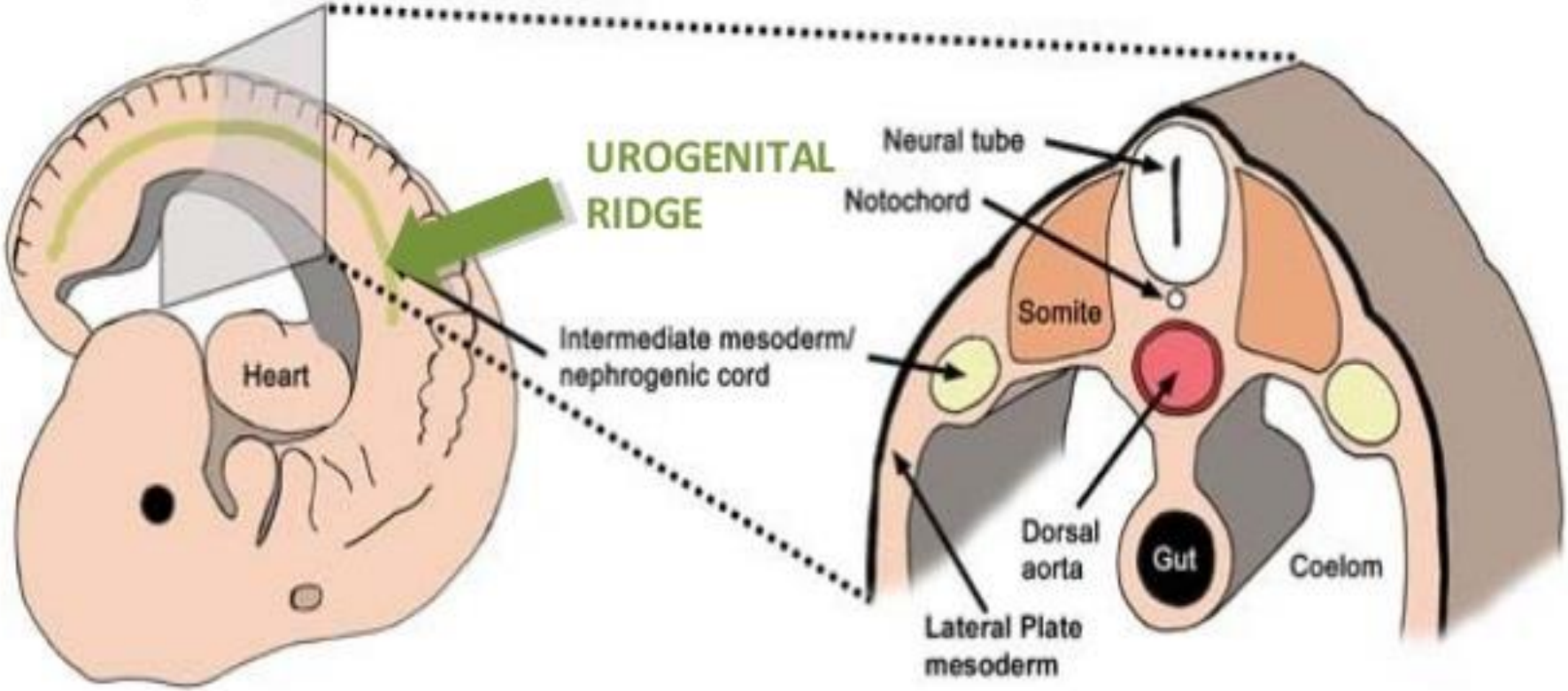
EVOLUTION & SUCCESSION OF KIDNEY IN DIFFERENT CLASSES OF VERTIBRATES

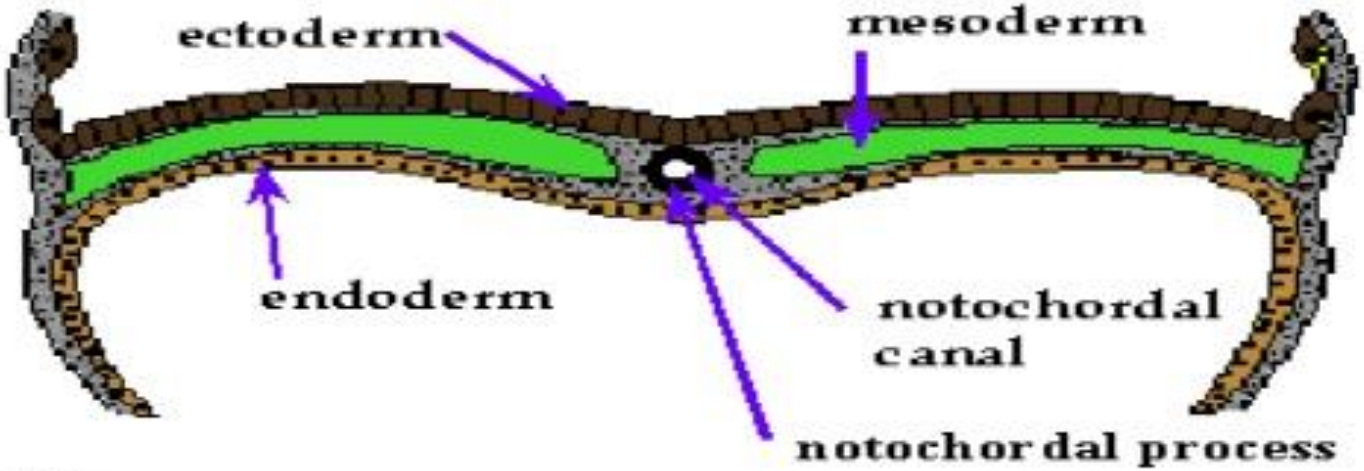
Mammalian Kidney Development

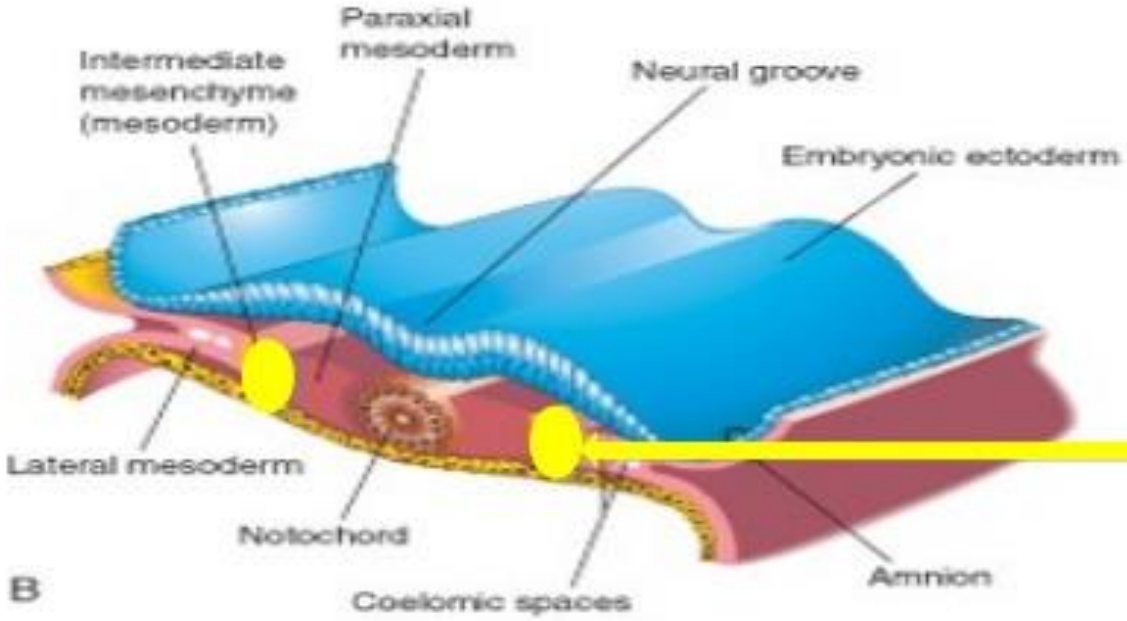
- After the folding of the embryonic disc, the intermediate mesoderm forms a bulging on the posterior abdominal wall, called the **NEPHROGENIC CORD/ UROGENITAL RIDGE**
- It extends from the cervical region to the sacral region of the embryo.



Basic Concepts

The 3 embryonic germ layers

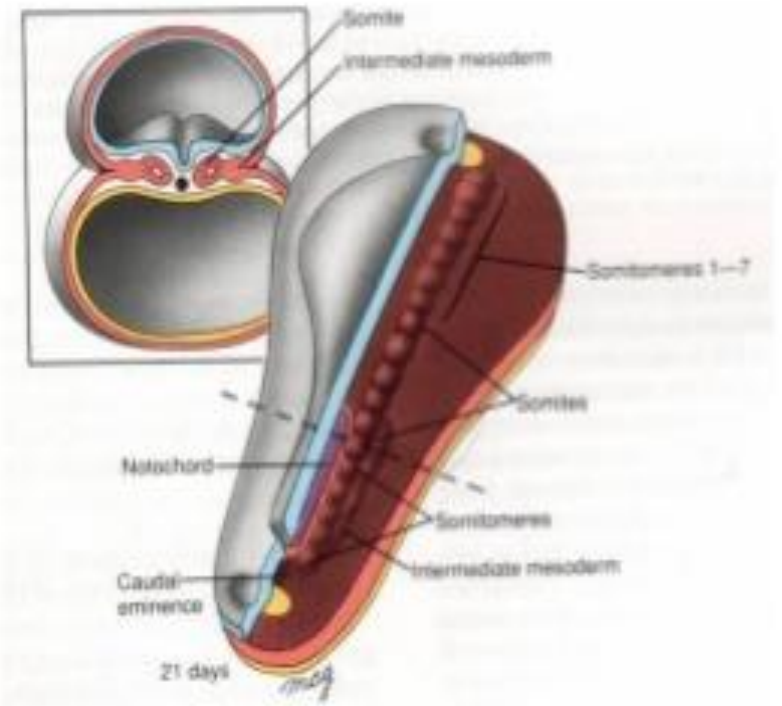




INTERMEDIATE MESODERM

INTERMEDIATE MESODERM

- Mesoderm appears in the 3 week embryo
  - Paraxial = somites
  - Intermediate
  - Lateral plate
    - Two layers separated by the Coelome
- Intermediate mesoderm gives rise to “Paired Glands” (Kidneys, Adrenals and Gonads)



Stages of Kidney Development

- The Human Kidney develops in 3 successive stages (rostral to caudal)

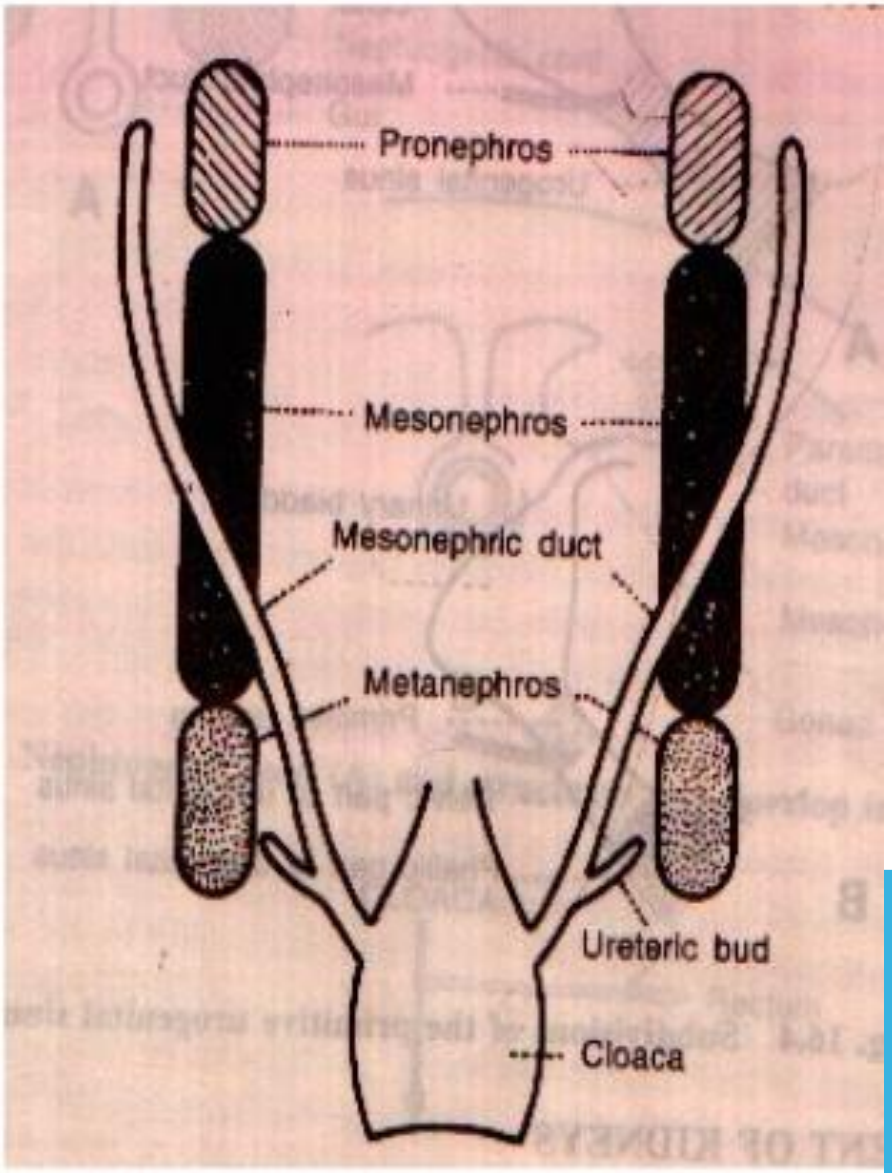
➢ PRONEPHROS

➢ MESONEPHROS

➢ METANEPHROS

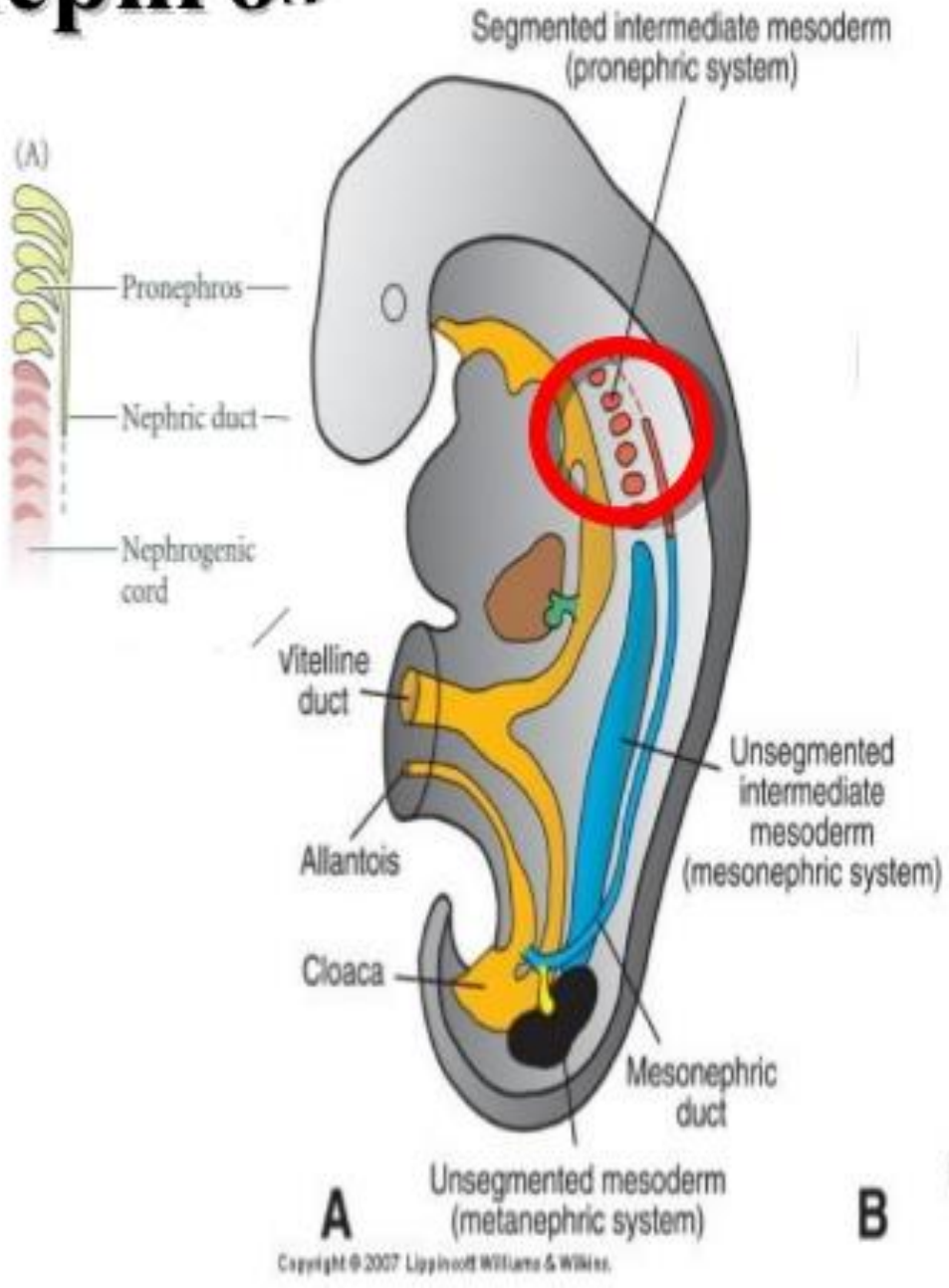
- They are aligned adjacent to the

Wolfian / Nephric Duct



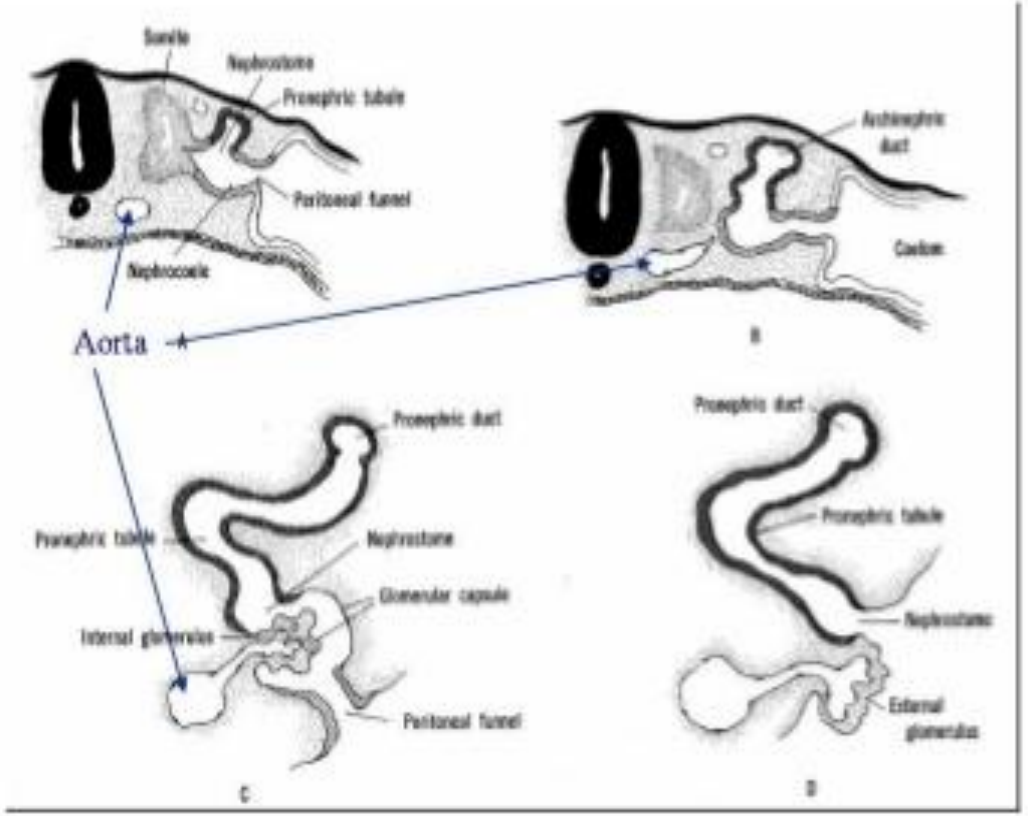
Pronephros

- The PRONEPHROS develops from the cranial most part of urogenital ridge.
- It is transitory and regresses completely by 5 weeks of gestation
- Forms the kidney in larval stages of amphibians and fish
- It is non functional in Humans.



Pronephros
the first kidney

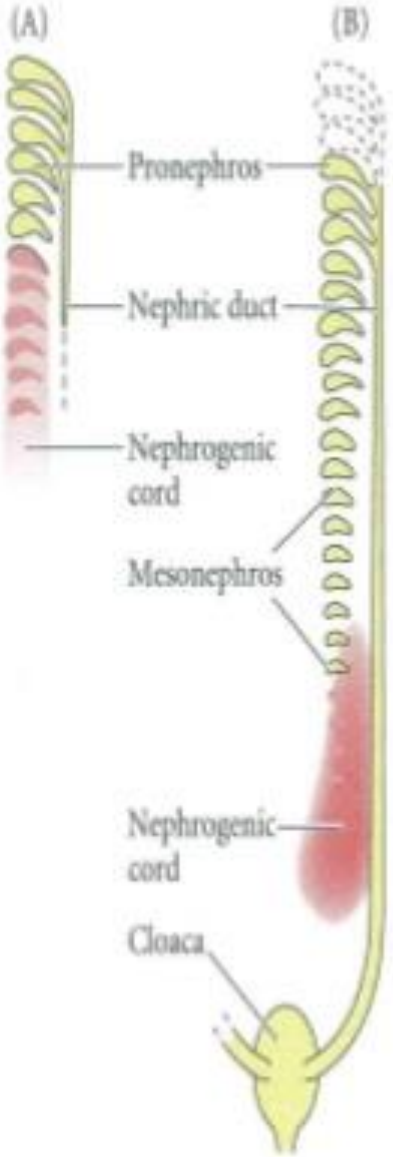
- A cavity, like the coelom develops inside the intermediate mesoderm
- Balls of bloods vessels from the aorta bulge into the space – The Glomerulus.
- The glomerulus allows excess water to leave the blood while salts and macromolecules are retained.
- This kind of kidney is found in primitive fish (eg Lampreys) and in the embryos of most vertebrates

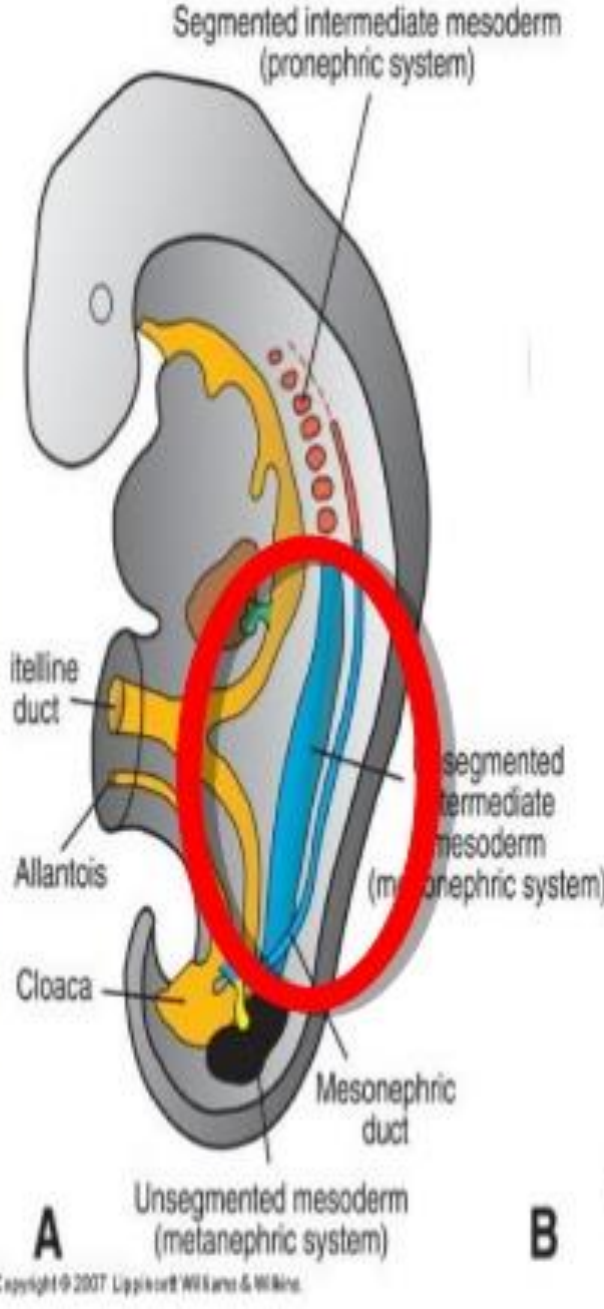


- Initially the water filters into the coelom
- Later, part of the cavity inside the intermediate mesoderm links up with similar parts in adjacent segments to form a duct.

Mesonephros

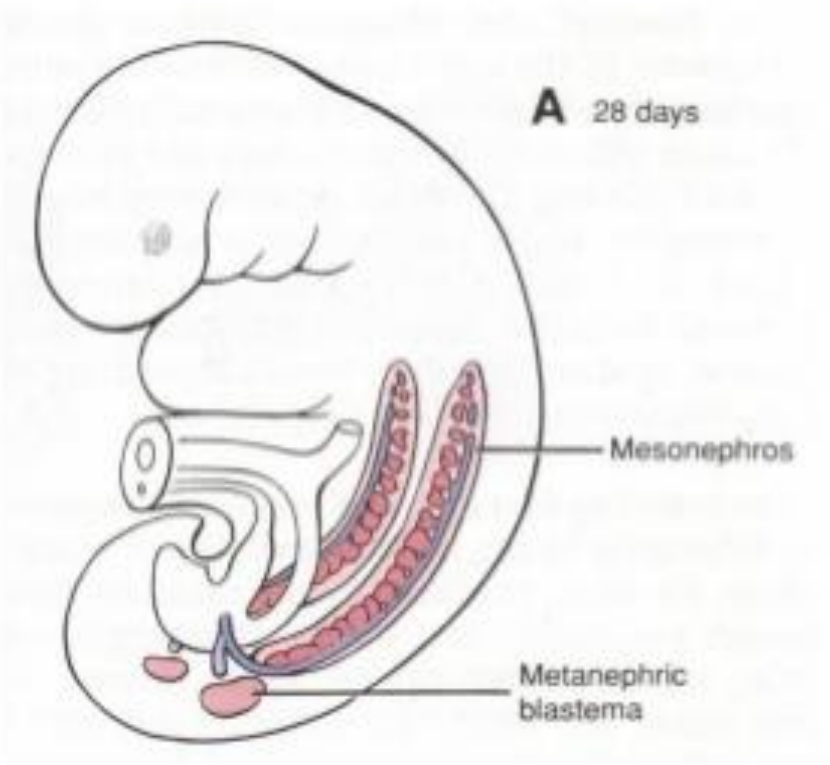
- MESONEPHROS develops caudal to the Pronephros.
- It consists of a series of tubules that drain into the nephric duct, which can be called the Mesonephric duct.
- Excretory organ for embryo until metanephros takes over.
- By the 4th month of gestation-completely disappears.
- Before its degeneration some of its cells migrate and ultimately form the
  Adrenal glands
  Gonads





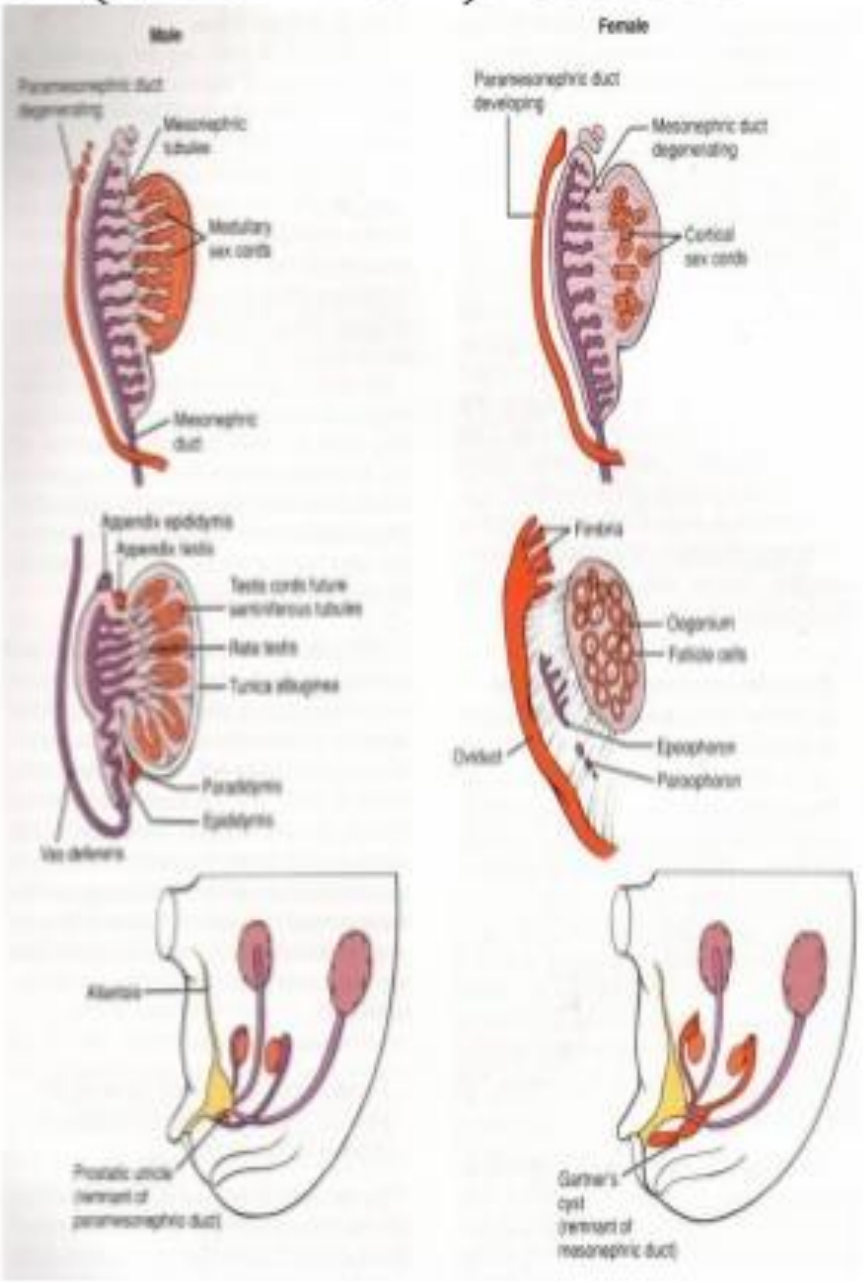
Mesonephros - in humans

- The Mesonephros first appears early in week 4
- In thoracic and lumbar segments of intermediate mesoderm.
- Urine is produced and drains along the mesonephric (Wolfian) duct to the cloaca/bladder
- In week 5 the thoracic segments regress but the mesonephric kidney continues functioning until week 10



Fate of the Mesonephric (Wolfian) ducts

- The development of the metanephric kidney accompanied the changes in the reproductive system.
- The gonads of primitive vertebrates release their eggs and sperm into the coelom, from there they pass via small pores into the cloaca.
- In higher vertebrates the eggs are still released into the coelom, but the cloacal pores have become specialised tubes which open adjacent to the ovary.
- In the embryo, this egg collecting tube (paramesonephric duct) lies parallel to the mesonephric duct.

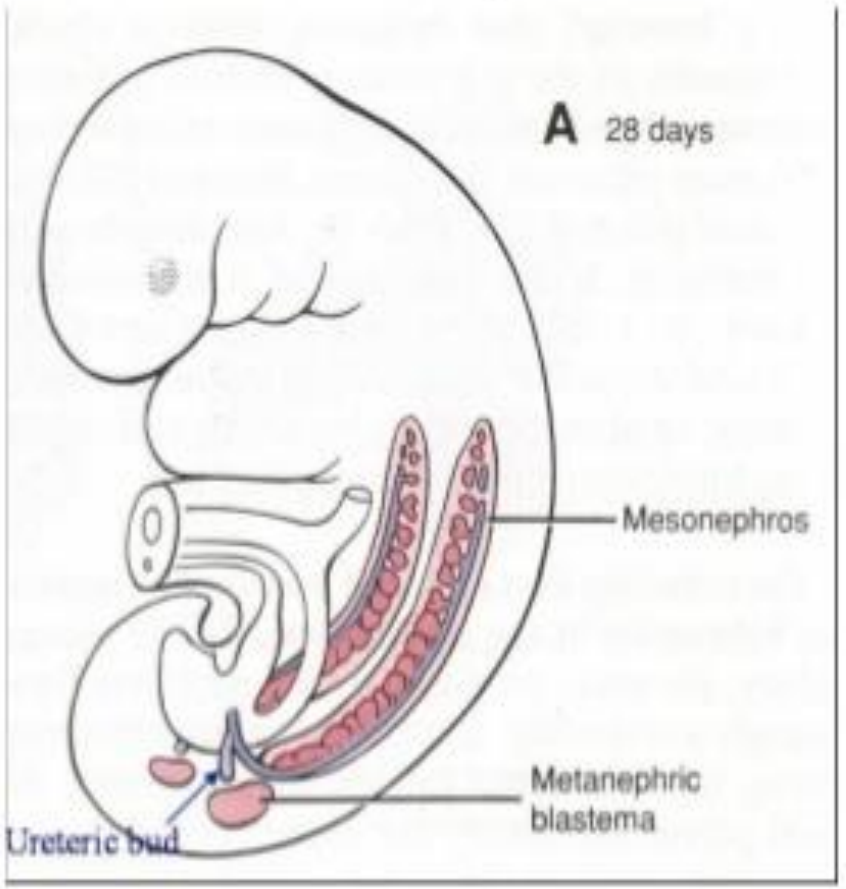


Male and Female genital ducts

- Initially both sexes have both mesonephric and paramesonephric ducts
- In females
  - Eggs are still released into the coelom (peritoneal cavity) but are gathered up in the uterine tubes.
  - The two paramesonephric ducts become the uterine tubes.
  - Distally the paramesonephric ducts fuse together to form the uterus and vagina.
  - The mesonephric duct degenerates completely.
- In higher vertebrates sperm is never released into the coelom but reaches the outside by passing through some derivative of the urinary system. In birds, reptiles and mammals the testis develops a connection with the mesonephric duct (at the time that the mesonephros is degenerating).
- In males
  - The mesonephric duct becomes the ductus deferens, seminal vesicle and parts of the prostate gland.
  - The paramesonephric duct degenerates completely.

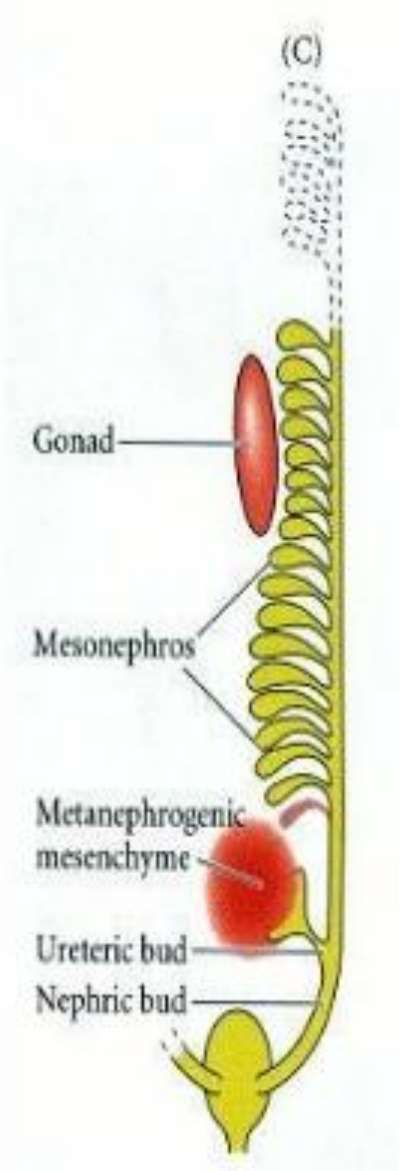
Metanephros – definitive kidney

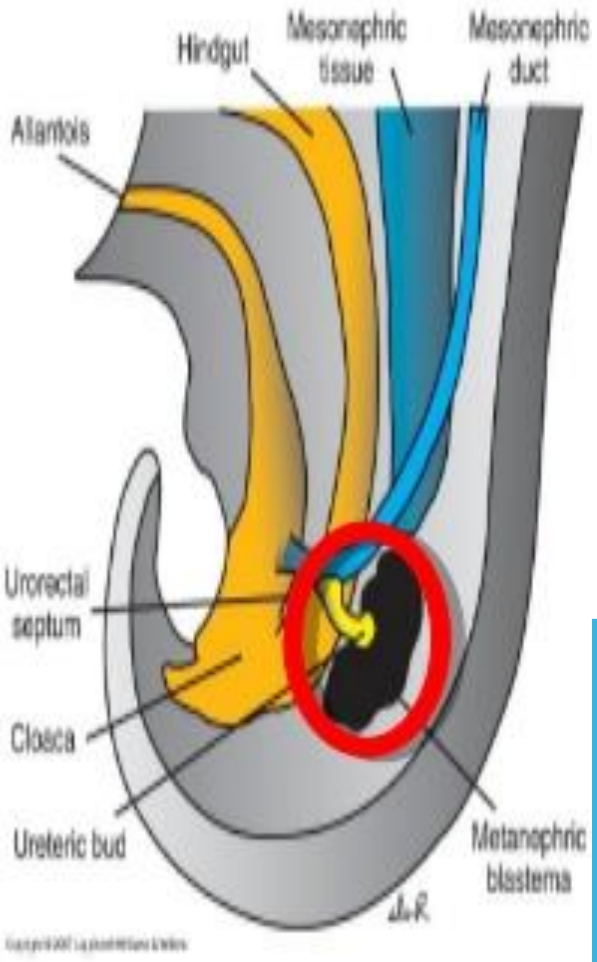
- The metanephros or definitive kidney of higher vertebrates, begins when the metanephric ducts (ureteric buds) sprout from the distal end of the mesonephric duct at about 5 weeks.
- The ureteric buds induce intermediate mesoderm in the sacral region to form a metanephric blastema which forms the glomeruli and tubules of the nephrons.



Metanephros

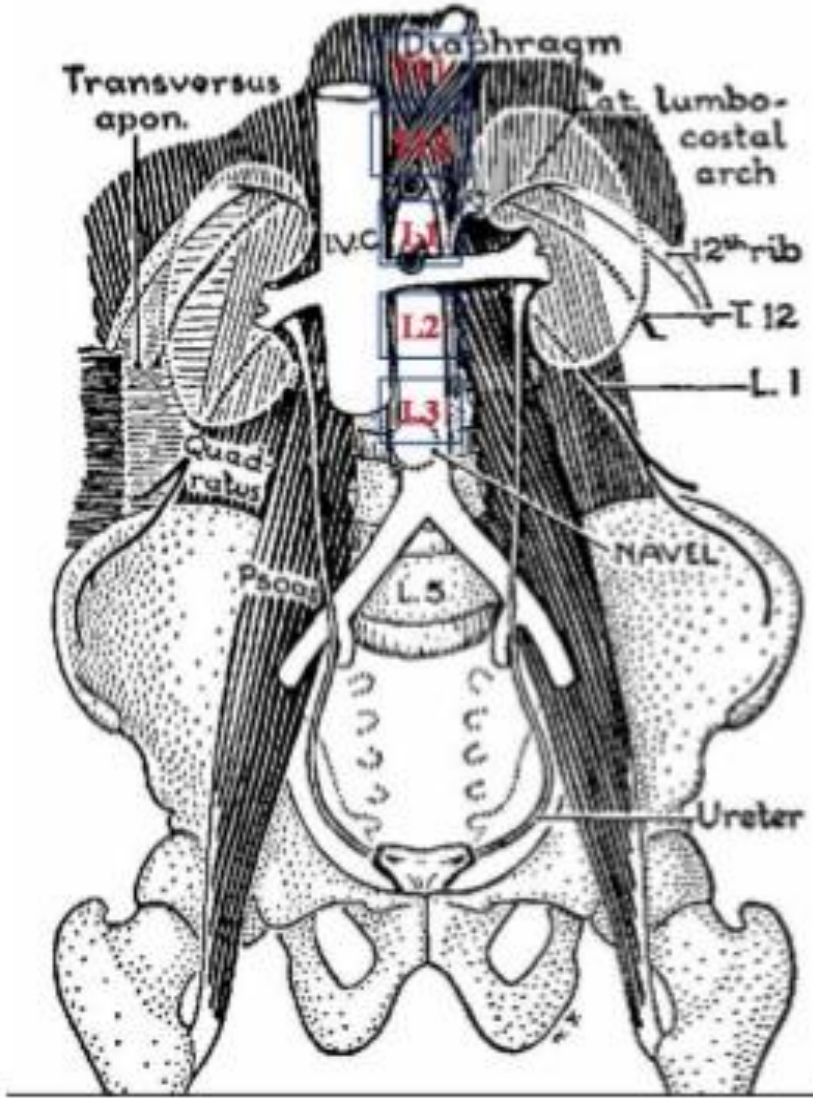
- METANEPHROS, third and final stage of Kidney development
- It results from Reciprocal inductive signals between the Metanephric Mesenchyme (MM) and the Ureteric Bud (UB) at the caudal end of the Urogenital bridge.
- Ureteric bud is an outgrowth at the distal end of the Wolfian duct, first visible at approx. 5 weeks of gestation.





Position of kidneys

- Kidneys lie on the psoas muscle beside the vertebral bodies.
- The diaphragm and 11th and 12th ribs lie behind the upper half of each kidney.
- Therefore they move with breathing
- Left is higher than right (liver)
- Upper poles T12
- Hilum is at L1/2
- Lower poles at L3
- Upper poles are more medial (psoas).
- In the hilum:
  - Renal vein is the most anterior.
  - Followed by renal artery & pelvis/ureter
- Note that the left renal vein is longer .



It crosses the aorta
Is crossed by the SMA
Receives left gonadal vein

Signaling Pathways in Kidney Development

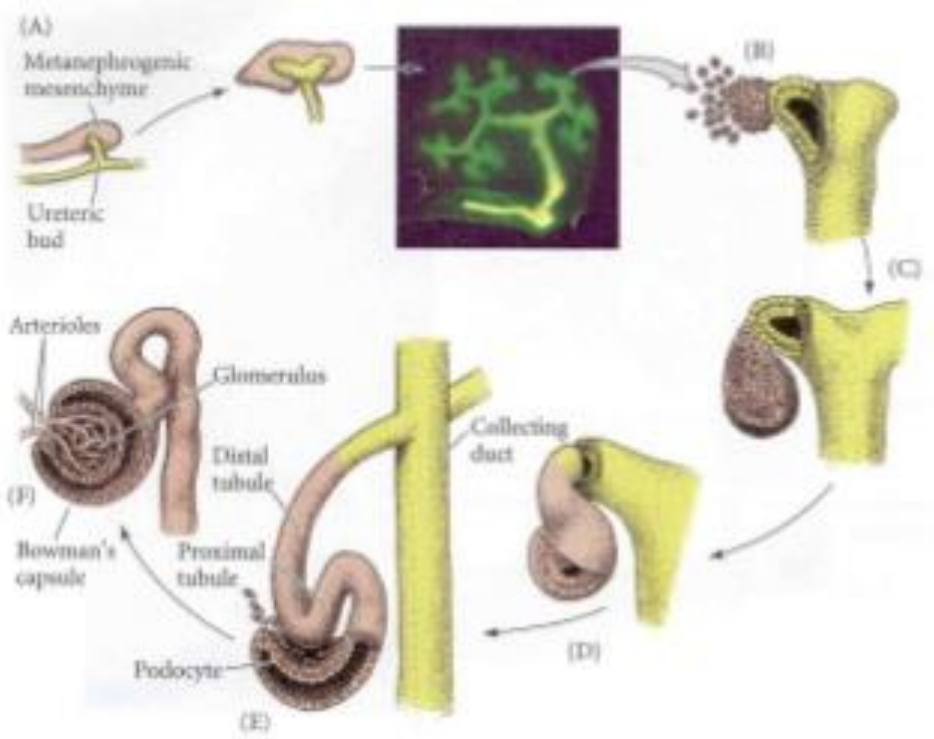
- From MM
  - WT 1
    - Hepatocyte Growth Factor(HGF) & MET
    - Glial derived nuerotrophic factor(GDNF) & RET
- From Ureteric bud
    - Bone morphogenic protein(BMP)
    - Fibroblast growth factor(FGF)

    - PAX-2
    - WNT-4

WT1

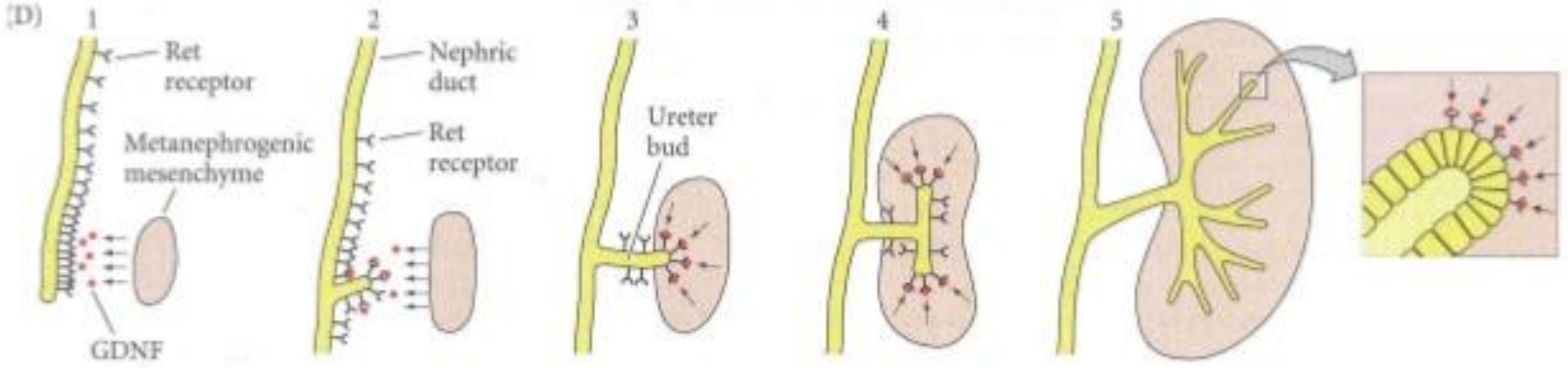
- Wt1 is a transcription factor
- WT1 was originally identified as a gene involved in Wilms tumor, a pediatric cancer in which kidney elements are incompletely differentiated and proliferate to form tumors.
- Wt1 is first expressed in intermediate mesoderm prior to kidney development, and then in the kidney, gonads and mesothelium.
- Makes MM tissue to respond to ureteric bud induction.

WT1 is expressed in the metanephric mesenchyme but not the Wolfian duct or ureteric bud.



As the differentiation proceeds, WT1 expression is lost in the cells of the proximal and distal tubules and retained only in the glomerular podocytes.

GDNF- ret Signaling in Kidney Development



Ret is a tyrosine kinase receptor
Ret is expressed in the Wolfian duct and the ureteric bud.
For stimulation of ureteric bud branching
By the time the bud has branched several times, expression is restricted to the tips of the branches.

Factors from Ureteral Bud

- **Bone morphogenic protein(BMP)**
- **Fibroblast growth factor(FGF)**

- Stimulate proliferation of metanephric mesenchyme

- Maintain production of WT 1.

Factors from Ureteral Bud

- **PAX-2**
- **WNT-4**

- Mainly cause mesenchyme **to epithelialise** in prepation for excretory tubule differentiation.
- Production of **Laminin** and **Type 4 Collagen** to form basement membrane.

Timeline of Kidney Embryology

- Week 4 : appearance of Wolffian or Mesonephric Duct
- Day 28 : formation of Ureteric Bud (UB)
- Week 4-8 : Initial MM induction and UB branching
- Week 8 : First nephrons are formed
- Week 6-8 : kidneys ascend from pelvis to lumbar location
- Week 8-15 : Period of UB branching with stochastic formation of UB ampulla and nephron units
- Week 10 : filtration begins
- Week 32-36: End of Nephrogenesis