nephrons in the kidney generate urine that is propelled to the ureters and then to the bladder for storage and excretion

The Urinary outflow tract:
- monitors and regulates extra-cellular fluids
- excretes harmful substances in urine, including nitrogenous wastes (urea)
- returns useful substances to bloodstream
- maintain balance of water, electrolytes (salts), acids, and pH in the body fluids

Formation of Urine:
- blood filtered to the glomerulus
capillary walls thin
blood pressure higher inside capillaries than in Bowman’s capsule

Formation of Urine
- nitrogen-containing waste products of protein metabolism, urea and creatinine, pass on through tubules to be excreted in urine
urine from all collecting ducts empties into renal pelvis
urine moves down ureters to bladder
empties via urethra
Formation of Urine

in healthy nephron, neither protein nor RBCs filter into capsule
in proximal tubule, most of nutrients and large amount of water reabsorbed back to capillaries
salts selectively reabsorbed according to body’s needs
water reabsorbed with salts

The urogenital system derives predominantly from intermediate mesoderm

During development, 3 successive kidneys form:

pronephros in an early embryo
A metanephros is always drained exclusively by one duct, the ureter. In birds and reptiles, the ureter separates from the nephric duct and enters the cloaca. In mammals, the ureter separates from the nephric duct and enters the bladder.

renal development begins when the ureteric bud invades kidney mesenchyme (the metanephric blastema)
How are the diverse cell types in the kidney, ureter and bladder formed?
The kidney forms via interactions between 3 main cell types:

- collecting ducts
- nephrons
- interstitium

Local proliferation at ureteric bud tips forms an ampulla.

The ampulla splits to form two new tips.

The collecting duct system grows by dichotomous branching.
Nephrons form exclusively at ureteric bud tips in response to local signals.

Nephron progenitors condense at ub tips, aggregate, and trans-differentiate into epithelial cells that make up Comma and S-shaped bodies.

Nephrons differentiate from mesenchymal progenitors.

Diverse cell types lining the nephron perform distinct functions.
Reciprocal signaling between epithelial and mesenchymal cell types is crucial for organ formation.

Reciprocal signaling is required for branching morphogenesis and for nephron differentiation during renal development.

co-culture experiments demonstrate reciprocal signaling between ureteric bud epithelial and nephron progenitors.

• no ureteric bud, nephron progenitors undergo apoptosis.
no nephron progenitors, no branching morphogenesis

signals from the ureteric bud control nephron induction

signals from nephron progenitors control branching morphogenesis

Ret/Gdnf signaling exemplifies a reciprocal loop

The Ret gene is expressed in ureteric bud tips where it controls branching morphogenesis

Gdnf secreted by nephron progenitors binds to Ret via the Ret receptor (Gfra1) inducing branching morphogenesis

GDNF signals through GFRα-1 and RET

GDNF

GFRα-1

RET

P

P

TYROSINE KINASE
deletion of Ret, Gdnf or the Ret receptor Gfra1 results in renal agenesis or hypoplasia

Connecting the upper and lower urinary tract

physical or functional blockage that impedes urine flow can cause renal scarring, hydronephrosis or end state renal disease

renal filtrate must be efficiently propelled to the bladder for storage and excretion
How does the lower urinary tract form?

The cloaca is partitioned into the hindgut and urogenital sinus by the urorectal septum.

As the embryo grows, the ureters lengthen, and the kidneys rotate and ascend along the dorsal body wall.

The urogenital sinus forms the bladder and the urethra.
The renal pelvis, ureters and bladder are lined with a transitional epithelium (the urothelium).

Urine transport depends on peristalsis.

Ureters are surrounded by 2-3 coats of longitudinal and circular muscle that mediate myogenic peristalsis.

Myogenic peristalsis is initiated in the renal pelvis moving a bolus of urine to the ureter then to the bladder.

The Bladder

The ureter is initially joined to the Wolffian duct (future vas deferens) not to the bladder.

Mature connections are established when the ureter orifice is transposed from the posterior Wolffian duct (the common nephric duct) to the bladder.
Urine transport depends on proper connections between the ureters and the **bladder trigone**

**Accepted model of ureter transposition**

- **Accepted model of ureter transposition**
- **form of the trigone from the common nephric duct** repositions the ureters in the bladder

- According to the accepted model, trigone formation is considered to be crucial for repositioning the ureter orifice

  - during ureter transposition, the **cnd** is incorporated into the bladder where it expands to form the **trigone** effectively separating the ureter orifice from the Wolffian duct

**The trigone** is defined as the portion of the urogenital sinus that lies between the ureters and sex ducts
the flap valve is an anti-reflux mechanism that prevents urine back flow

its function depends on proper insertion of the ureter orifice in the bladder

proper positioning of the ureter orifice is necessary for:
- formation of patent connections along the outflow tract
- preventing reflux

defects in position, can cause obstruction or reflux, inducing severe renal damage

using mouse models to re-assess the mechanism of ureter transposition:

expression of Jelly Fish green fluorescent protein in the mouse common nephric duct of this transgenic mouse enables us to follow its fate during ureter insertion

Ureter transposition depends on apoptosis of the common nephric duct, which does not form the trigone
A revised model of ureter transposition

- E11: the common nephric duct is absorbed into the expanding urogenital sinus. The ureter makes direct contact with and inserts into the urogenital sinus.
- E12: apoptosis of the common nephric duct enables the ureter orifice to detach from the Wolffian duct.
- E13: continued growth and expansion of the urogenital sinus moves the ureter orifice further anterior to the bladder neck.

**Forget this revised model of ureter transposition when you take your boards; the new model is published but not in the text books yet. Remember it however as an example of how modern tools will allow us to directly examine other embryological models of organogenesis!!**