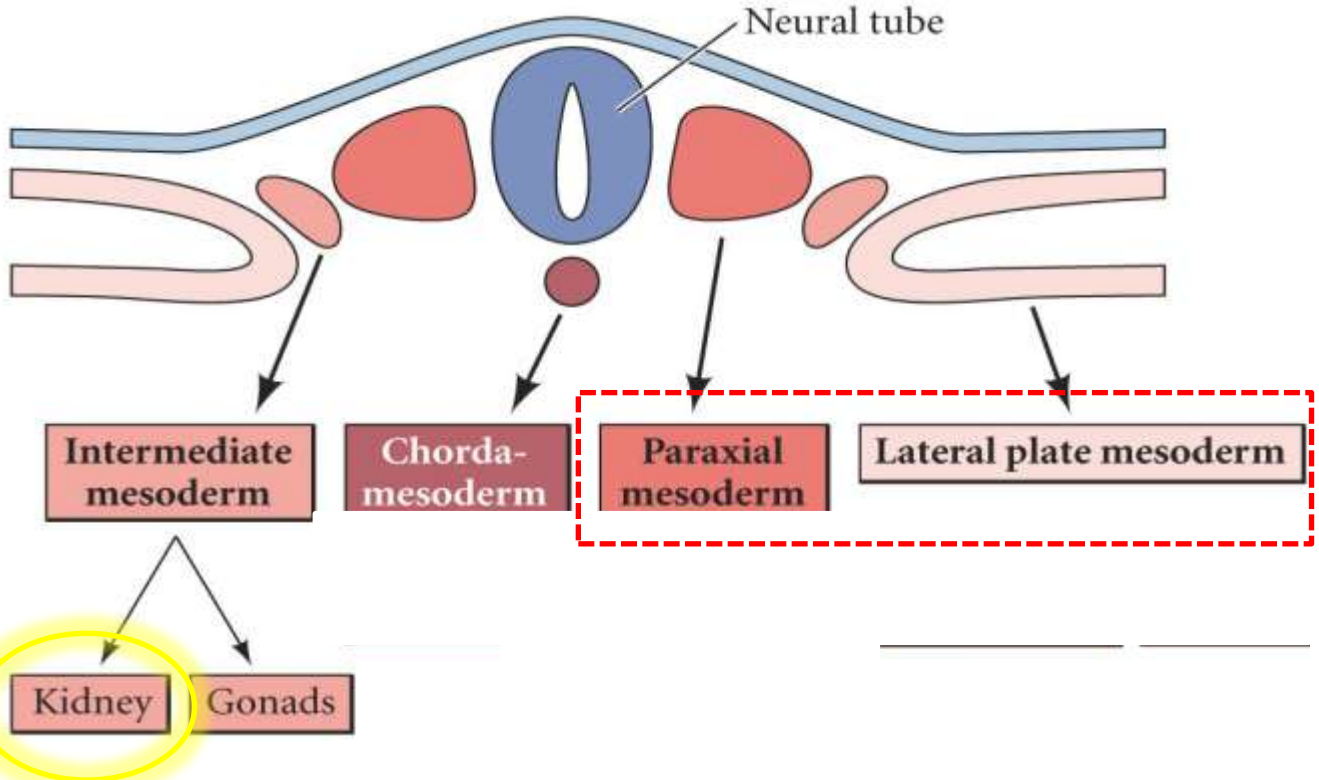
URINARY SYSTEM DEVELOPMENT

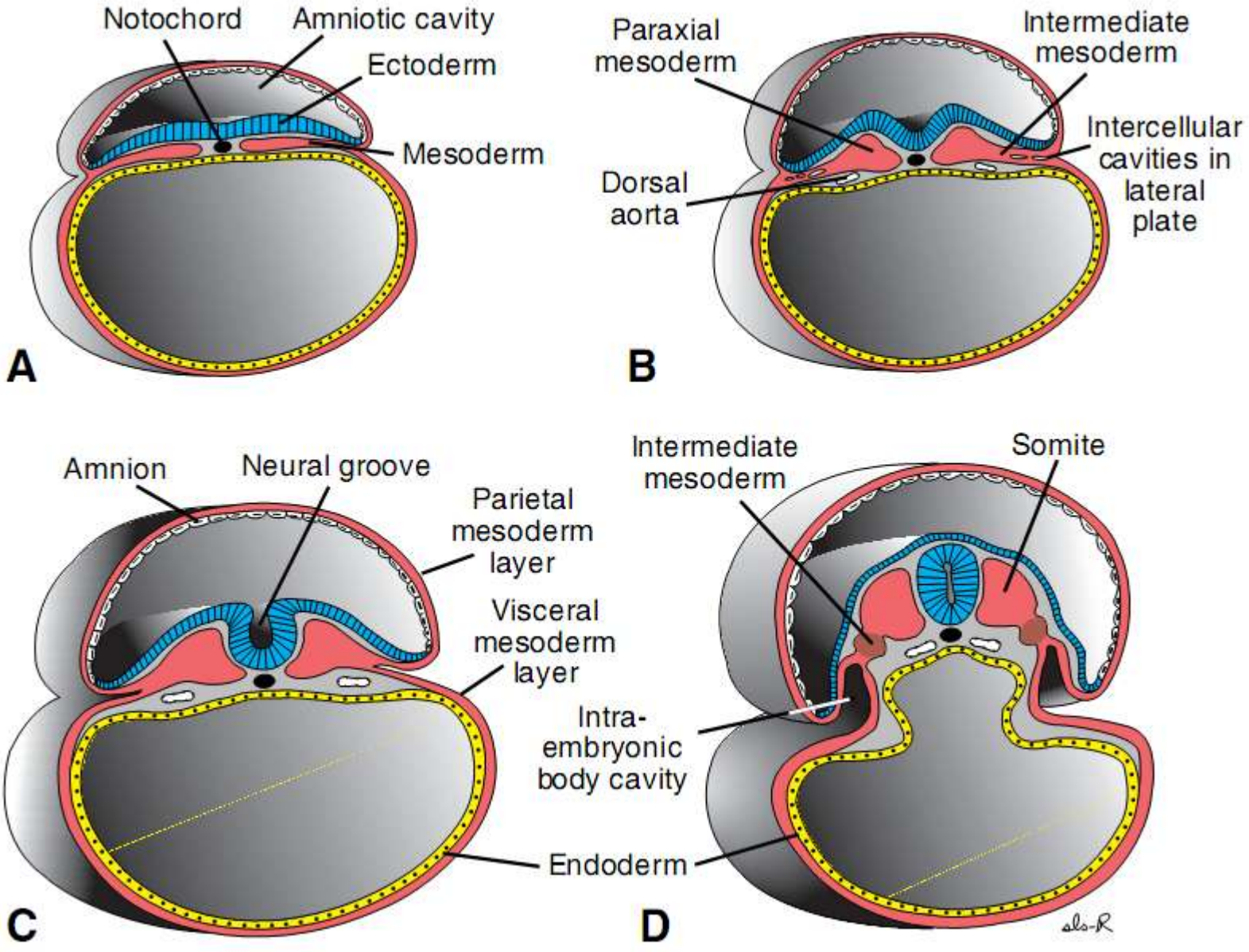
Laboratorium Anatomi-Histologi
FK Universitas Brawijaya

Pokok bahasan

- Tractus uropoetica
  - Ren
  - Ureter
  - Vesica urinaria
- Tractus genitalis
  - Stadium indiferen : - Perkembangan gonad
    - Perkembangan saluran
    - Perkembangan genitalia externa
  - Stadium diferensiasi seksual
    - Perkembangan gonad menjadi laki dan perempuan
    - Perkembangan ductus Mulleri dan ductus Wolffi
    - Perkembangan genitalia externa
- Kelainan bawaan


Primitive node
Primitive streak
Epiblast
Amnioblasts
Yolk sac
Invaginating mesoderm cells
Hypoblast
B


Neural tube
Intermediate mesoderm
Chorda-mesoderm
Paraxial mesoderm
Lateral plate mesoderm
Kidney
Gonads


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

URINARY SYSTEM DEVELOPMENT

- the urinary system and the genital system 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.
- Generally : from cranial to caudal.
- CONSIST OF
  - Excretory system : nephron
  - Collecting system

RENAL

1. pronephros, rudimentary and nonfunctional;
2. Mesonephros, function for a short time during the early fetal period;
3. metanephros. forms the permanent kidney

@ CONSIST OF

- Excretory system : nephron
- Collecting system


"… dan, Dia telah menciptakan segala sesuatu, dan Dia menetapkan ukuran-ukurannya dengan serapi-rapinya." (QS Al Furqaan:2)

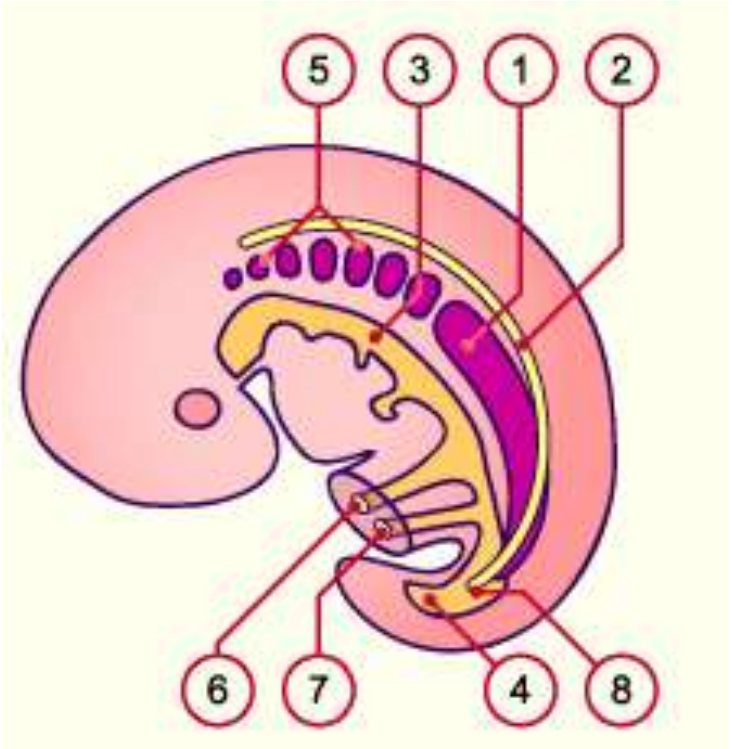
Pronephros

Mesonephros

Metanephros

Pronephros

- beginning of the fourth week (days 22)
- 7 to 10 solid cell groups in the cervical region → *nephrotome*
- By the end of the fourth week, all indications of the pronephric system have disappeared.
- vestigial and has no function.



1	Nephrogenic cord
2	Mesonephric duct
1+2	Mesonephros
3	Intestine
4	Cloaca
5	Atrophied nephrotome
6	Yolk sac (umbilical vesicle)
7	Allantois
8	Outflow of the mesonephric duct into the cloaca

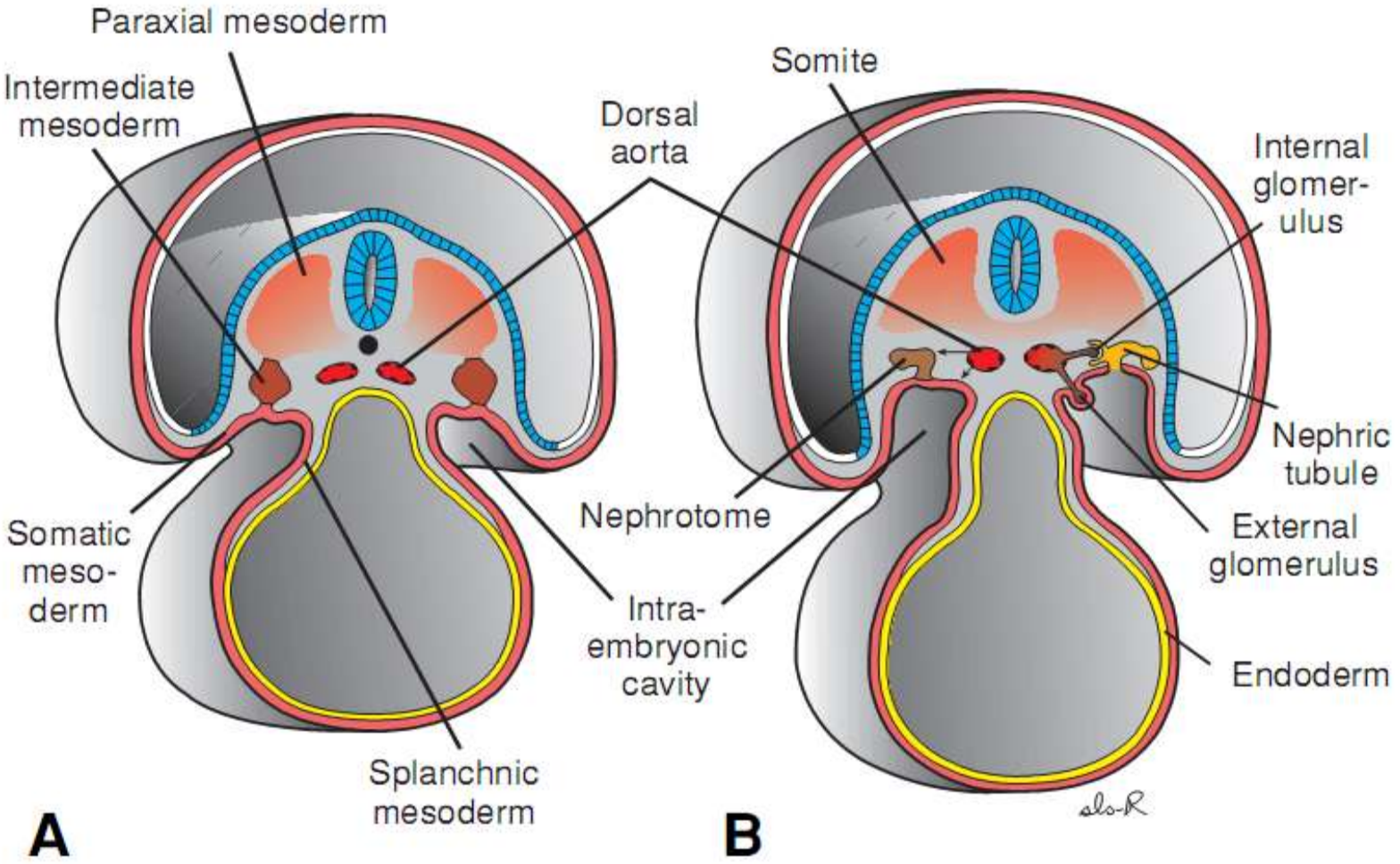


Figure 14.1 Transverse sections through embryos at various stages of development showing formation of nephric tubules. **A.** 21 days. **B.** 25 days. Note formation of external and internal glomeruli and the open connection between the intraembryonic cavity and the nephric tubule.

Pronephros

Mesonephros

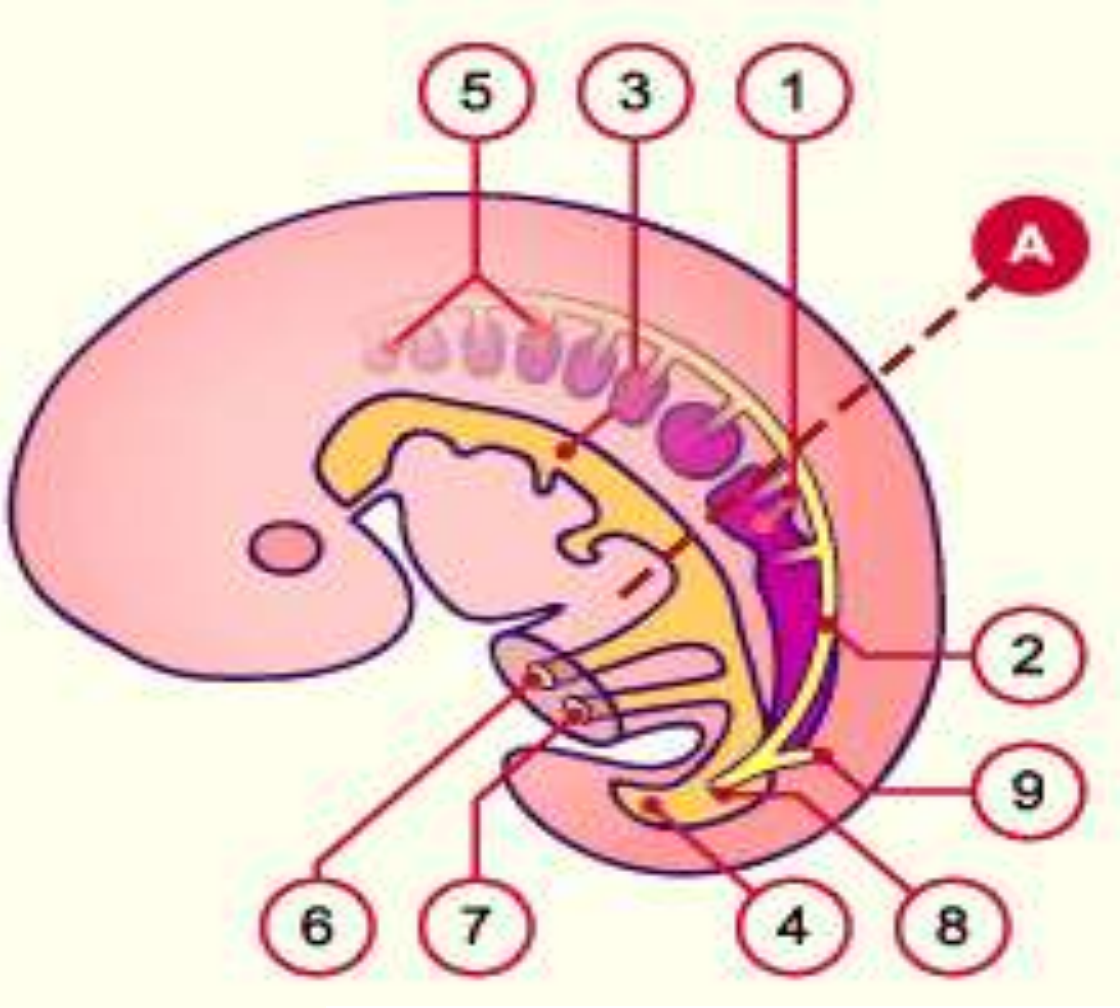
Metanephros

Mesonephros (Wolffian)

- It is the second kidney to appear
- In the thoracic and upper lumbar region.
- In the 4^{th} week
- The mesonephric tubules (as a row) end in the pronephric duct which is now called mesonephric duct (Wolffian duct)
- Mesonephric duct undergoes canalization – transformation from mesenchyme to epithelium
- Mesonephros is functional until 10 weeks
- Mesonephric Duct regression depends on sex (Genital Development)

- Early in the 4th week of development, during regression of the pronephric system, 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**

- In the middle of the second month the mesonephros forms a large ovoid organ on each side of the midline (gonad) → = urogenital ridge
- While caudal tubules are still differentiating, cranial tubules and glomeruli show degenerative changes,
- By the end of the 2nd month the majority have disappeared.
- In the male : a few of the caudal tubules and the mesonephric duct persist and participate in formation of the genital system.
- In female : all gone.



1	Nephrogenic cord
2	Mesonephric duct
1+2	Mesonephros
3	Intestine
4	Cloaca
5	Atrophied nephrotom
6	Yolk sac (umbilical vesicle)
7	Allantois
8	Outflow of the mesonephric duct into the cloaca
9	Ureter bud (anlage)

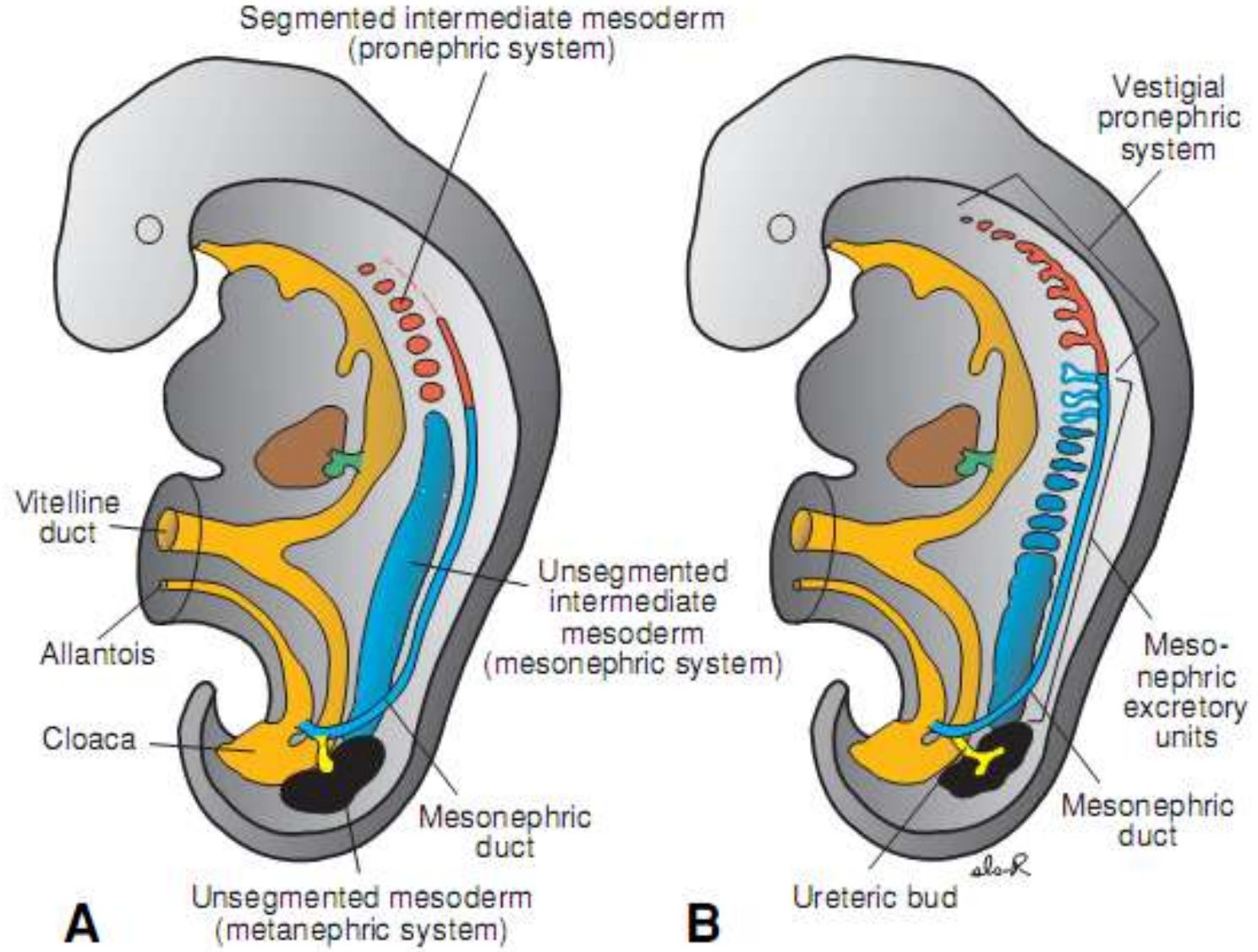


Figure 14.2 A. Relationship of the intermediate mesoderm of the pronephric, mesonephric, and metanephric systems. In cervical and upper thoracic regions intermediate mesoderm is segmented; in lower thoracic, lumbar, and sacral regions it forms a solid, unsegmented mass of tissue, the nephrogenic cord. Note the longitudinal collecting duct, formed initially by the pronephros but later by the mesonephros. **B.** Excretory tubules of the pronephric and mesonephric systems in a 5-week-old embryo.

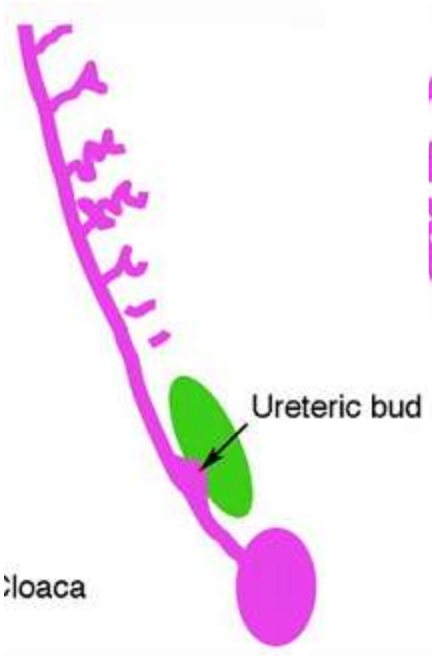
Pronephros

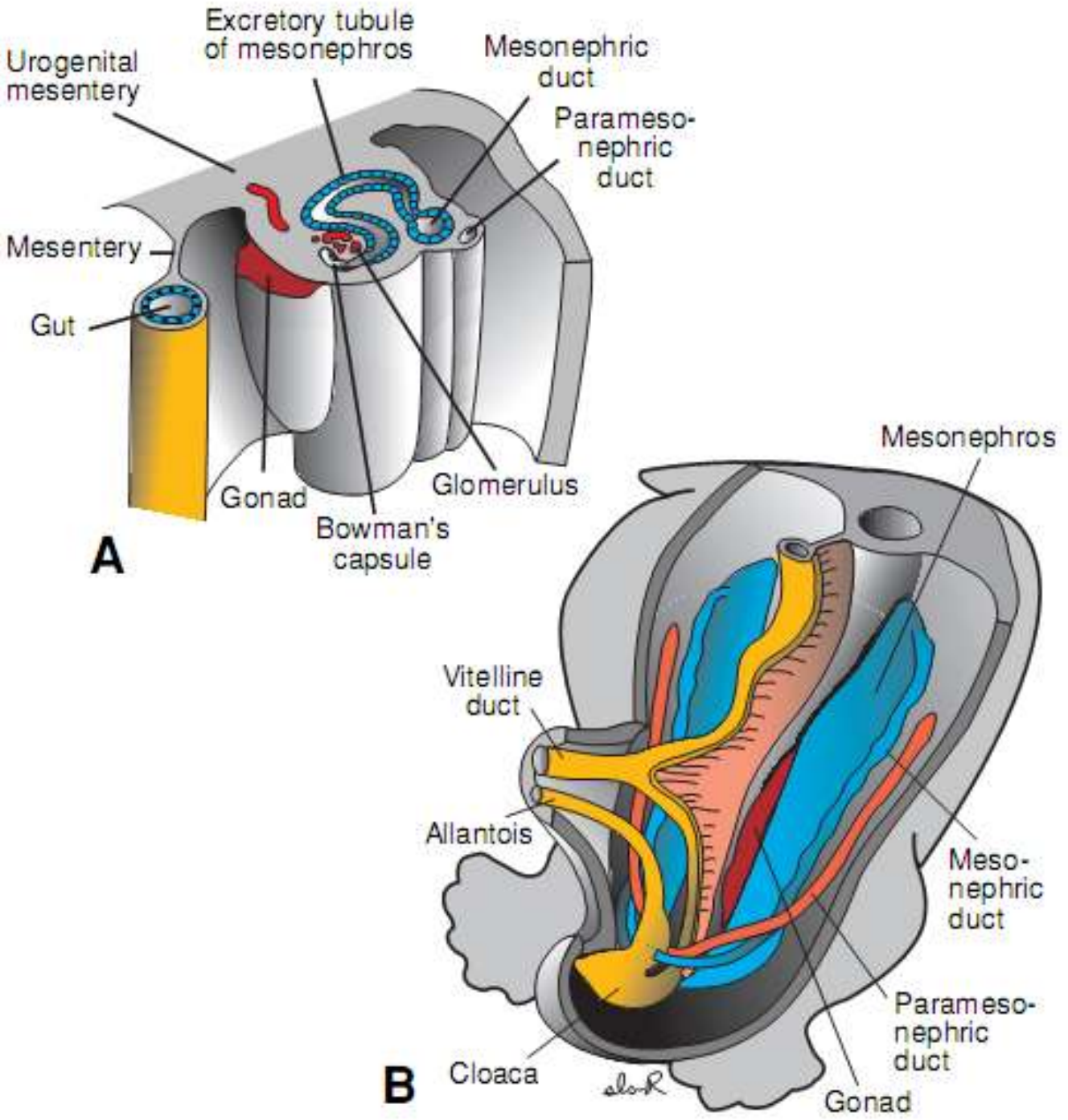
Mesonephros

METANEPHROS

Metanephros

- The third urinary organ, as permanent kidney
- Appears in the 5th week.
- Its excretory units develop from **metanephric mesoderm** in the same manner as in the mesonephric system
- The development of the duct system (Collecting system) : from **Ureteric bud** : an outgrowth of the mesonephric duct close to its entrance to the cloaca




Excretory tubule of mesonephros
Urogenital mesentery
Mesonephric duct
Paramesonephric duct
Mesentery
Gut
Gonad
Glomerulus
Bowman's capsule
A
Mesonephros
Vitelline duct
Allantois
Mesonephric duct
Paramesonephric duct
Cloaca
Gonad
B

Collecting System.

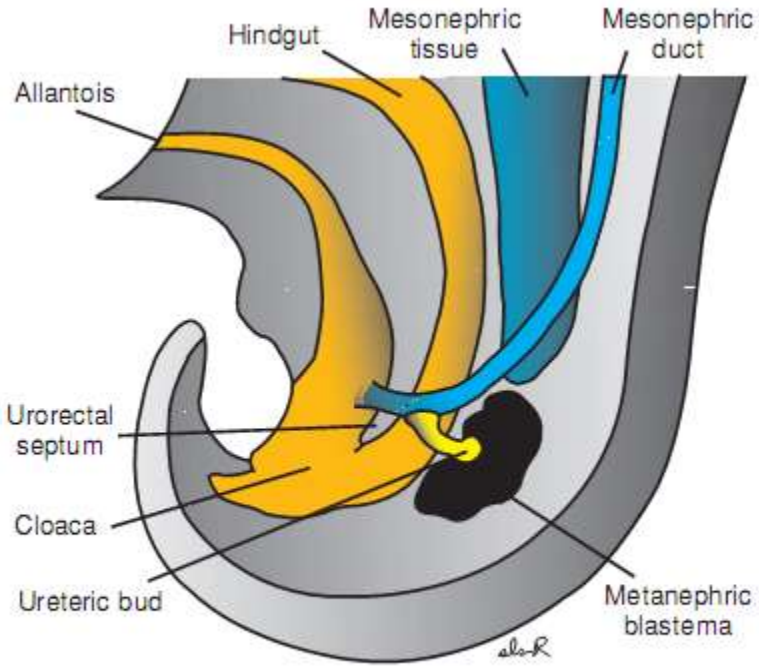
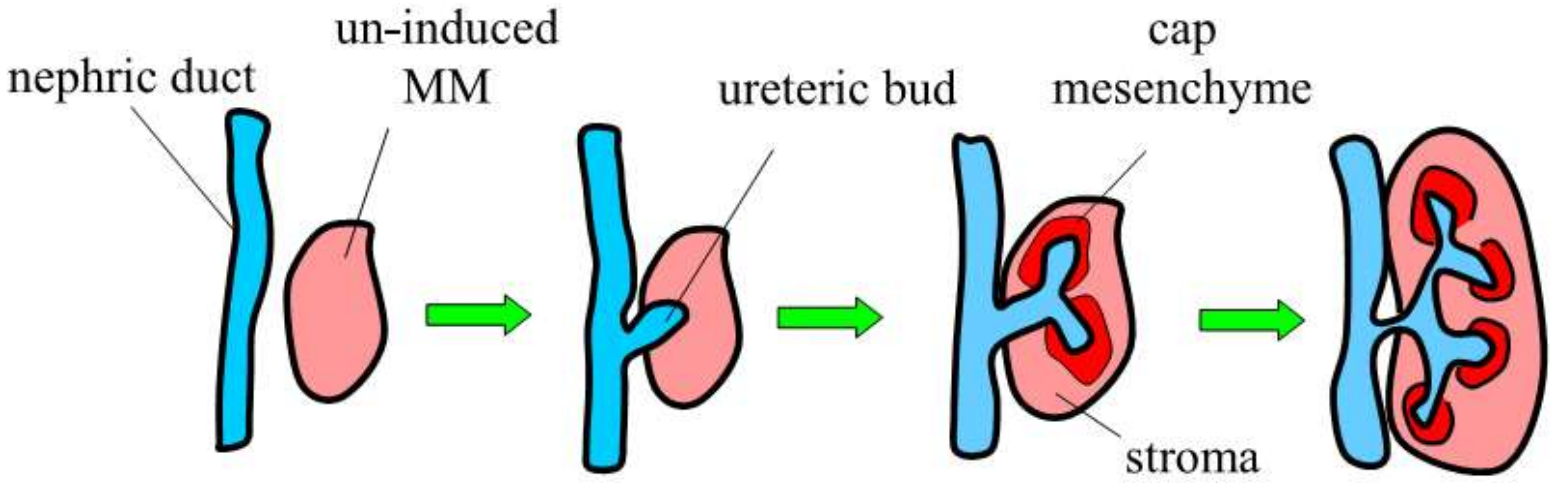


Figure 14.4 Relation of the hindgut and cloaca at the end of the fifth week. The ureteric bud penetrates the metanephric mesoderm (blastema).

Collecting System.

- The bud penetrates the **metanephric tissue**, which is molded over its distal end as a cap
- the bud dilates, forming the primitive renal pelvis, and splits into cranial and caudal portions, the future major calyces
- @ calyx → forms 2 new buds while penetrating the metanephric tissue → continue to subdivide until 12 or more generations .
- The tubules of the second order enlarge and absorb those of the third and fourth generations, forming the minor calyces.
- collecting tubules of the fifth and successive generations elongate considerably and converge on the minor calyx, forming the renal pyramid
- END : ureteric bud membentuk : ureter, renal pelvis, calyx mayor dan minor, dan tubulus colectivus



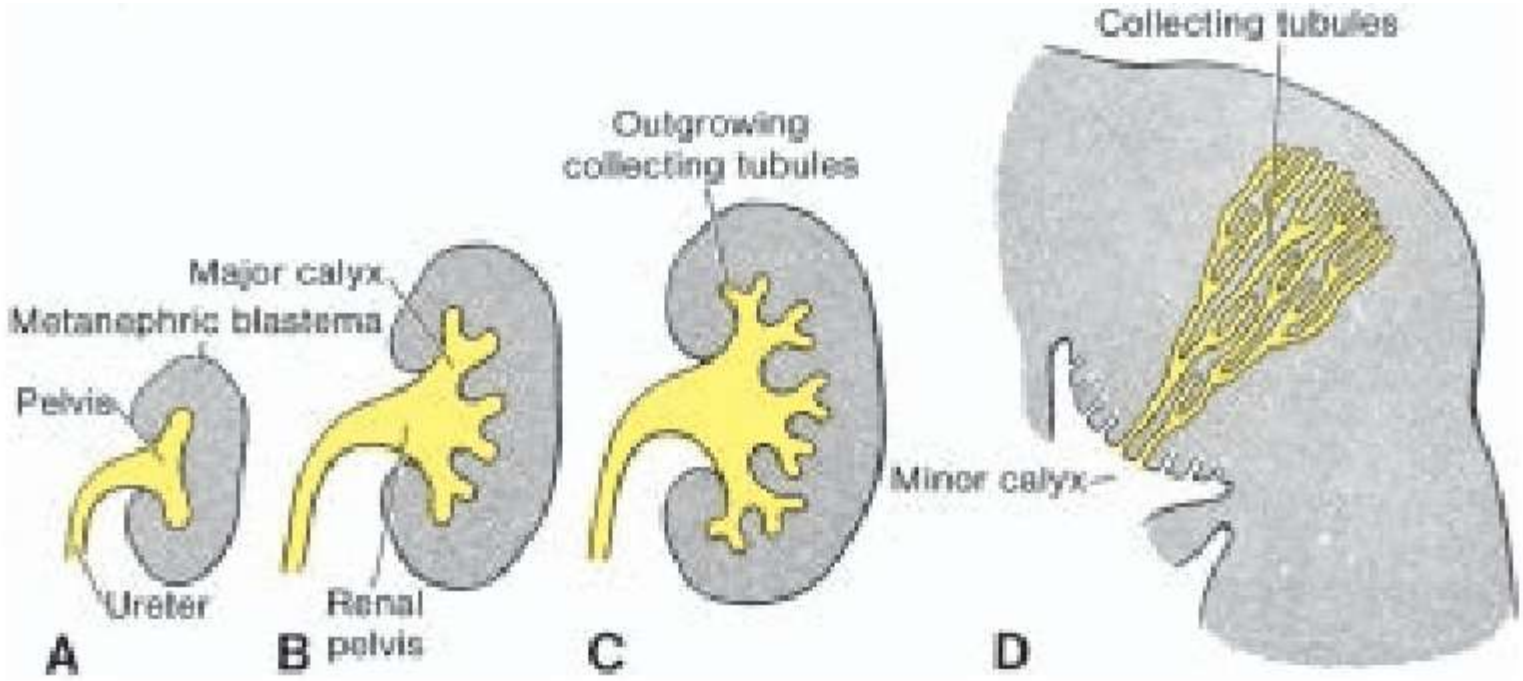
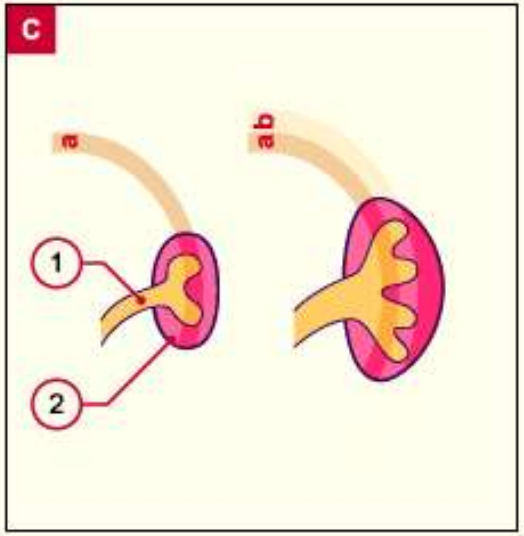
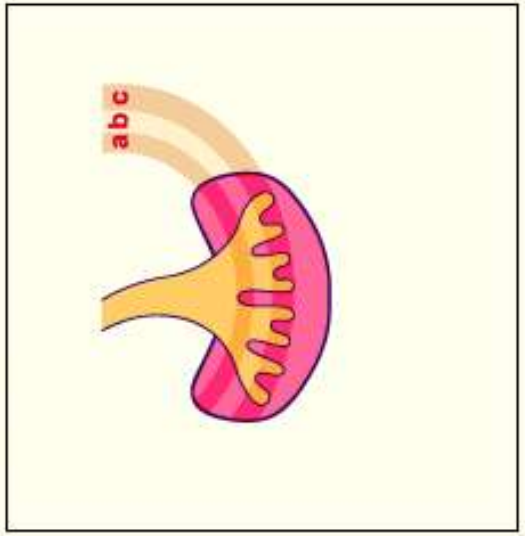
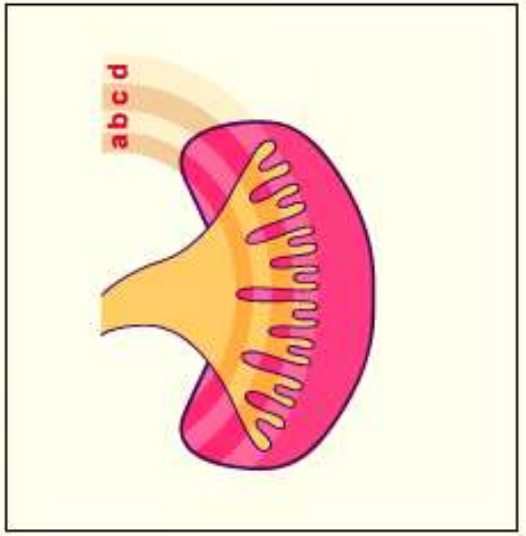
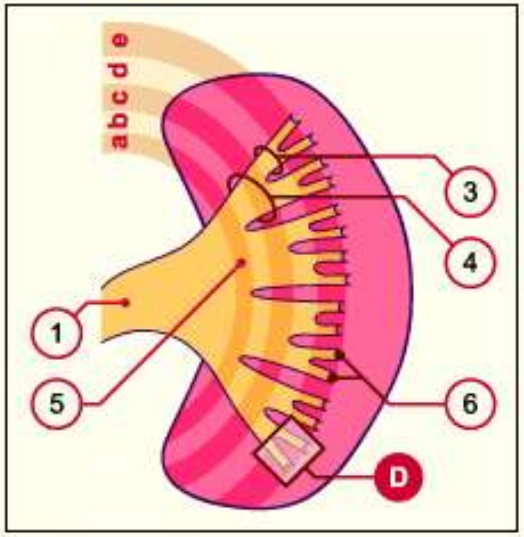


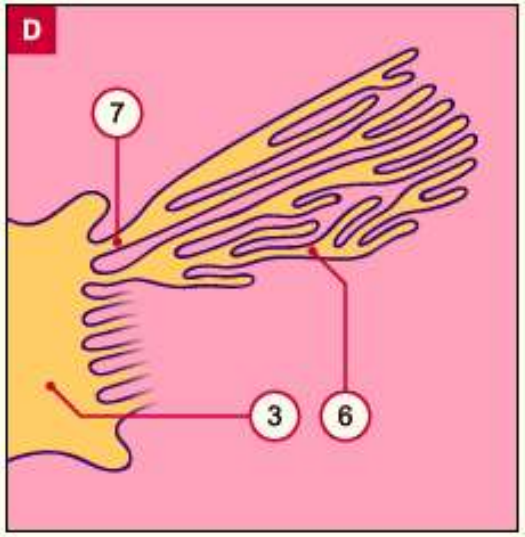
Figure 14.5 Development of the renal pelvis, calyces, and collecting tubules of the metanephros. **A.** 6 weeks. **B.** At the end of the sixth week. **C.** 7 weeks, **D.** Newborn. Note the pyramid form of the collecting tubules entering the minor calyx.











Atrophy of the previous partitions
(16 branches)

1 Ureter
2 Metanephric blastema
3 Minor calix
4 Major calix
5 Renal pelvis
6 Collecting duct
7 Papillary duct

a 1st dichotomous partition
b (two branches) 2nd dichotomous
c partition (4 branches)
d 3rd dichotomous partition
e (8 branches) 4th dichotomous

Excretory System.

- Each newly formed collecting tubule is covered at its distal end by a **metanephric tissue cap**
- cells of the tissue cap form small vesicles, the **renal vesicles**, which in turn give rise to small S-shaped tubules
- Capillaries invasion: differentiate into **glomeruli**
- Tubuli + glomeruli = nephrons (excretory units)
- The proximal end of each nephron forms Bowman's capsule, indented by a glomerulus
- The distal end forms an open connection with one of the collecting tubules.
- Continuous lengthening of the excretory tubule results in formation of the TCP , loop of Henle, and TCD

Excretory System.

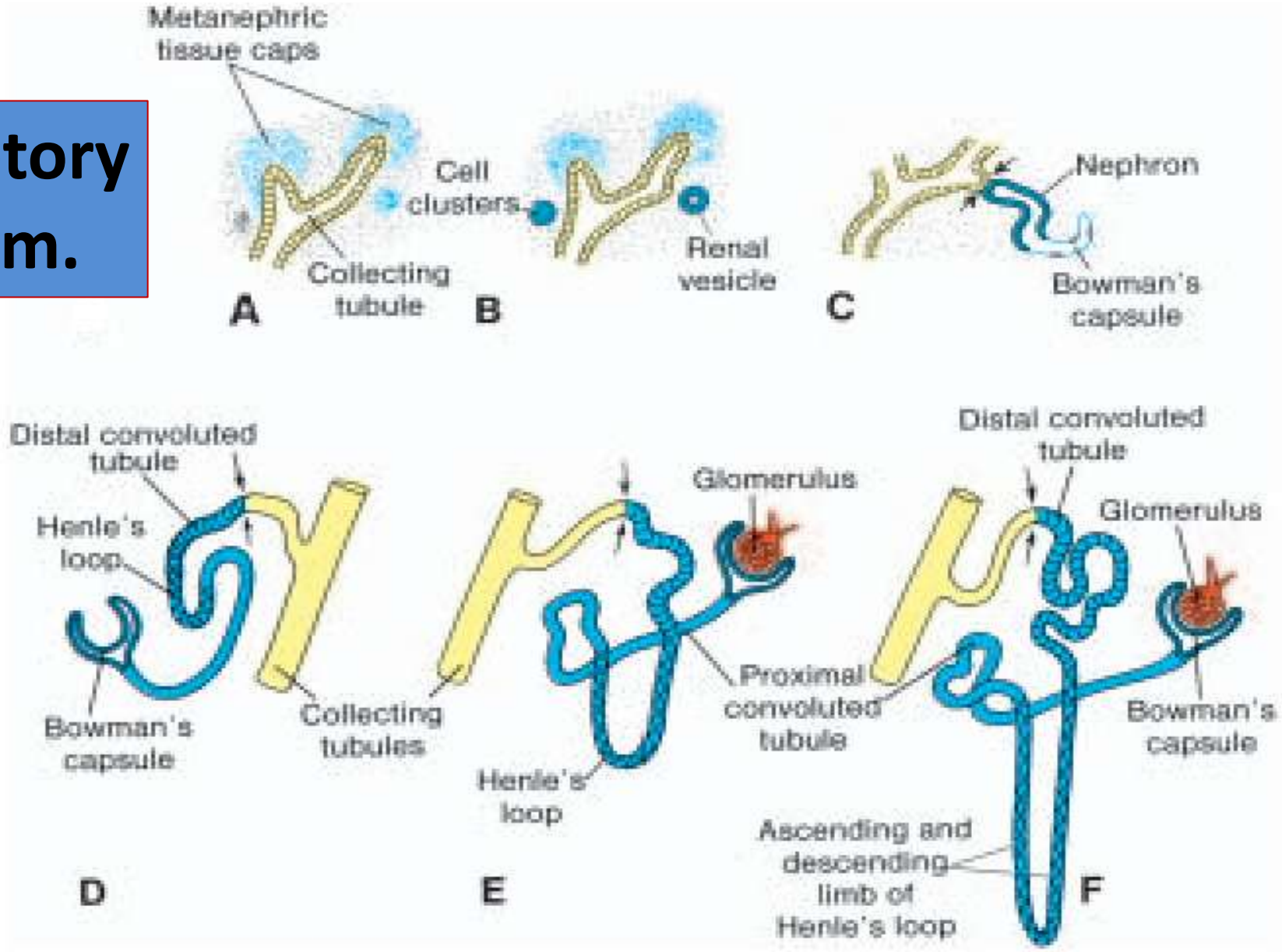
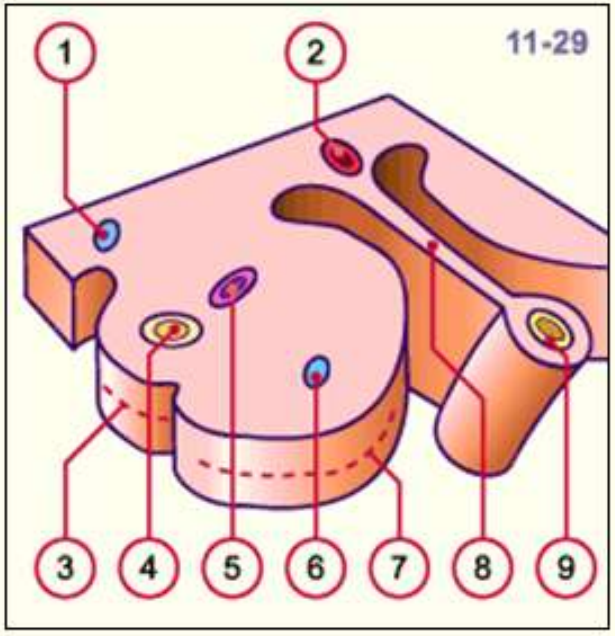
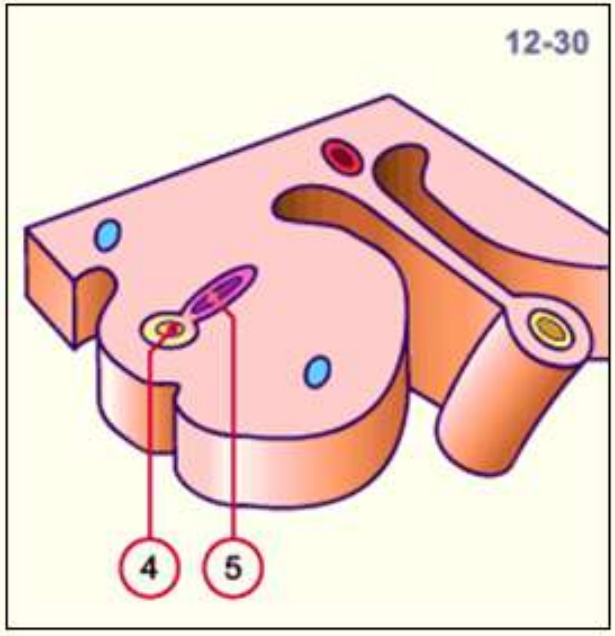
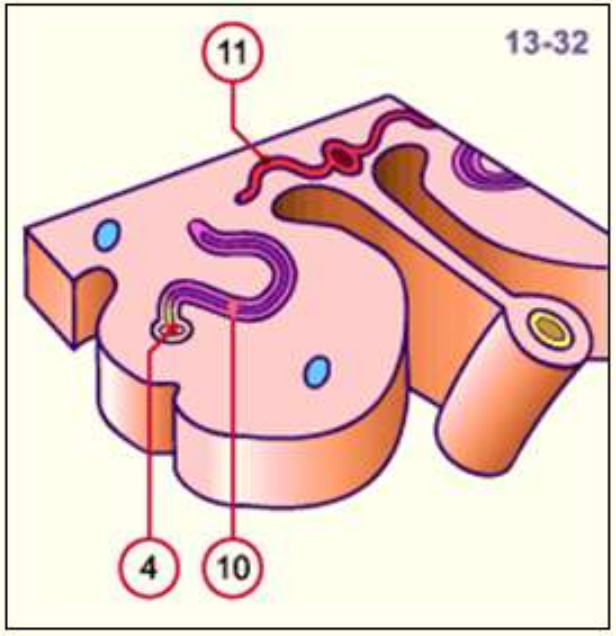
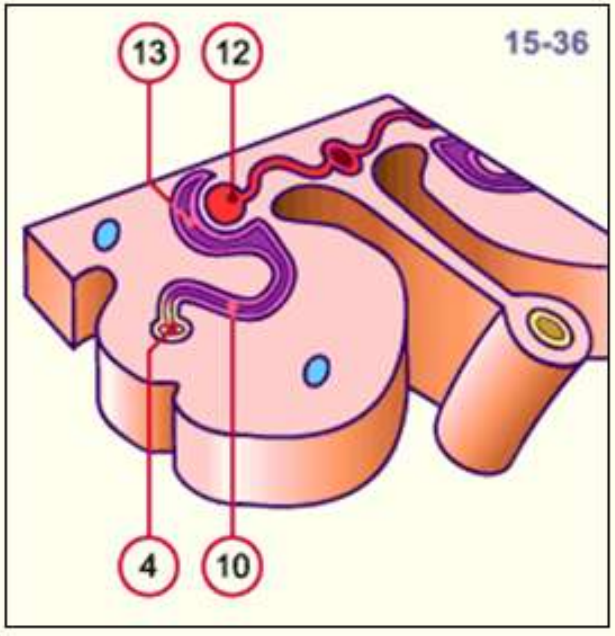


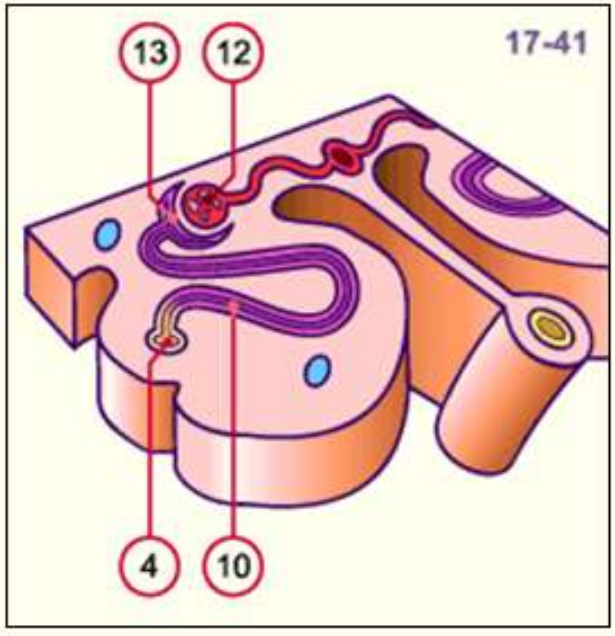
Figure 14.6 Development of a metanephric excretory unit. *Arrows*, the place where the excretory unit (*blue*) establishes an open communication with the collecting system (*yellow*), allowing flow of urine from the glomerulus into the collecting ducts.



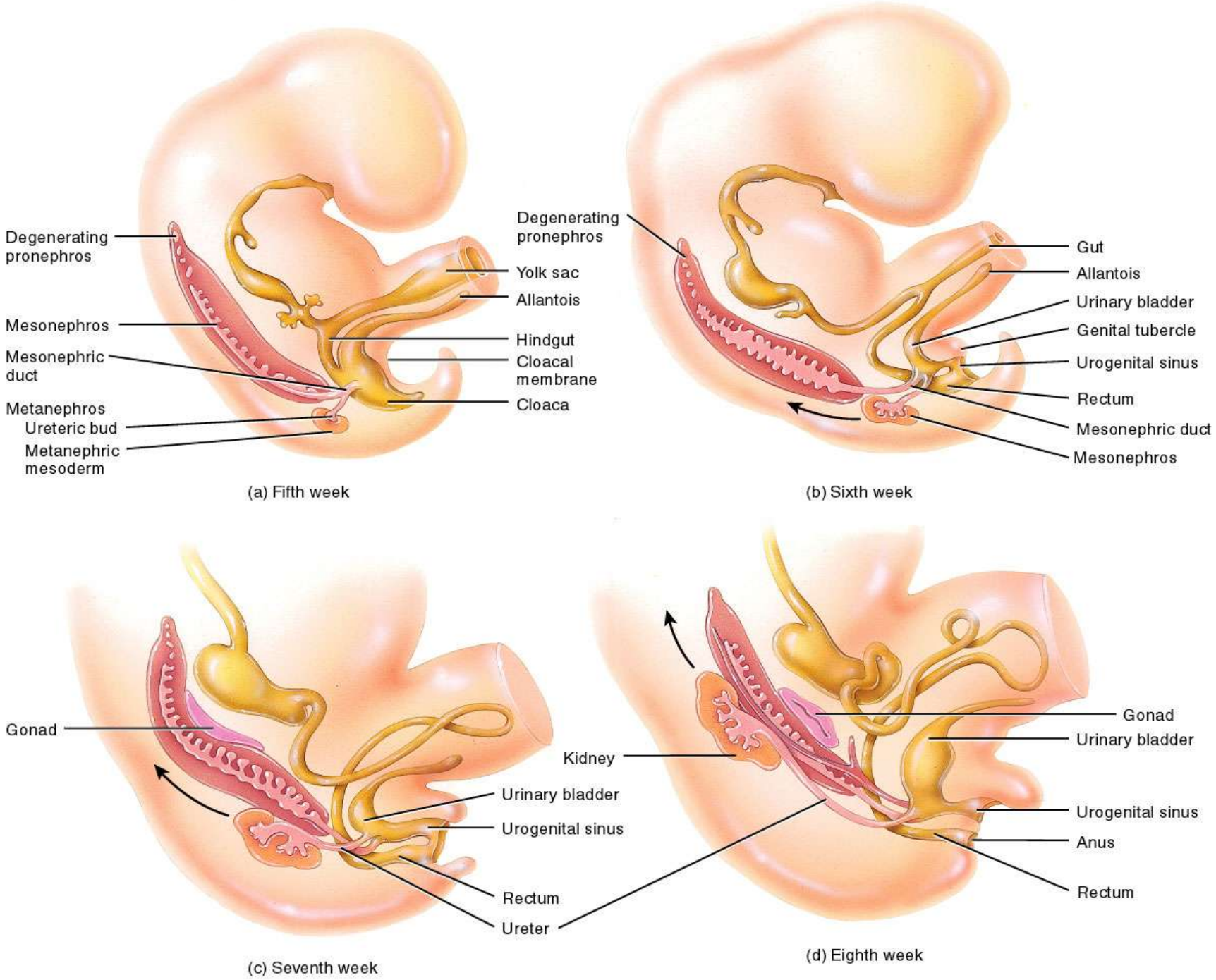








1 Inferior cardinal vein
2 Aorta
3 Nephrogenic cord
4 Mesonephric duct (Wolffian duct)
5 Mesonephric vesicle
6 Subcardinal vein
7 Genital ridge
8 Dorsal mesentery
9 Intestinal tube
10 Mesonephric tubule
11 Lateral (visceral) branch of the aorta
12 Glomerulus
13 Bowman's capsule


Degenerating pronephros
Yolk sac
Allantois
Mesonephros
Hindgut
Mesonephric duct
Cloacal membrane
Metanephros
Cloaca
Ureteric bud
Metanephric mesoderm
(a) Fifth week
Degenerating pronephros
Gut
Allantois
Urinary bladder
Genital tubercle
Urogenital sinus
Rectum
Mesonephric duct
Mesonephros
(b) Sixth week
Gonad
Urinary bladder
Urogenital sinus
Rectum
Ureter
(c) Seventh week
Gonad
Kidney
Urinary bladder
Urogenital sinus
Anus
Rectum
(d) Eighth week

Snapshot of renal physiology

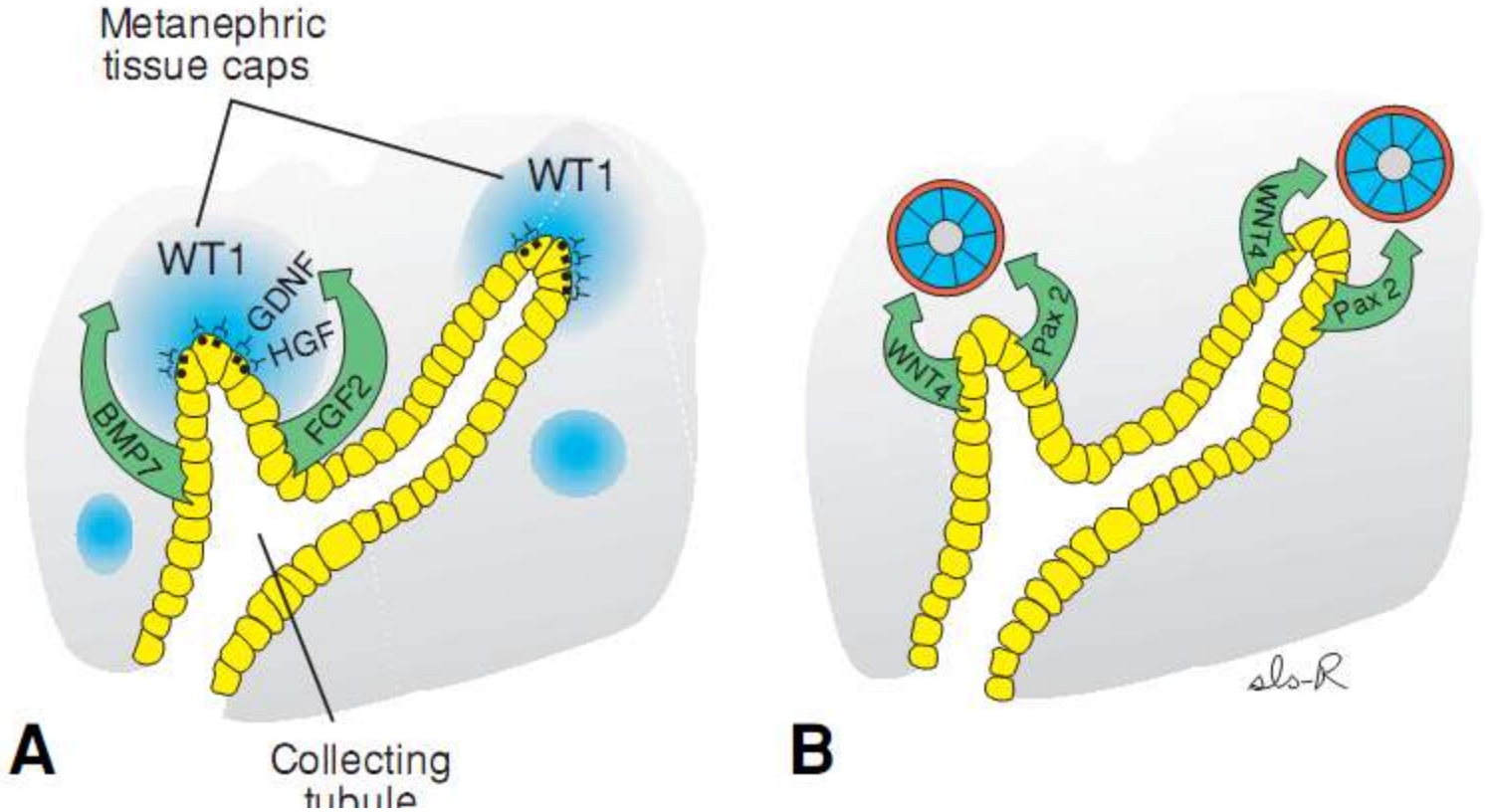
- Nephrons are formed until birth
- Urine production begins early in gestation, soon after differentiation of the glomerular capillaries, which start to form 10th week
- Urine → amniotic cavity
- At birth the kidneys have a lobulated appearance, but the lobulation disappears during infancy as a result of further growth of the nephrons.
- But there is no increase in their number.

MOLECULAR REGULATION

- involves epithelial mesenchymal interactions.
- **epithelium of the ureteric bu**d 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. WT1 also regulates production of glial-derived neurotrophic factor (**GDNF**) and hepatocyte growth factor (**HGF,** or scatter factor) by the mesenchyme. GDNF &HGF 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**,

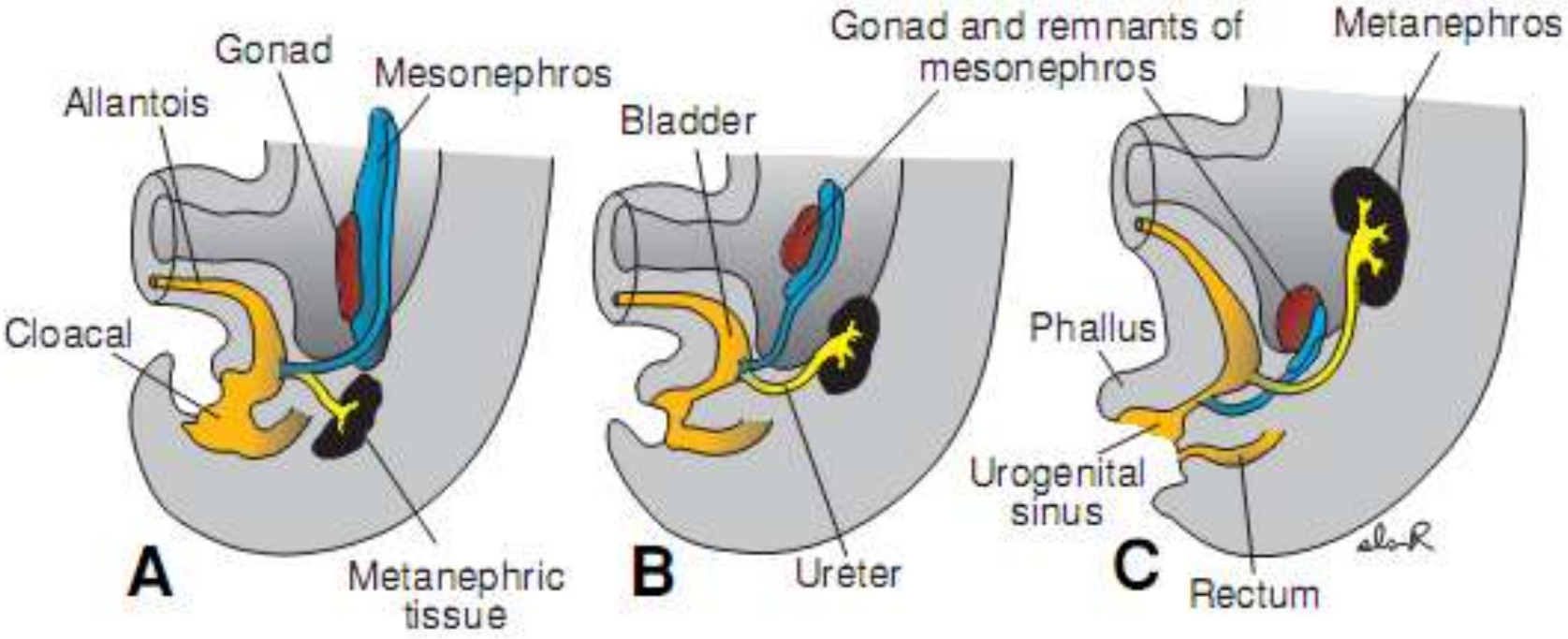
- **the buds** induce the mesenchyme via fibroblast growth factor-2 **(FGF-2)** and bone morphogenetic protein-7**(BMP-7**) as growth factors → block apoptosis and stimulate proliferation in the metanephric mesenchyme while maintaining production of WT1.
- Conversion of the mesenchyme to an epithelium for nephron formation is also mediated by the **ureteric buds** by **PAX2 and WNT4.**
- fibronectin, collagen I, and collagen III are replaced with laminin and type IV collagen, characteristic of an epithelial basal lamina.
- the cell adhesion molecules syndecan and E-cadherin for for condensation of the mesenchyme into an epithelium

- Conversion of the mesenchyme to an epithelium for nephron formation : bronectin, collagen I, and collagen III are replaced with laminin and type IV collagen, characteristic of an epithelial basal lamina. Diregulasi a.l oleh PAX2 and WNT4.
- In addition, the cell adhesion molecules syndecan and E-cadherin,


Metanephric
tissue caps
WT1
WT1
GDNF
HGF
BMP7
FGF2
Collecting
tubule
A
WNT4
Pax 2
WNT4
Pax 2
B

The MIGRATION & ROTATION

- Iniatially : pelvic region → ascent cranially to abdomen.
- Fx : diminution of body curvature and by growth of the body in the lumbar and sacral regions

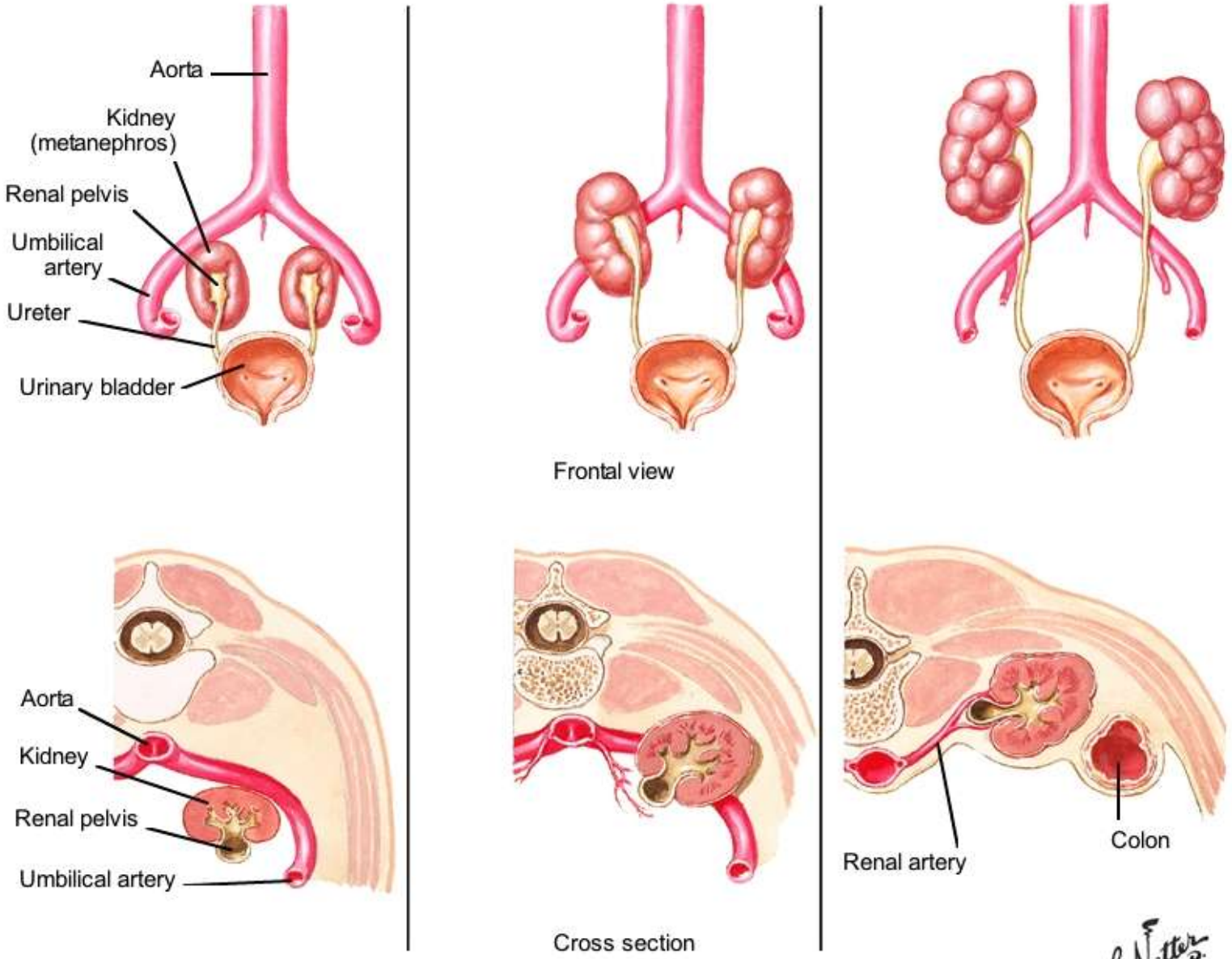


Rotation of the kidney

- At first the convex border of the kidney is directed posterioly while the hilum lies ventrally
- Later the kidney rotates about 90 degrees and the dorsal convex border becomes lateral.

Ascent and Rotation of the Metanephric Kidneys

Apparent "ascent and rotation" of the kidneys in embryological development



Vesica Urinaria & Urehtra

- during the 4th to 7th weeks of development, the cloaca divides into the **urogenital sinus** anteriorly and **the anal canal** posteriorly , separated by **urorectal septum** (a layer of mesoderm between the primitive anal canal and the urogenital sinus). The tip of the septum will form the perineal body

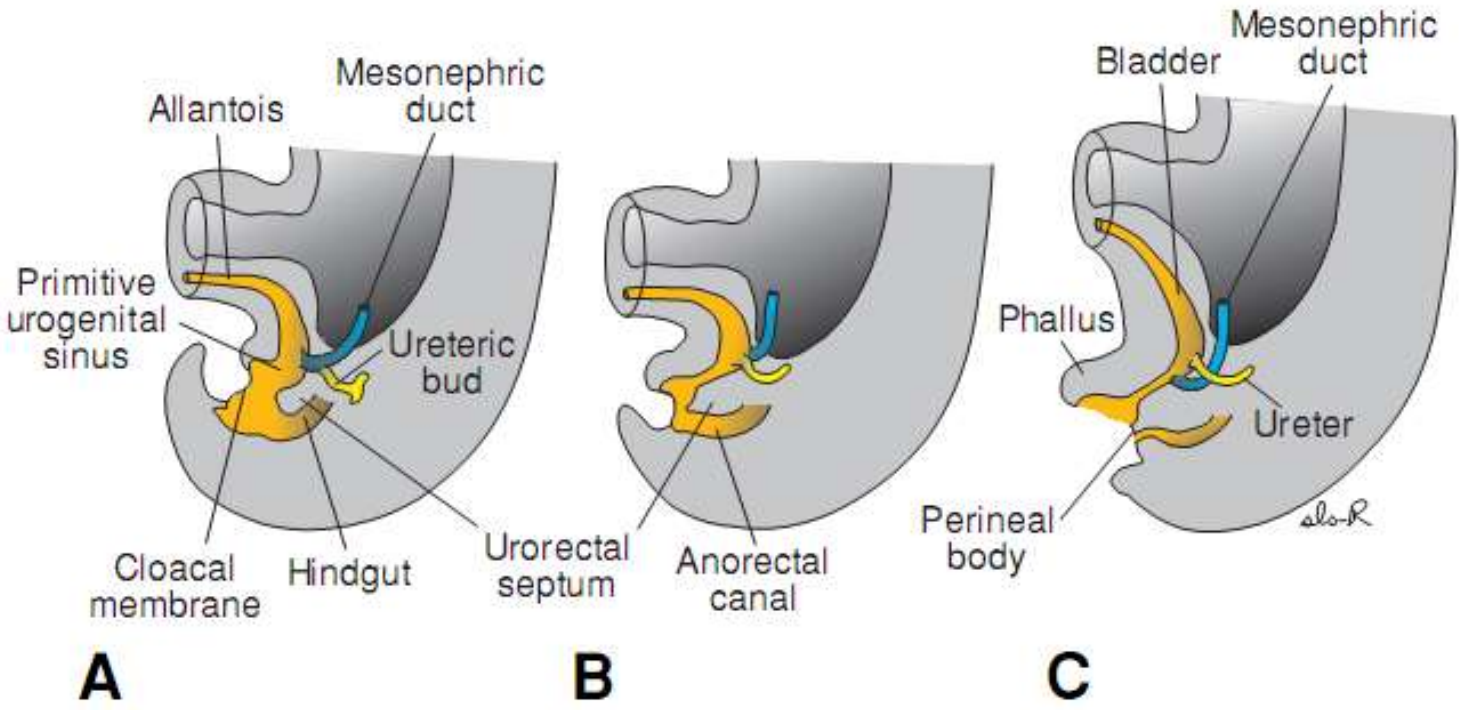


Figure 14.12 Divisions of the cloaca into the urogenital sinus and anorectal canal. The mesonephric duct is gradually absorbed into the wall of the urogenital sinus, and the ureters enter separately. **A.** At the end of the fifth week. **B.** 7 weeks. **C.** 8 weeks.

- The upper and largest part of Sinus urogenital Superior is the vesica urinaria. Initially the V.U is continuous with the allantois.
- When the lumen of the allantois is obliterated, a thick fibrous cord, the urachus, remains and connects the apex of the bladder with the umbilicus (adult → median umbilical ligament)
- The next part of UGS : the pelvic part; sex dependent!

  male → prostatic and membranous parts of the urethra.
- The last of UGS : the phallic part. It is flattened from side to side, and as the genital tubercle grows, this part of the sinus will be pulled ventrally

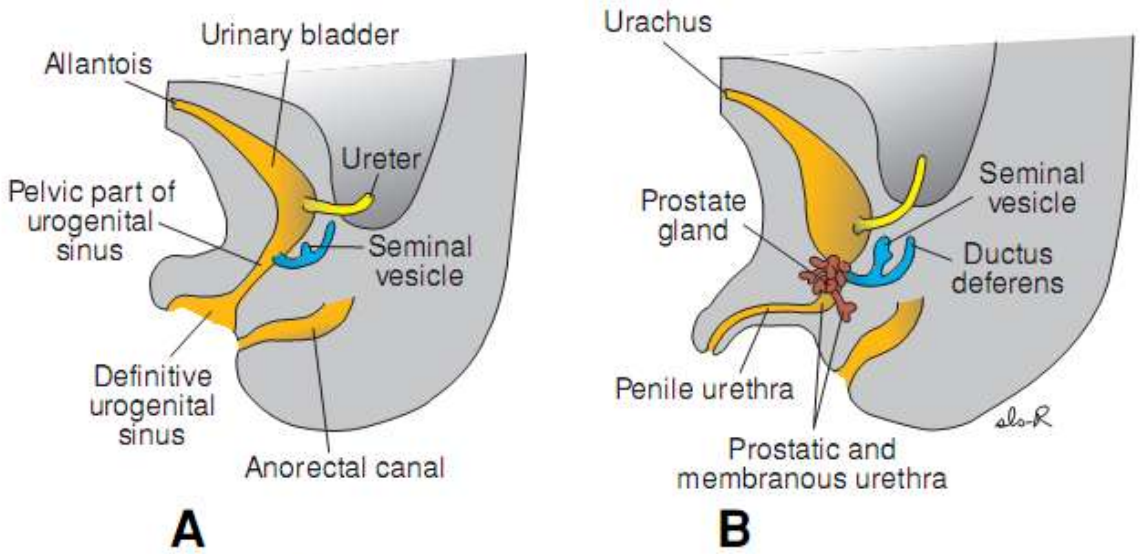


Figure 14.13 A. Development of the urogenital sinus into the urinary bladder and definitive urogenital sinus. **B.** In the male the definitive urogenital sinus develops into the penile urethra. The prostate gland is formed by buds from the urethra, and seminal vesicles are formed by budding from the ductus deferens.

- During differentiation of the cloaca, the caudal portions of the mesonephric ducts are absorbed into the wall of the urinary bladder.
- mesonephric ducts move close together to enter the prostatic urethra and in the male become the ejaculatory ducts
- **Ureters,** enter the bladder separately. The orifices of the ureters move farther cranially.
- Mucosal (endodermal) epithelial change inside VU → trigonum area

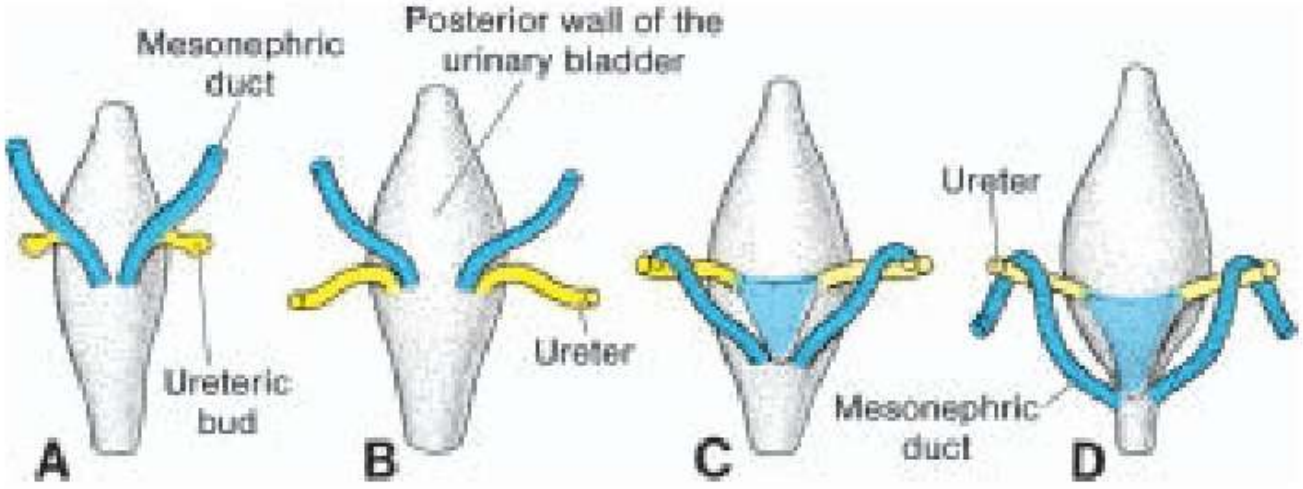


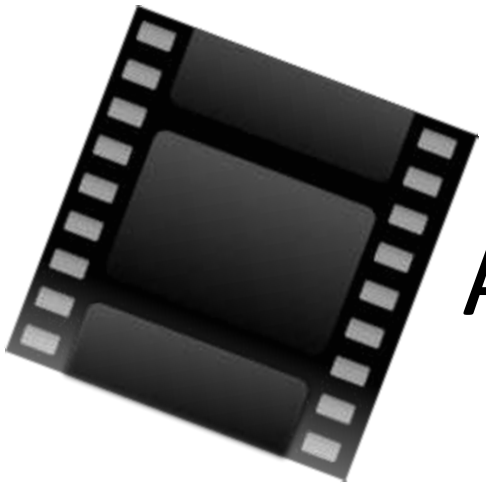
Figure 14.14 Dorsal views of the bladder showing the relation of the ureters and mesonephric ducts during development. Initially the ureters are formed by an outgrowth of the mesonephric duct **(A),** but with time they assume a separate entrance into the urinary bladder **(B–D)**. Note the trigone of the bladder formed by incorporation of the mesonephric ducts **(C** and **D)**.

- the mucosa of the bladder formed by incorporation of the ducts (the trigone of the bladder) is 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.
- the mesonephric ducts move close together to enter the prostatic urethra and in the male become the ejaculatory ducts

URETHRA

- Epithel : endoderm derivates
- the surrounding connective and smooth muscle tissue is derived from splanchnic mesoderm
- end of the 3rd 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



ANIMATION

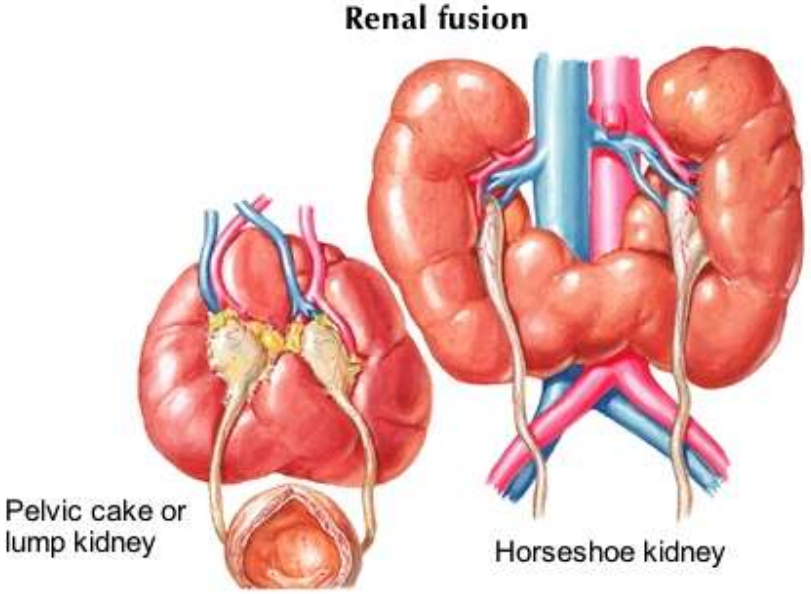
Source : youtube.com

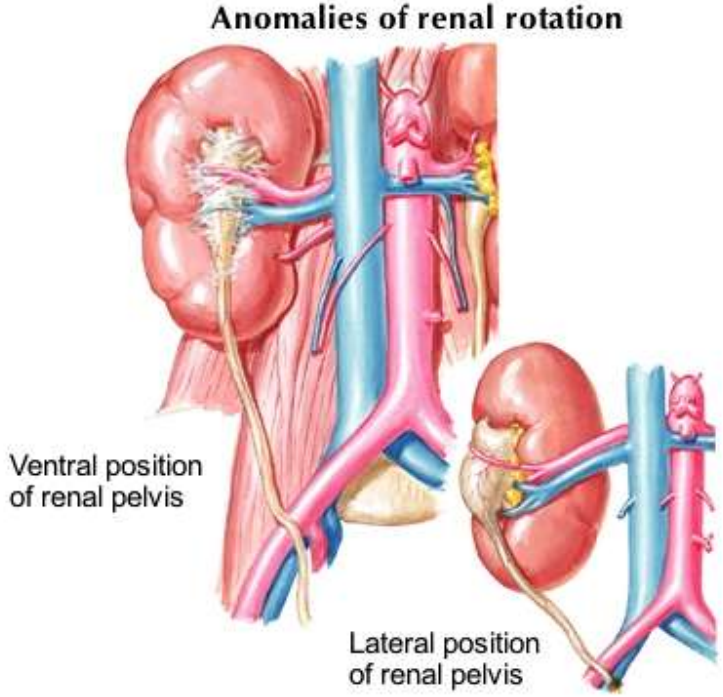
Source : youtube.com

CLINICAL CORRELATION

Klinis	Pathogenesis
Renal agenesis	Kegagalan interaksi ureteric bud vs metanephric mesoderm
Horse-shoe kidney (*)	(?) abnormal migration of nephrogenic cells
Double ureter	Early splitting ureteric bud
Congenital cystic kidney (ADPKD)	Dilatasi abnormal dalam nefron
Pelvic kidney	Abnormality in ascent
Wilms tumor	mutations in the WT1 gene on 11p13 →kegagalan diferensiasi normal

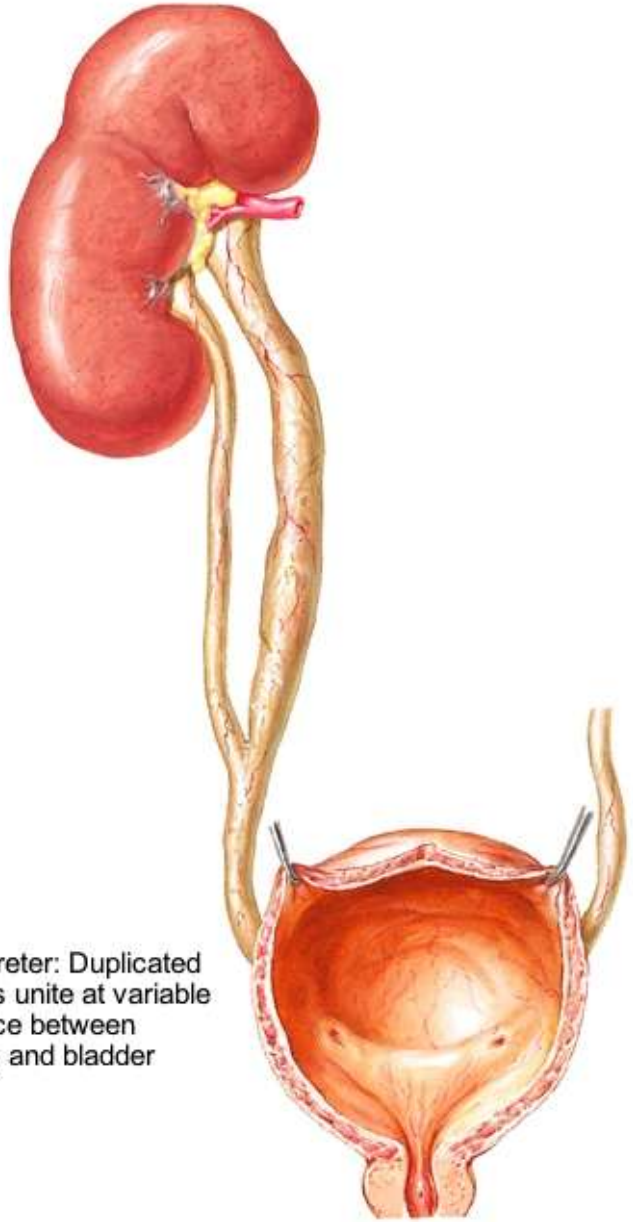
Kidney Rotation and Migration Anomalies





Ureteric Bud Duplication

Incomplete duplication of ureter

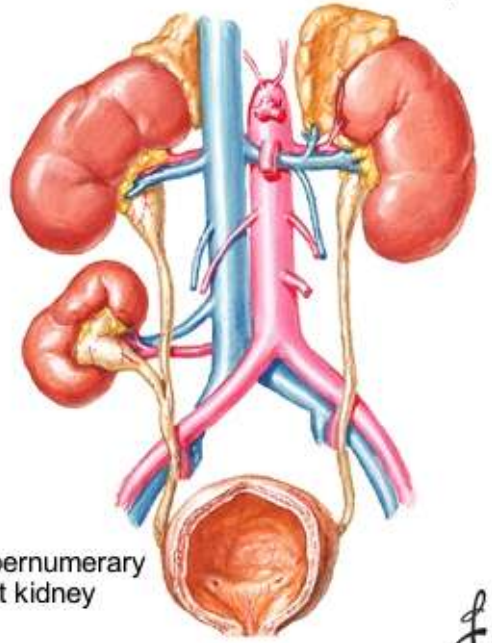


Bifid ureter: Duplicated ureters unite at variable distance between kidney and bladder

Anomalies of renal pelvis and calyces

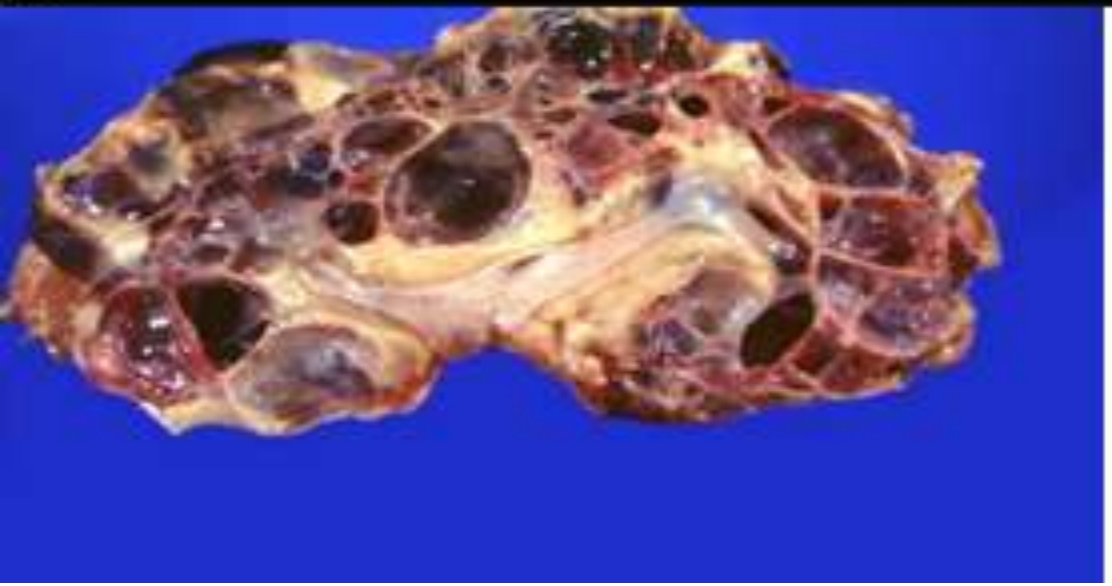
Duplicated renal pelvis

Anomalies in number of kidneys



Supernumerary right kidney

F. Netter M.D. ©IGN



Cystic diseases of the kidney: nephronophthisis and polycystic kidney disease

Probable causes: protein defects in primary cilia on renal **tubular** epithelium

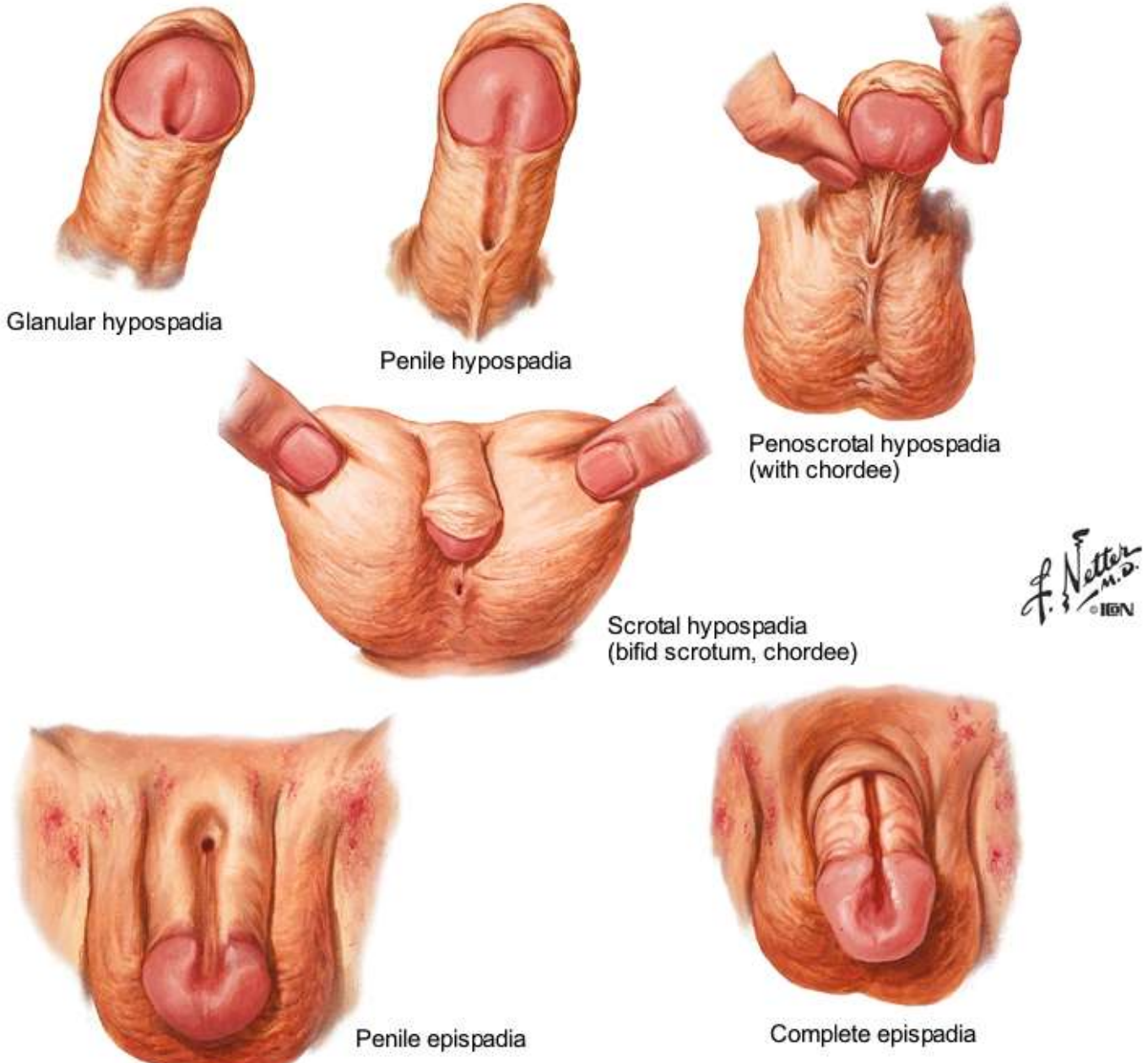
www.ndt-educational.org/images/hildebrandt-13.jpg

Anomalies of urethra

- Hypospadias : external urethral orifice opens in the ventral part of the penis,scrotum or perineum

- Epispadias: the external urethral orifice is situated on the dorsal surface of the penis

Hypospadia and Epispadias



“ Sungguh, Kami telah menciptakan manusia dalam bentuk yang sebaik-baiknya. ”

(QS. At-Tin: 4)

struktur	timing	Asal (derivat dr)	produk	dll
Ureteric bud	Mgg V	Mesonephric duct	- ureter	
dst				
dsb				