

# KIDNEY DEVELOPMENT

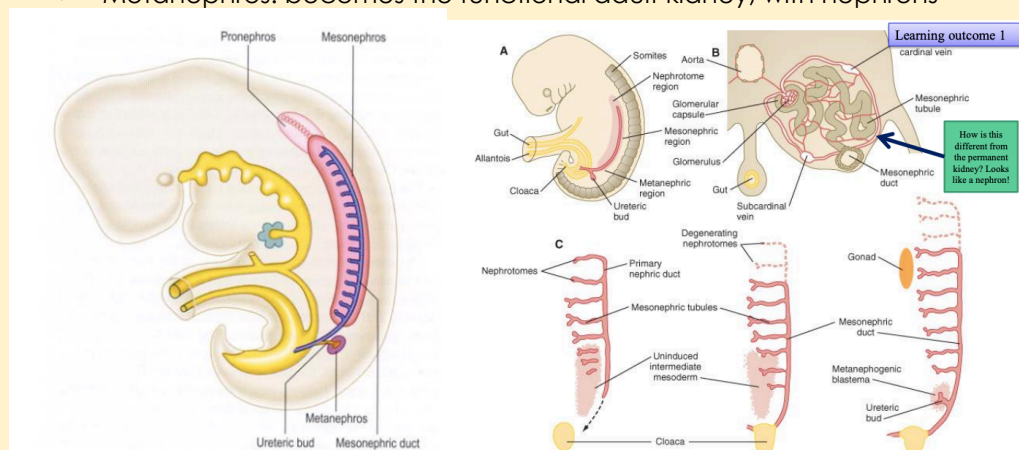
## THREE STAGES OF KIDNEY DEVELOPMENT

Kidney development involves the formation of three distinct excretory organs, each arising from the intermediate mesoderm.

|                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|----------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Pronephros                 | <ul style="list-style-type: none"> <li>The earliest stage of kidney development</li> <li>Begins around 22 days of gestation</li> <li>Consists of about 5-7 nephric vesicles (mesoderm), small hollow epithelial balls</li> <li>Pronephric duct: continuous with the mesonephric duct, which later becomes essential in further kidney development</li> <li>Non-functional in humans, purely a transient structure</li> <li>It degenerates quickly and has no excretory function in humans</li> </ul>                                                                                                                                                                                                                                                                                                                                              |
| Mesonephros                | <ul style="list-style-type: none"> <li>Develops caudally to the pronephros</li> <li>Appears late in the 4<sup>th</sup> week of gestation</li> <li>Contains around 40-42 mesonephric units, though only 30-32 are present at one time</li> <li>Acts as a temporary kidney, providing some basic renal functions such as blood filtration during early development</li> <li>Mesonephric tubules have limited capacity for water retention, distinguishing them from mature nephrons in adults</li> <li>The mesonephros degenerate by the end of the first trimester but leave behind important adult structures (in males, the epididymis, vas deferens, and some lesser-known female structures)</li> <li>In lower vertebrates (like fish), the mesonephros persists as their functional kidney since they don't need to conserve water</li> </ul> |
| Metanephros (adult kidney) | <ul style="list-style-type: none"> <li>The definitive kidney of mammals</li> <li>Emerges late in the first trimester and continues developing postnatally</li> <li>Develops from the most posterior intermediate mesoderm</li> </ul> <p>Key structures:</p> <ul style="list-style-type: none"> <li>Ureteric bud: a critical outgrowth of the mesonephric duct, which induces the formation of the metanephric kidney. It interacts with surrounding metanephric mesenchyme, which eventually forms nephrons</li> <li>Nephrons: the functional units of the kidney responsible for blood filtration and water retention</li> <li>The interactions between the ureteric bud and metanephric mesenchyme are crucial for nephron development and the formation of nephron tubules</li> </ul>                                                          |

## Summary

- Pronephros: transient, non-functional
- Mesonephros: temporary excretory organ, degenerates but leaves essential structures in males
- Metanephros: becomes the functional adult kidney, with nephrons



The development of the kidney involves the interaction between two major components:

- Ureteric bud: derived from the mesonephric duct
- Metanephric mesenchyme: derived from the intermediate mesoderm

These two components undergo reciprocal inductive interactions to form the functional kidney, including the nephrons and the collecting duct system.

### ADULT DERIVATIVES OF THE URETERIC BUD

The ureteric bud gives rise to the collecting duct system which includes:

- Collecting ducts: tubular structures that drain the urine formed in the nephron
- Renal calyces: includes the minor calyces and major calyces
- Minor calyces: receive urine from the collecting ducts of a single renal pyramid
- Major calyces: formed by the convergence of multiple minor calyces
- Renal pelvis: the funnel-shaped cavity that collects urine from the major calyces and directs it into the ureter
- Ureter: the duct through which urine passes from the kidney to the bladder

### ADULT DERIVATIVES OF THE METANEPHRIC MESENCHYME

The metanephric mesenchyme forms the nephrons, the functional units of the kidney that filter blood and urine. Specifically, it gives rise to:

- Nephrons: the functional units of the kidney. Consisting of:
- Glomerulus: a cluster of capillaries that filters blood to form the initial urine (ultrafiltrate)
- Proximal convoluted tubule: the first part of the renal tubule, responsible for reabsorbing nutrients, water, and ions
- Loop of Henle: a long, u-shaped segment that plays a key role in concentrating urine and preserving water
- Distal convoluted tubule: the last part of the renal tubule, involved in further ion exchange and secretion
- Renal interstitium: the connective tissue surrounding the nephron

### MORPHOLOGICAL STAGES IN NEPHROGENESIS

Nephrogenesis, the process of nephron formation, involves the transformation of metanephric mesenchymal cells into epithelial cells, which then form the functional components of the nephron. This process is marked by a series of morphological changes:

#### Mesenchymal condensation

- At the tips of the branches of the ureteric bud, metanephric mesenchyme cells condense to form a pre-tubular aggregate
- These cells are unpolarised at this stage

#### Formation of epithelial vesicle

- The pre-tubular aggregate undergoes mesenchymal-to-epithelial transformation (MET), forming an epithelial vesicle
- The cells become polarised, meaning they develop an apical and basal surface with a small lumen in the centre

#### Comma-shaped body

- The vesicle elongates and forms a structure resembling a comma, called the comma-shaped body
- This marks the early formation of the nephron structure

#### S-shaped body

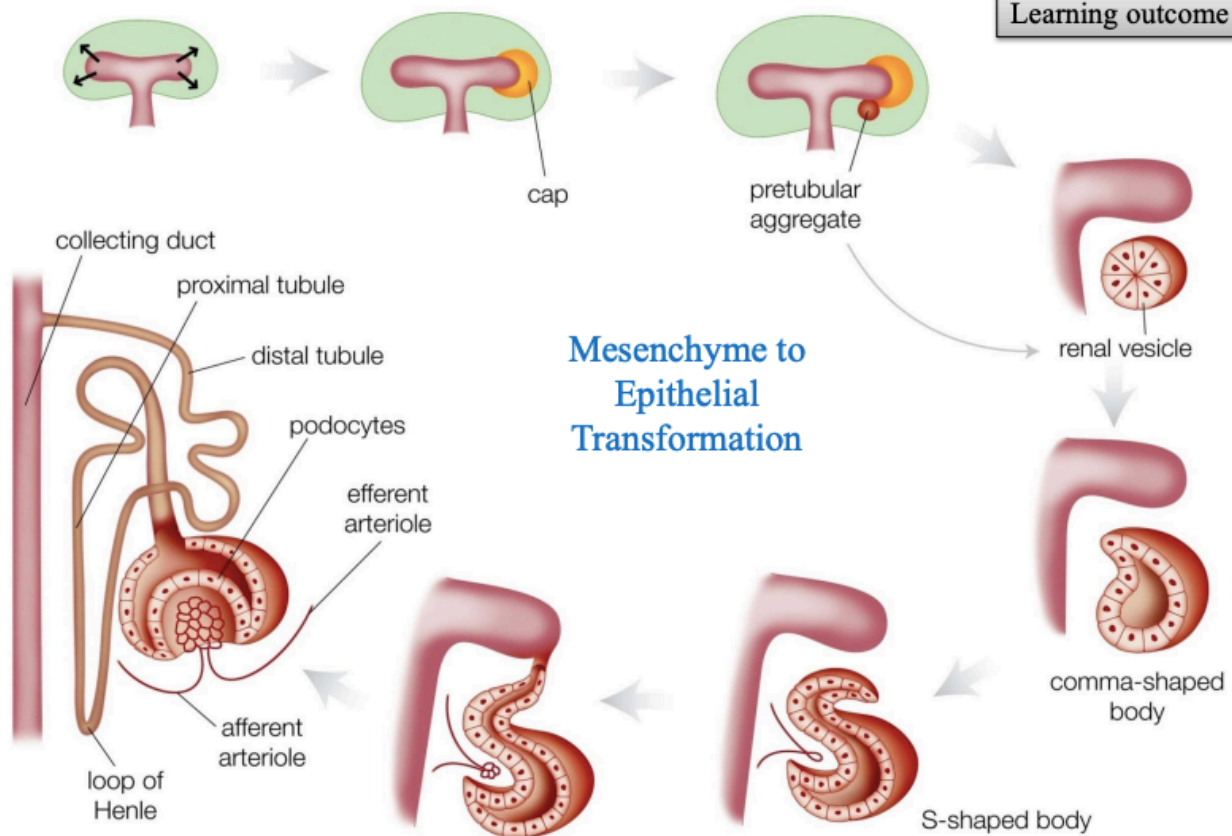
- The comma-shaped body further develops into the s-shaped body
- This structure starts to resemble the nephron and includes the glomerular capillaries forming at one end, alongside the early renal tubules

#### Capillary loop stage

- The glomerulus begins to form fully, with capillaries invaginating into the nephron, creating the Bowman's capsule
- At this stage, the nephron connects to the collecting duct system derived from the ureteric bud

#### Mature nephron formation

- The S-shaped body matures into a fully formed nephron, composed of:
- Glomerulus: The site of blood filtration
- Proximal convoluted tubule: For reabsorption
- Loop of Henle: For water conservation and concentration of urine
- Distal convoluted tubule: Final adjustment of ion balance
- The nephron attaches to the collecting duct system, forming a continuous tubular structure through which urine flows to the renal pelvis



### NEPHROGENIC ZONE

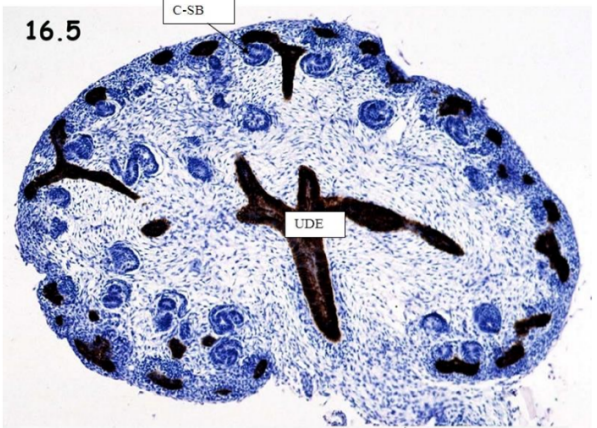
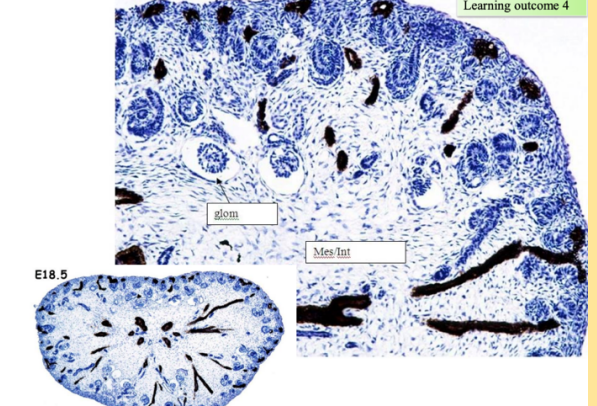
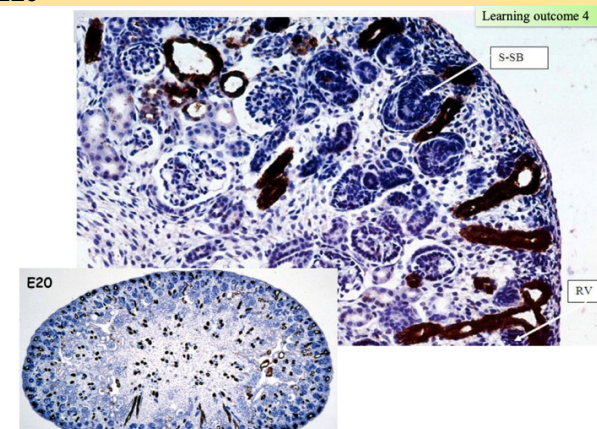
- The nephrogenic zone is the outermost region of the kidney, located in the cortex
- It is where nephrogenesis, or the formation of new nephrons, occurs
- Nephron formation happens at the tips of the ureteric buds through reciprocal inductive interactions between the ureteric bud and the metanephric mesenchyme
- Nephrogenesis continues postnatally, but the nephrogenic zone can be observed in embryos at various stages of development

### Key structures identified in nephrogenesis

In rat kidney development (stained with DBA for ureteric bud epithelium), the stages of nephron formation can be clearly seen at different embryonic stages (E16, E18, E20):

|                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ureteric bud (epithelium)        | <ul style="list-style-type: none"> <li>• The ureteric bud appears brown when stained with DBA and is responsible for the formation of the collecting ducts.</li> <li>• Branching morphogenesis of the ureteric bud occurs, and at the tips of these branches, nephrons begin to form.</li> <li>• The ureteric bud is clearly seen in cross-sections of the kidney cortex at each stage of development (E16, E18, E20).</li> </ul> |
| Metanephric mesenchyme           | <ul style="list-style-type: none"> <li>• Appears blue in stained sections and surrounds the ureteric bud.</li> <li>• Interacts with the ureteric bud to form nephrons, contributing to the development of glomeruli and tubules.</li> </ul>                                                                                                                                                                                       |
| Comma-shaped and s-shaped bodies | <ul style="list-style-type: none"> <li>• Nephron formation begins with the appearance of comma-shaped bodies, followed by S-shaped bodies, both located at the tips of the ureteric bud branches.</li> <li>• These bodies represent the early stages of nephron development.</li> <li>• The nephrogenic zone is highly active with these structures at E16.5 and E18.5, indicating ongoing nephrogenesis</li> </ul>               |

## EMBRYONIC DEVELOPMENTAL STAGES IN THE NEPHROGENIC ZONE

|                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>E16.5</p>  <p>16.5</p> <p>C-SB</p> <p>UDE</p>                                 | <ul style="list-style-type: none"> <li>Nephrogenesis is very active, with the presence of S-shaped bodies and vesicles.</li> <li>No mature glomeruli are present at this stage, but the nephrogenic zone is clearly visible at the periphery of the kidney.</li> <li>The staining of the ureteric bud epithelium and the surrounding metanephric mesenchyme highlights the ongoing interactions that lead to nephron formation.</li> </ul>                                |
| <p>E18.5</p>  <p>Learning outcome 4</p> <p>glom</p> <p>Mes/Int</p> <p>E18.5</p> | <ul style="list-style-type: none"> <li>Mature glomeruli start to appear in the cortex, marked by the formation of Bowman's capsules and the urinary space for plasma ultrafiltrate.</li> <li>Nephrogenesis is still occurring, with S-shaped bodies, renal vesicles, and comma-shaped bodies visible in the nephrogenic zone.</li> <li>This indicates that even as mature nephrons form, new nephrons are still being induced at the tips of the ureteric buds</li> </ul> |
| <p>E20</p>  <p>Learning outcome 4</p> <p>S-SB</p> <p>RV</p> <p>E20</p>         | <ul style="list-style-type: none"> <li>Mature glomeruli are more prevalent, and fully formed nephrons can be observed.</li> <li>However, nephrogenesis is still ongoing, as indicated by the presence of S-shaped bodies in the nephrogenic zone.</li> <li>The nephrogenic zone remains a highly active area at the periphery of the kidney, where new nephrons continue to be induced and developed</li> </ul>                                                           |

### SIGNIFICANCE OF THE NEPHROGENIC ZONE

- The nephrogenic zone is responsible for the ongoing development of nephrons during both prenatal and postnatal life.
- The deeply stained nephrogenic zone at the kidney's periphery marks the site of active nephron formation, highlighting the developmental gradient from immature to mature nephrons.
- Even as mature glomeruli and collecting ducts form deeper in the kidney, the outer nephrogenic zone remains active, supporting new nephron formation

#### Key points of nephrogenic zone development

- Nephron formation occurs only at the tips of the ureteric ducts through reciprocal induction between the ureteric bud and metanephric mesenchyme.
- Mature glomeruli begin to appear by E18.5, but nephrogenesis continues well into later stages, evidenced by the presence of S-shaped bodies.
- The periphery of the kidney remains a highly active site for nephron formation, even as the kidney matures