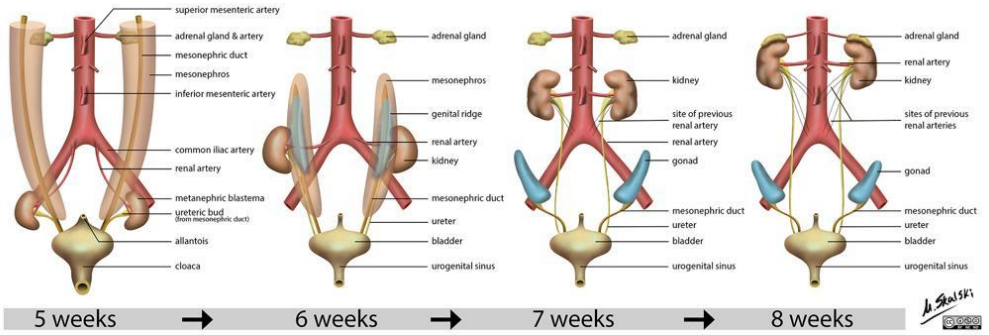
Development of the Urinary System
Malformations



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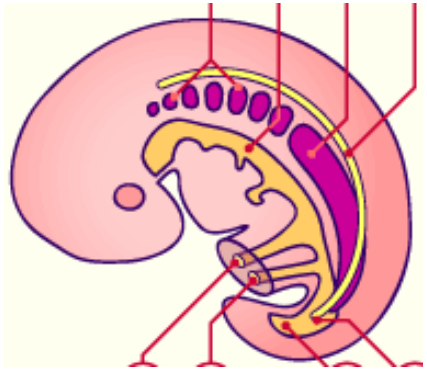
LEARNING OBJECTIVES

- identify the divisions of the intermediate mesoderm
- identify the location of the nephrogenic primordium
- understand the sequential development of pronephros, mesonephros, and metanephros
- list the derivatives of the mesonephric duct
- describe the development of the definitive kidneys, ureters, urinary bladder, and urethra

THE DEVELOPMENT OF URINARY ORGANS STARTS DURING WEEK 3.

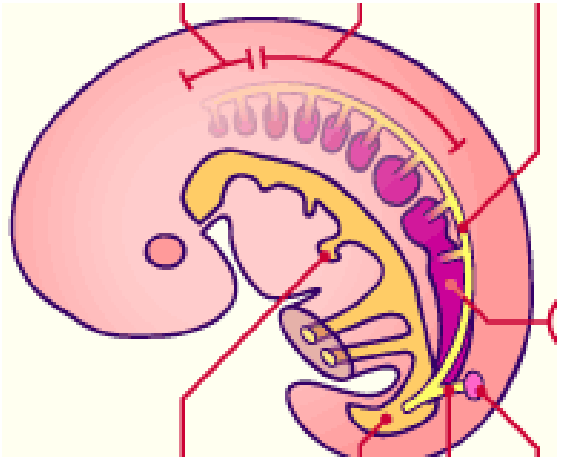
During the intrauterine life the PLACENTA is responsible for **water and electrolyte content** of the body.

The urinary system develops together with the genital apparatus (basically from the same primordium).



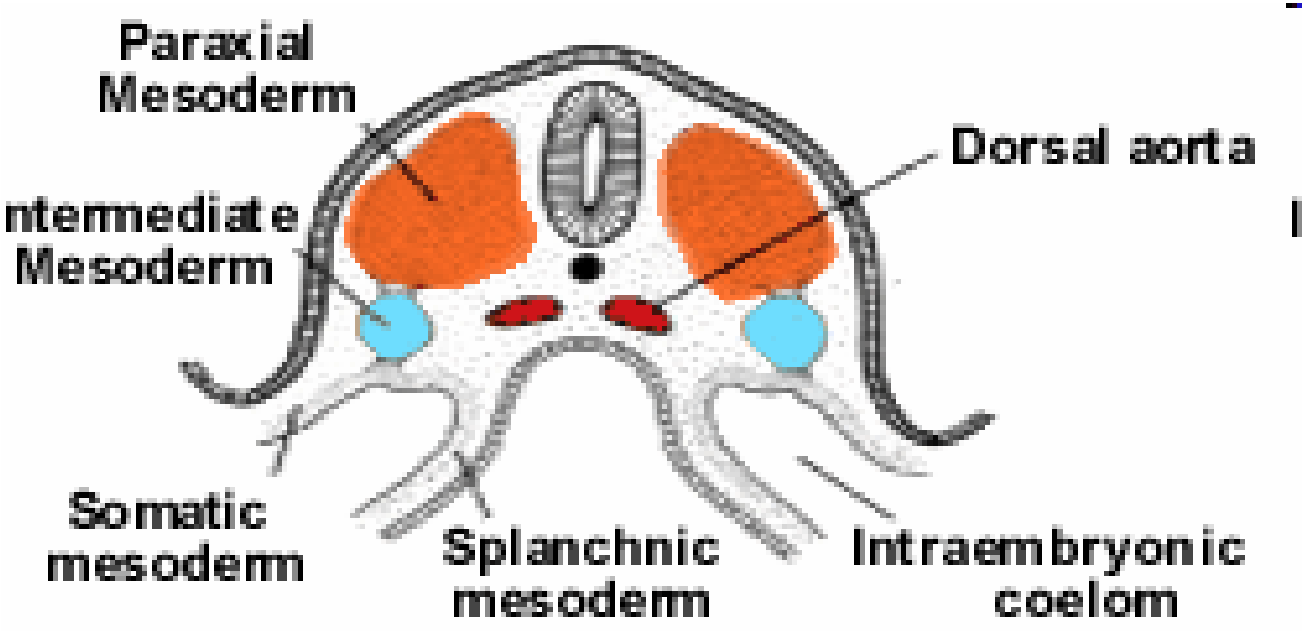
The primordium derives from intermediate mesoderm (**nephrogenic tissue**) as well as from the **urogenital sinus**

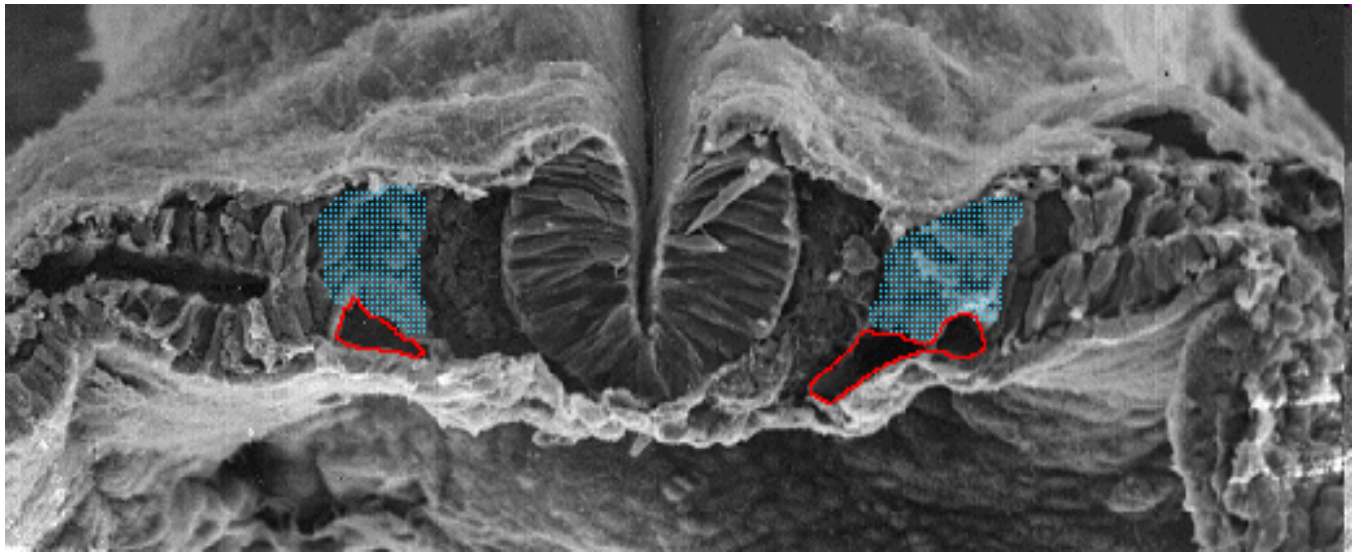
Cranio-caudal direction/gradient



The fetal kidneys start working during the **12. week.** They produce fetal urine which makes up cca 80% of the amniotic fluid.

WHERE DOES THIS ALL START?



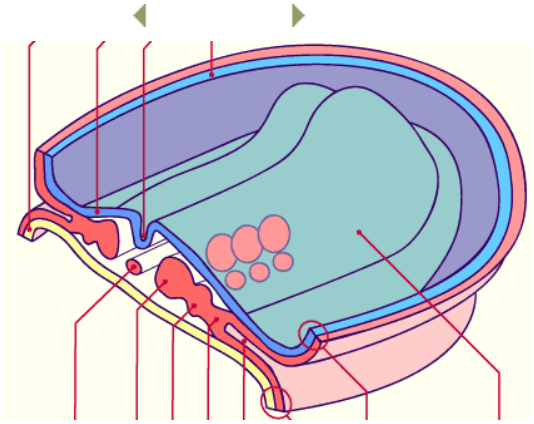


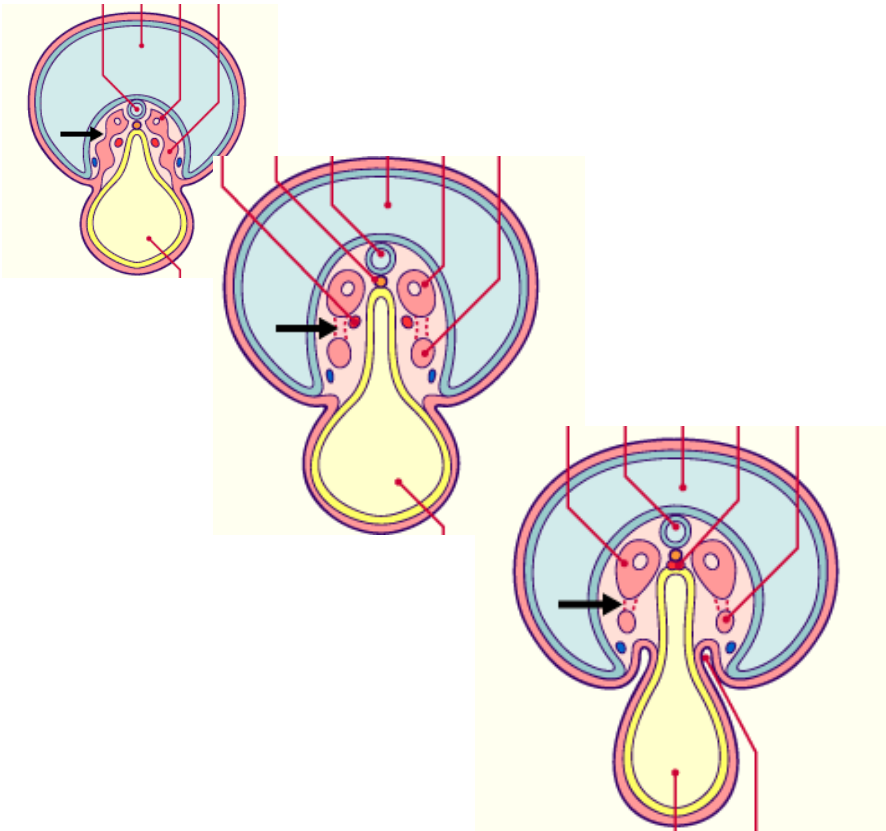
LATERAL FOLDING

The **nephrogenic cord** develops out of the **intermediate mesoderm and extends from the cervical to the caudal region.**

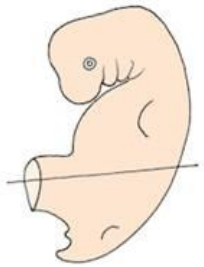
It becomes segmented like the paraxial mesoderm (somites) This segmentation is easily seen in the cranial region, and is **rudimentary** in the middle region. In the caudal region it is **no longer present**

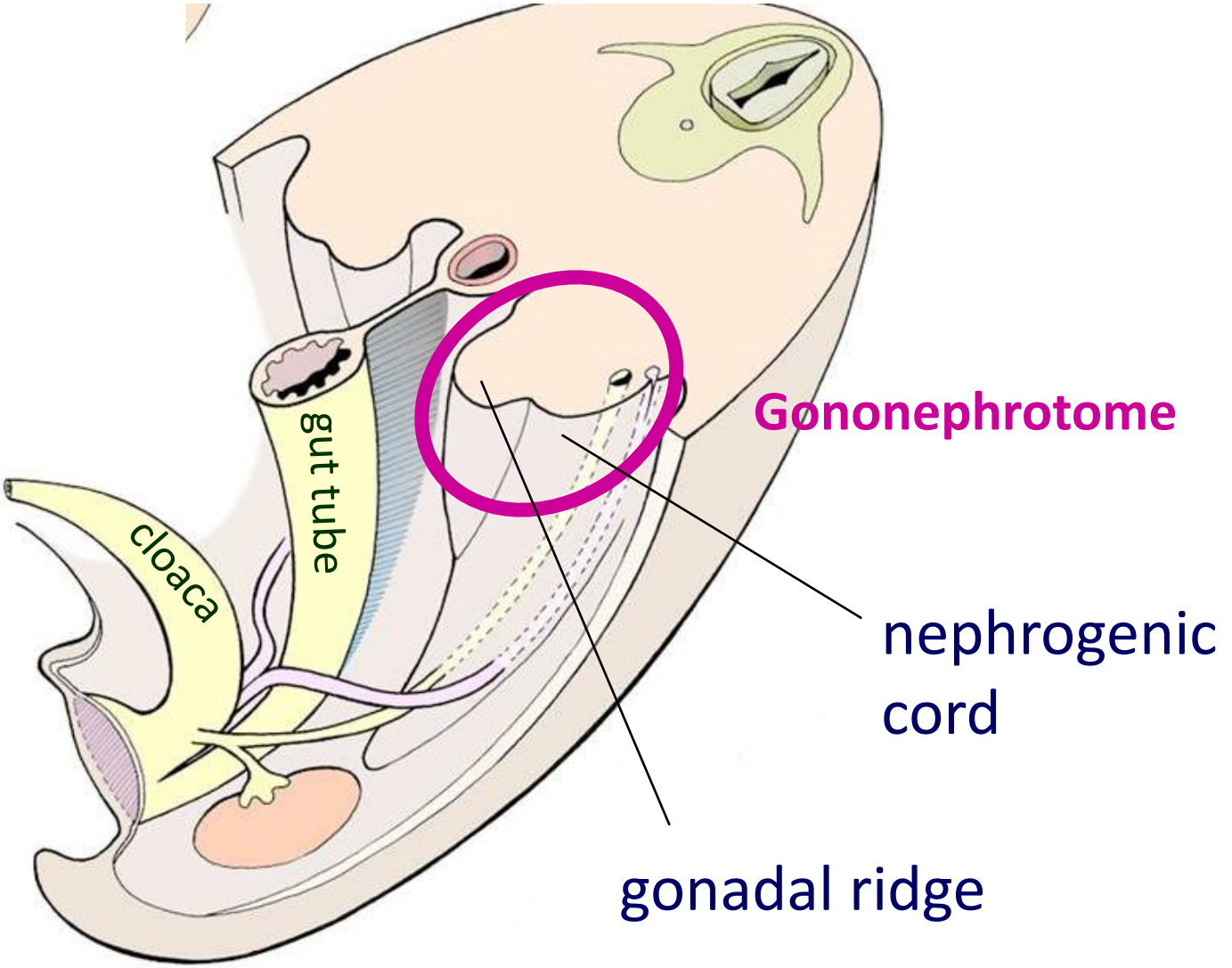
Due to the growth of the inner structures of the embryo, the tissue lying most laterally is displaced ventrally. This leads not only to a **separation of the nephrogenic cord** from the paraxial and lateral mesoderm, but also to a coalescence of certain median structures such as the two dorsal aortas **which fuse to form the definitive (median) aorta.**



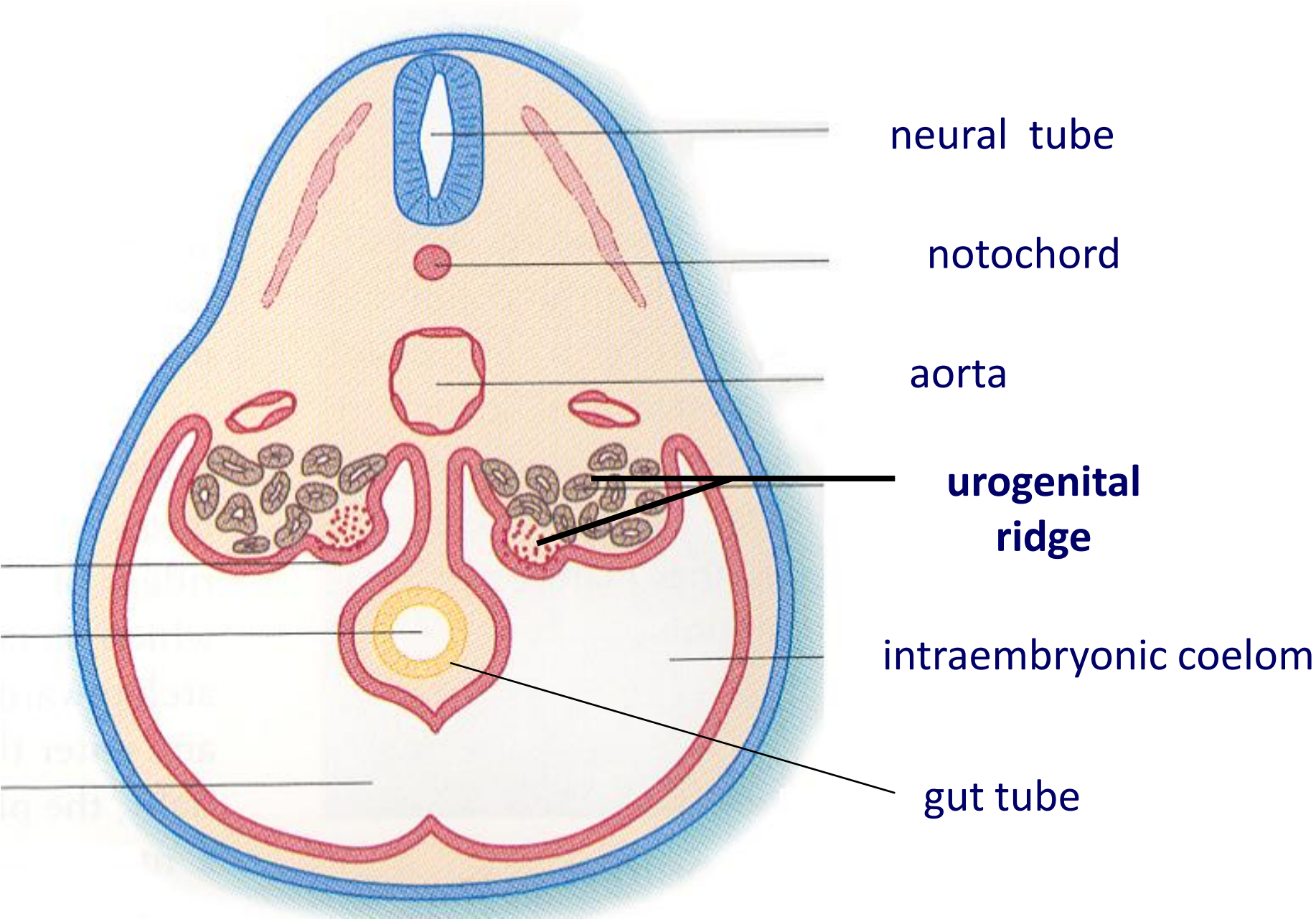


INTERMEDIATE MESODERM



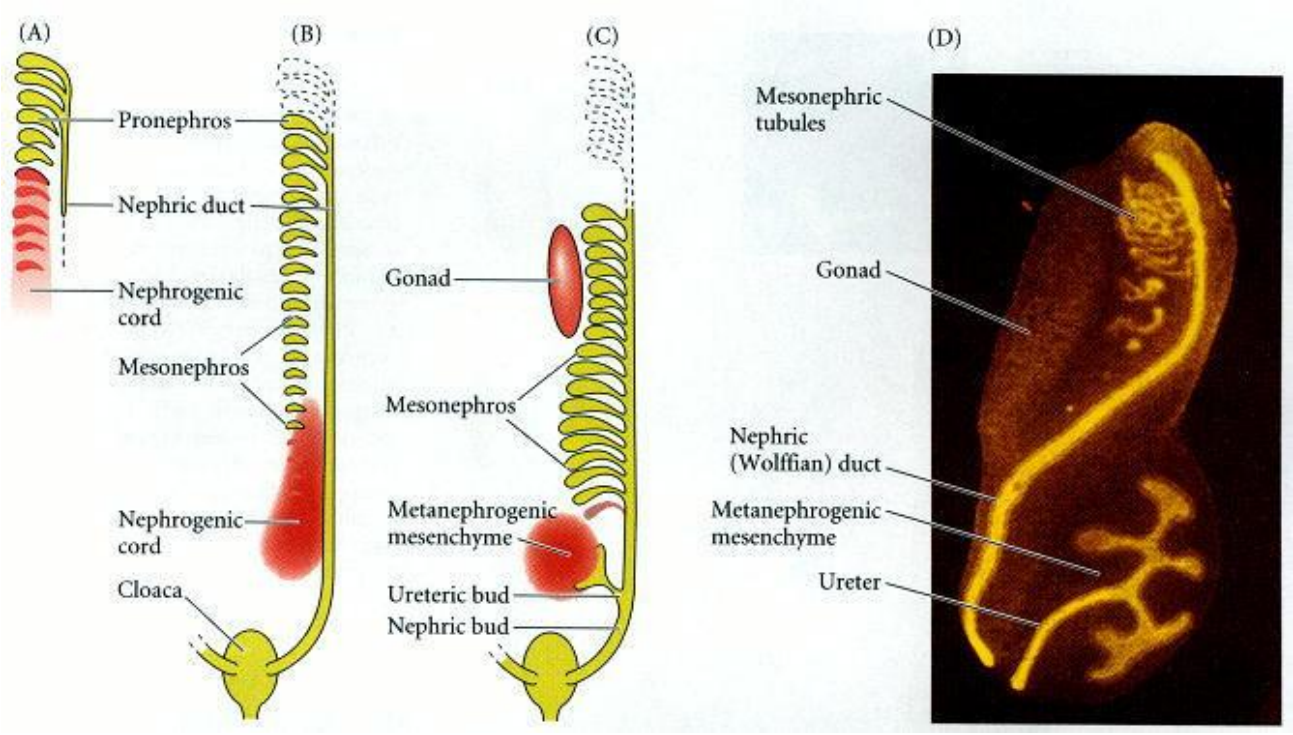


INTERMEDIATE MESODERM



CHRONOLOGY OF KIDNEY DEVELOPMENT
PRO-, MESO- AND METANEPHROS

1. 2. 3. 4.



20. day of embryonic life

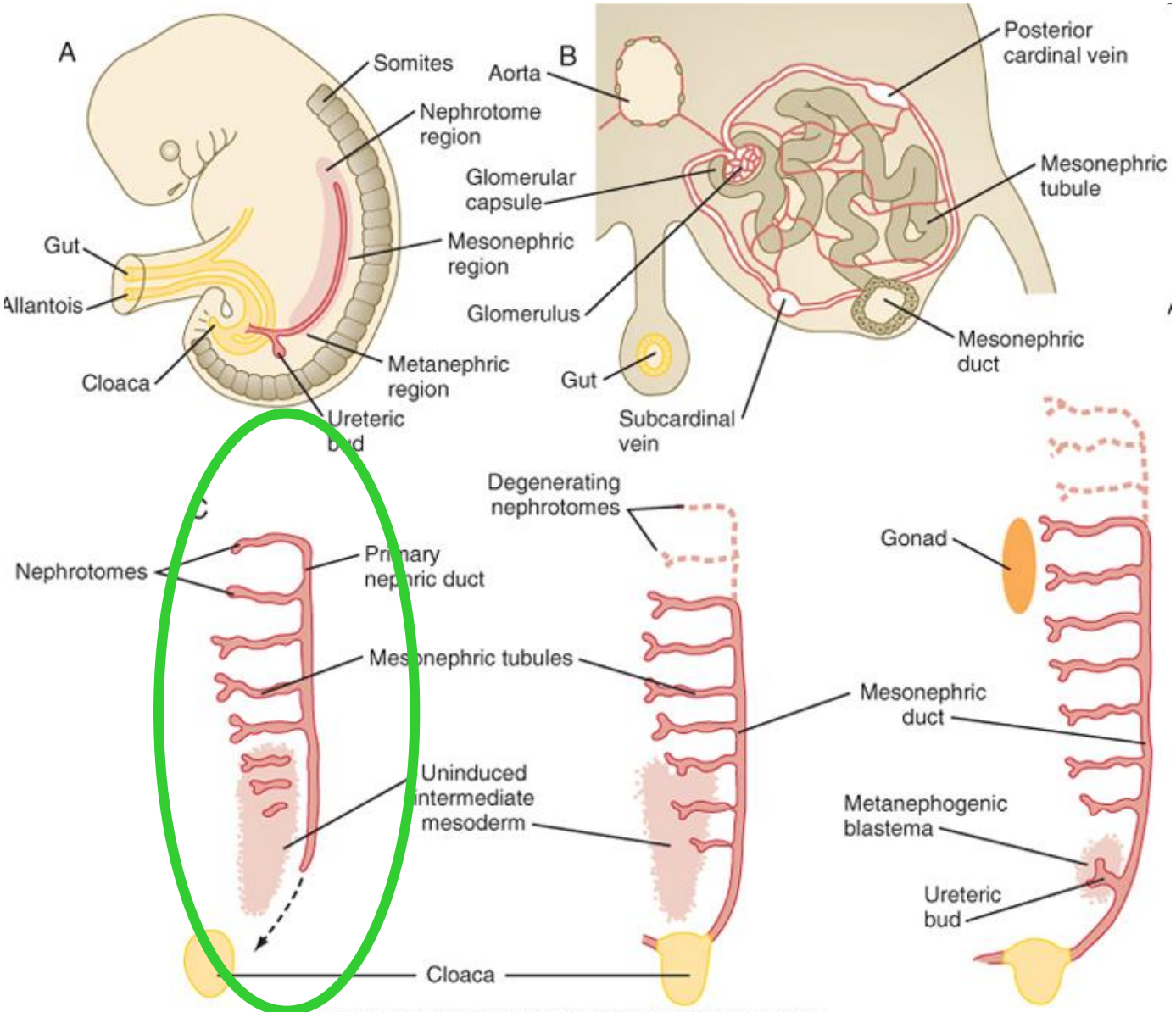
25. day of embryonic life

35. day of embryonic life

Cytokeratin fluorescence immunostaining of mouse embryo. Cytokeratin is present in nephric duct and its derivates.

Nagy Nándor

PRONEPHROS

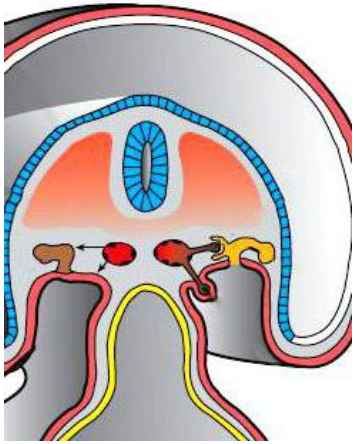


PRONEPHROS

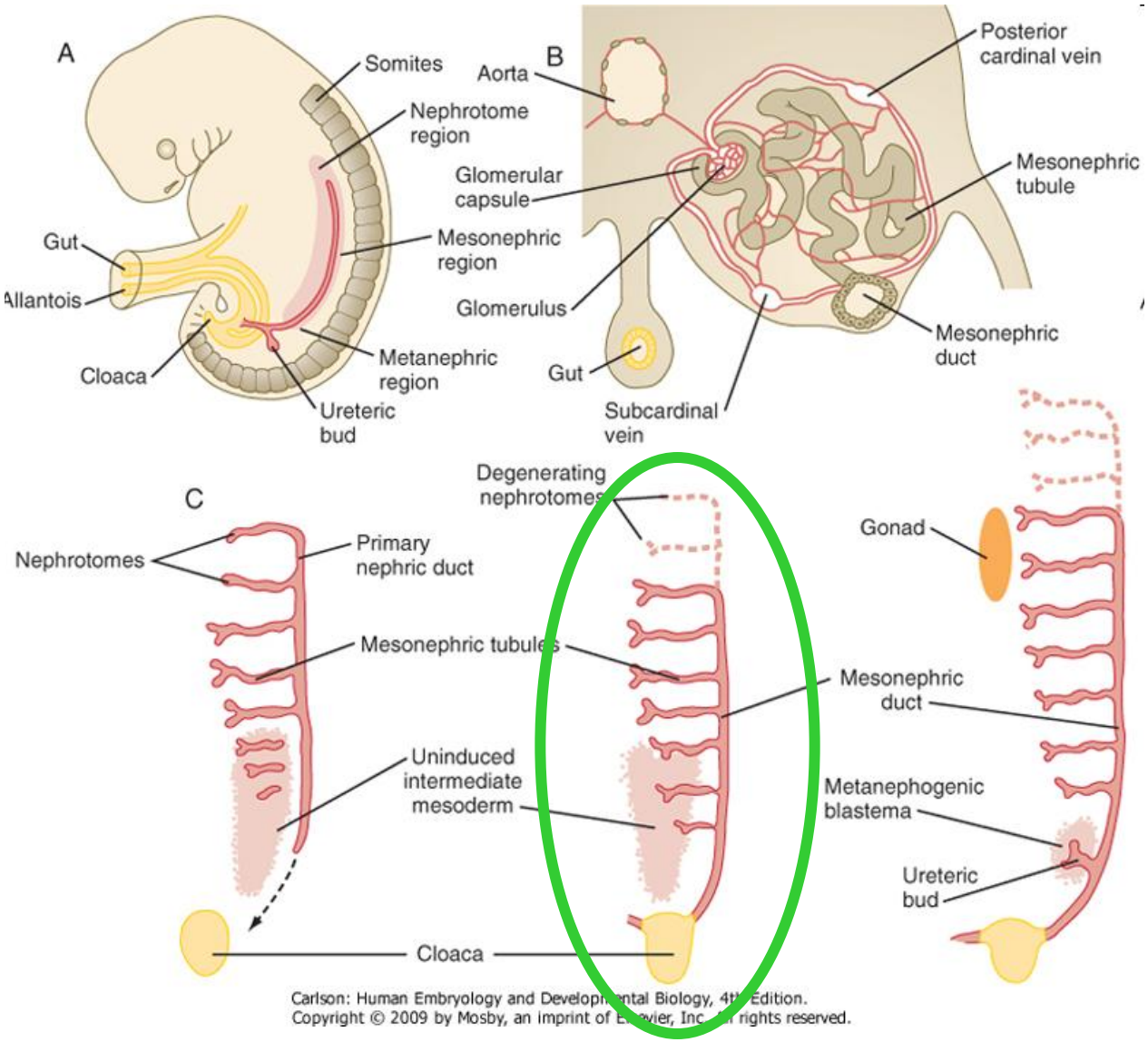
Beginning with the **4th week**, conforming to the cranio-caudal gradient, the **pronephros** in the **neck region** divides into independent masses of cells, the ***nephrotomes*.**
Each nephrotome develops into an epithelialized pronephros glomerulus. Laterally, they form the **pronephros tubules** that can partly bind with the coelom. Via the fusion of these tubules between two nephrotomes the **hollow pronephros duct** arises that is the anlage of the pronephric collecting duct. In humans, this pronephros system corresponds more to a **primitive and transient structure** that is functionally of no importance. According to the classical view, the **pronephros duct** stops in the caudal region at the level of the 13th -14th somite and then goes over into the **mesonephric duct** (Wolffian duct).

It has 3 distinctive features

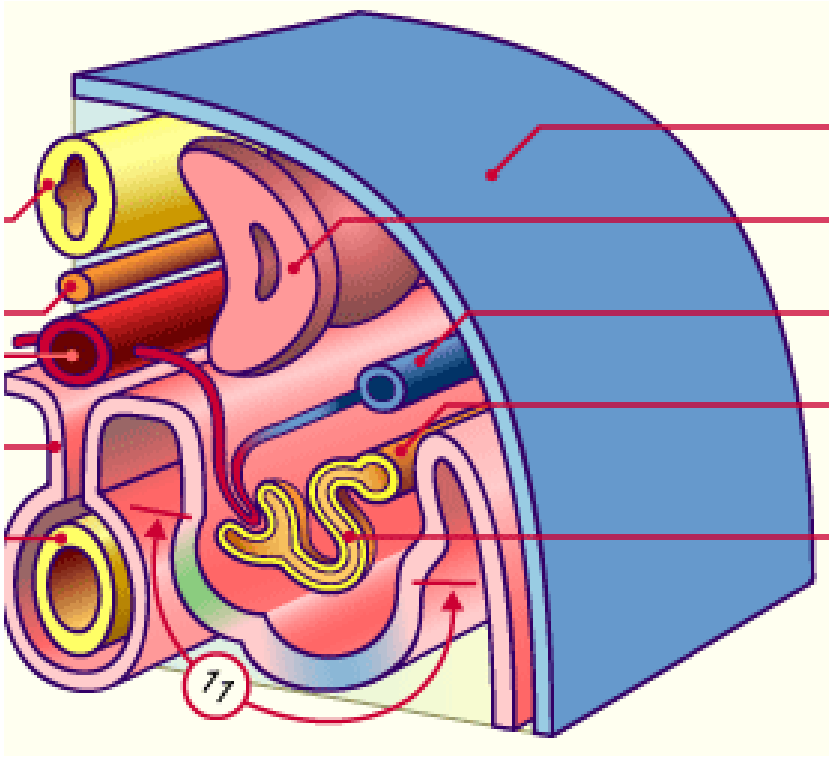
pronephric duct
pronephric tubuli
external (celomic) glomeruli



MESONEPHROS



MESONEPHROS



It differentiates between the upper thoracic) and lumbar region (L3).
The mesonephric units elongate to form tubuli with a blind but fenestratedmedial end **(Bowman's capsule)**.

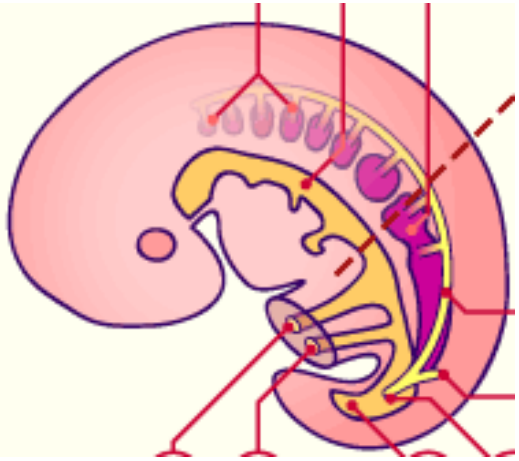
The ***urogenital ridge*** projects into the lumen of the coelom. With the ***S-shaped mesonephric tubules*** the mesonephric duct (Wolffian duct) forms a transitory precursor of the adult excretory system. The medial end of the mesonephric tubule is closed and forms a funnel (Bowman's capsule) that surrounds a tuft of capillaries (the glomerulus). ***The capillaries come from lateral branches of the dorsal aorta and drain into the inferior cardinal vein***.
This functional unit is also termed the excretory unit of the mesonephros.

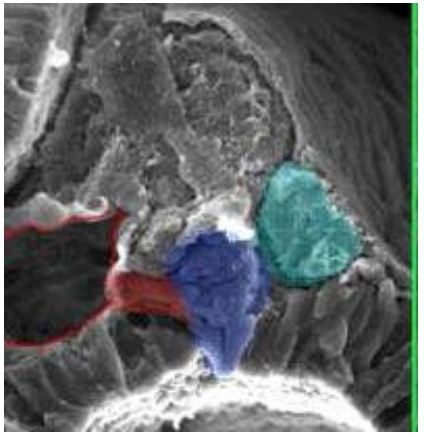
http://www.embryology.ch/allemand/turinary/devebauche03.html

MESONEPHROS

The mesonephric duct forms on the dorsal side of the nephrogenic cord at the level of the **9th somite**. Initially it consists of a **solid mesenchymal cord of cells. It releases itself from the nephrogenic cord and is finally localized under the ectoderm**, which probably plays an inductive role in its formation **.**
Released from the nephrogenic cord, it develops in the caudal direction and canalizes itself at the same time**, in order to finally end in the cloaca**. As soon as it is canalized one calls it the **mesonephric duct (Wolffian duct)**. At the site where the mesonephric duct (Wolffian duct) discharges into the cloaca, the **rear wall of the bladder** forms.

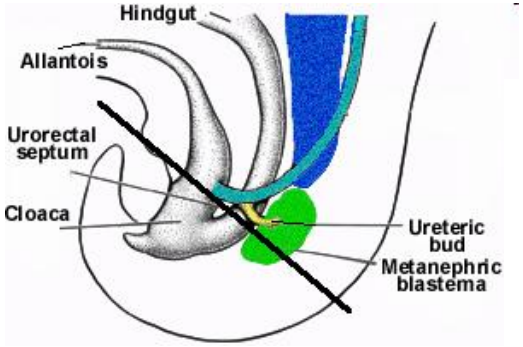
It has 3 distinctive features
nephrogenic fold
mesonephric duct
true glomeruli

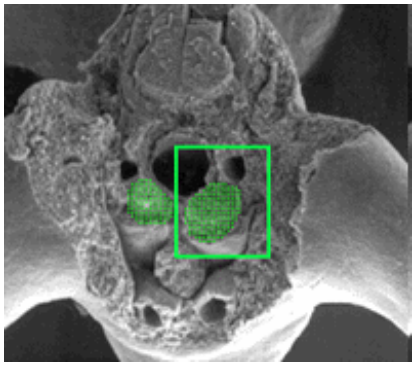


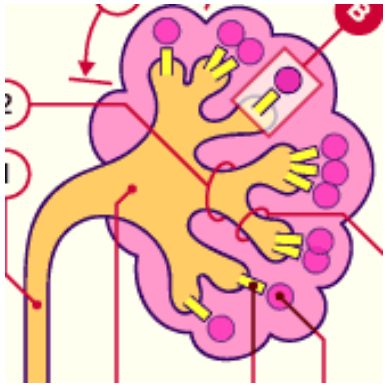


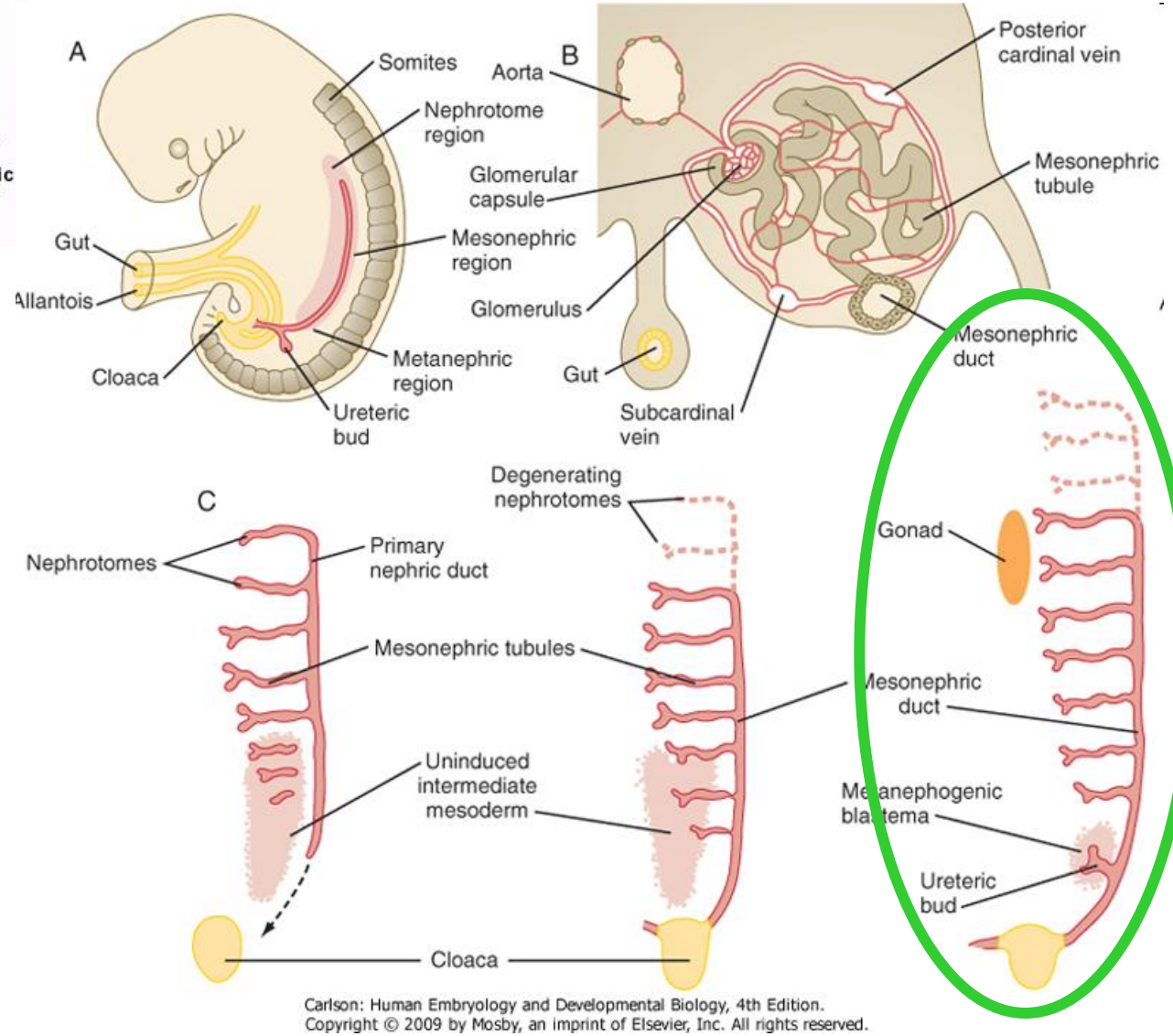
The mesonephric duct (Wolffian duct)
Animal experiments have shown that the growth and the caudal extension of the mesonephric duct depend on the presence of the extracellular molecule fibronectin (an integrin). The differentiation of the solid cord into a duct depends on the secretion of the BMP4 (bone morphogenetic protein 4) by the ectoderm

METANEPHROS

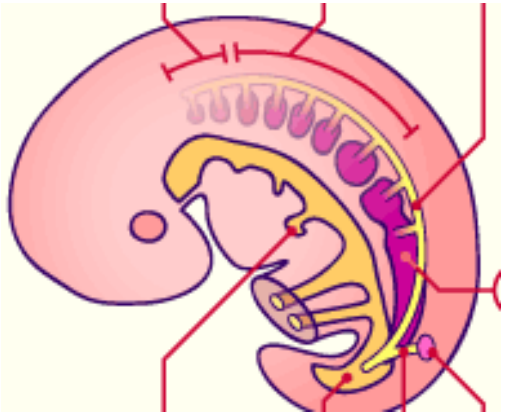








METANEPHROS



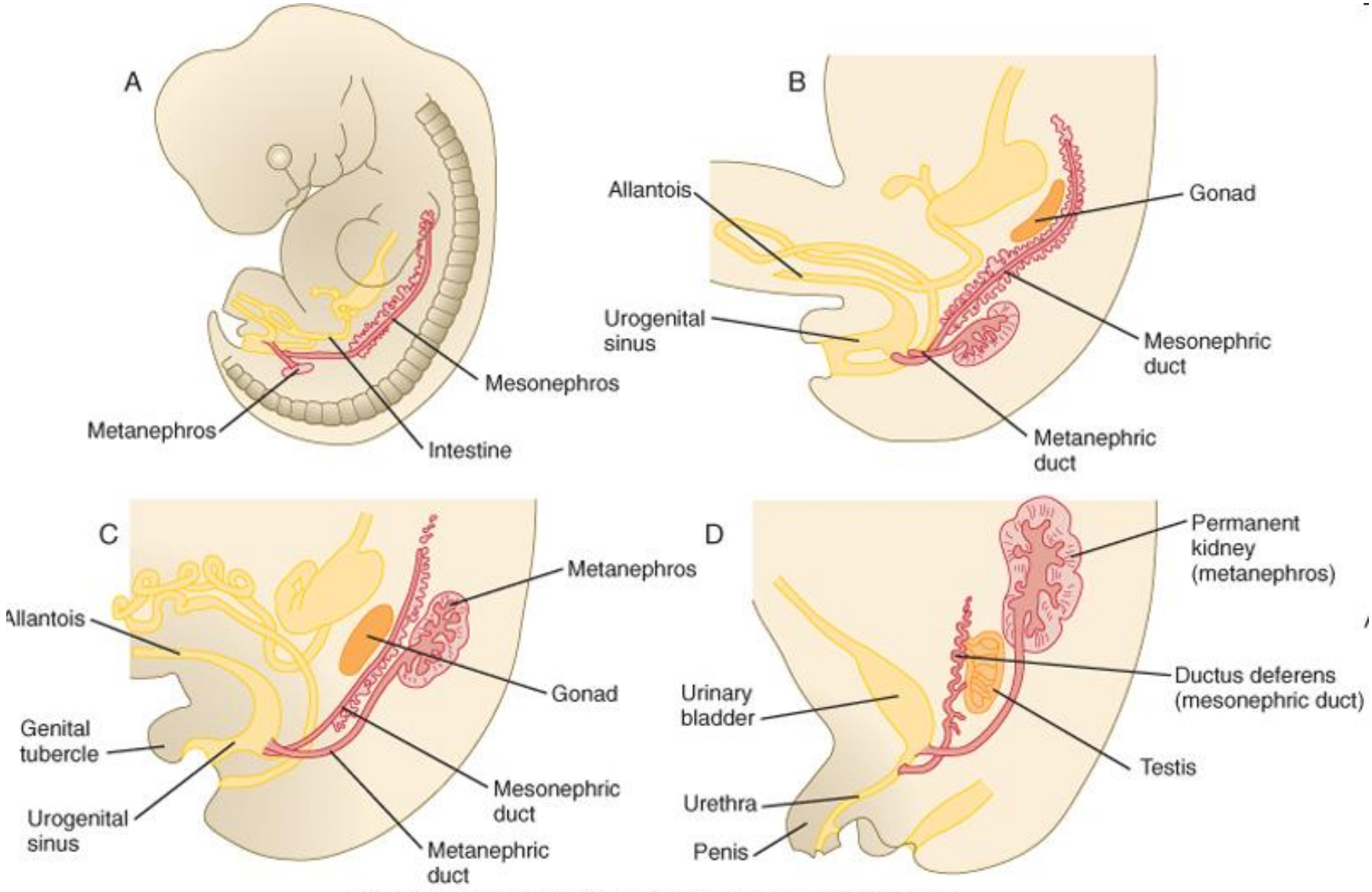
The **metanephros** develops from **three intermediate mesoderm structures** of the ***sacral*** region:

- **Ureter anlage**
- **Metanephric vesicle**
- **Glomerular capillary network**

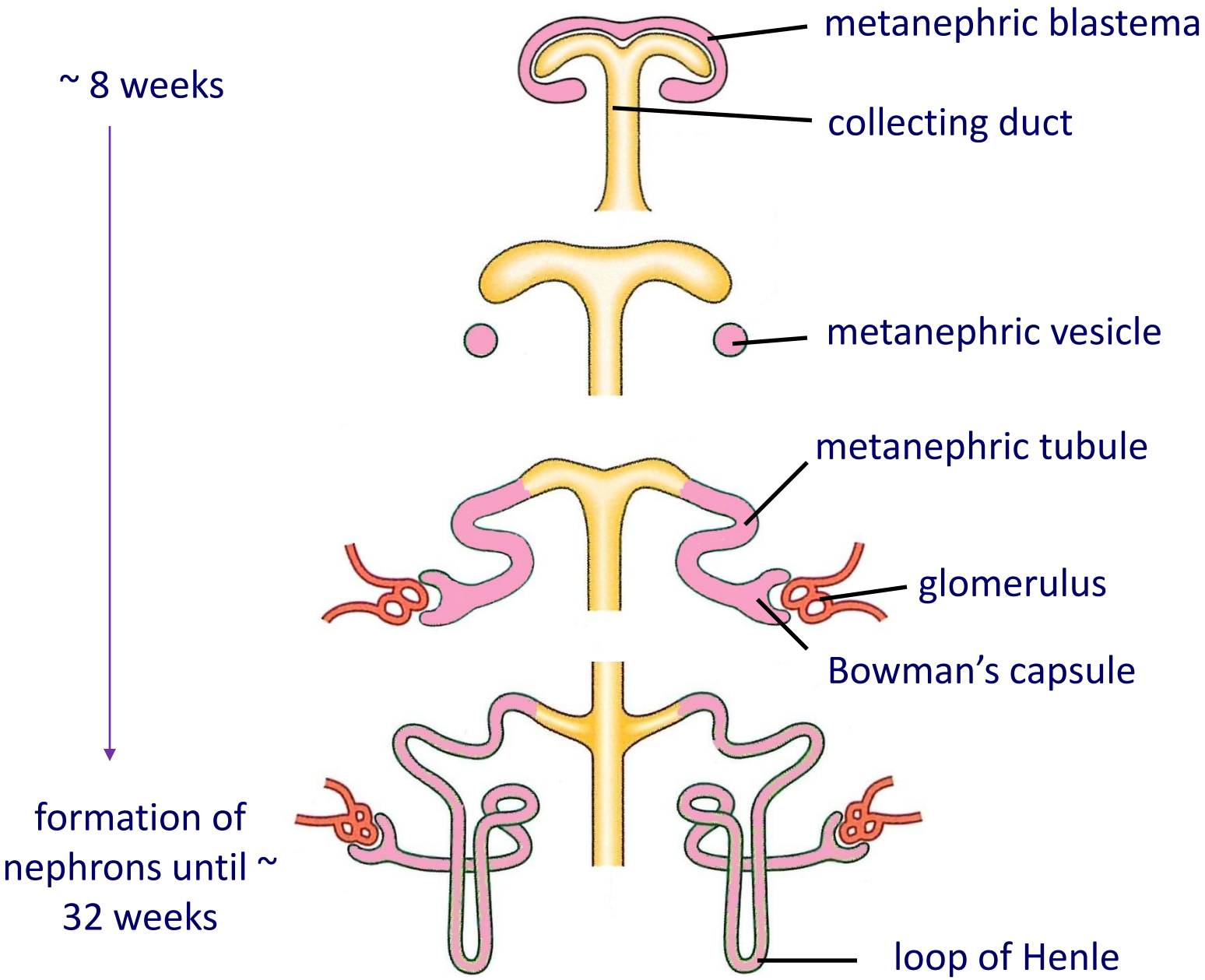
The **ureter anlage is an epithelial diverticulum** from the **caudal part of the mesonephric duct (Wolffian duct)** in the area of the ***first sacral vertebra (S1***).
The anlage intrudes into the metanephric vesicle and forms the extra- and intrarenal excretory passages.
The metanephric blastema corresponds to the sacral part of the nephrogenic cord below L3.
It is mesenchymal tissue out of which the **metanephric vesicles** arise. From these originate the **nephrons** (= functional units of the kidneys).

At present it is still not clear whether the glomerular capillary network develops through vasculogenesis (direct development of vessels from the metanephric vesicles) or through angiogenesis (development from existing vessels of the metanephros)

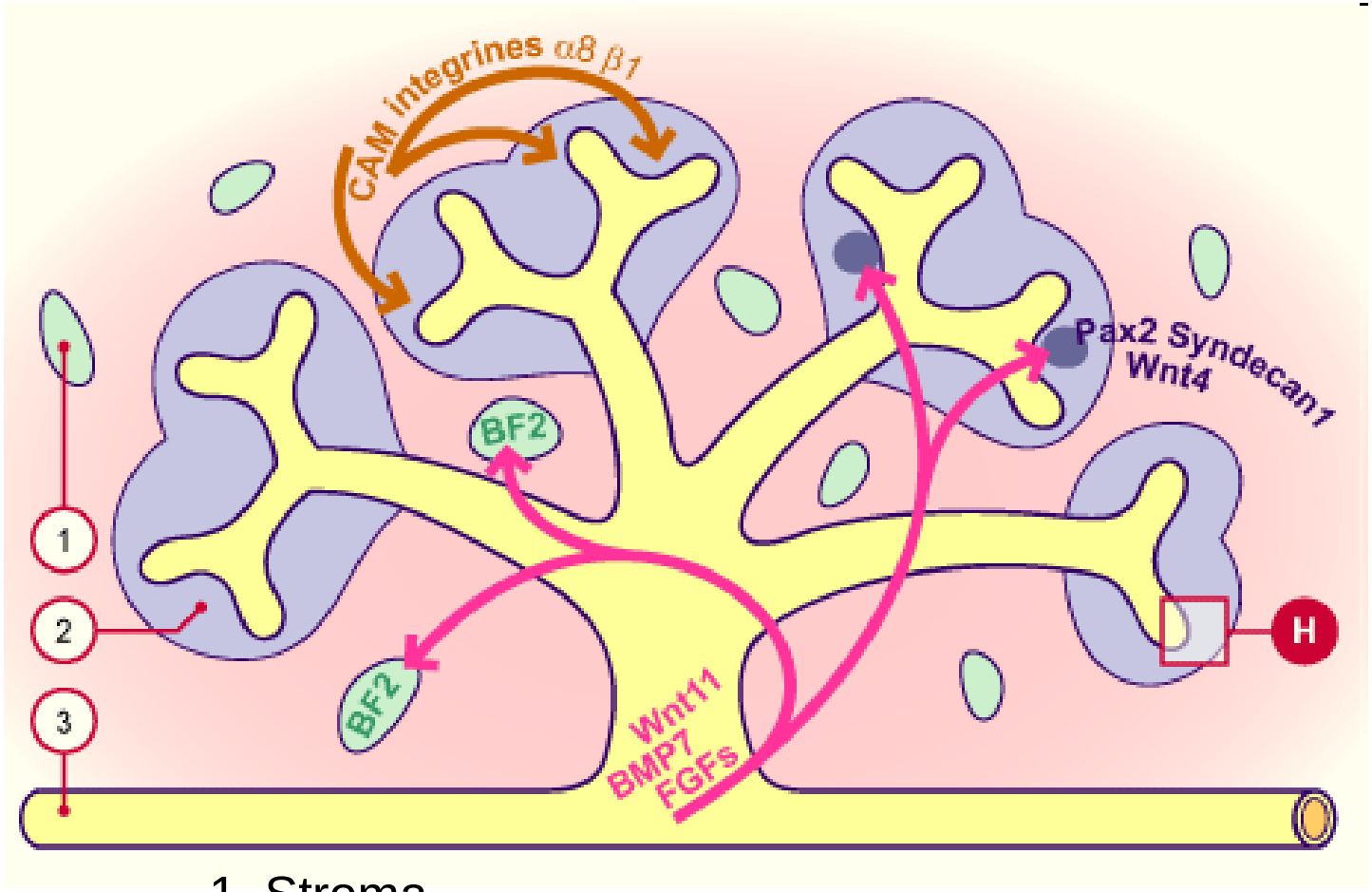
DIFFERENTIATION OF THE PERMANENT KIDNEY



DIFFERENTIATION OF THE METANEPHRIC BLASTEME

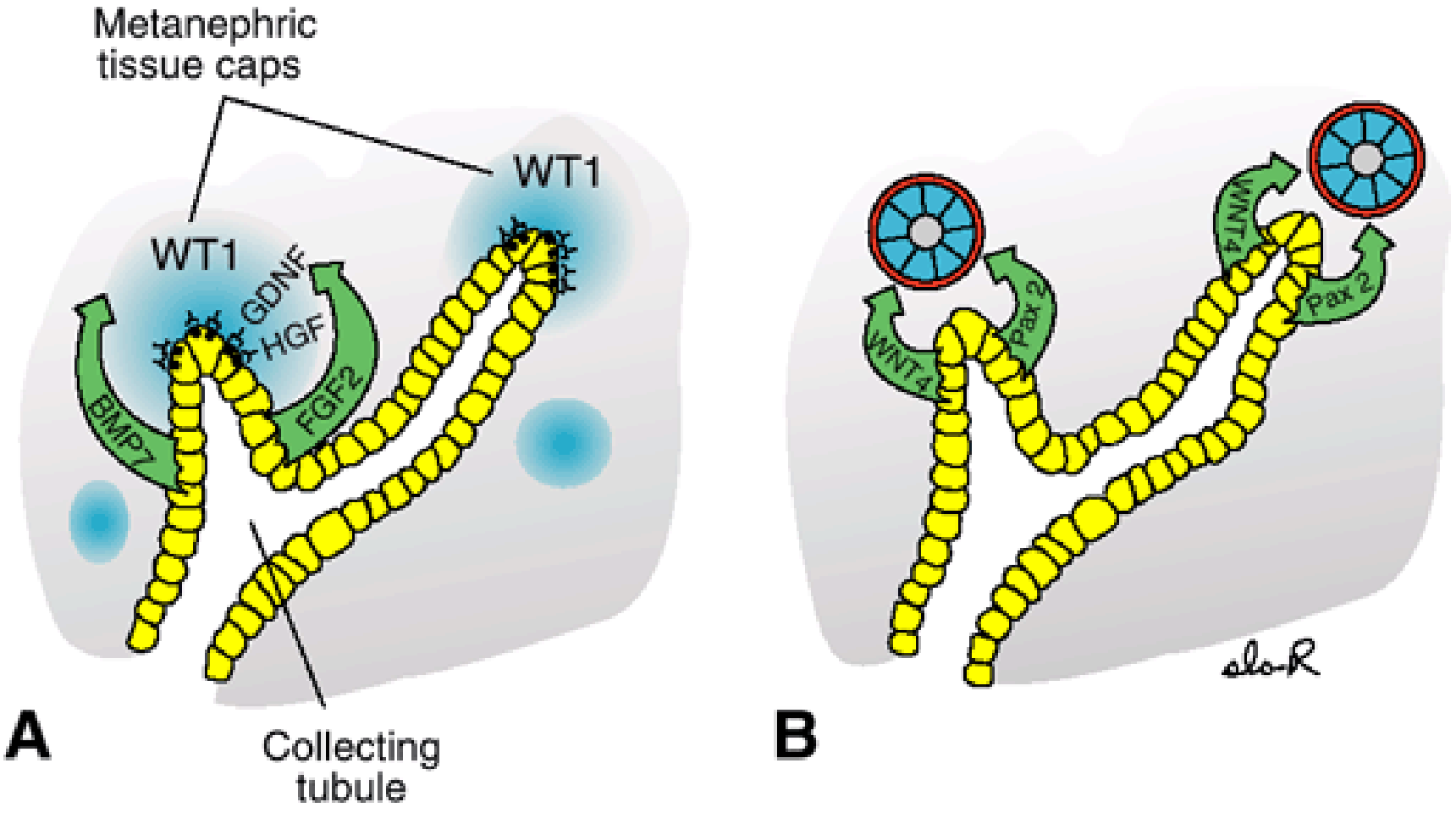


GENETIC REGULATION OF THE DEVELOPMENT OF THE NEPHRON

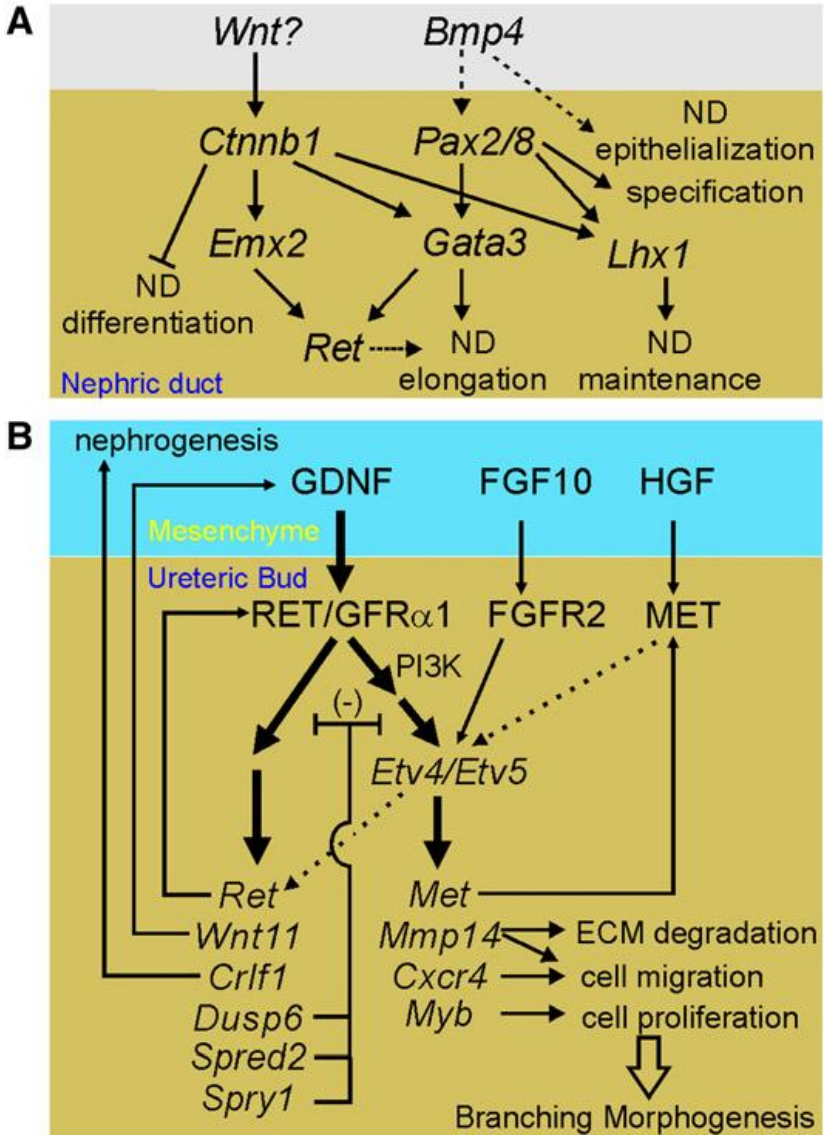


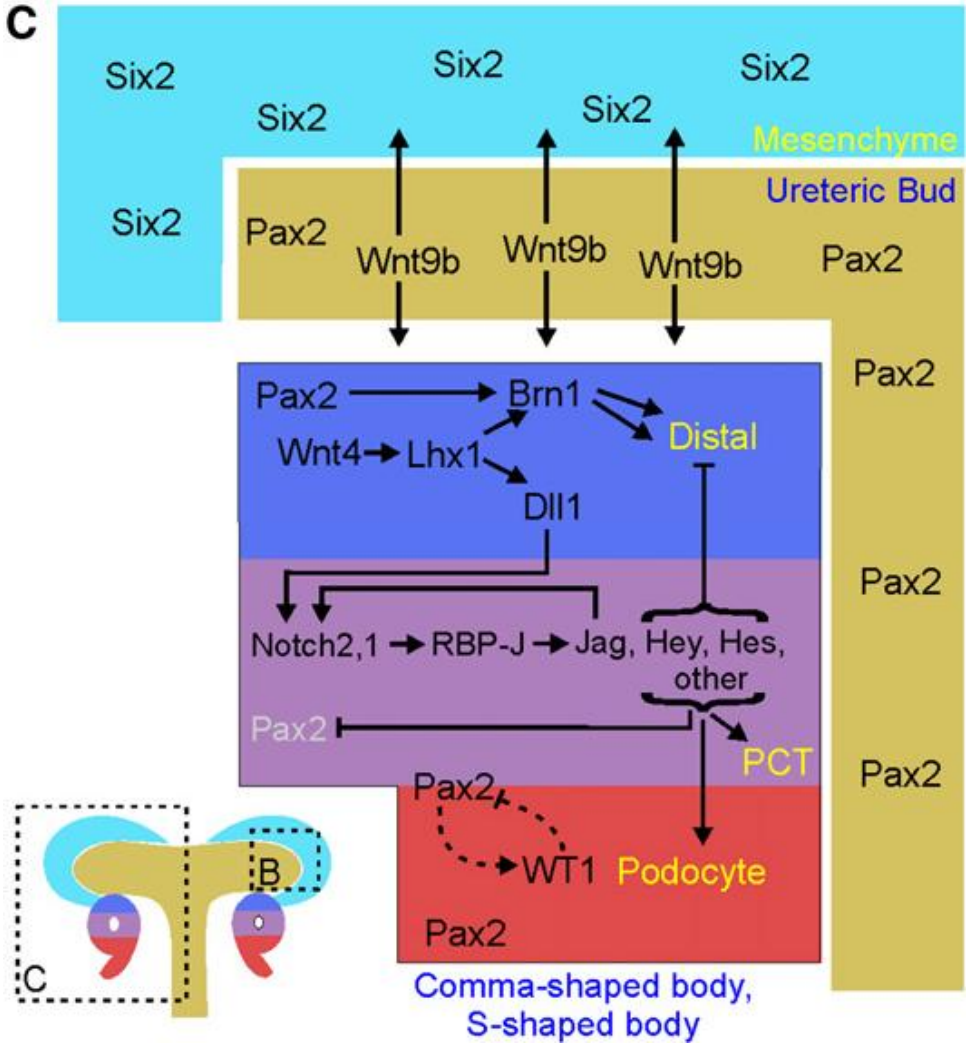
1. Stroma
2. Metanephric blastema
3. Mesonephric duct (Wolffian duct)

FORMATION OF COLLECTING DUCTS AND NEPHRONS

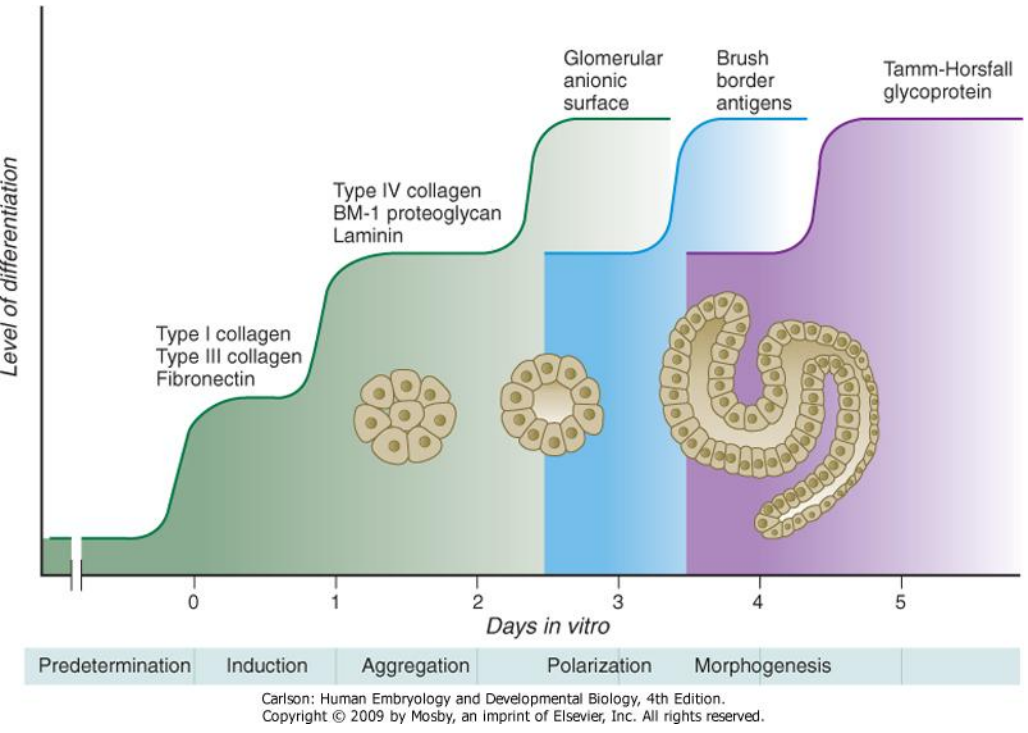


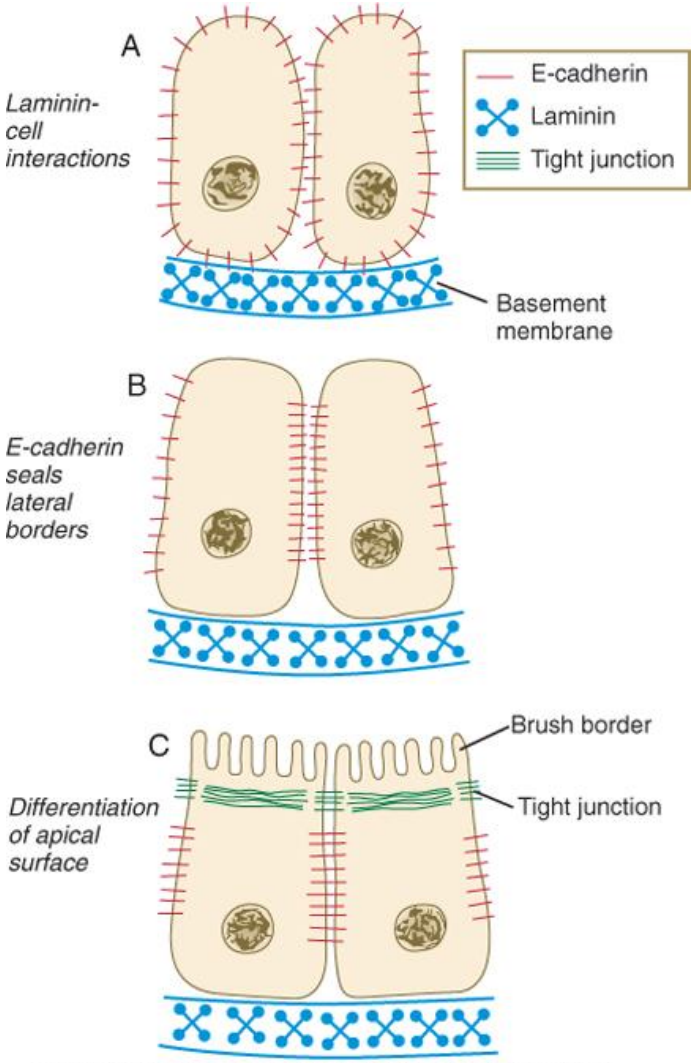
The genetic orchestra of metanephric development





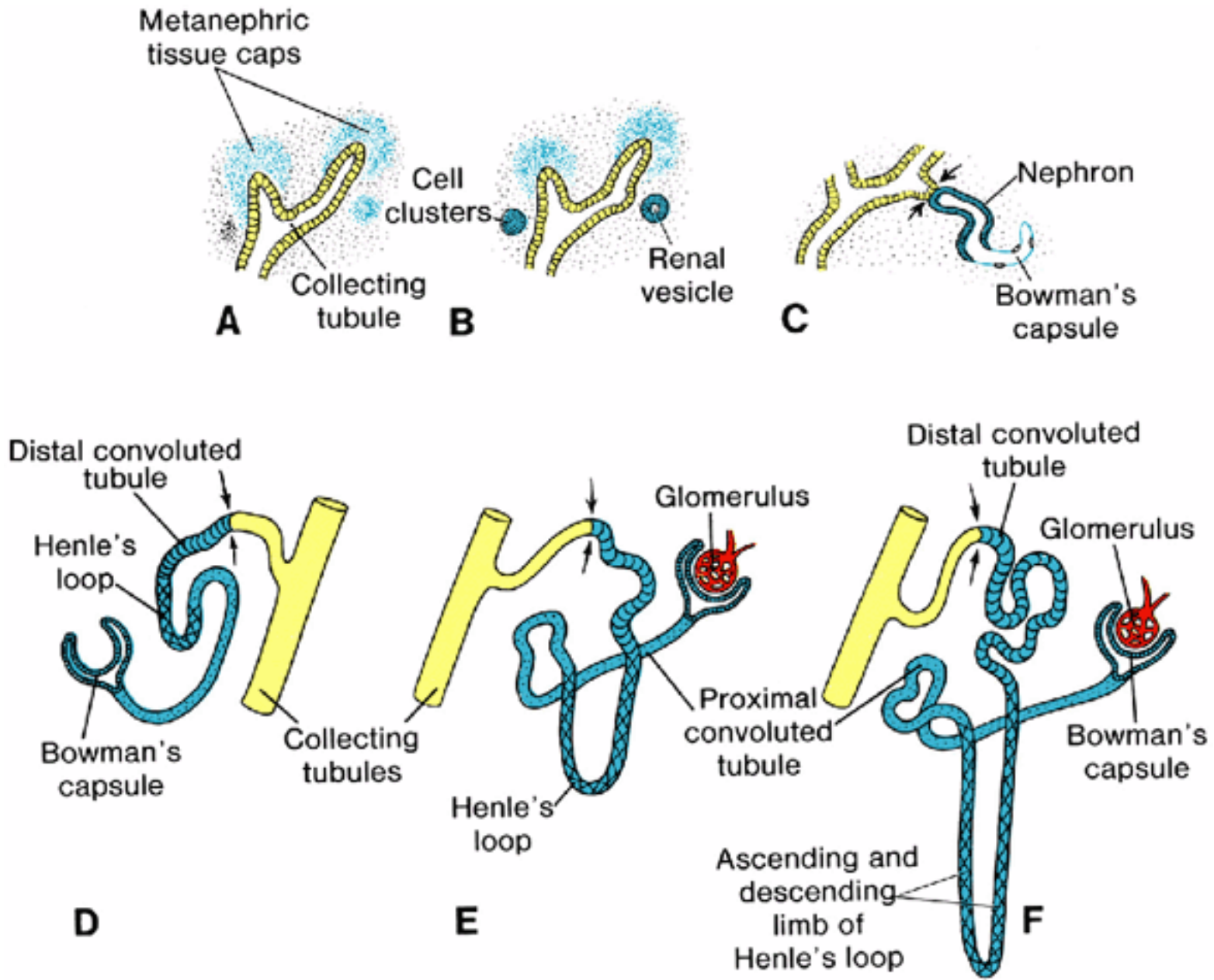
Nephron differentiation



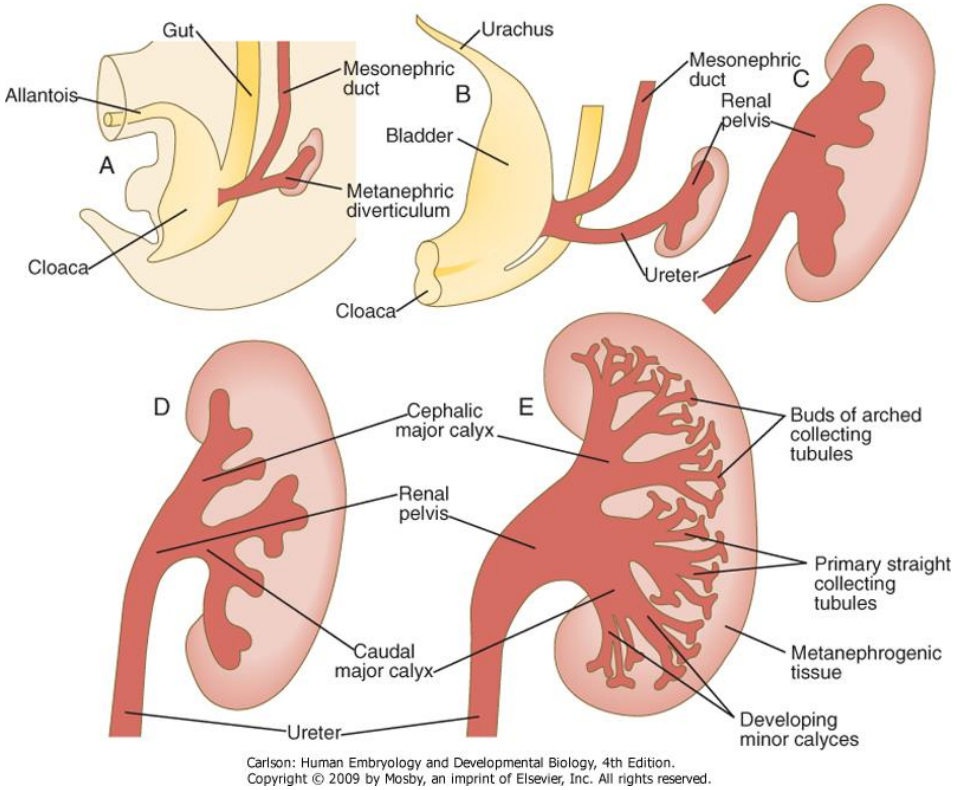


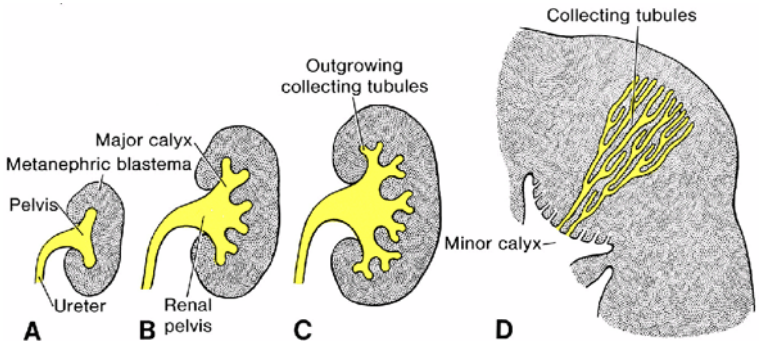
Proximal convoluted tubule

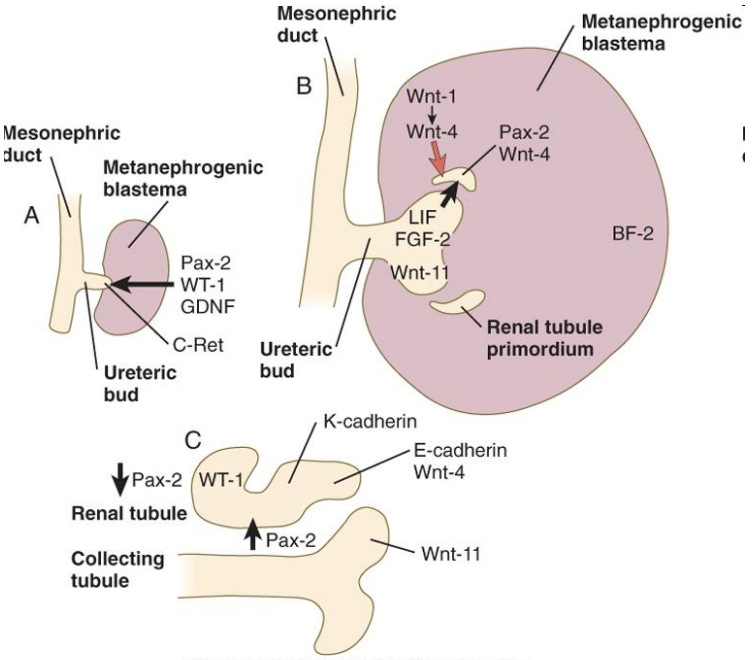
DIFFERENTIATION OF THE METANEPHRIC BLASTEME



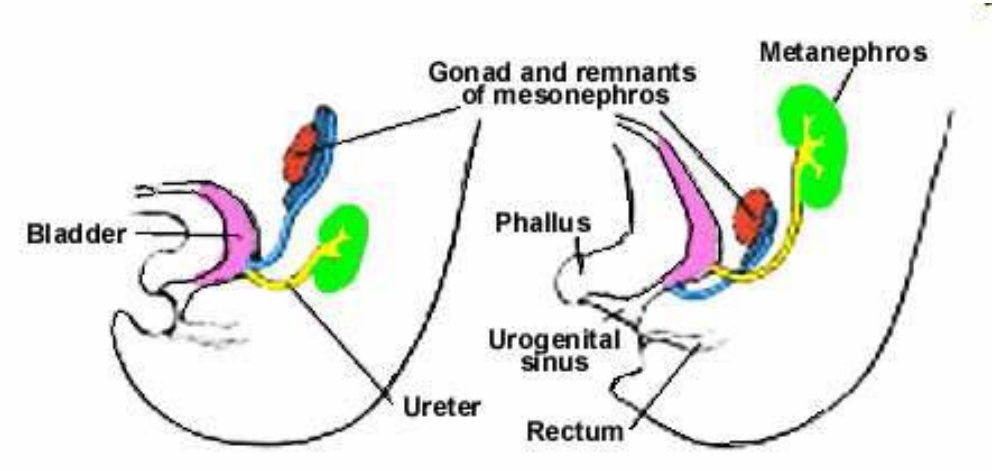
DEVELOPMENT OF THE URETER

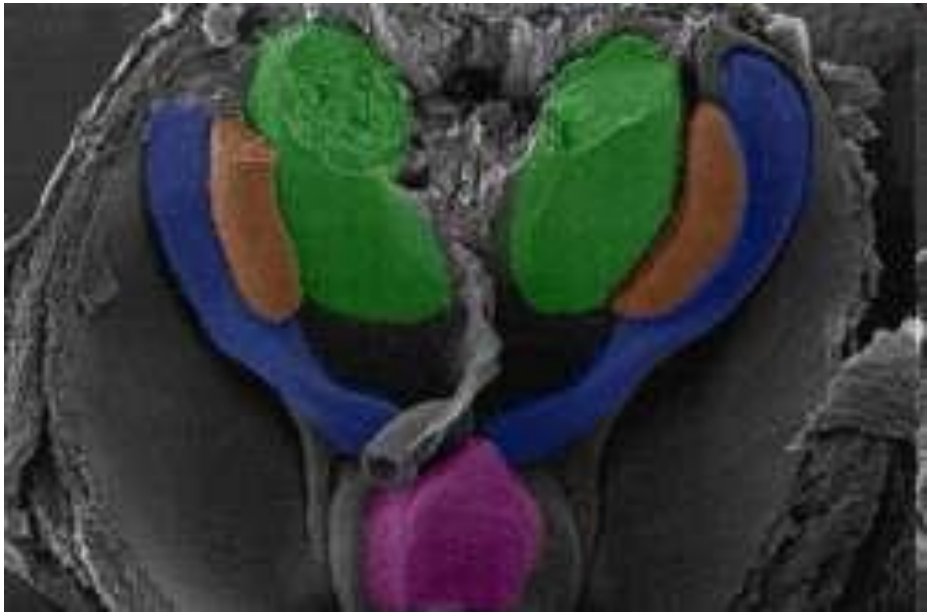


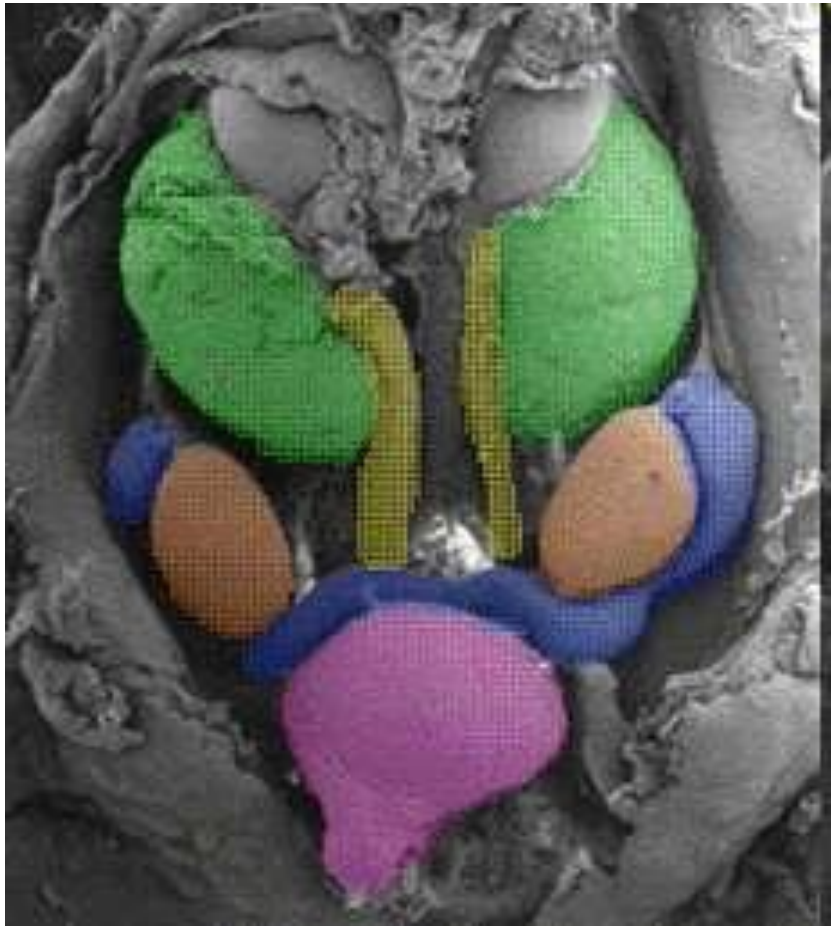




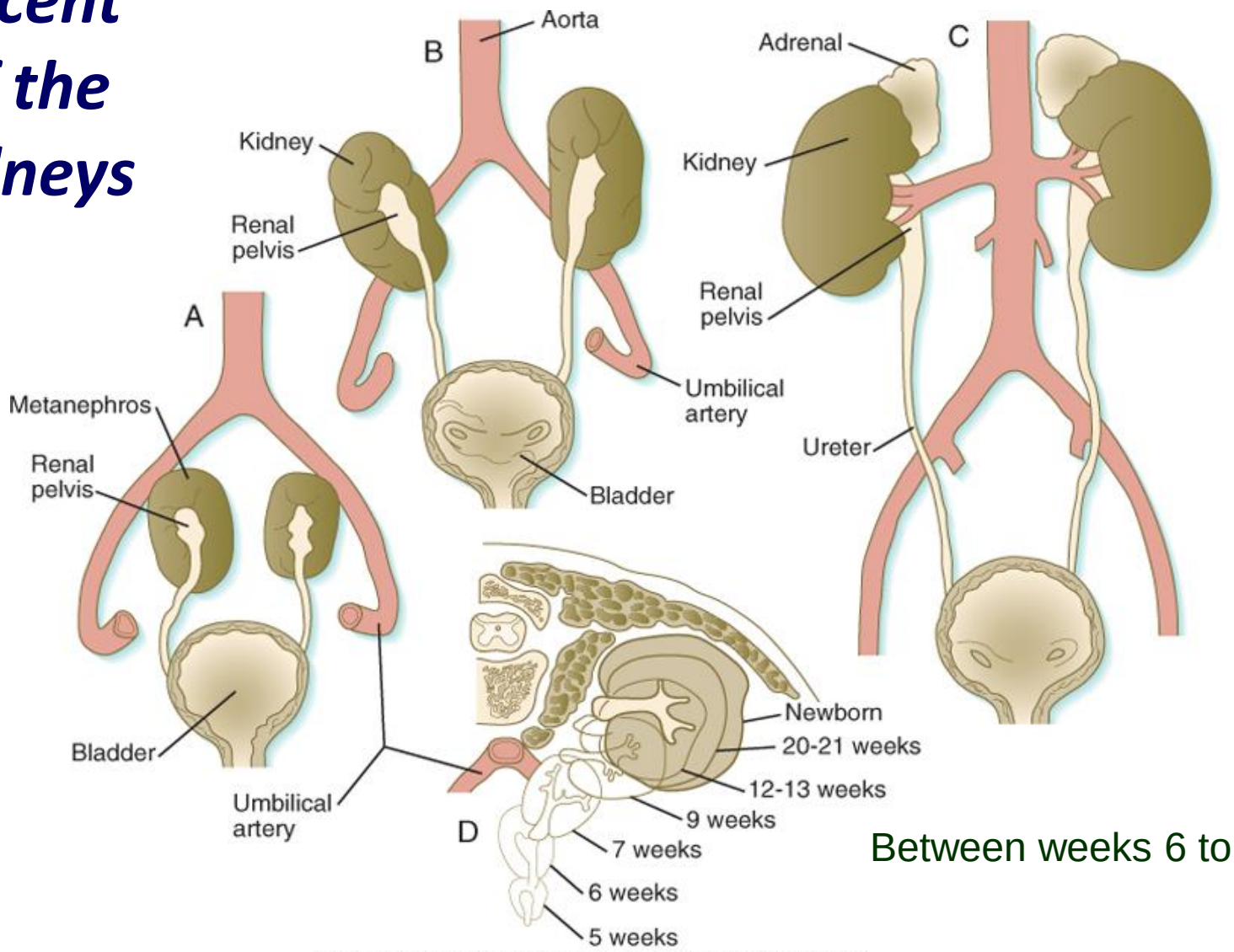
URETER (KUPFFER DUCT)







Ascent of the kidneys



Between weeks 6 to 9.

PRODUCTION OF URINE BY FETUS

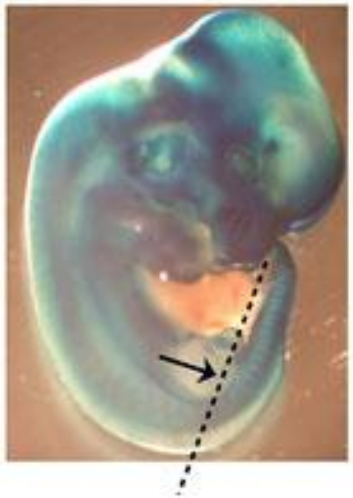
- Fetal urine mixes with amniotic fluid

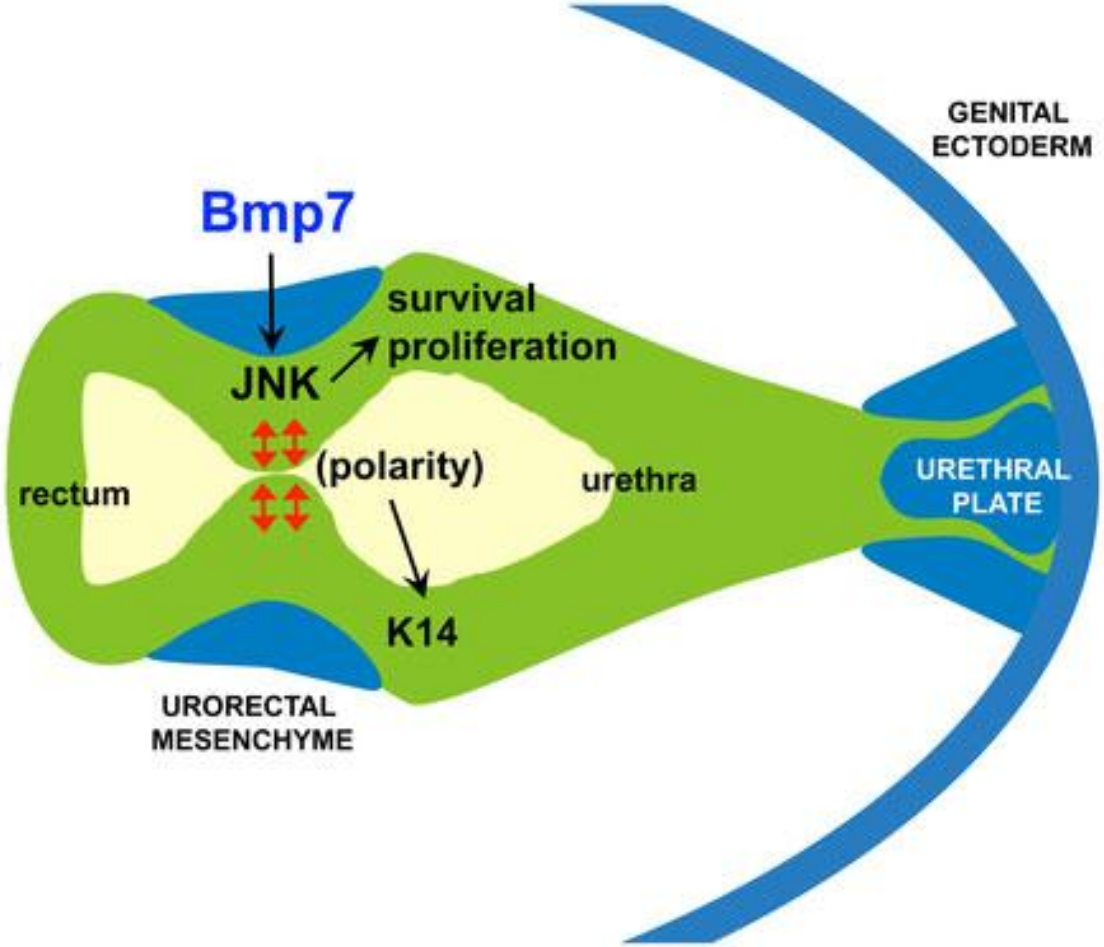
- Amniotic fluid enters fetal intestinal tract where it is absorbed into bloodstream

- From the bloodstream to the placenta which transfers metabolic waste to the mother

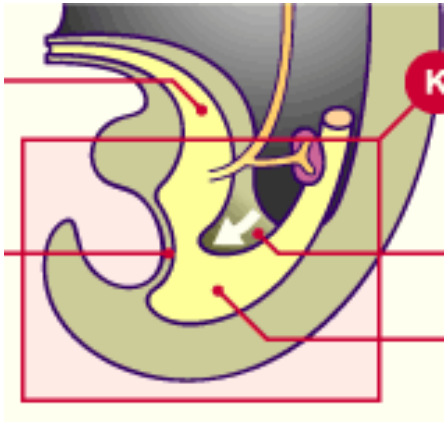
- Fetal kidneys are not necessary for exchange of waste products

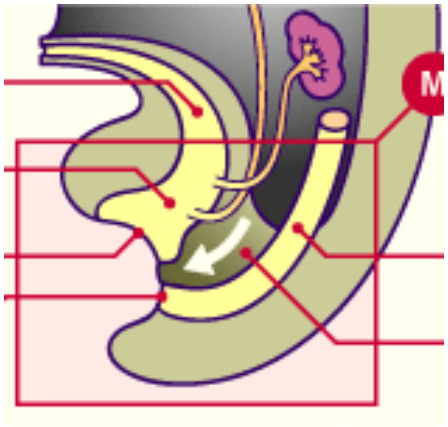
SEPTATION OF THE CLOACA

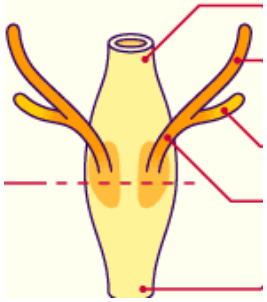




SEPTATION OF THE CLOACA





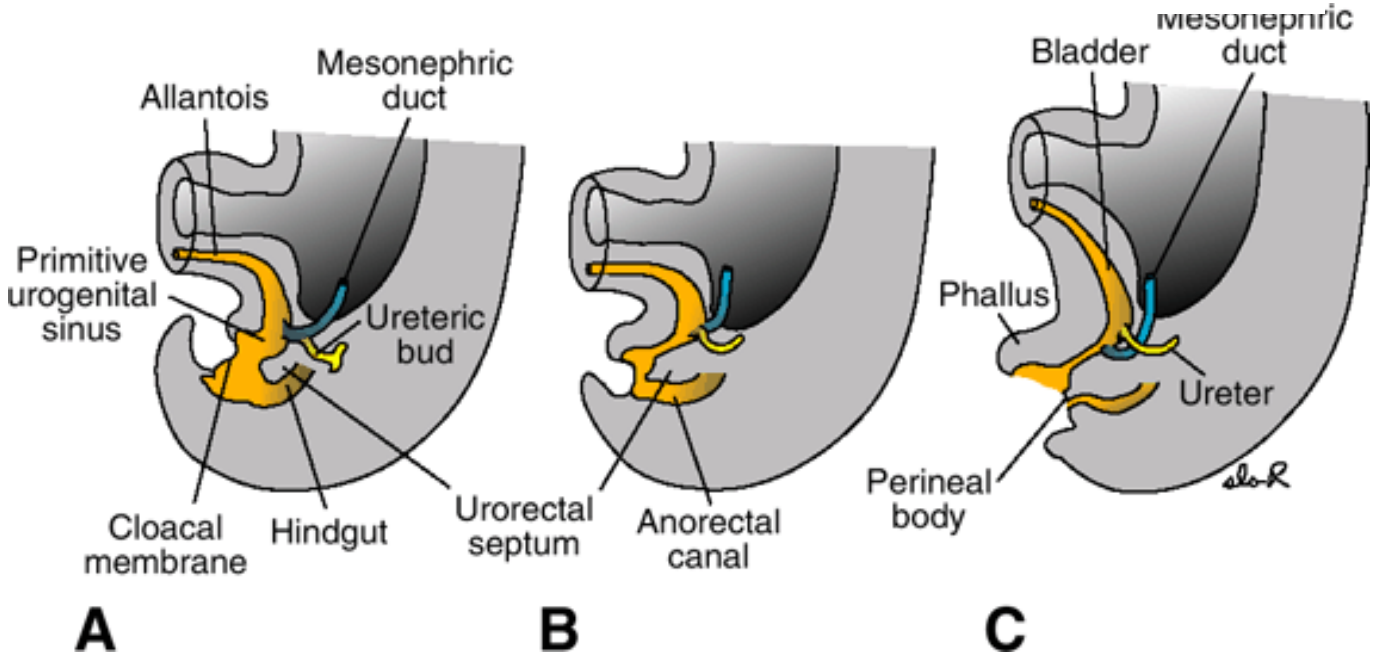


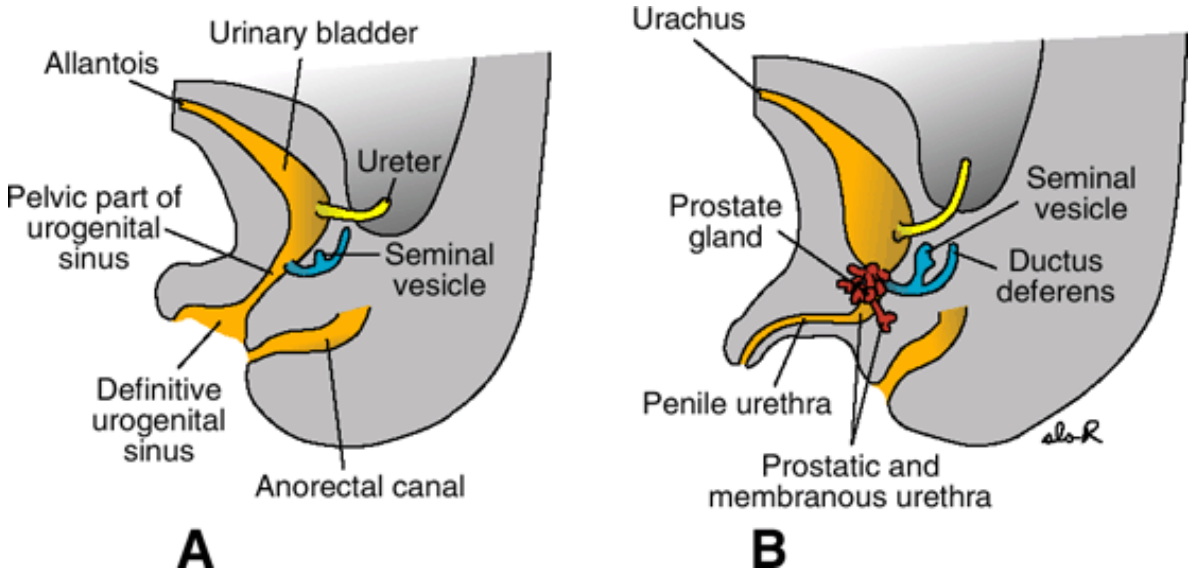
The cloaca is the common end of the rectal tube and the urogenital tract. Towards the outside it is closed by the cloacal membrane.
Between the ***4th and 6th weeks*** the **urorectal septum** separates the cloaca into a **primary urogenital sinus** (ventrally) and the **rectum** (dorsally).

- The ***bladder*** and the ***pelvic part of the urethra*** arise from the ***primary urogenital sinus***
- The ***caudal portion of the urethra*** comes from the ***definitive urogenital*** sinus
- The ***urorectal septum*** divides the cloacal membrane into two membranes: the ***urogenital membrane*** (ventrally) and the ***anal membrane*** (dorsally).

These two membranes atrophy, like the bucco-pharyngeal membrane, in order to form the intestinal and urogenital openings.

Urinary bladder
Septation of the cloaca

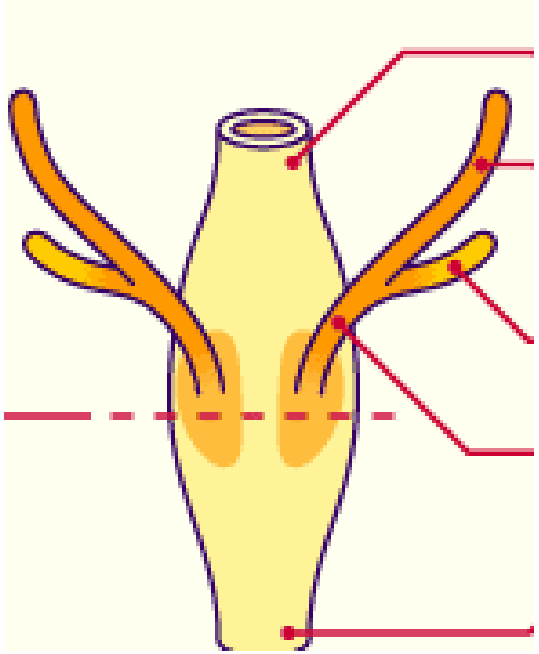




DEVELOPMENT OF THE URINARY BLADDER

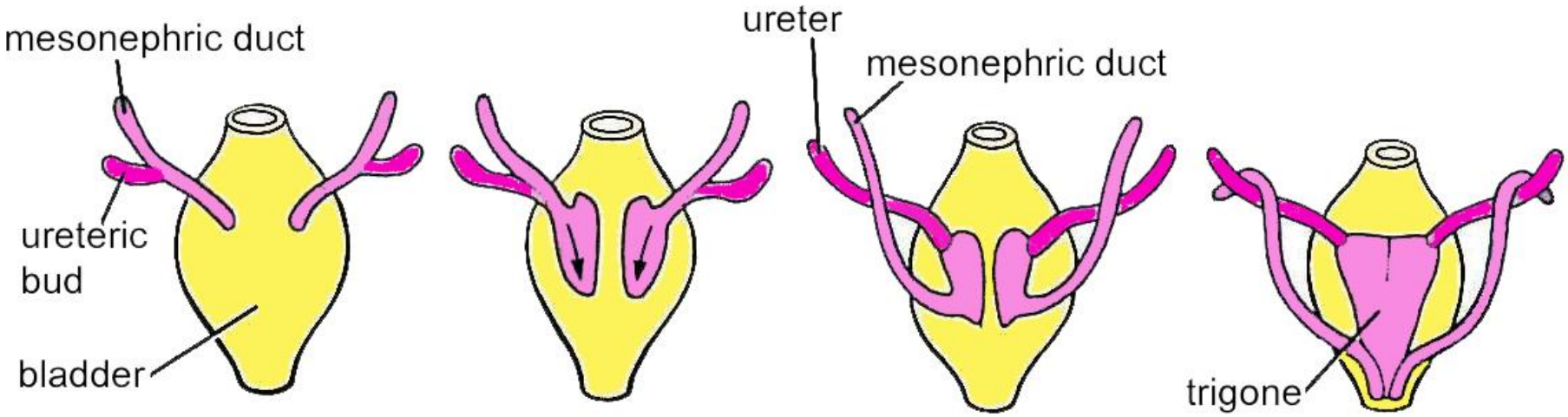
The **bladder** develops from the **upper part of the urogenital sinus (UGS)** and is connected with the allantois.
The allantois is obliterated during the development and forms a fibrous cord, the urachus, which following birth becomes the **median umbilical ligament**.

While the cloaca is being divided, the caudal, originally common part of the mesonephric duct (Wolffian duct) and the ureter anlage is taken up into the upper, postero-lateral wall of the urogenital sinus (future bladder).



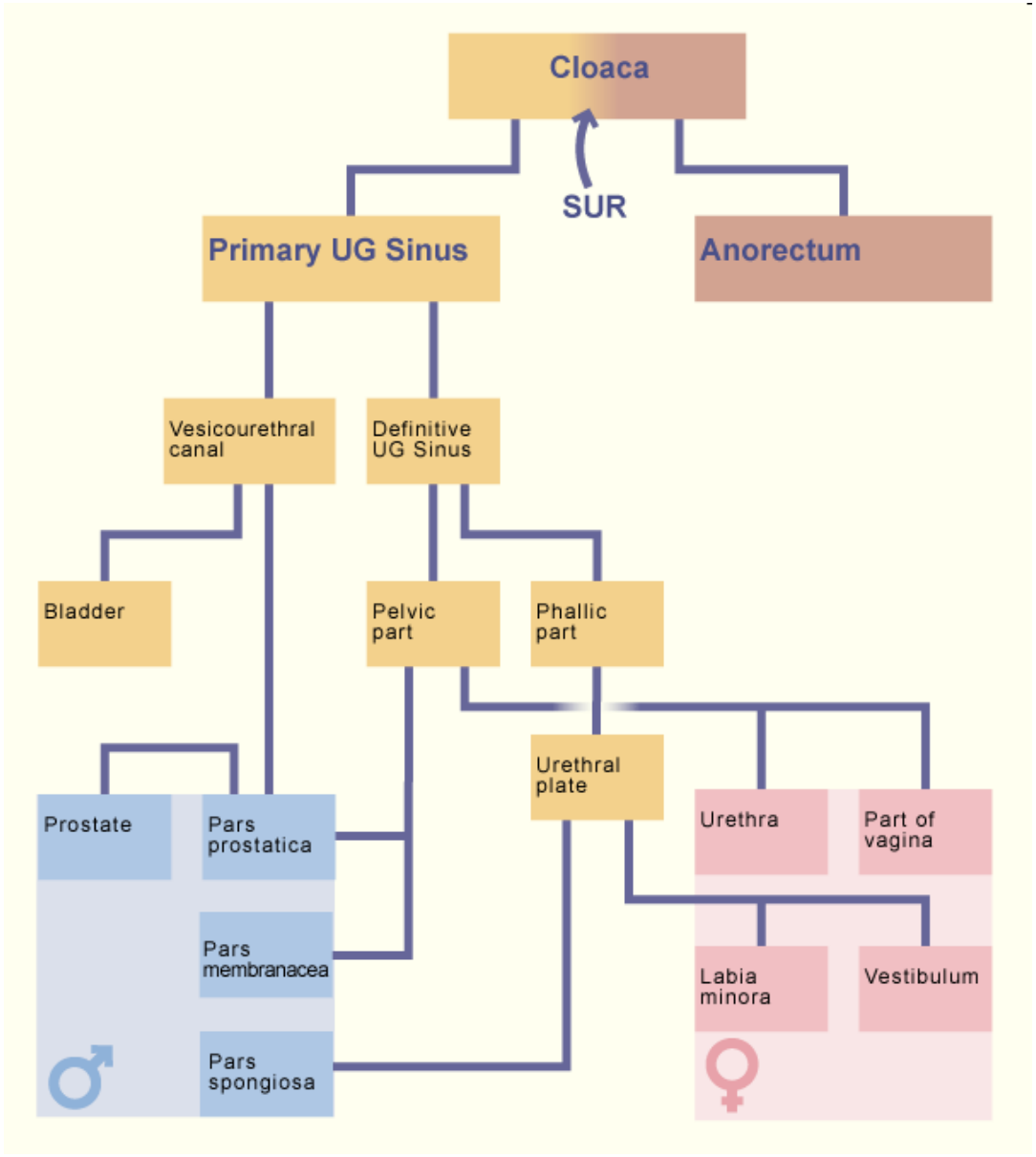
The **trigonum** thus originates from the **mesoderm** while the ***ventral bladder wall has an endodermal origin.***
Later, though, ***the trigonum will be completely covered by endodermal epithelial cells***.
The smooth musculature of the bladder develops during the 12th week from the splanchnopleural mesoderm, which coats the endoderm on the outside.

PARTS OF THE URINARY BLADDER



4 weeks → **6 weeks**

URETHRA



The urethra forms itself from the lower part of the urogenital sinus (UGS).

In a **man** the prostate and membranous part of the urethra arise from the pelvic part of the UGS while the spongy urethra comes from the phallic part (urethral plate).

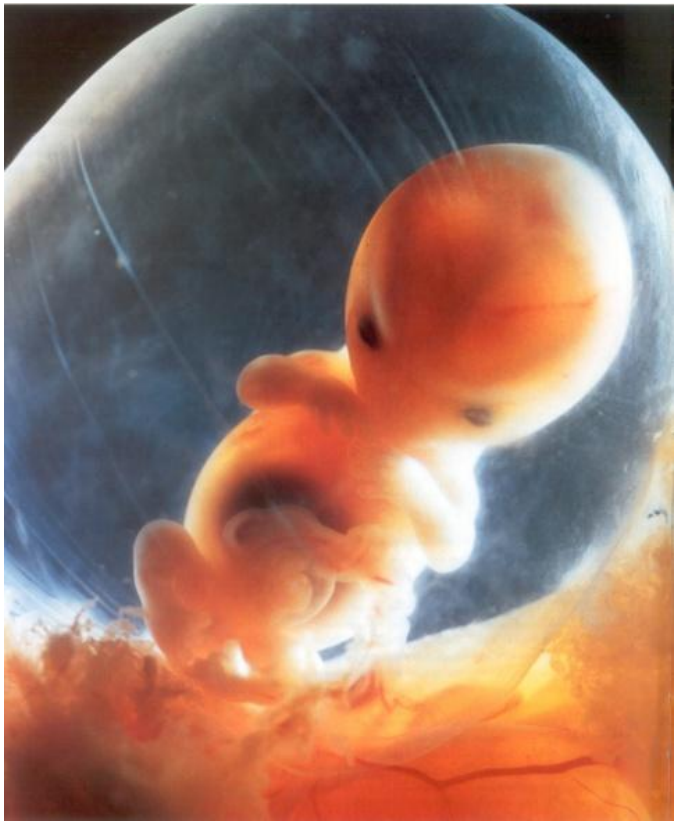
In a **woman** the whole urethra and part of the vagina arise from the pelvic part of the UGS while the phallic part (urethral plate) forms the vestibule and the labia minora.

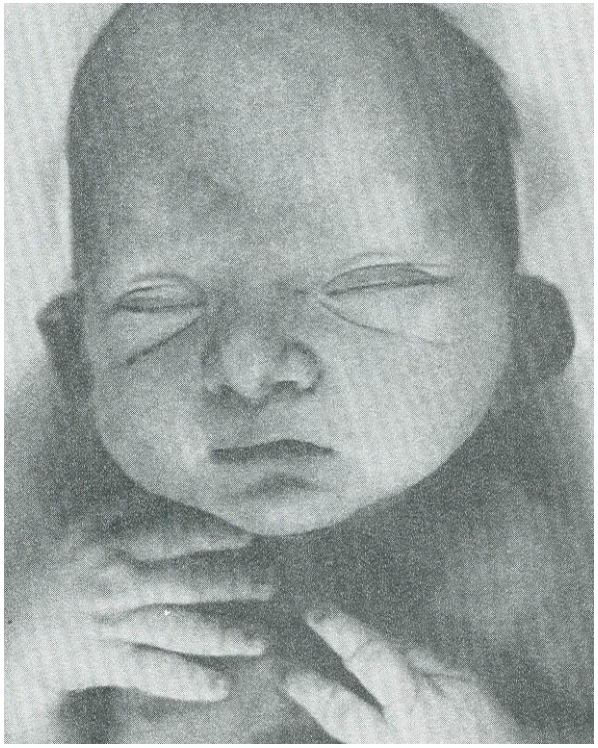
FEHLBILDUNG

- **AGENESIS** *(13, 18-as Trisomie, als Nachfolge zB einer mütterlichen Rubeola -Infektion)*
  - Unilaterale *(überlebt)*
  - Bilaterale *(meistens lethal)*
- **HYPOPLASIE** *(Parenchymverloss)*
- **KONGENITALE NIERENZYSTE** (*mehrere Typen sind vorhanden: autosomal dominant, 13-15, 18, 21, 22 trisomie – erscheint **bilateral**, auch von mechanischer Obliteration verursacht – erscheint **unilateral**)*
- **HUFEISENNIERE**, ***FUSION*** *(vitamin A Mangel,13, 18-as Trisomie, Turner- syndrome)*
- **WILMS – TUMOR** (*meistens in Kinder, Fehlbildung des Mesoderms in der Differenzierungsphase)*

FATE OF EXCRETED URINE IN FETAL LIFE

Renal agenesis
oligohydramnion



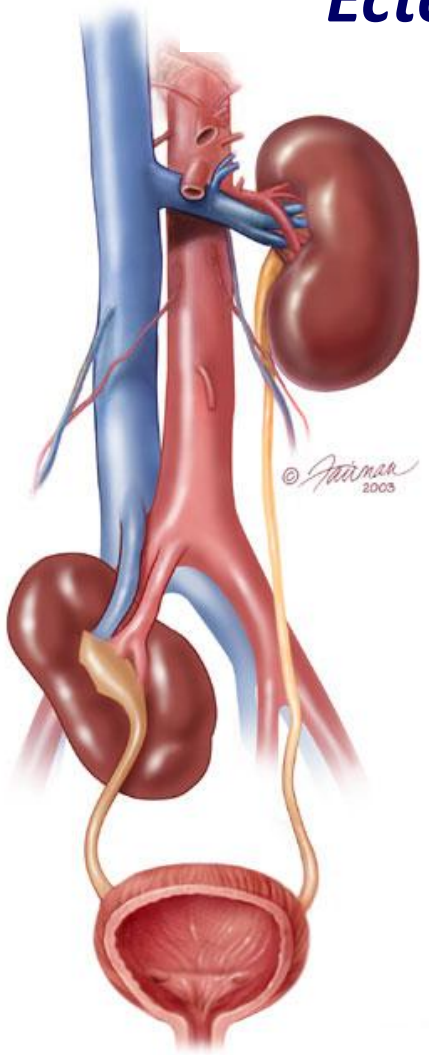


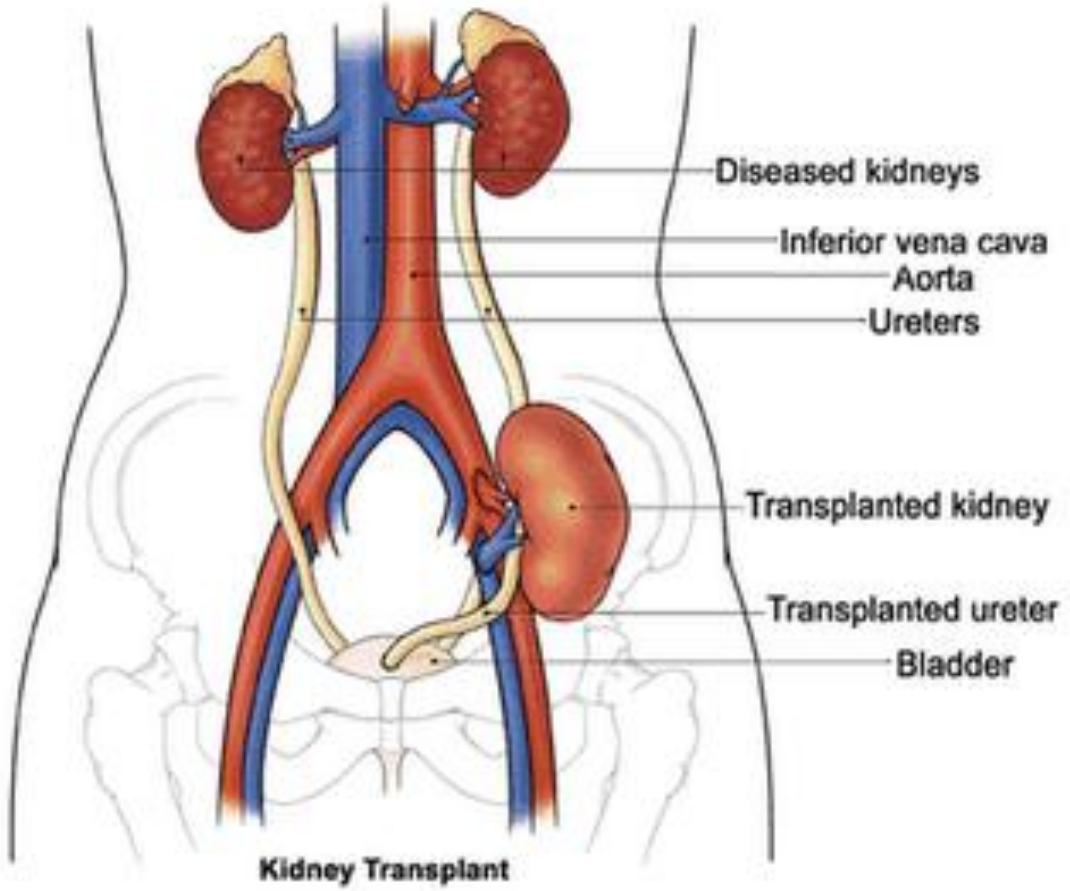
Potter's face

The fetal kidneys regulate the amount of amniotic fluid.

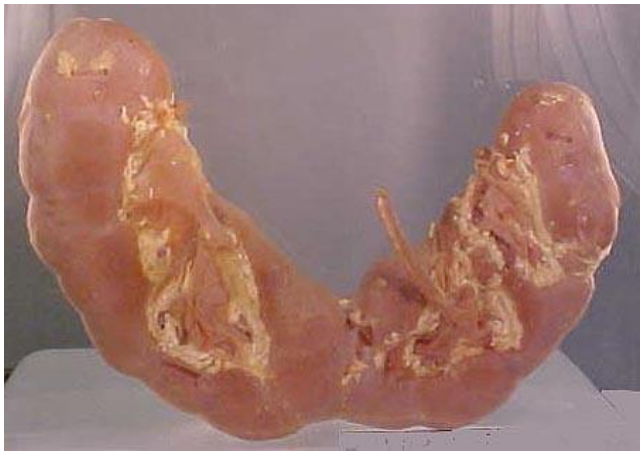
MALFORMATIONS

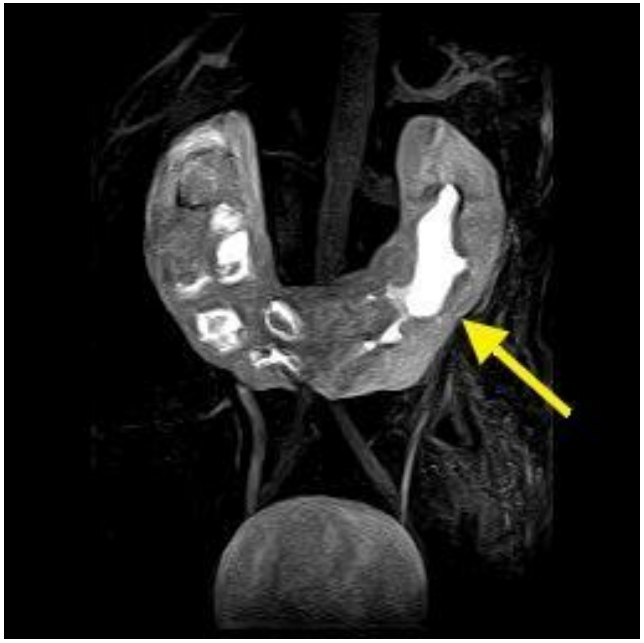
Ectopic kidney (or a transplant)

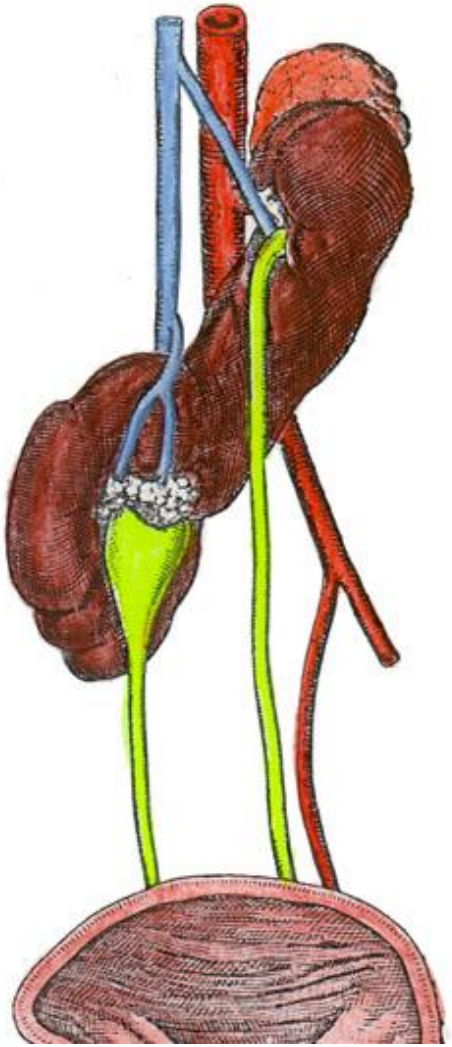




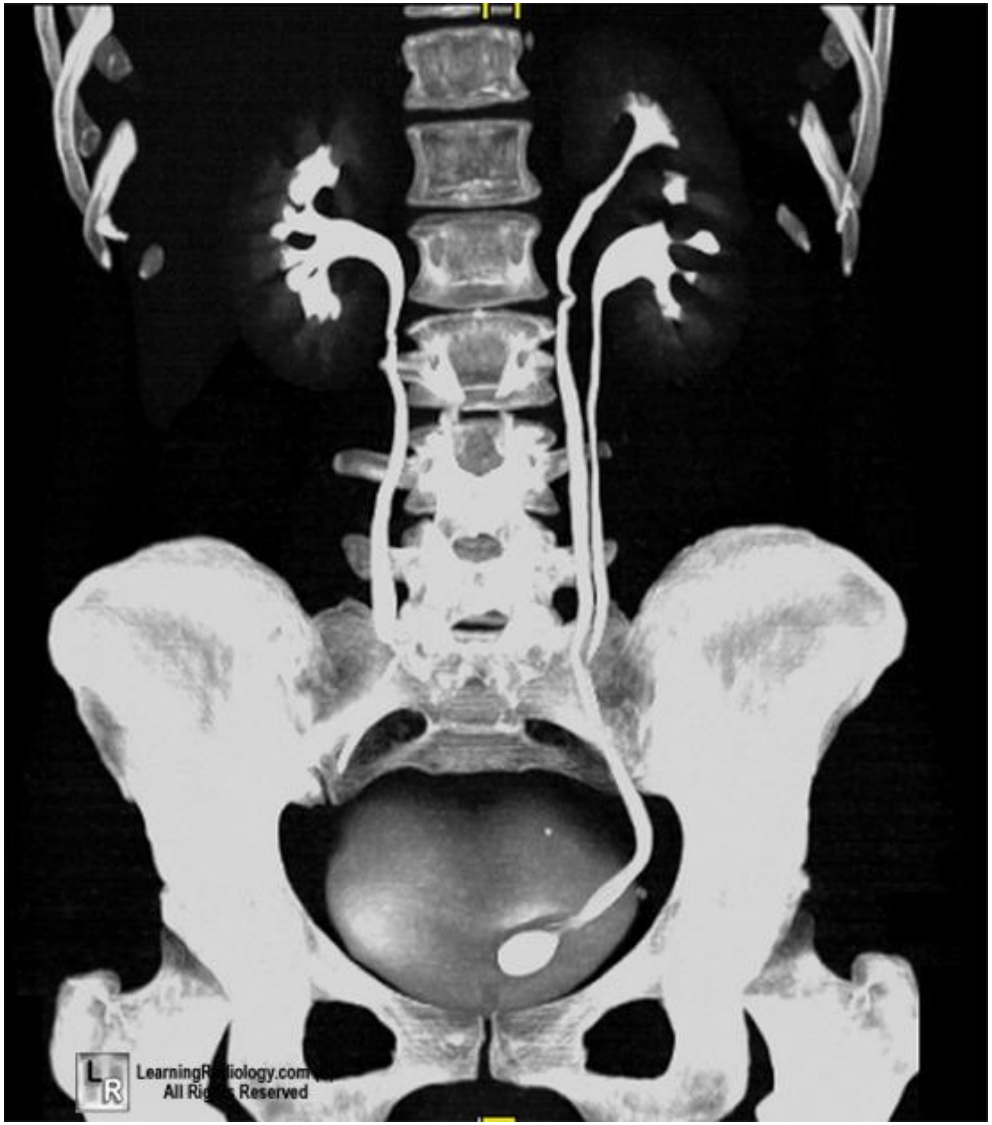
HORSESHOE KIDNEY





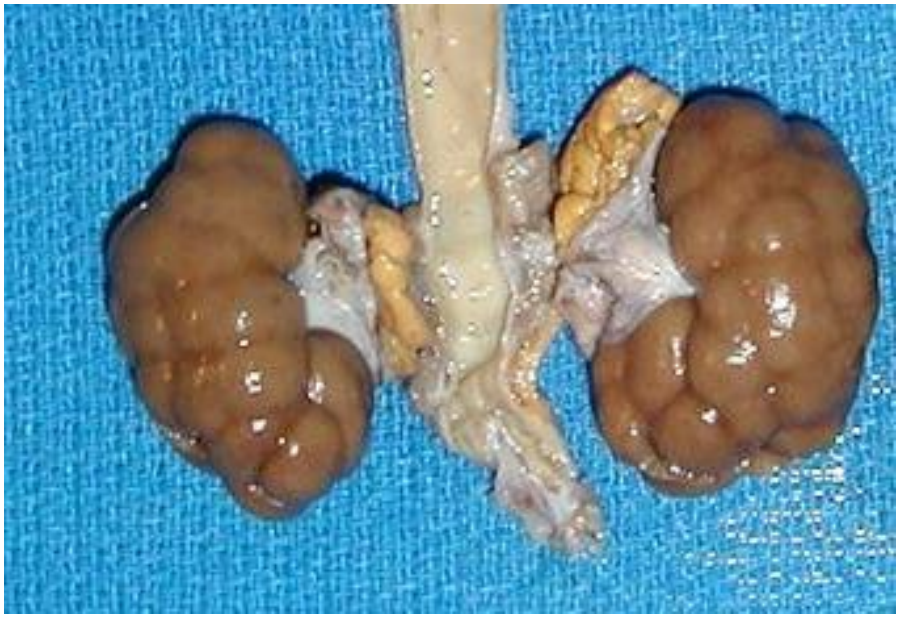


URETER DUPLEX



FETAL HUMAN KIDNEY

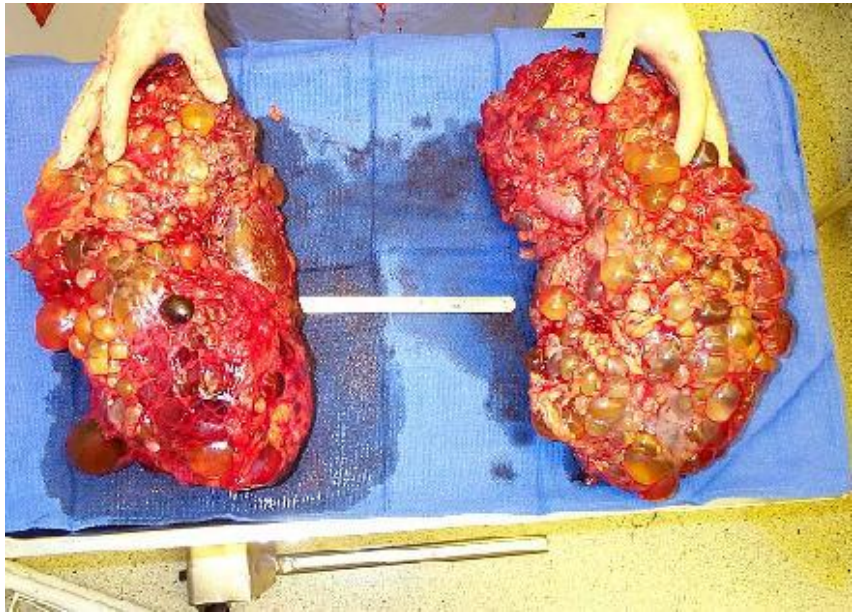
FIRST SEGMENTED BUT LATER SMOOTH

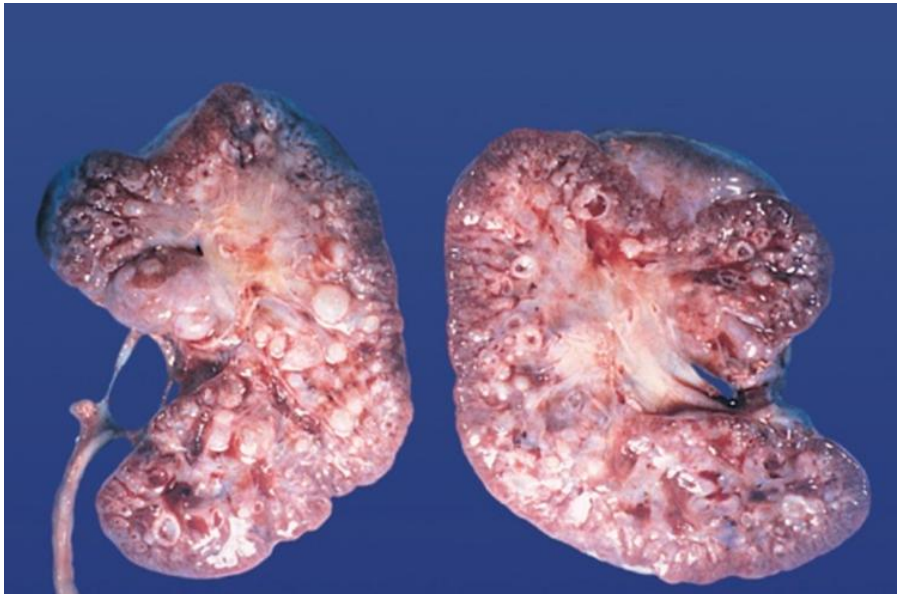


COW KIDNEY

STAYS SEGMENTED

POLICYSTIC KIDNEY





Congenital polycystic disease of kidney (1:800 live birth), PKD1 and PKD2 mutations

Thank you for your attention!