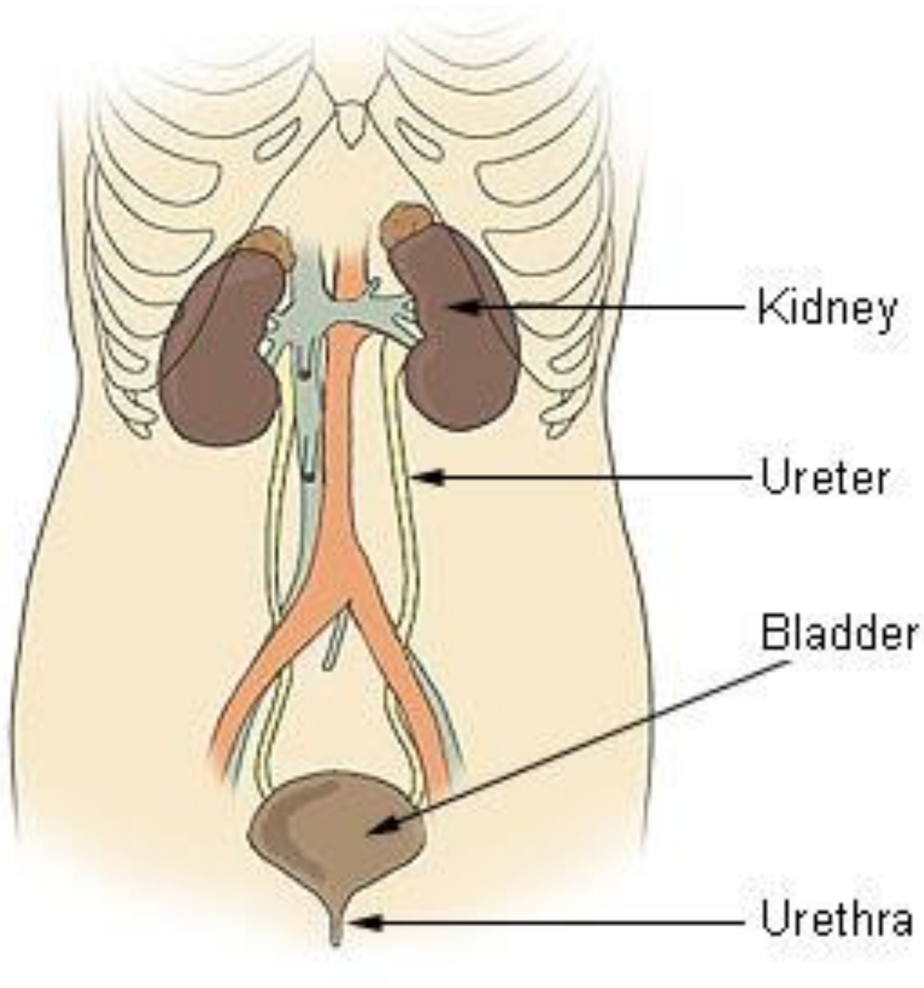
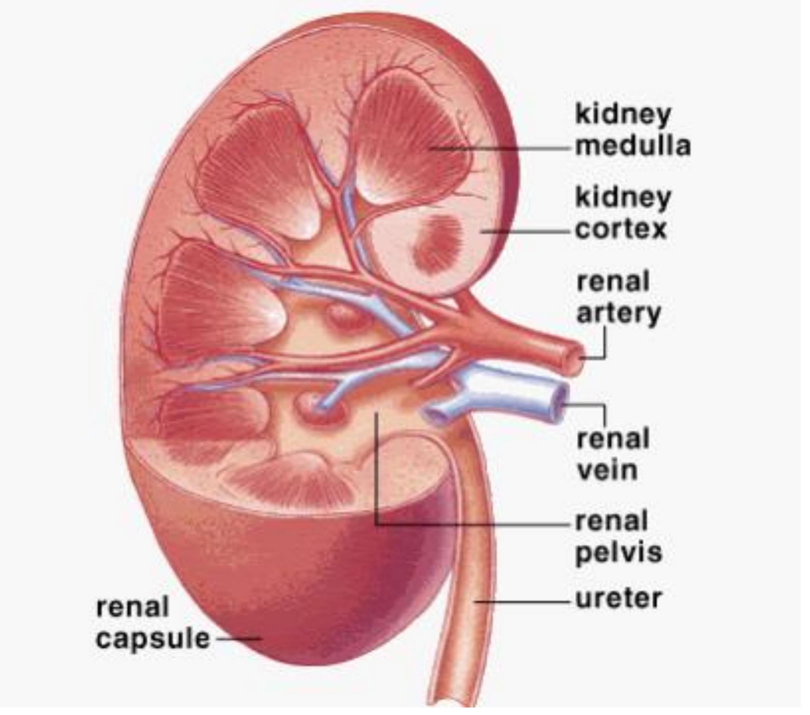
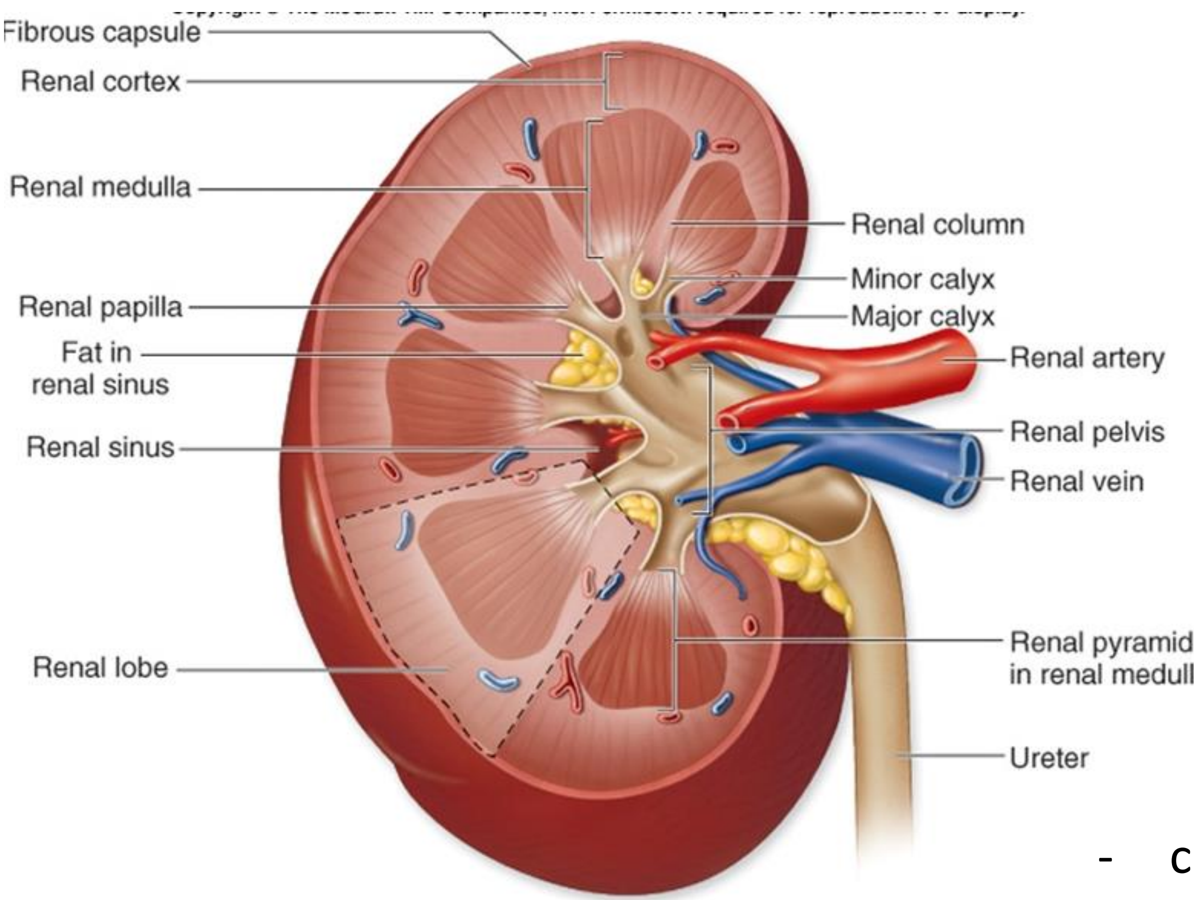
URINARY SYSTEM



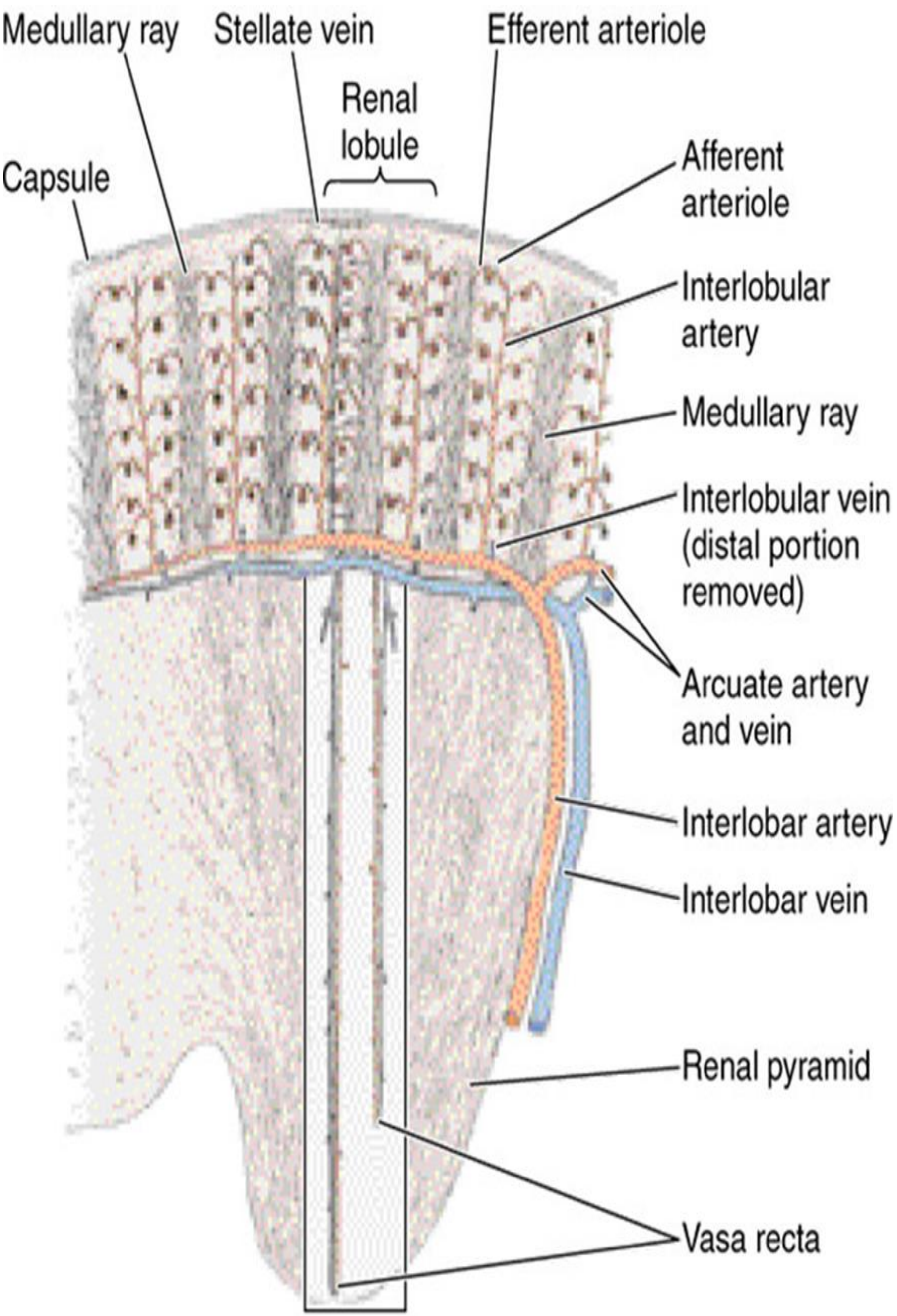
FUNCTIONS

- ✓ formation of urine (elimination of metabolic waste products)
- ✓ regulation of fluid and electrolyte balance
- ✓ regulation of blood pressure
- ✓ synthesis and release of erythropoietin



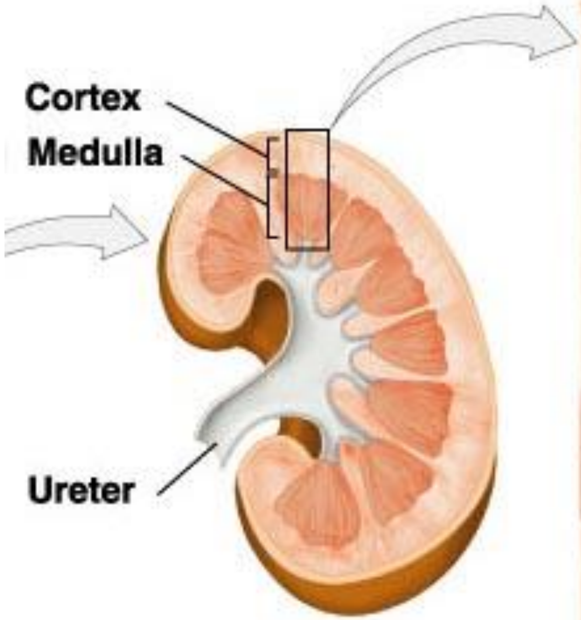


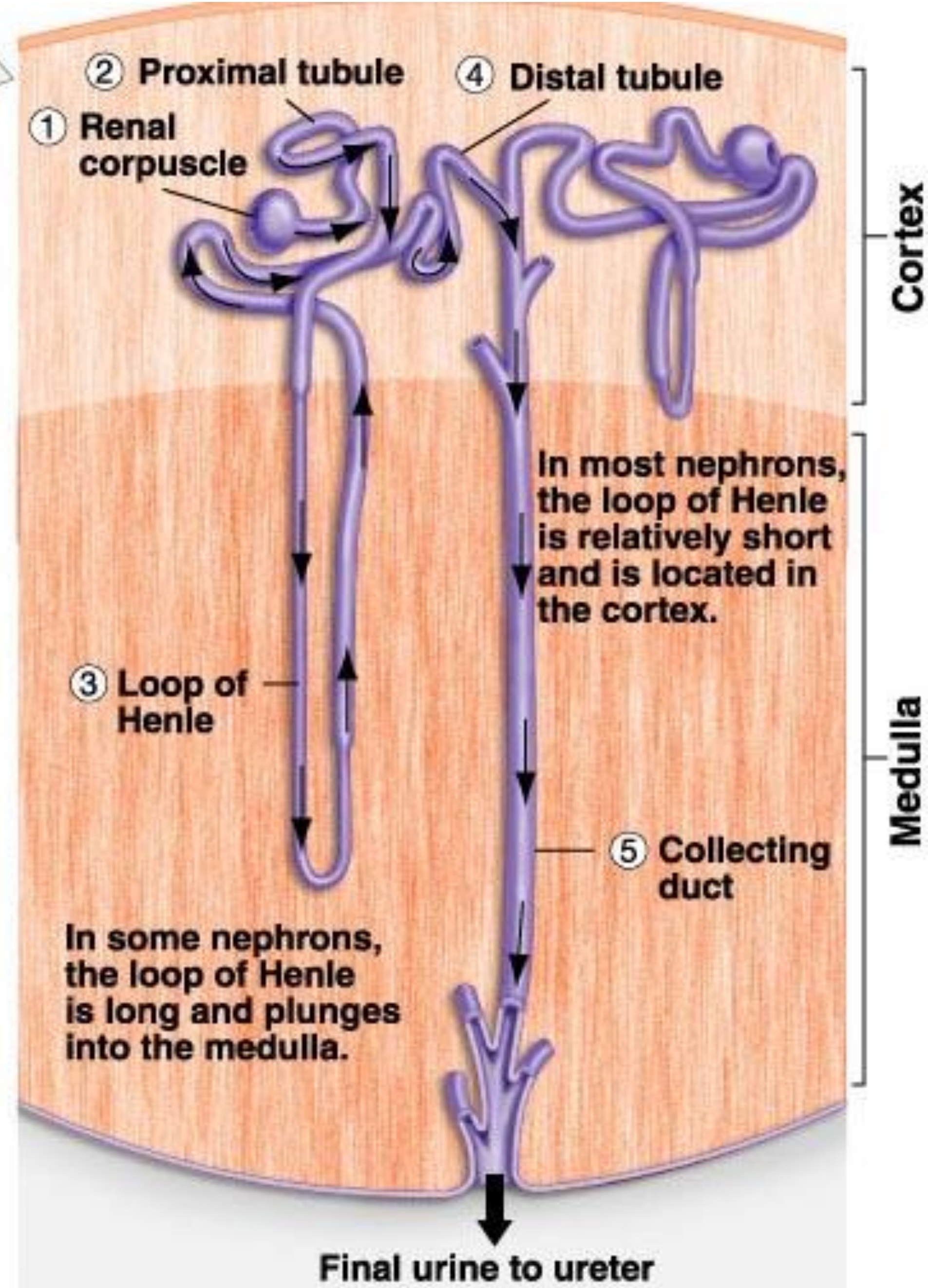
- connective tissue **capsule**
- is subdivided into an outer **cortex** and inner **medulla**
- **medulla** forms **renal pyramids (27 – 30)**



Kidney - blood supply

- receive blood from the **renal arteries**
- each renal artery branches into **segmental arteries**, dividing further into **interlobar arteries**
- the interlobar arteries supply blood to the **arcuate arteries** (run through the boundary of the cortex and the medulla).
- each arcuate artery supplies several **interlobular arteries** that feed into the **afferent arterioles** that supply the glomeruli
- the veins follow the same pattern

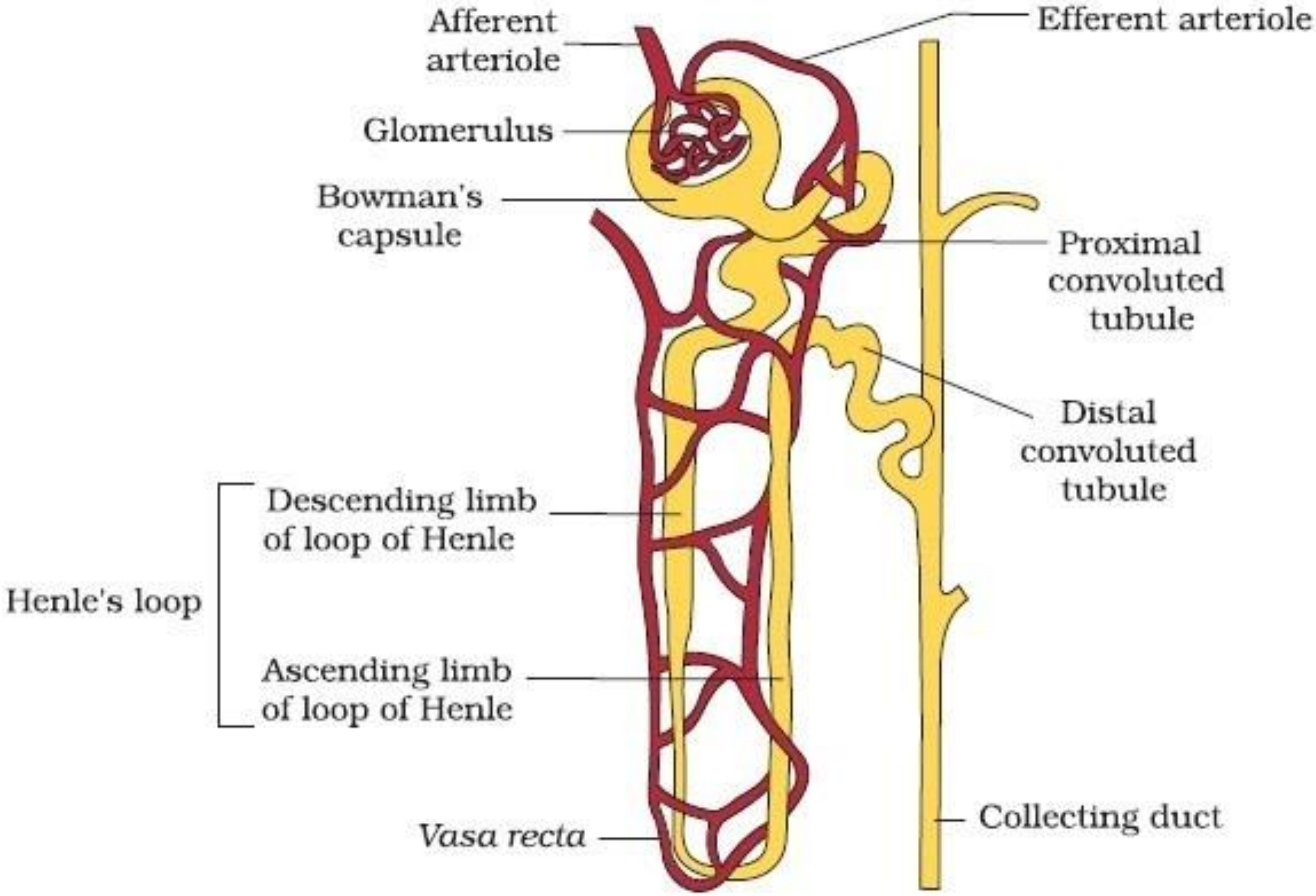




Nephron

- each nephron is composed of **renal corpuscle, proximal tubule, loop of Henle** and **distal tubule**
- two types of nephrons:

Cortical nephrons
Juxtamedullary nephrons



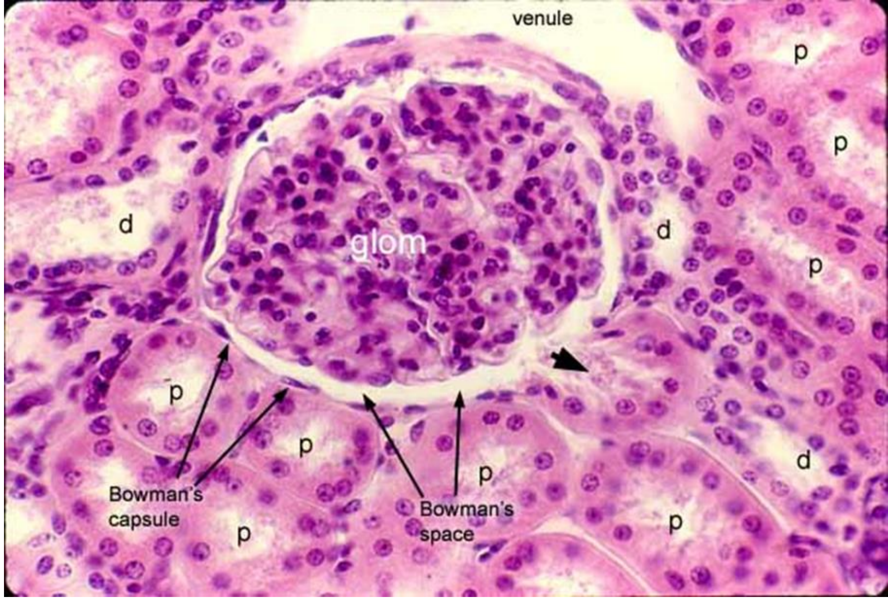
- glomerulus is supplied by **afferent glomerular arteriole** and drained by **efferent glomerular arteriole**
- **efferent glomerular arteriole** of juxtamegullary nephrons branches off, enters the medulla, and surrounds the loop of Henle – form **vasa recta**
- **vasa recta** are necessary for the concentration of urine

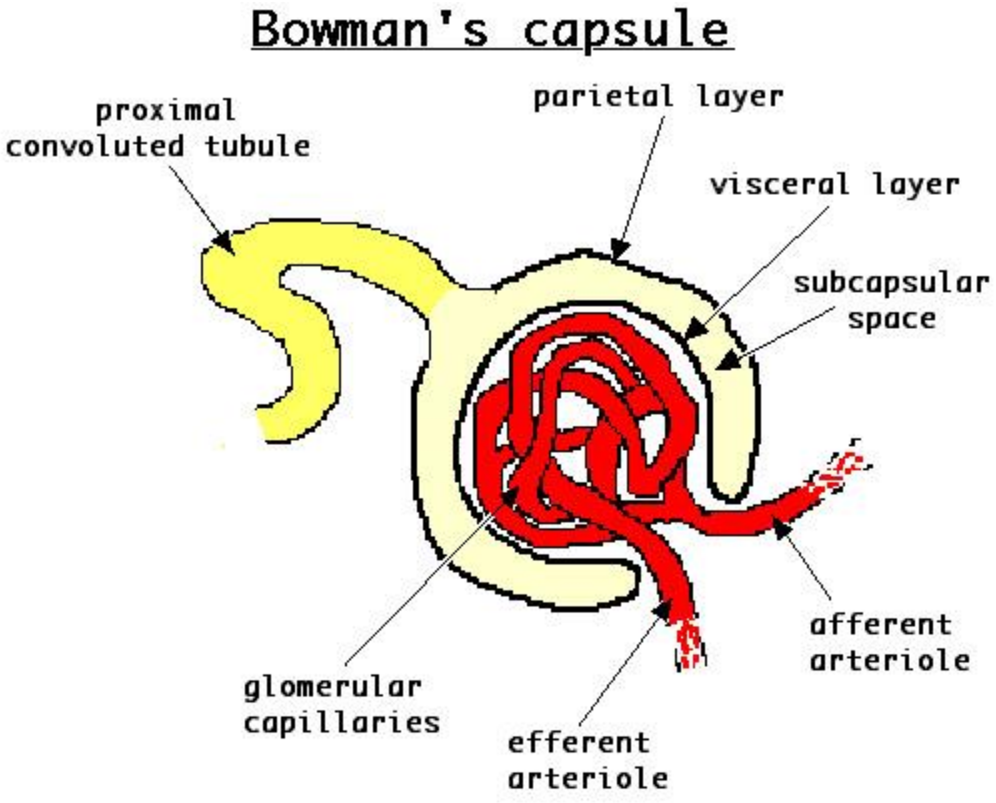
Renal corpuscle - Bowman's capsule

Visceral layer of Bowman's capsule
- composed of modified epithelial cells - **podocytes**

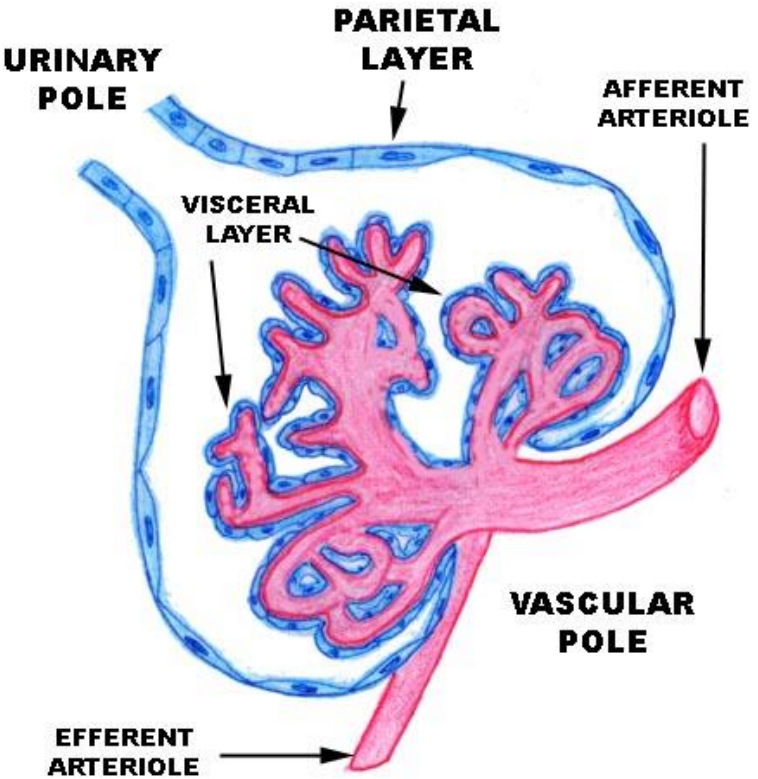
Parietal layer of Bowman's capsule
- simple squamous epithelium

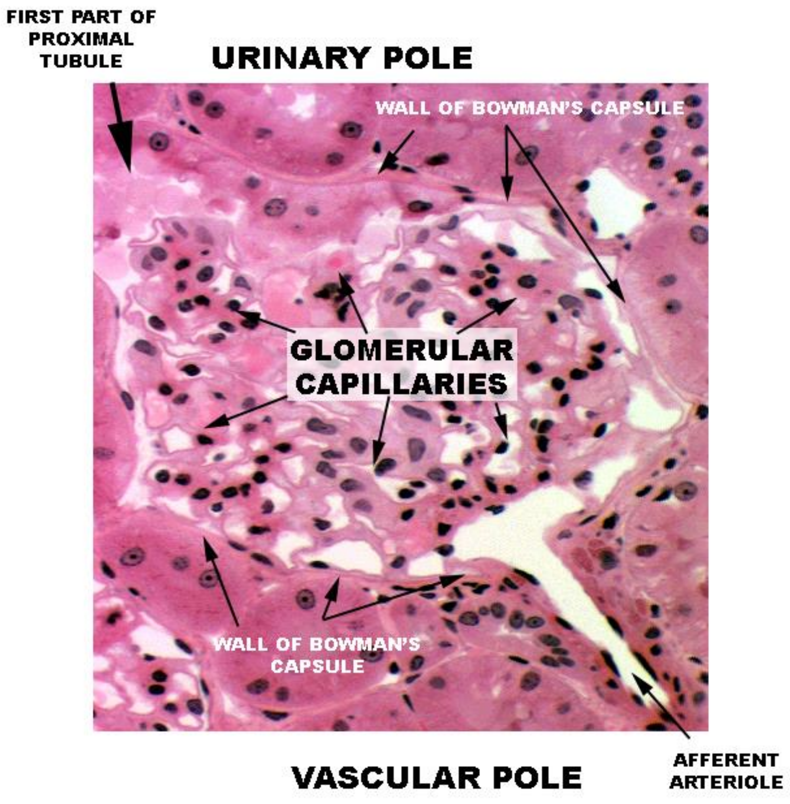
Bowman's space (urinary space) – between the visceral and parietal layers, of Bowman's capsule into which the filtrate enters after filtration.





Glomerulus is completely **arterial bed** –
is supplied by **afferent glomerular arteriole**
and drained by **efferent glomerular arteriole**

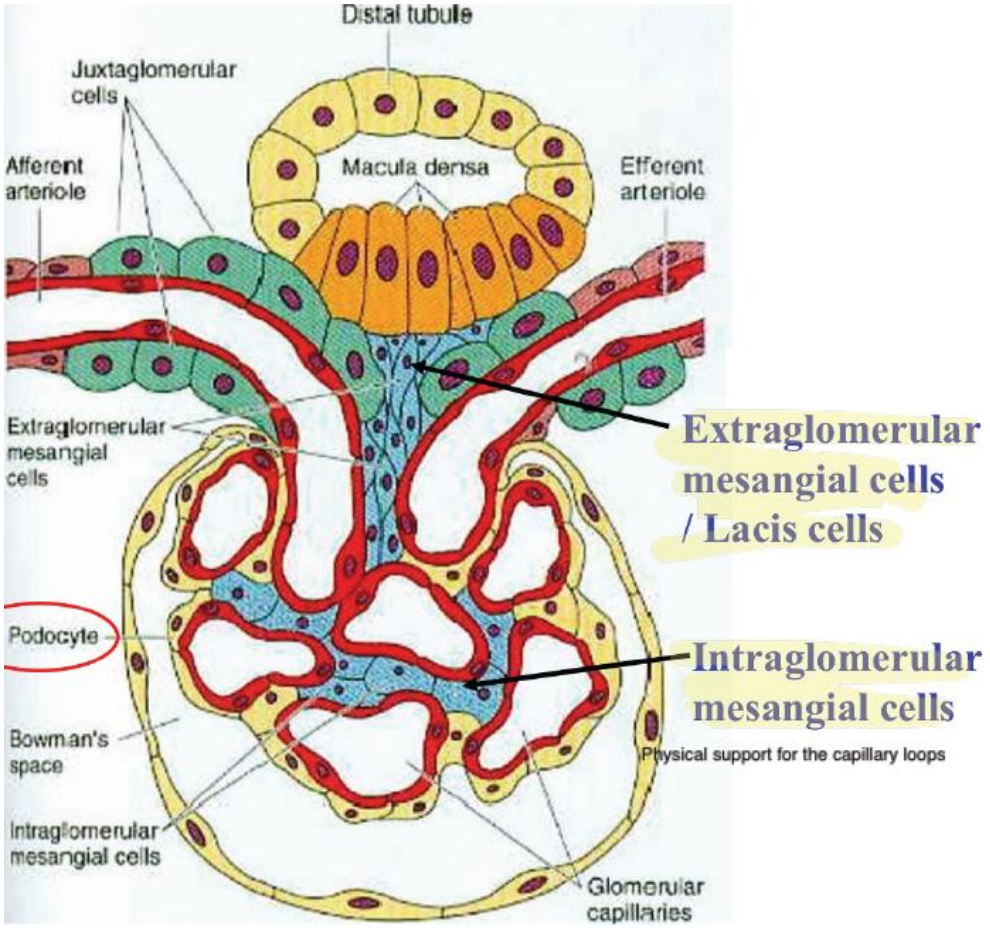




Glomerulus

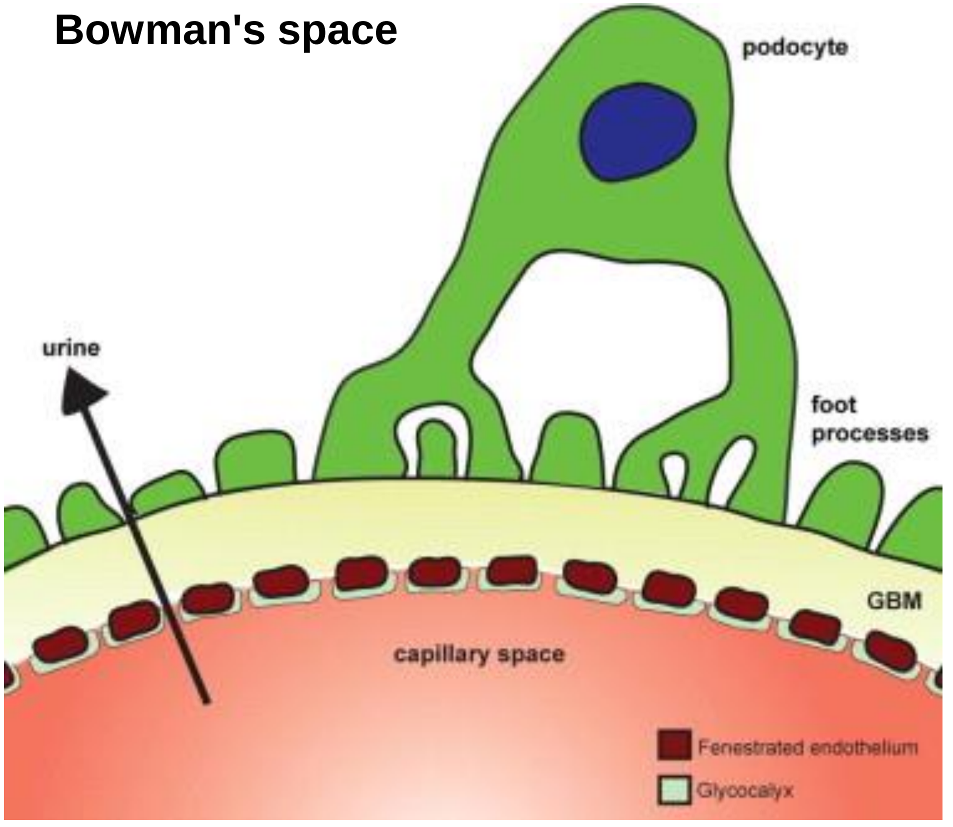
- is composed of **fenestrated capillaries** and **mesangial cells**

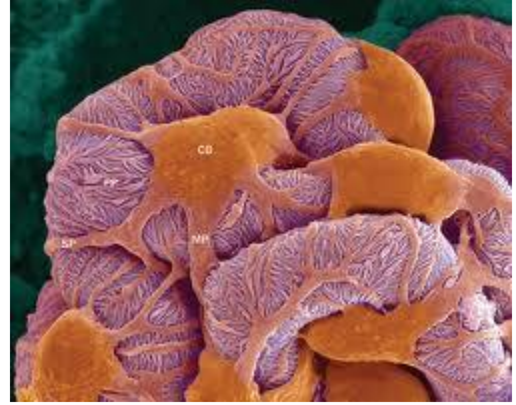
- **extraglomerular mesangial cells**
- located at the vascular pole
- **intraglomerular mesangial cells**
- pericyte-like cells situated within the renal corpuscle – provide **physical support** to the capillary, **phagocytosis** and **regulate blood flow** of the glomerular capillaries by their contractile activity



Filtration barrier

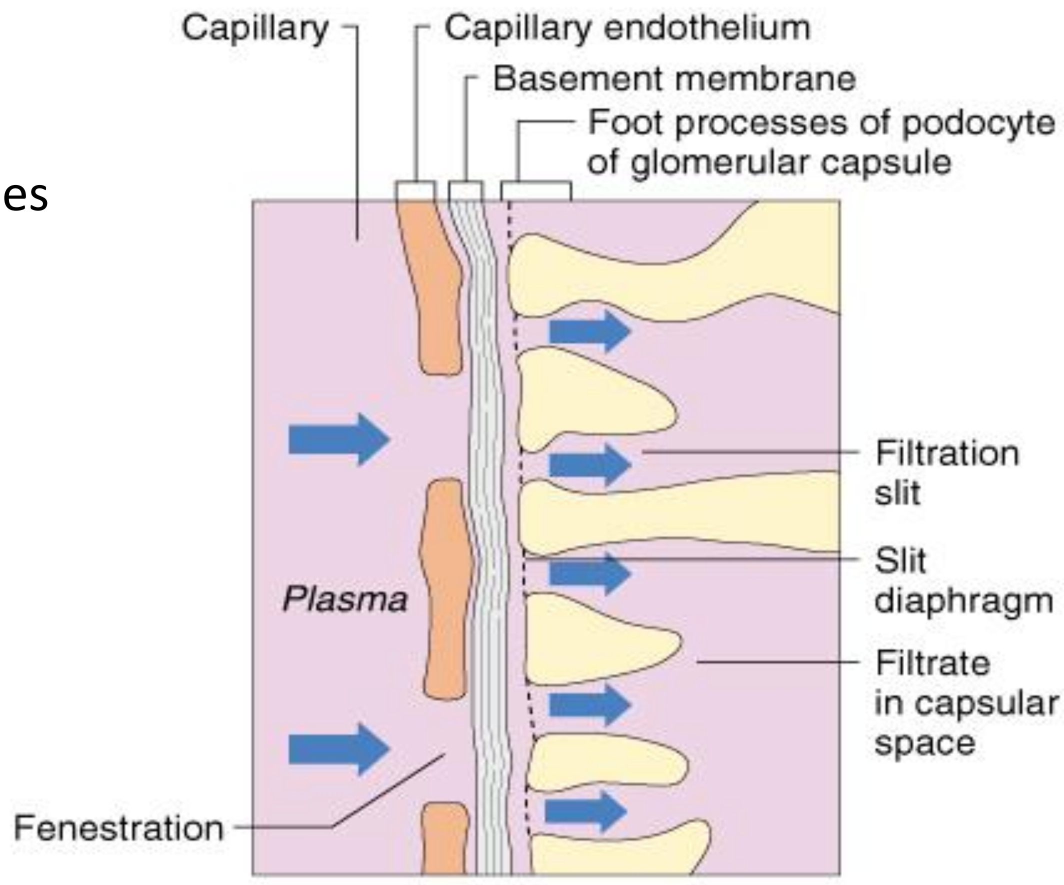
- the blood plasma is filtered through the capillaries of the glomerulus
- **glomerular capillary endothelial cells (**contain numerous pores – fenestrae)**, glomerular basement membrane (**very thick)**, and podocytes** (visceral layer of Bowman's capsule) into the Bowman's space





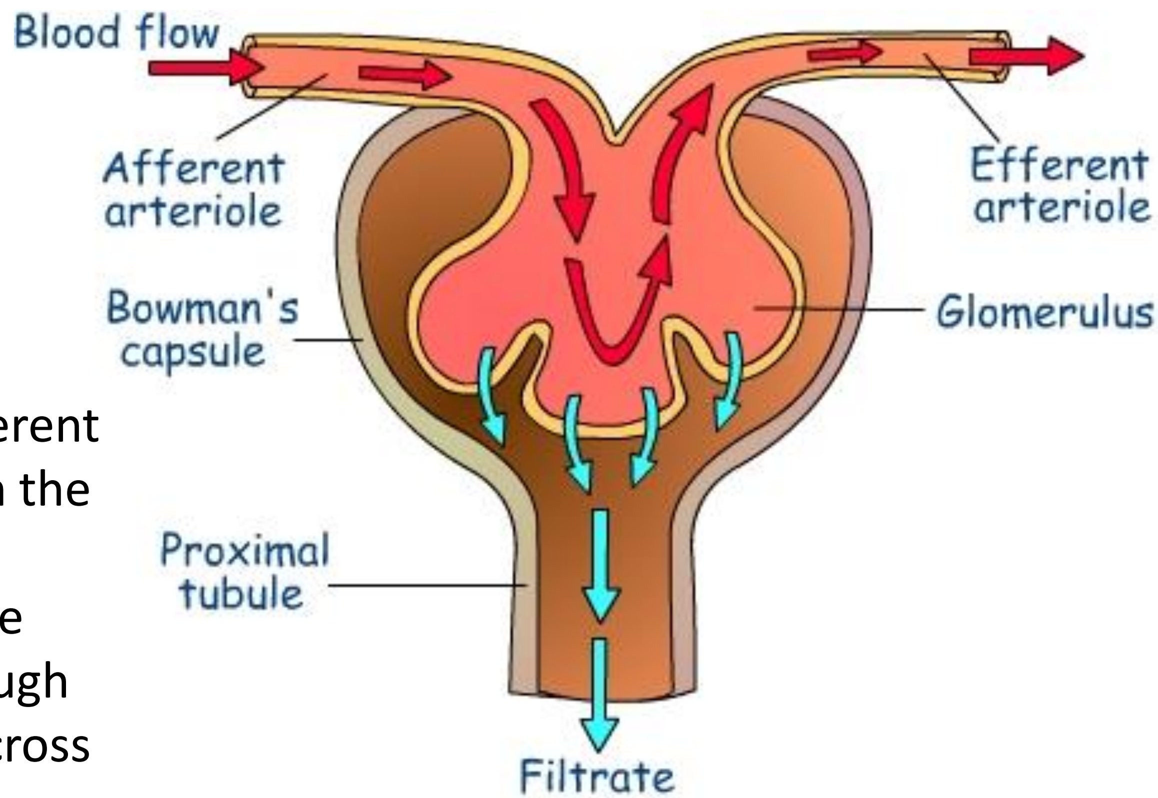
Podocytes

- cells of visceral layer of Bowman's capsule
- highly modified to perform a filtering function
- have numerous, long processes and secondary processes – **pedicels**



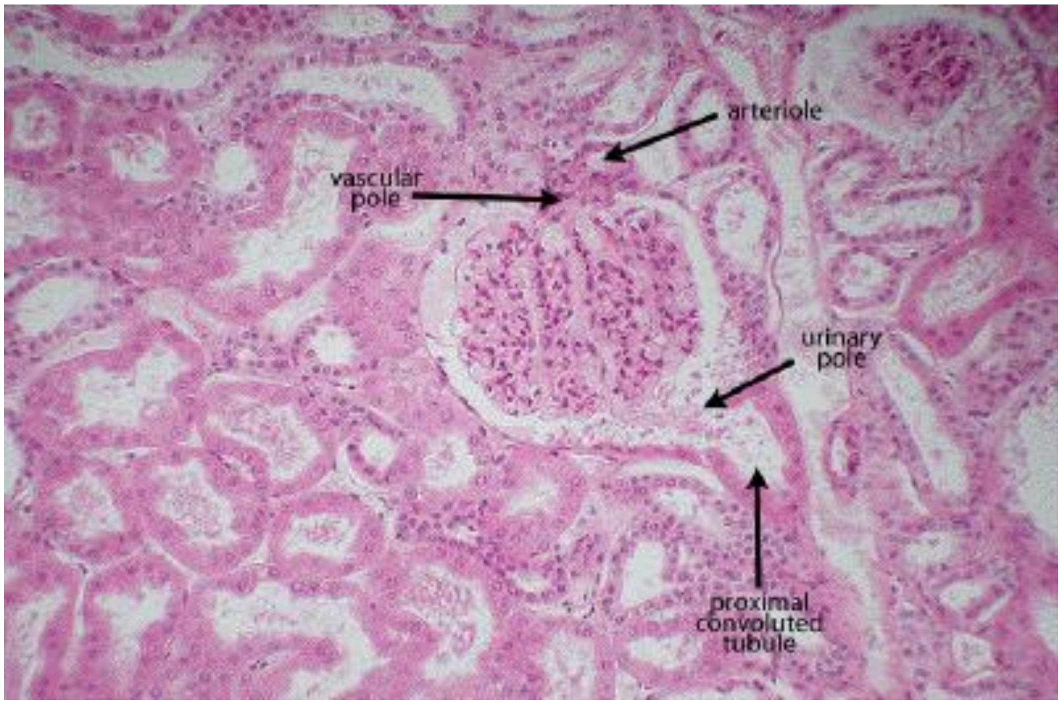
(c)

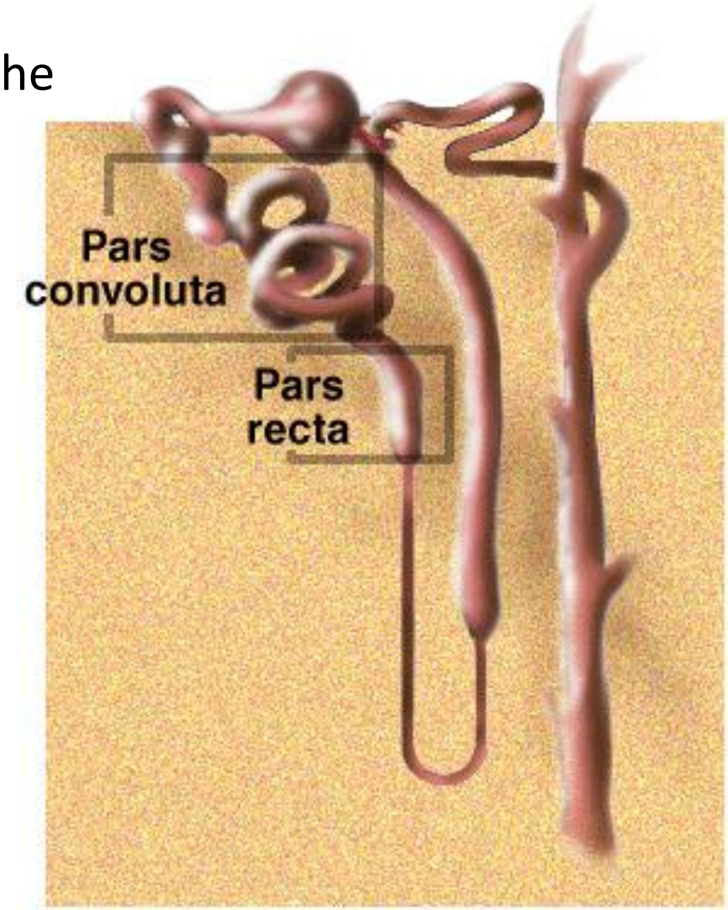
Filtration process – glomeular filtrate, ultrafiltrate



- blood flows through the afferent arteriole and leaves through the efferent arteriole
- the high hydrostatic pressure forces small molecules through the filter, from the blood, across the filtration barrier
- strong anions of basement membrane (collagen type IV) push away negatively charged proteins (e.g. albumins)

From Bowman’s space glomerular filtrate flows to the **proximal tubule** at the urinary pole

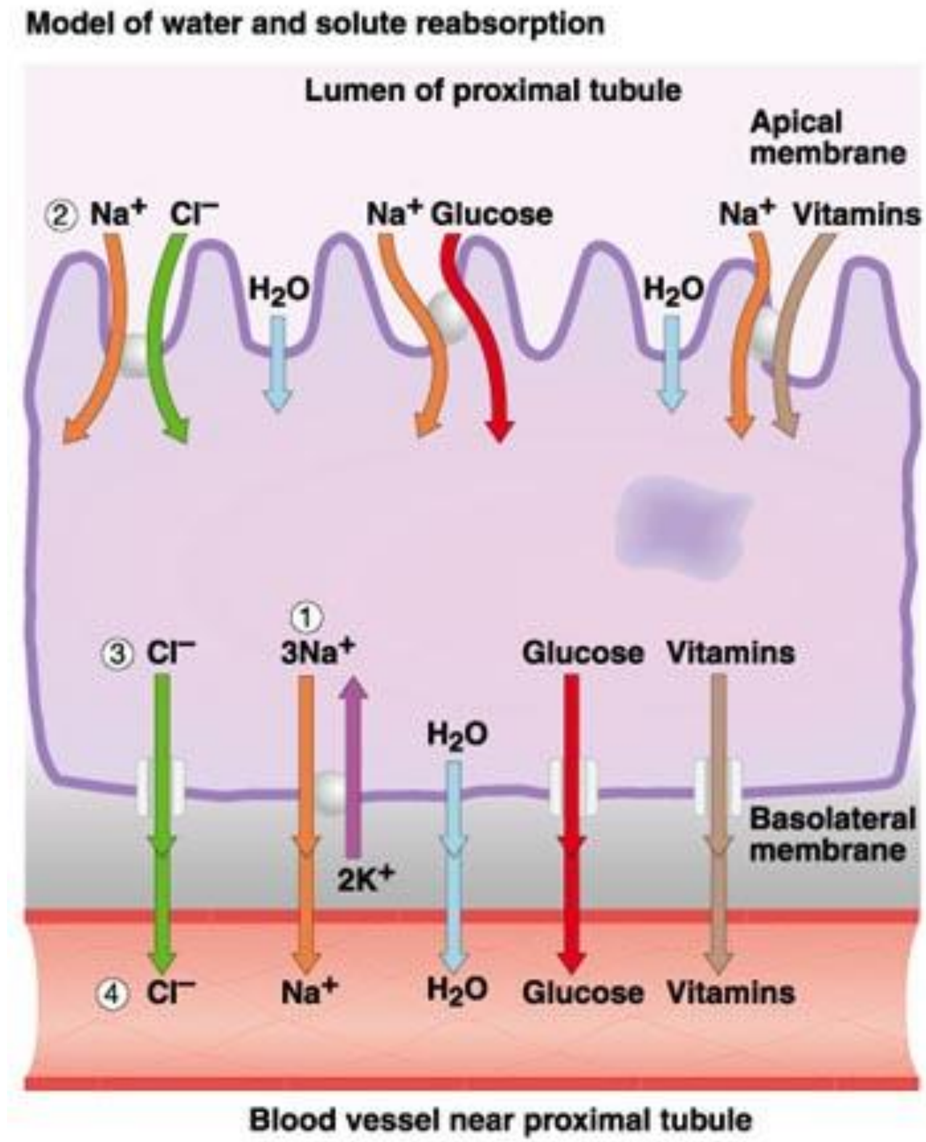




Function of proximal tubule

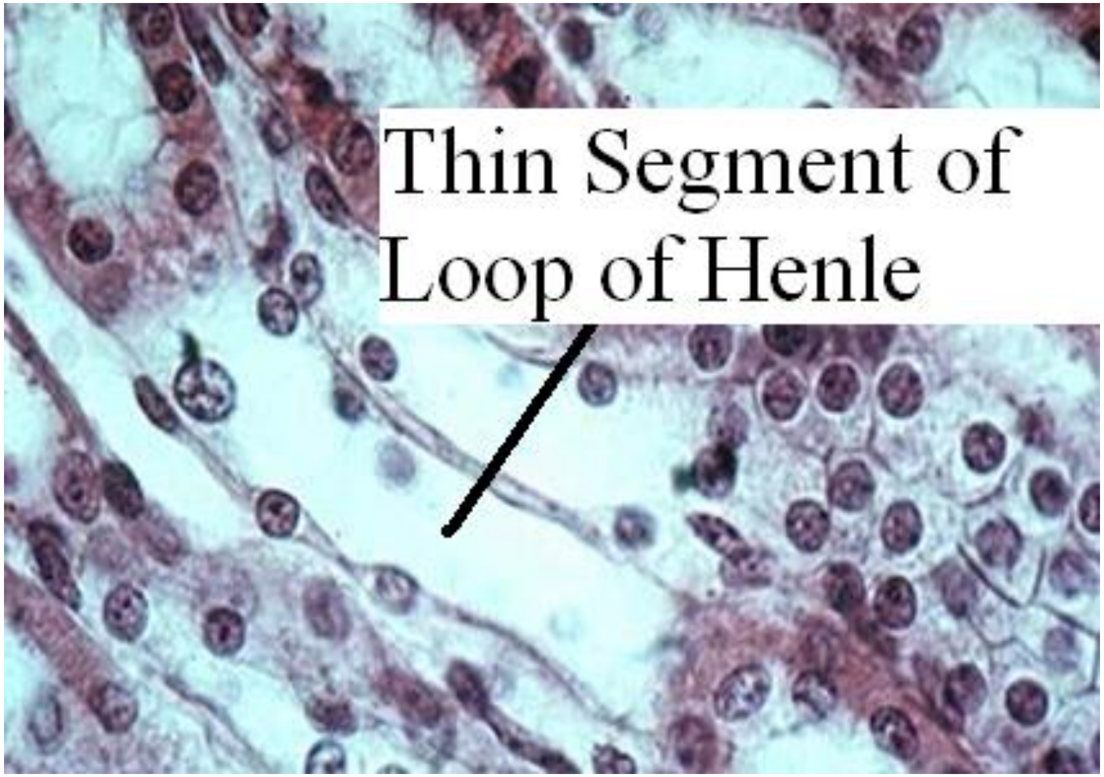
Cells of proximal tubule transport from the ultrafiltrate into the connective tissue stroma:

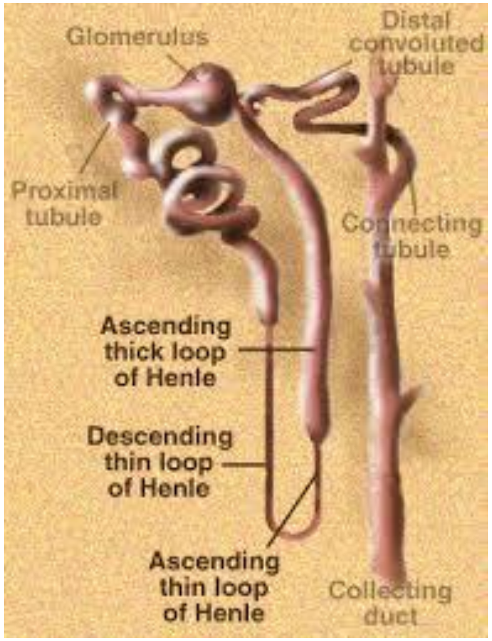
- **Na^+ and Cl^- ions**
- **Water (aquaporin channels)**
- **Glucose, amino acids and vitamins (endocytosis)**



Thin limbs of Henle's loop

- leads from the proximal convoluted tubule to the distal convoluted tubule

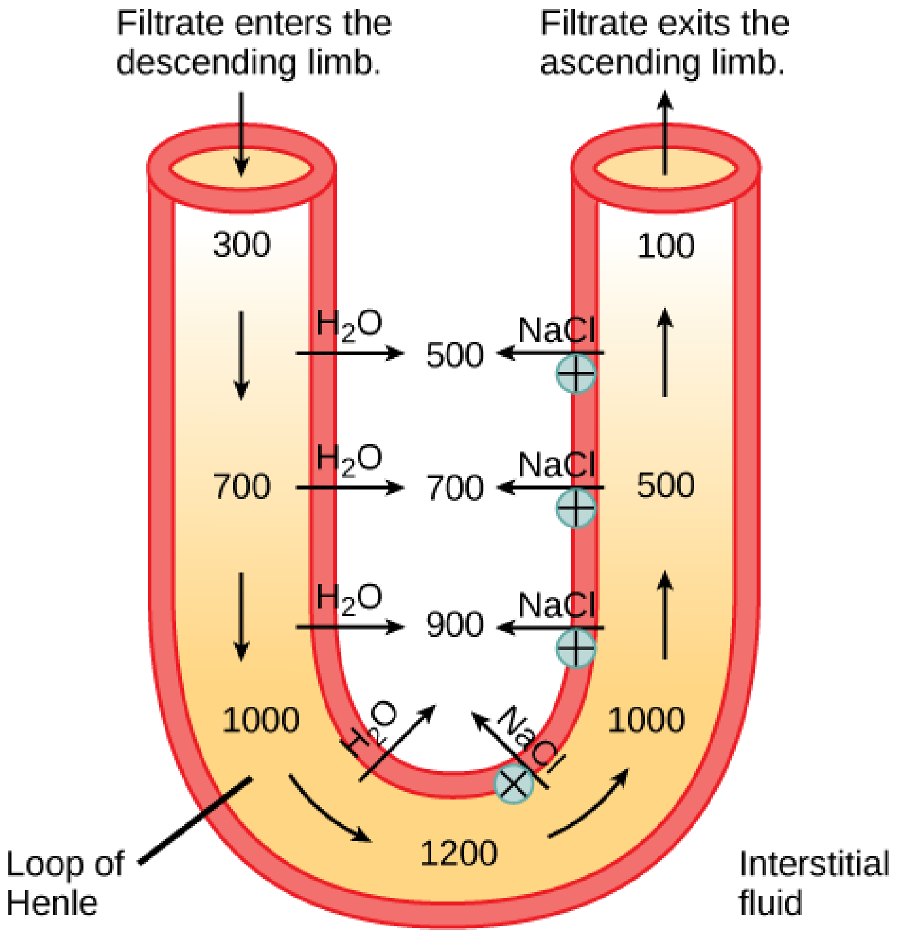




- Descending thin limb
- Henle's loop
- Ascending thin limb

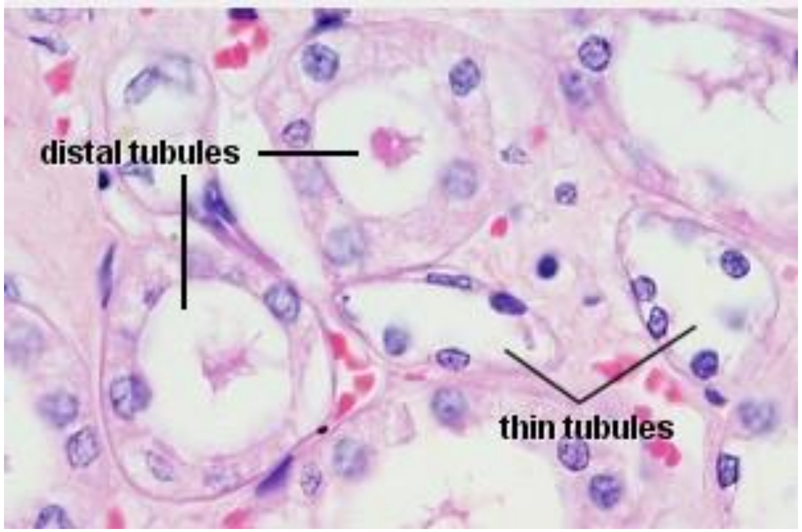
Thin limbs of Henle's loop – stromal gradient formation and concentration of urine

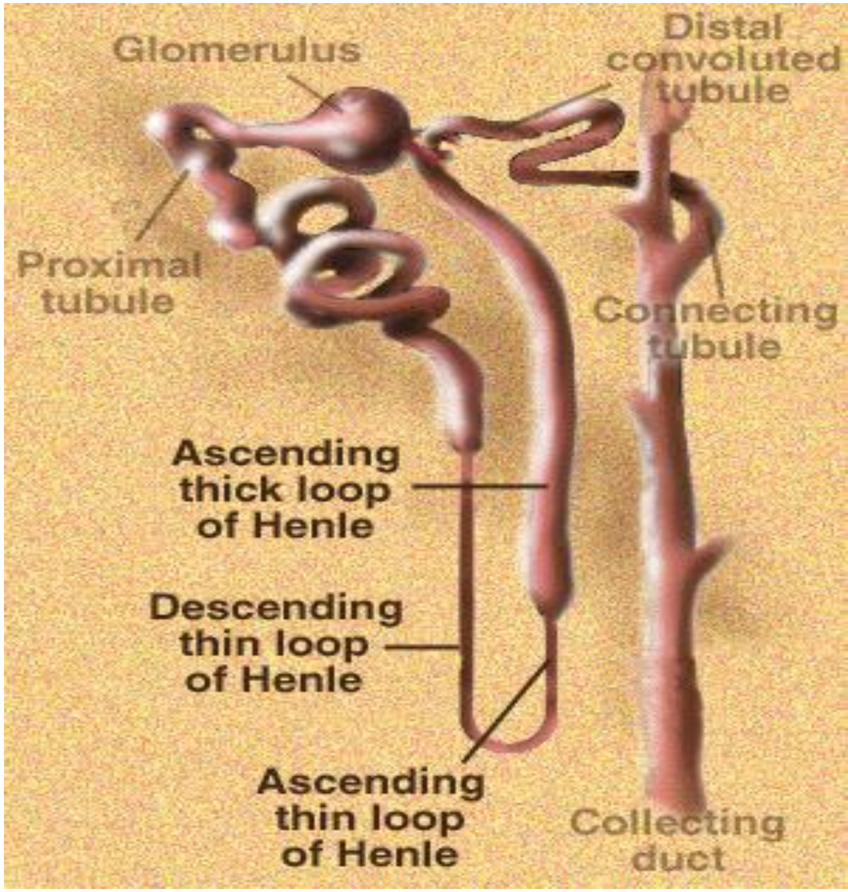
- the thin **descending** limb has low permeability to ions and urea, while being highly **permeable** to water (the concentration of the urine increases dramatically)
- the thin **ascending** limb is **impermeable** to water, but it is permeable to ions



Distal tubule

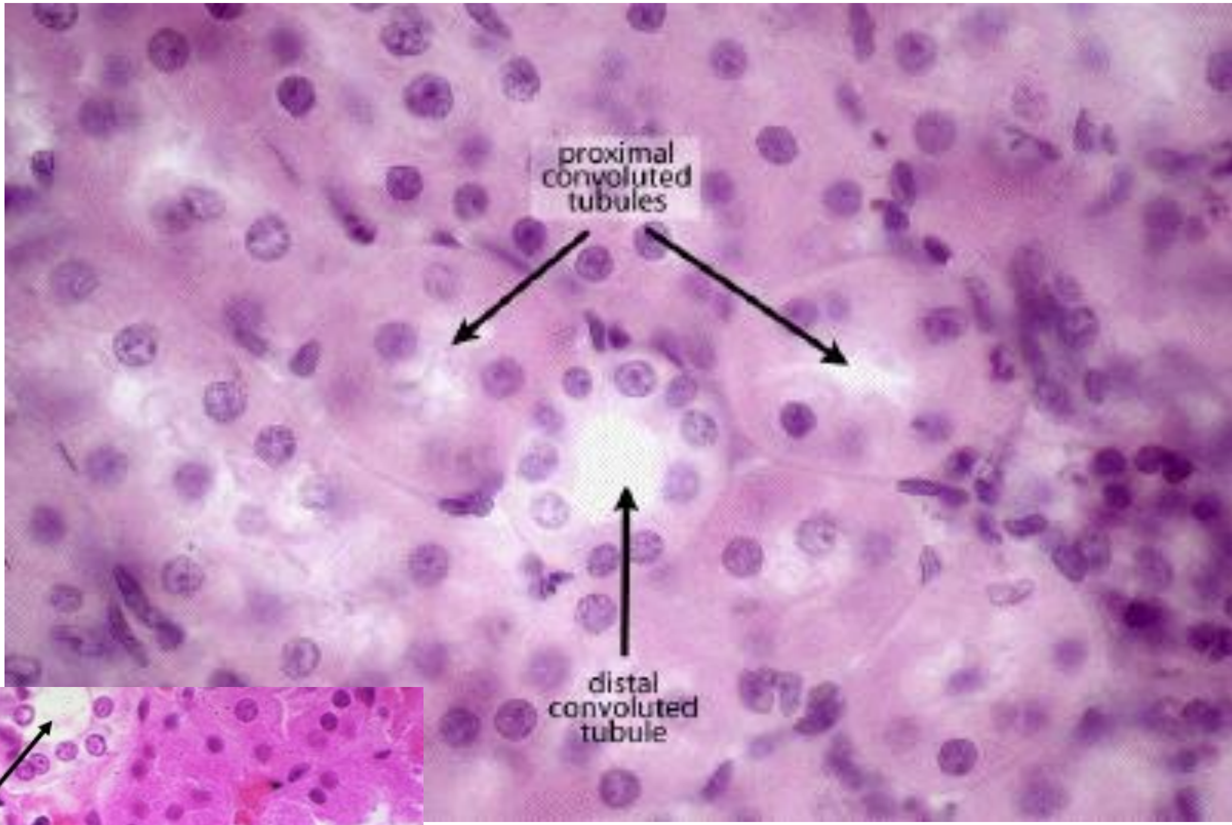
- the pars recta (the ascending thick limb of Henle's loop)
- the **macula densa** (closely packed specialized cells lining the wall of the distal convoluted tubule)
- the pars convoluta (the distal convoluted tubule)

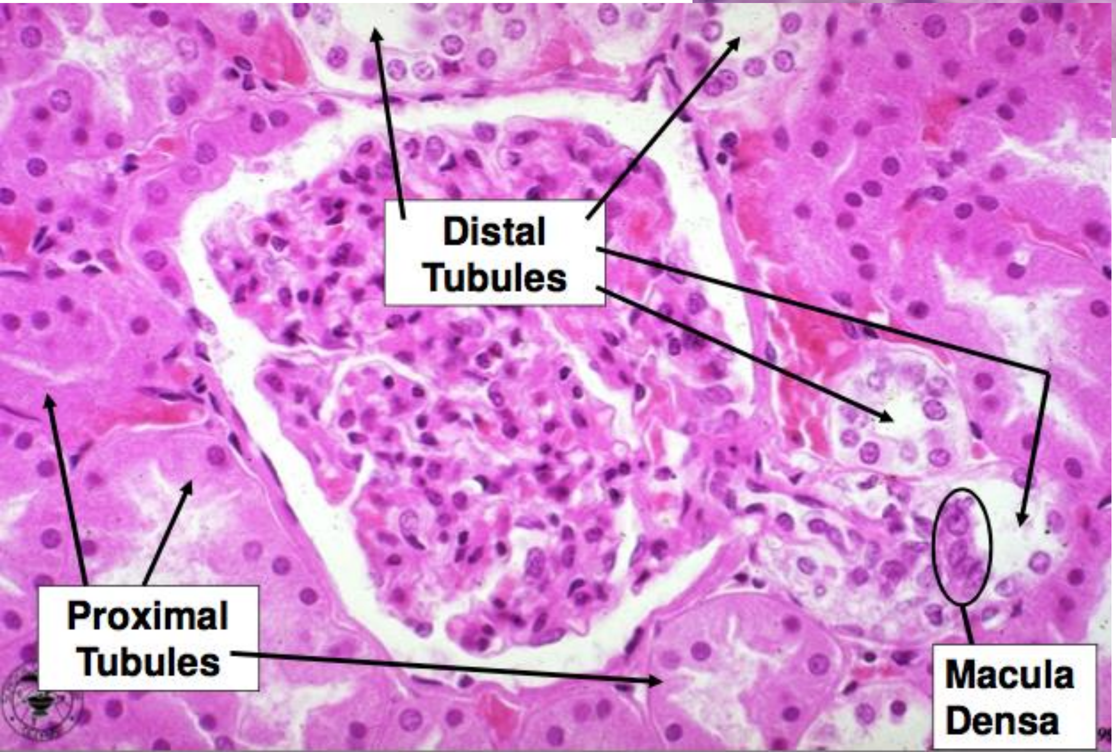




Proximal tubul

- cuboidal cells with eosinophilic cytoplasm
- only six to eight nuclei are included in the plane of section





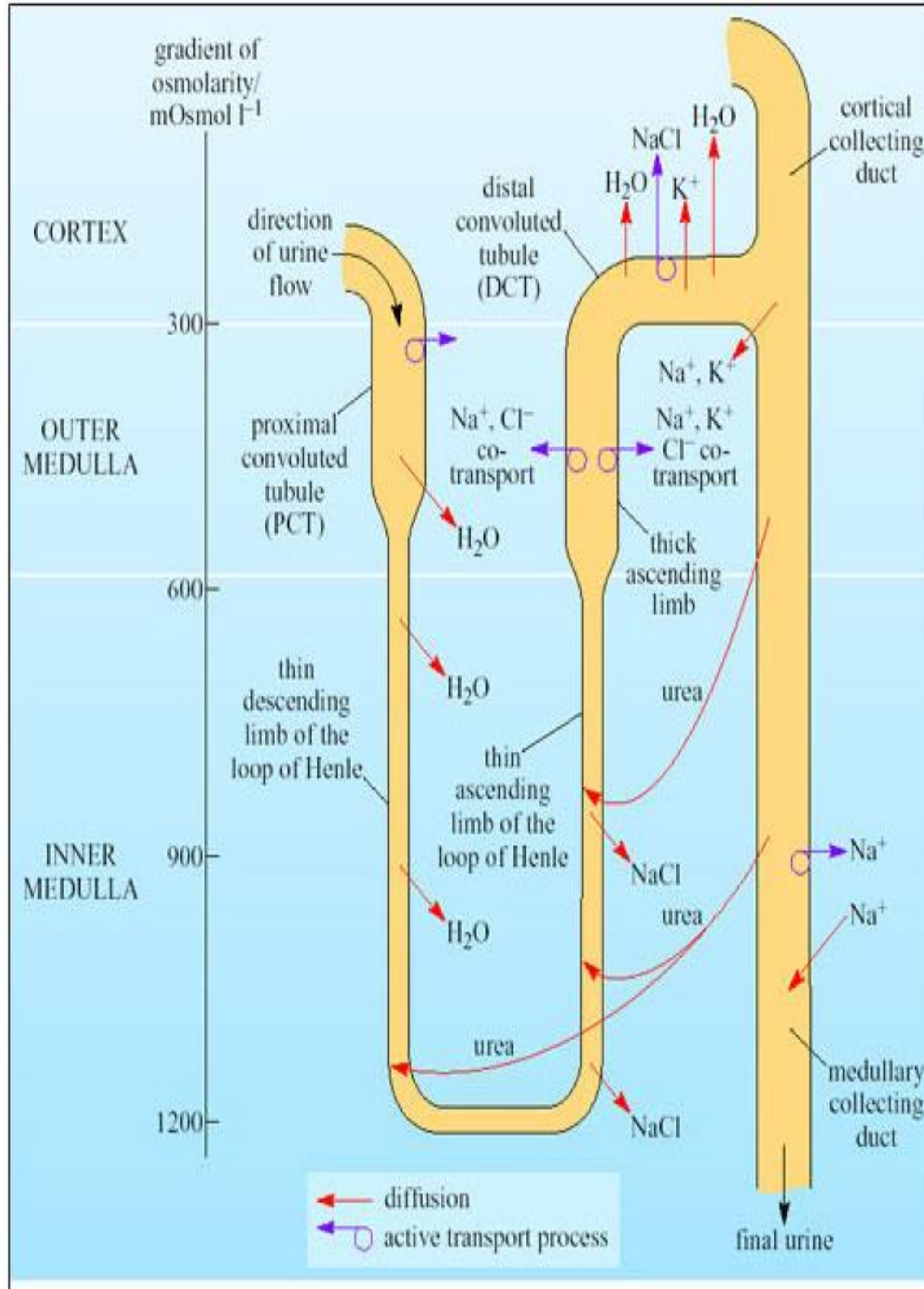
Distal tubul

- low cuboidal cells with paler cytoplasm
- cells are narrower – more nuclei are apparent in cross section
- the lumina of tubules are wide-open

Distal tubule – function

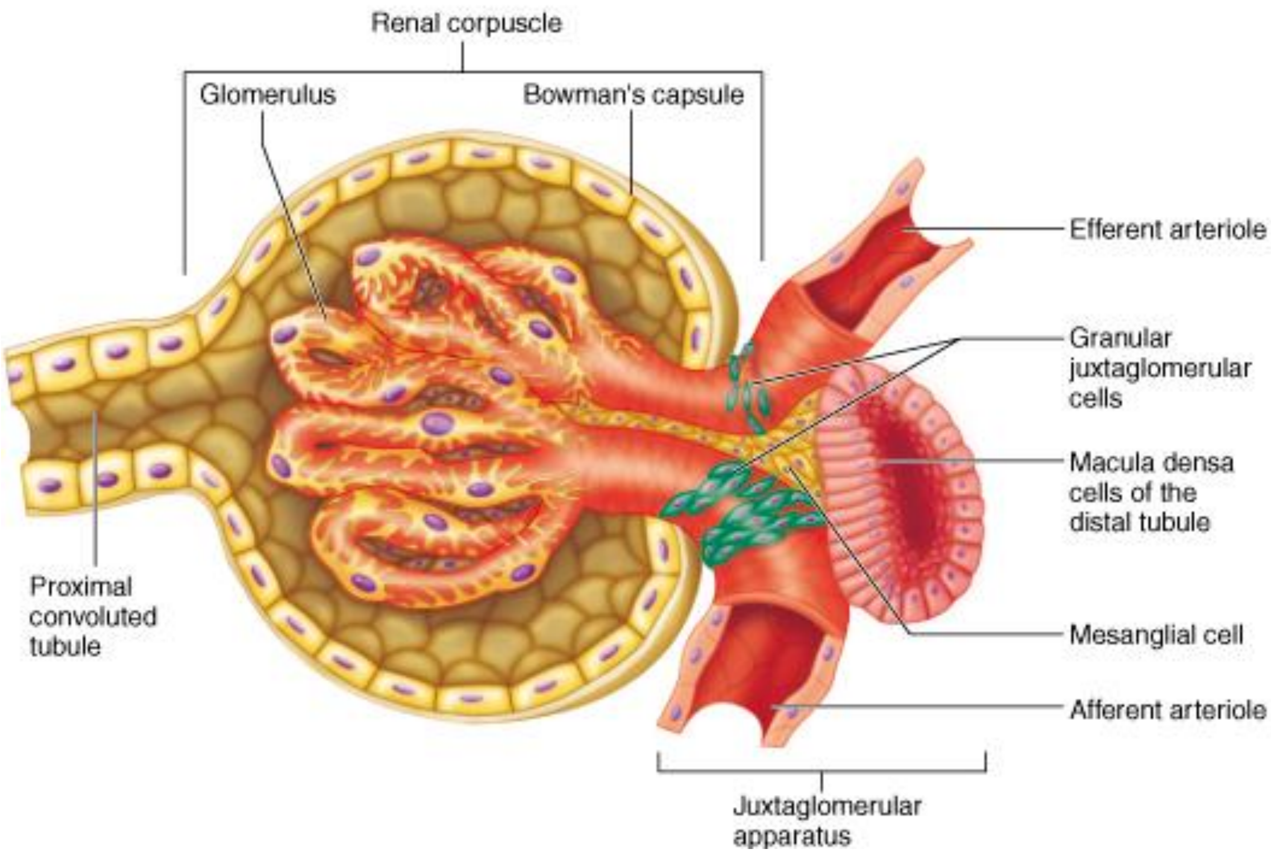
Thick ascending limb of Henle's loop
- is **impermeable** to water
- cells have chloride and sodium pumps (active transport of ions from the lumen of the tubule)

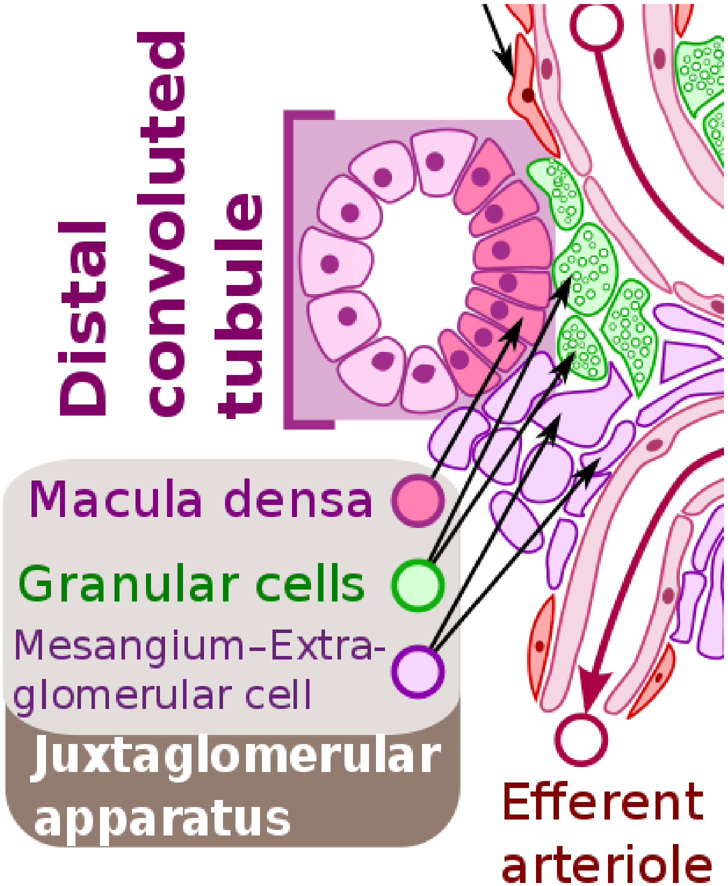
Distal convoluted tubule
- is partly responsible for the regulation of potassium, sodium, calcium concentration (cells have pumps for ions)
- sodium absorption by the distal tubule is mediated by the hormone **aldosterone (**zona glomerulosa of the adrenal cortex)



Juxtaglomerular apparatus

- is composed of the **macula densa** of the distal convoluted tubule, smooth muscle cells of the afferent arteriole known as **juxtaglomerular cells**, and **extraglomerular mesangial cells**



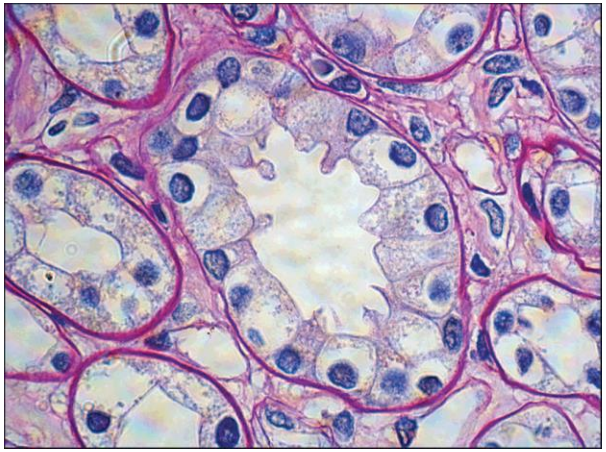


extraglomerular mesangial cells found outside the glomerulus, near the vascular pole and macula densa.

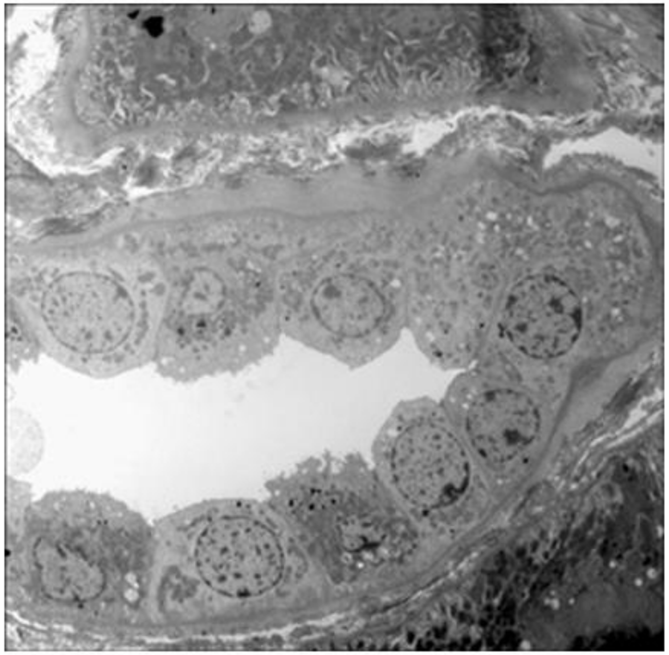
macula densa is an area of closely packed specialized cells lining the wall of the distal convoluted tubule (are sensitive to the concentration of sodium chloride)

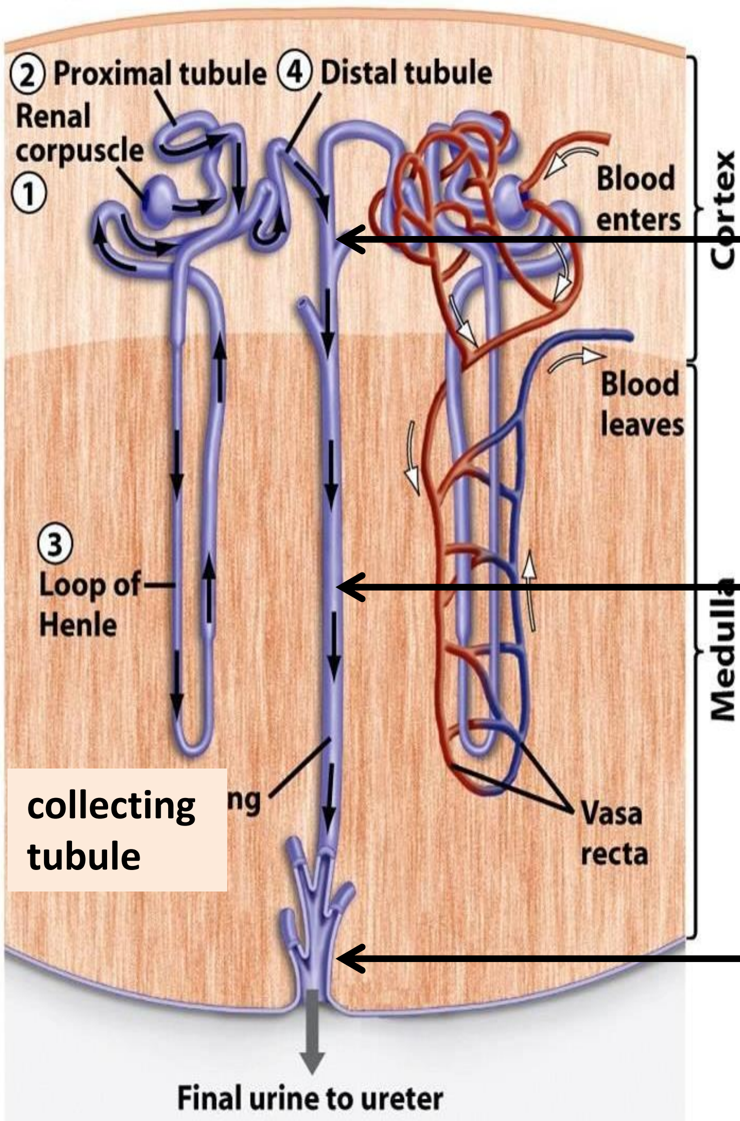
juxtaglomerular cells are specialized smooth muscle cells mainly in the walls of the afferent arterioles (synthesize, store, and secrete the enzyme **renin**)

Collecting tubules



- Principal cells (2/3 of cells)
  - Light cells with few organelles
  - ADH sensitive and role in K+ secretion
- Intercalated cells (1/3 of cells)
  - Dark cells
  - Acid base regulation
  - Type A: H^+ secretion
  - Type B: $HCO3^-$ secretion





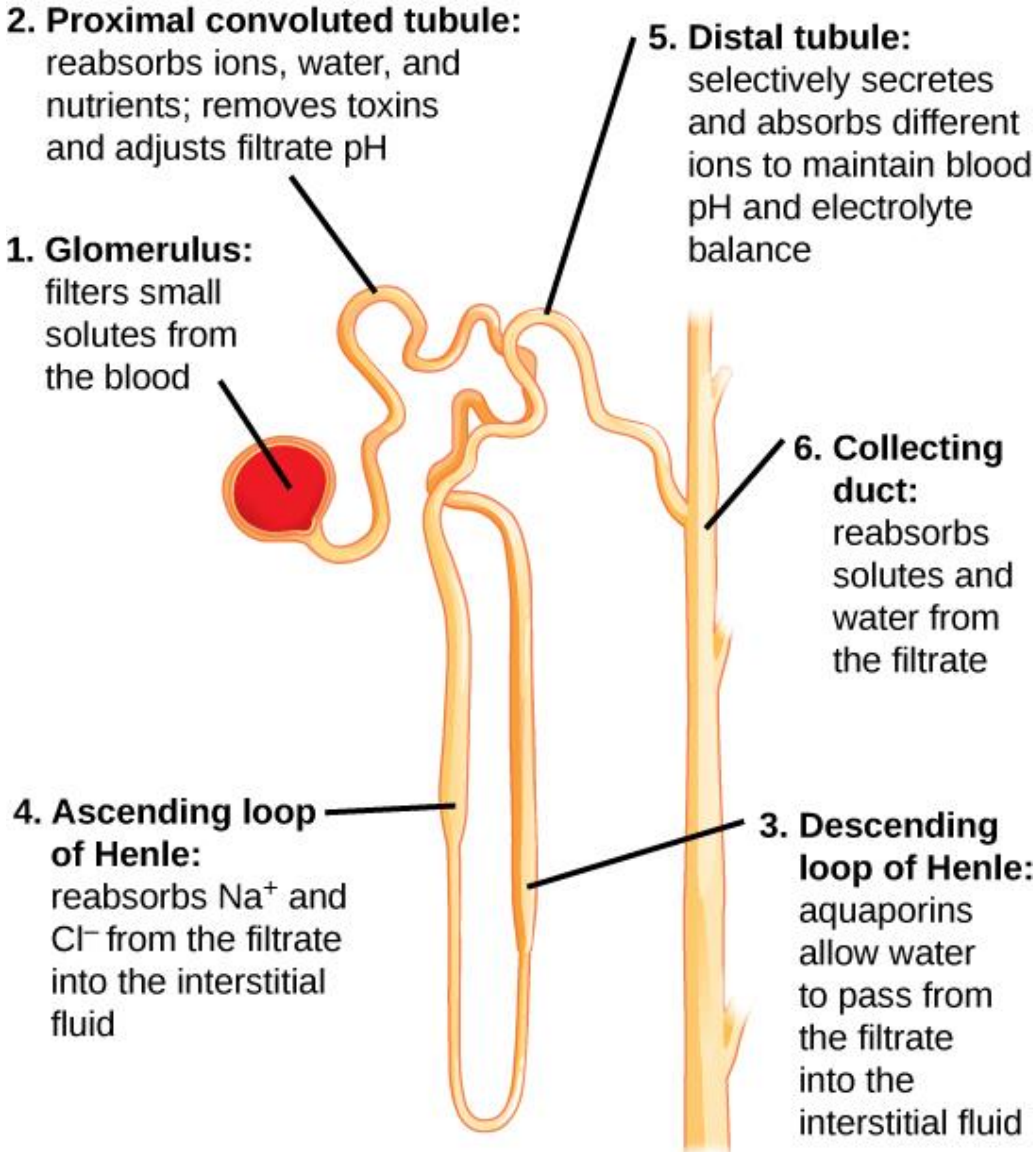
cortical collecting tubule

medullary collecting tubule

papillary collecting tubule (duct of Bellini)

Collecting tubule - function

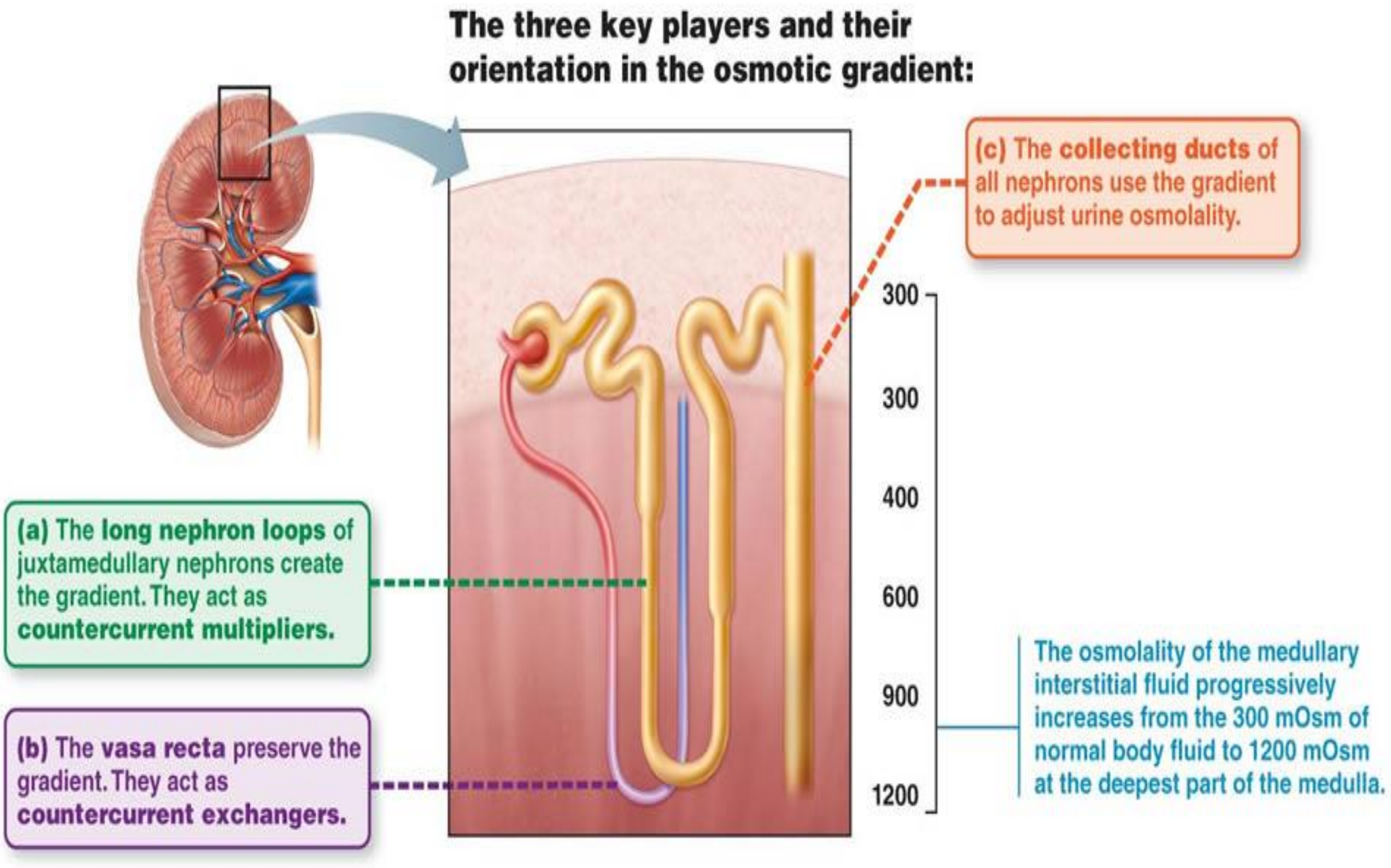
- reabsorption of **sodium and water**.
- depends on **hormonal activation (ADH)**



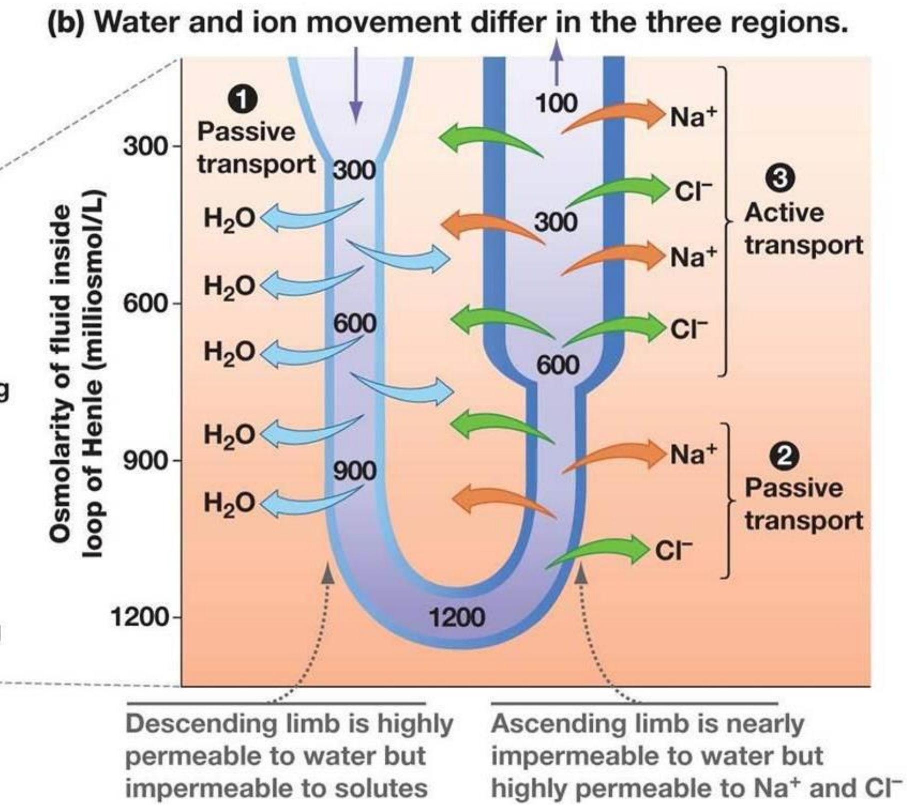
Urine formation

- about 180 L of glomerular filtrate is formed each day but only 1% is excreted

Osmotic gradient in the kidney interstitium is necessary for the concentration of urine



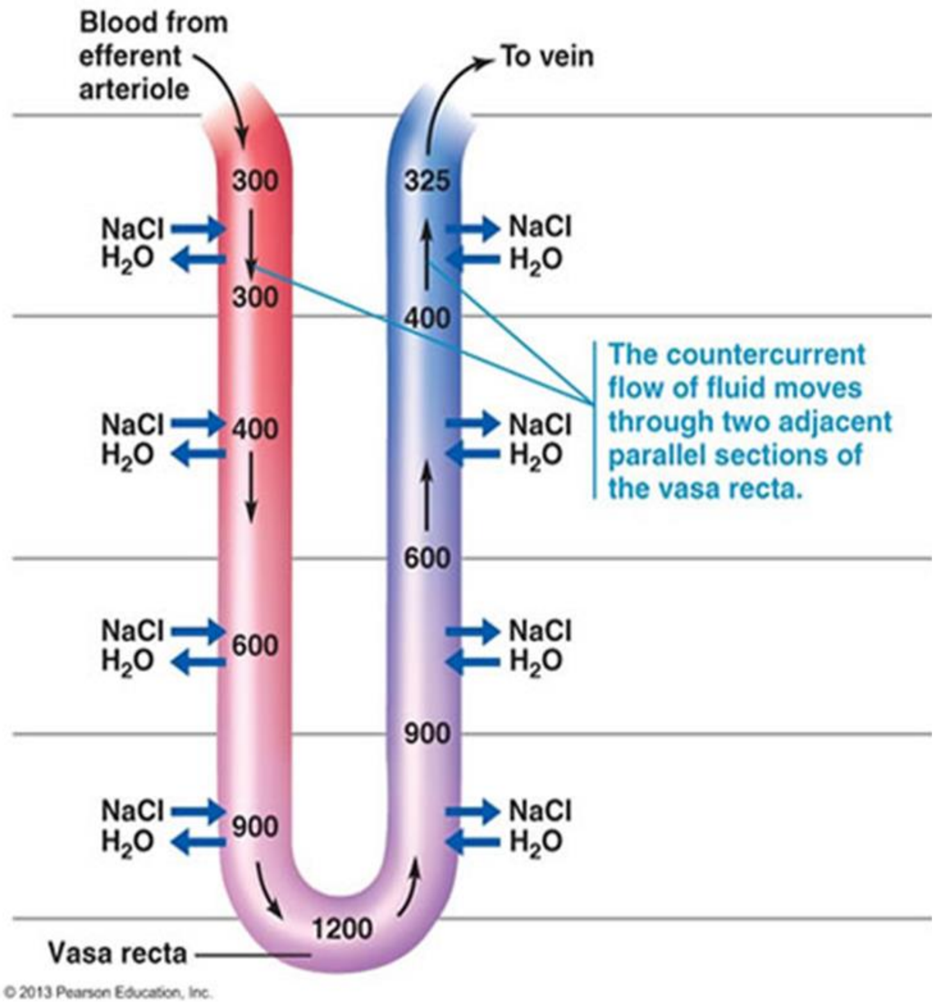
Countercurrent multiplier system – creates a gradient of osmolality in the renal interstitium



The **descending** loop of Henle has low permeability to ions and urea, but is **highly permeable to water (**water moves across the tubular wall into the medullary space, making the urine hypertonic)

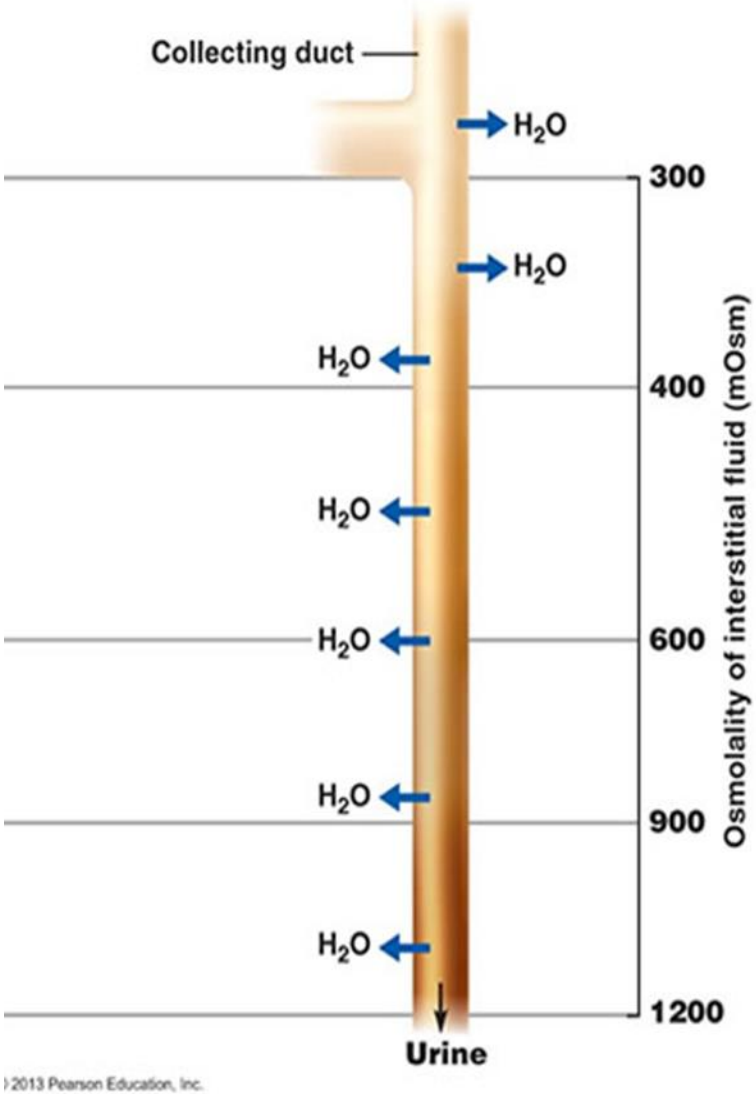
The ascending thin limb is **impermeable to water, but it is permeable to sodium and chloride ions** (ions are transported into the medullary space, making the filtrate hypotonic)

Countercurrent exchanger system
Vasa recta helps maintain the osmotic gradient in the medulla

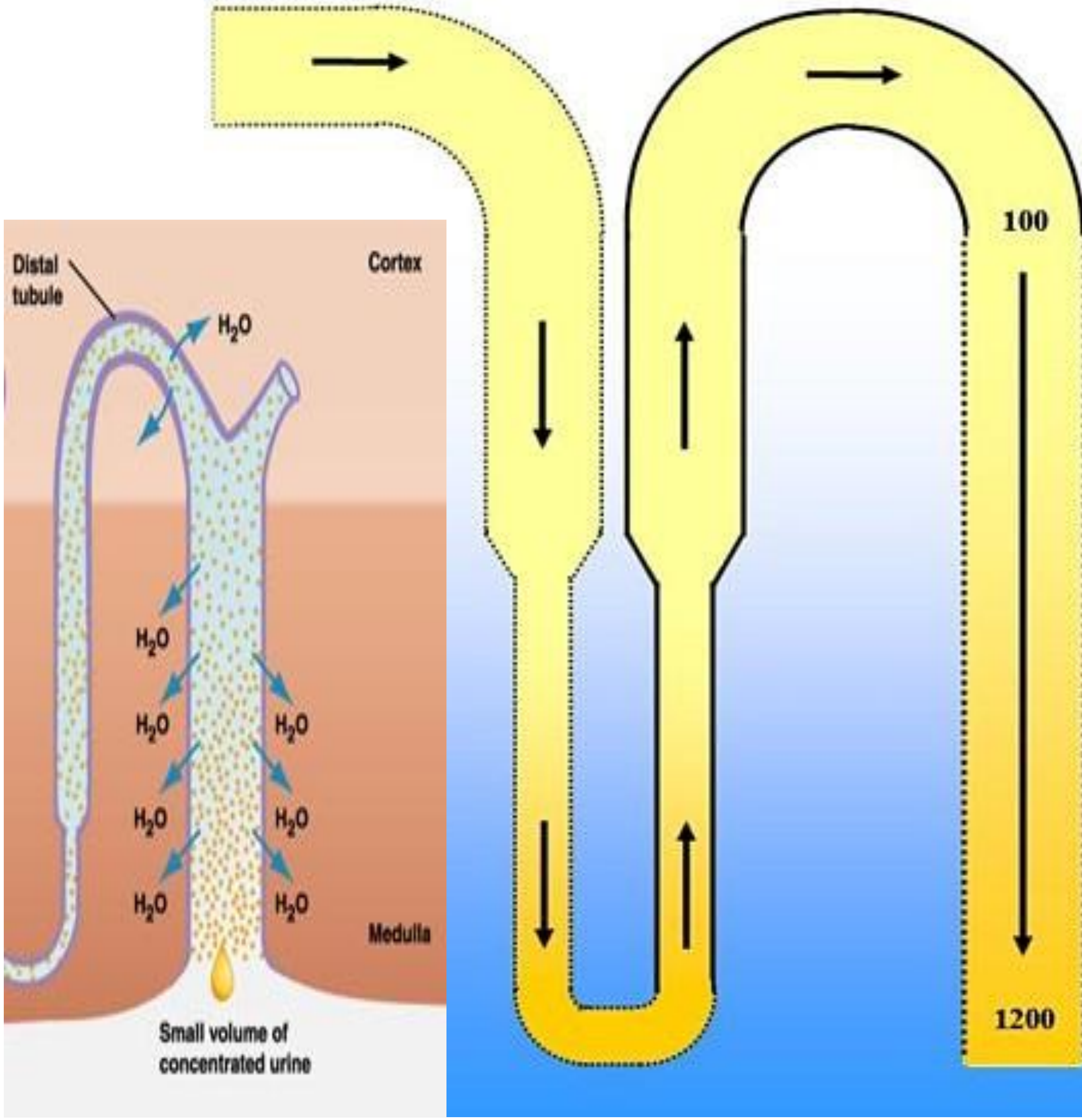


- the blood courses down the arterial limb - loses water and gains salts as it returns via the venous limb, it loses salts and gains water
- osmotic gradient in the medulla remains undisturbed
- osmolality of the blood in vessels is equilibrated with that of the interstitium
- this exchange system causes salt and water to be resorbed (returned back to the body) because of the concentration gradient in the renal medulla

Collecting tubule uses an **osmotic gradient** of the medulla for the concentration of the urine



- filtrate entering collecting tubule is **hypotonic**
- under the influence of **ADH** cells of collecting tubule become permeable to water
- as filtrate descends through the renal medulla in the collecting tubule, is subjected to the osmotic pressure gradient
- water leaves the lumina of collecting tubule
- urine becomes **concentrated** and **hypertonic**



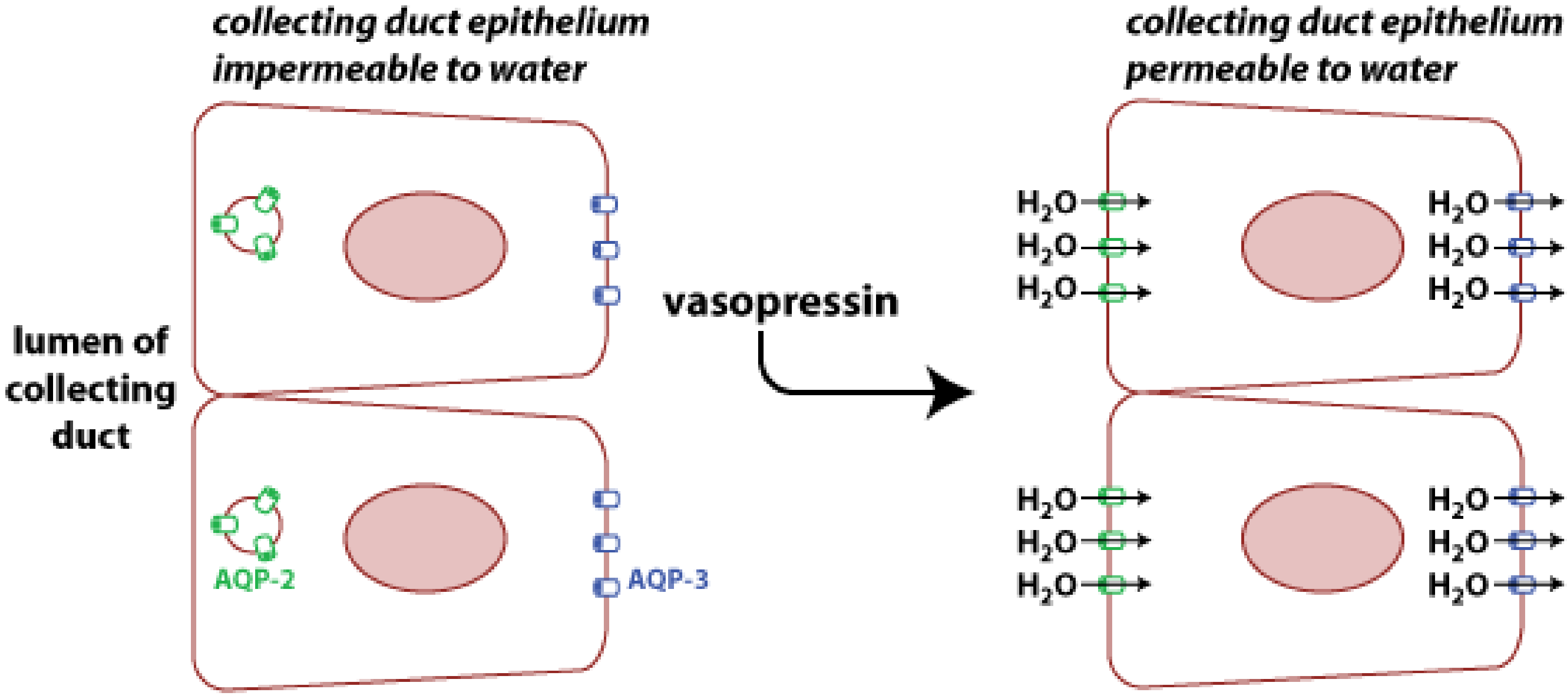
Vasopressin

- Anti-diuretic hormone (ADH)
- Secreted by posterior pituitary
- Acts on collecting duct and distal tubule
- Increases permeability of tubule epithelium

No vasopressin
collecting duct
impermeable to water
DILUTE URINE

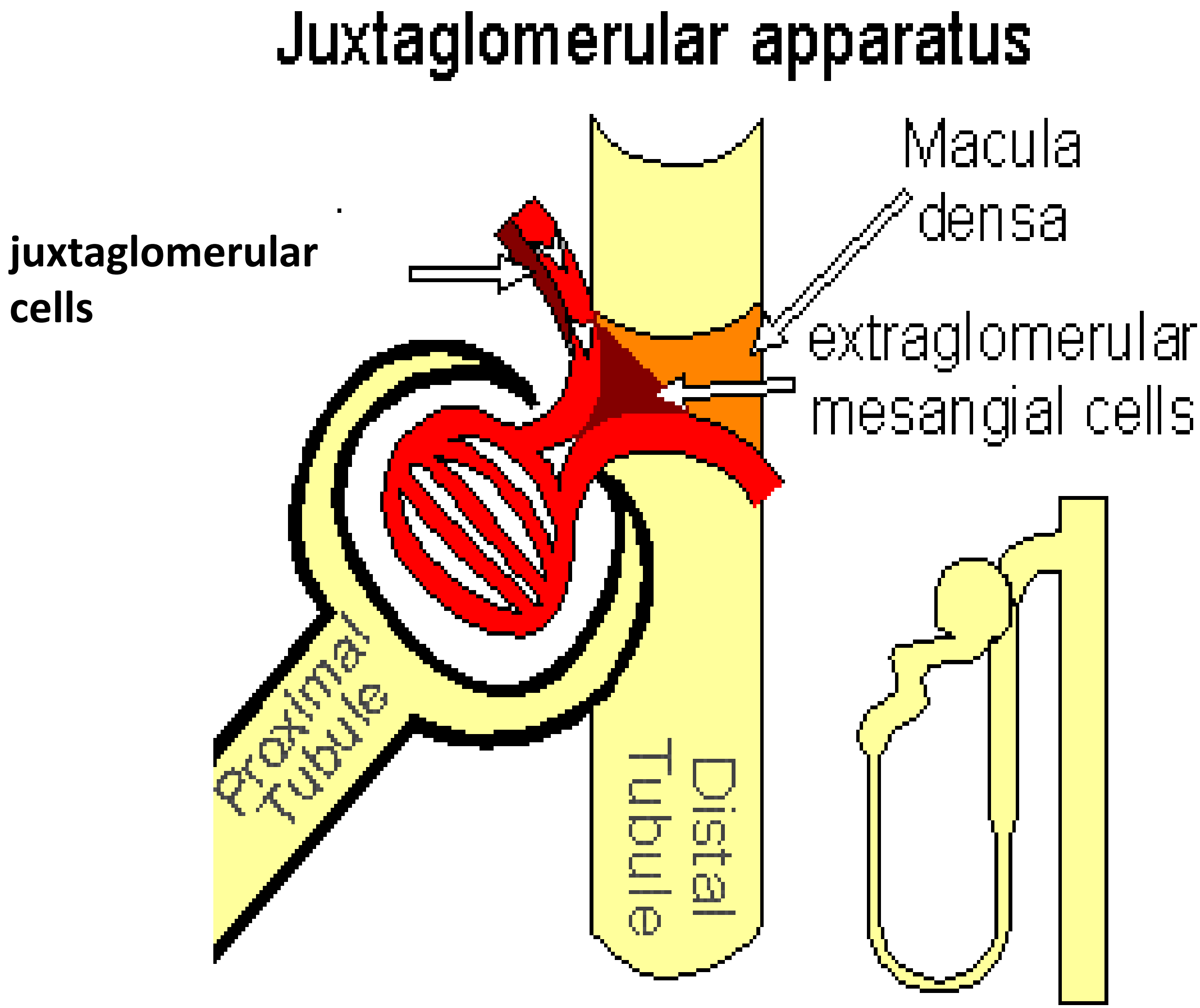
With vasopressin
collecting duct
permeable to water
CONCENTRATED URINE

Mechanism of action of antidiuretic hormone (vasopressin)



Function of nephron is regulateed by Juxtaglomerular apparatus

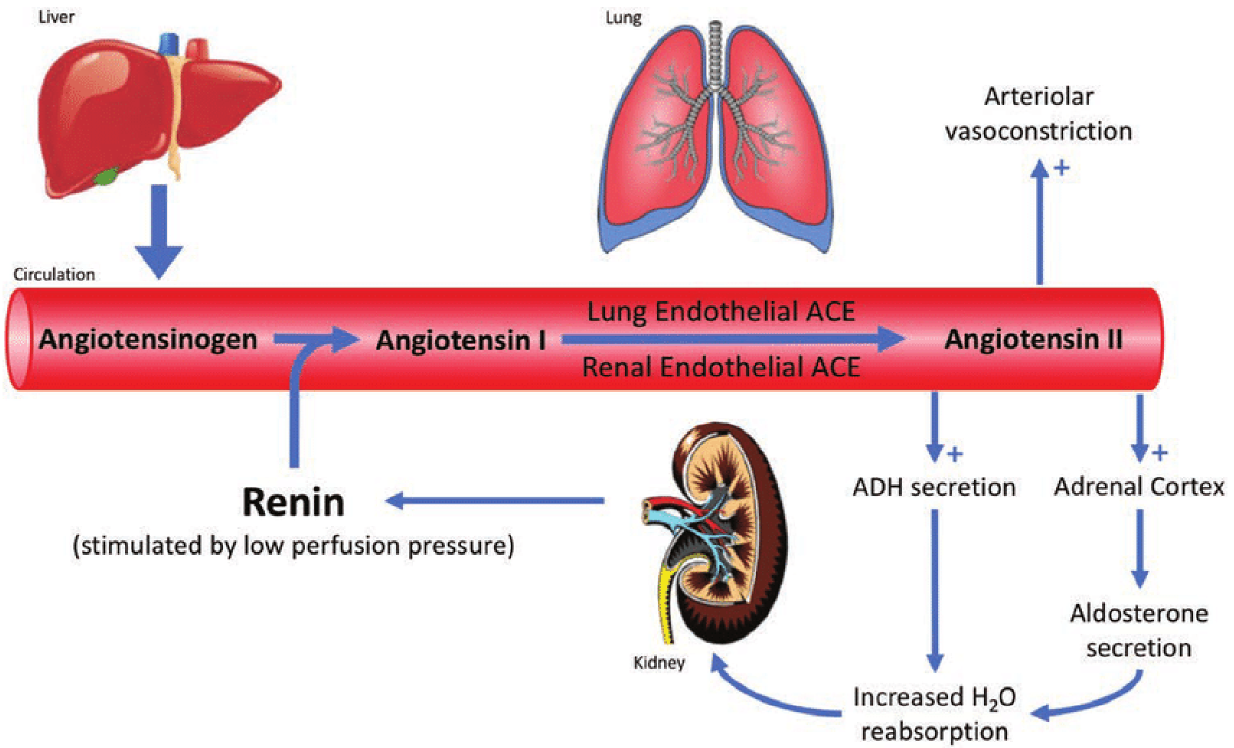
The **macula densa** senses any increase in the **sodium chloride** concentration in the distal tubule of the kidney and secretes a locally active **vasopressor**, which acts on the adjacent afferent arteriole to decrease glomerular filtration rate, and instruct juxtaglomerular cells to release the **renin**



- **Renin** converts **angiotensinogen** (bloodstream) into **angiotensin I**
- In capillaries of lungs (mainly) **angiotensin-converting enzyme (ACE)** converts **angiotensin I** to **angiotensin II** (vasoconstrictor)

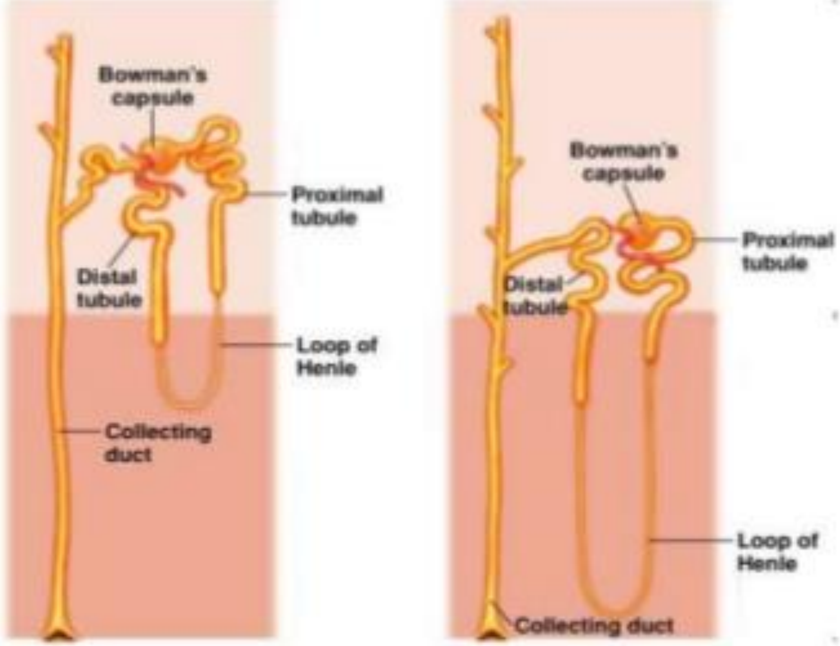
ANGIOTENSIN II

- causes vasoconstriction, which, in turn, increases blood pressure
- enhances the reabsorption of sodium and chloride ions by the cells of distal convoluted tubules of the nephron
- stimulates ADH release (increasing water reabsorption)

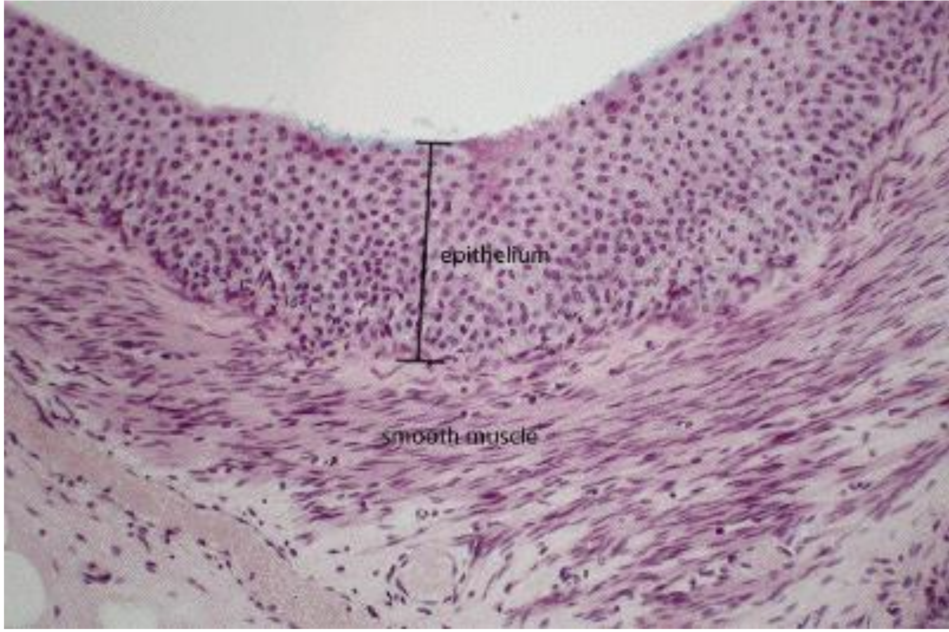


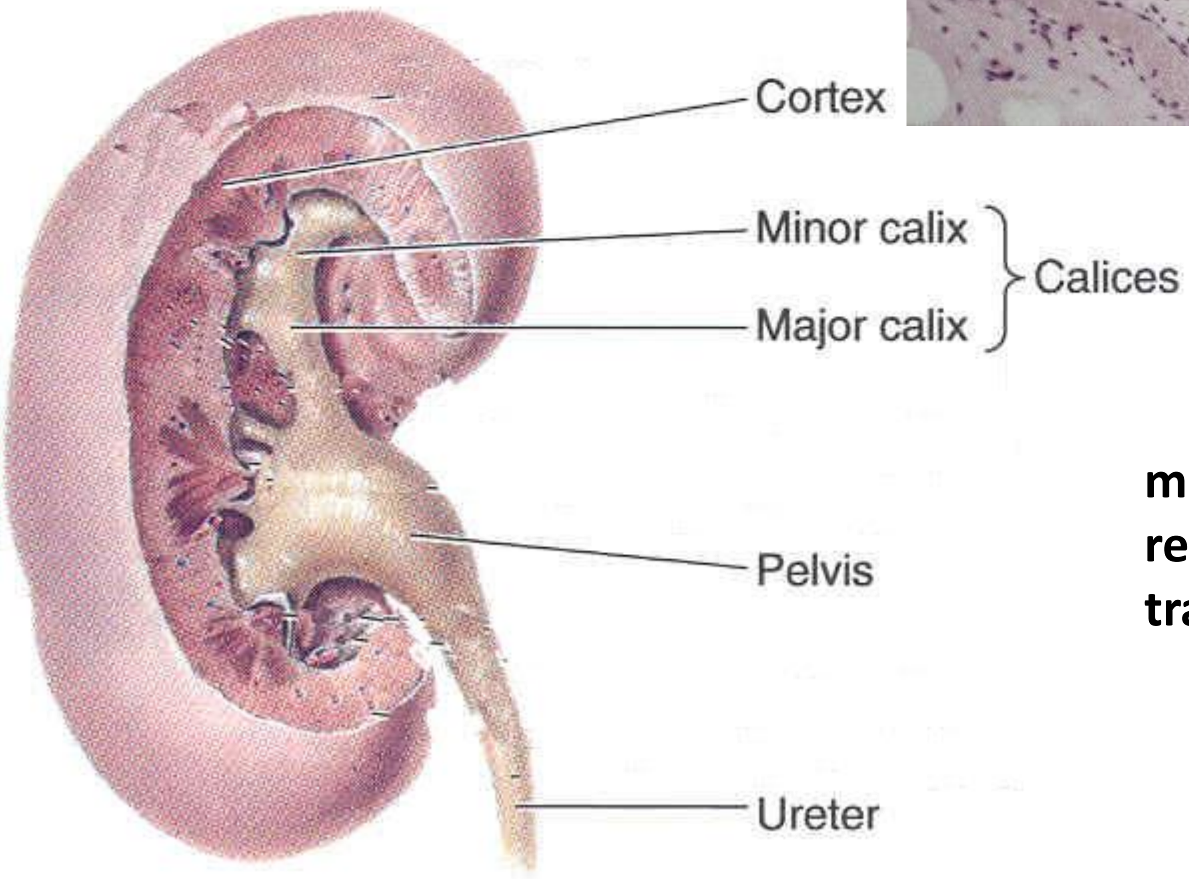
11.3 U.8 The length of the loop of Henle is positively correlated with the need for water conservation in animals.

Length of the loop of Henle and water conservation: The kangaroo rat's kidneys are especially efficient and produce only small quantities of highly concentrated urine. They have very long loops of Henle which builds a higher ion concentration in the **medulla (dark orange below).** The longer the loop the more water will be reabsorbed in the collecting duct.



Urine moves from the nephrones collecting duct system to the **minor calyx** and then the **major calyx** before entering the **renal pelvis**



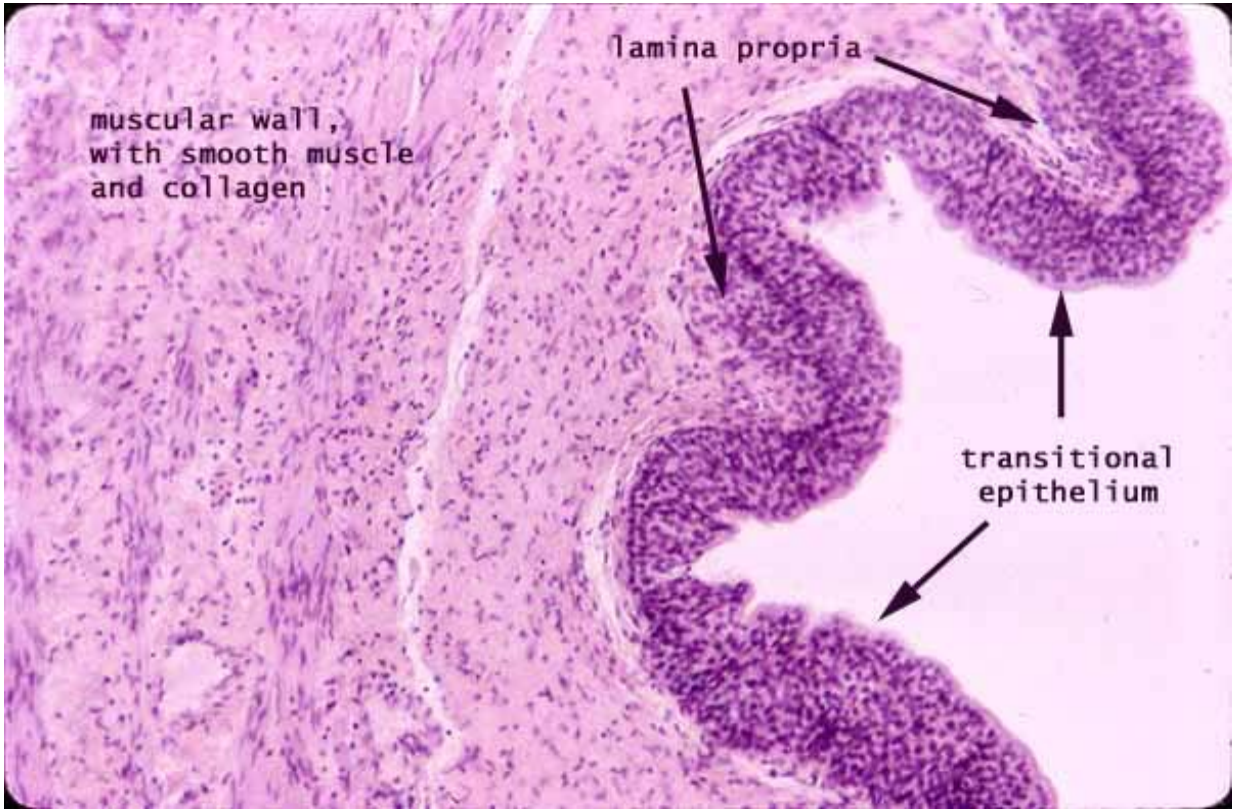


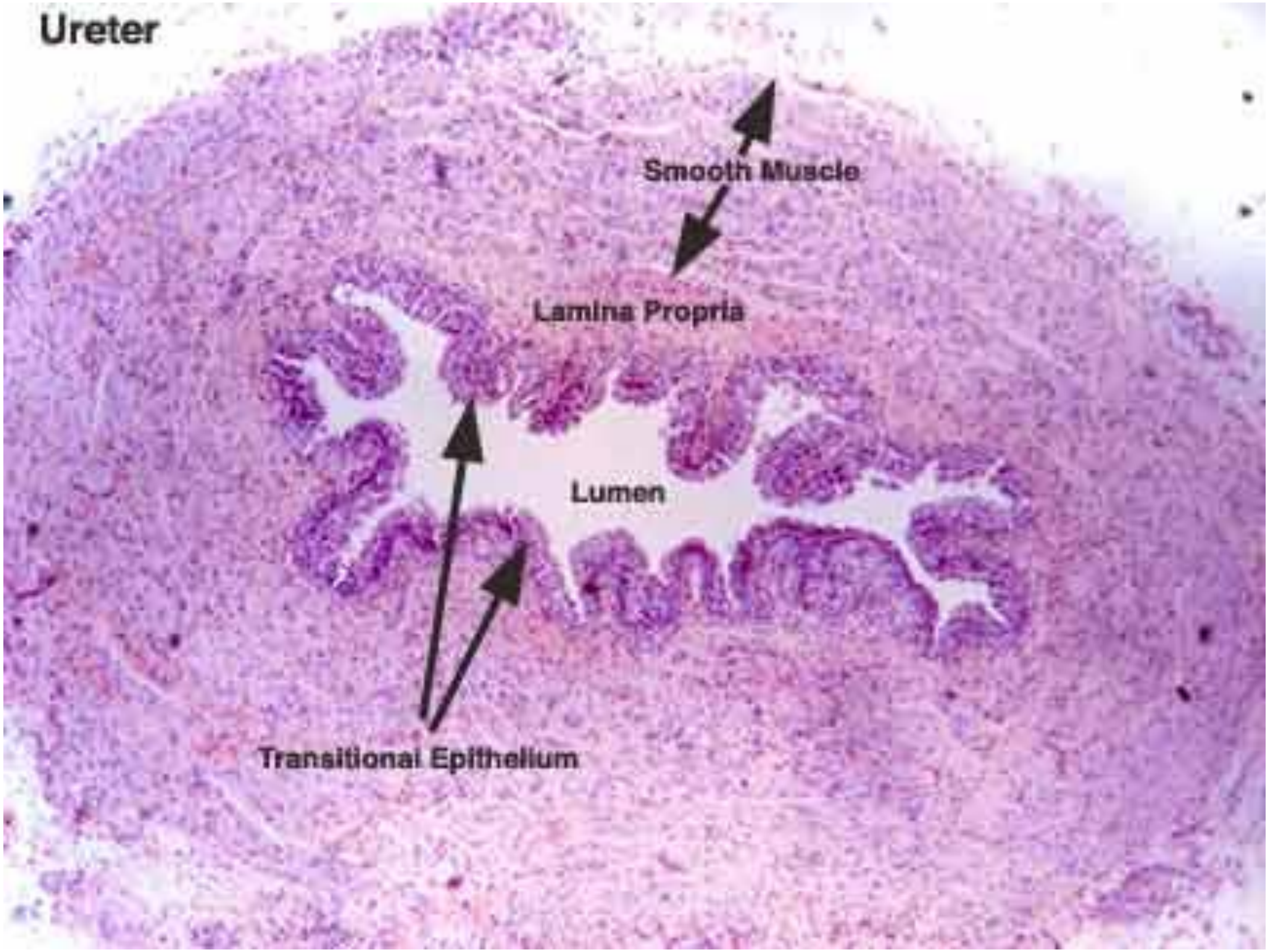
minor calyx, major calyx and **renal pelvis are lined by the transitional epithelium**

The **ureters** are tubes that deliver
urine from the kidneys to the urinary bladder.

The wall of the ureter contains:

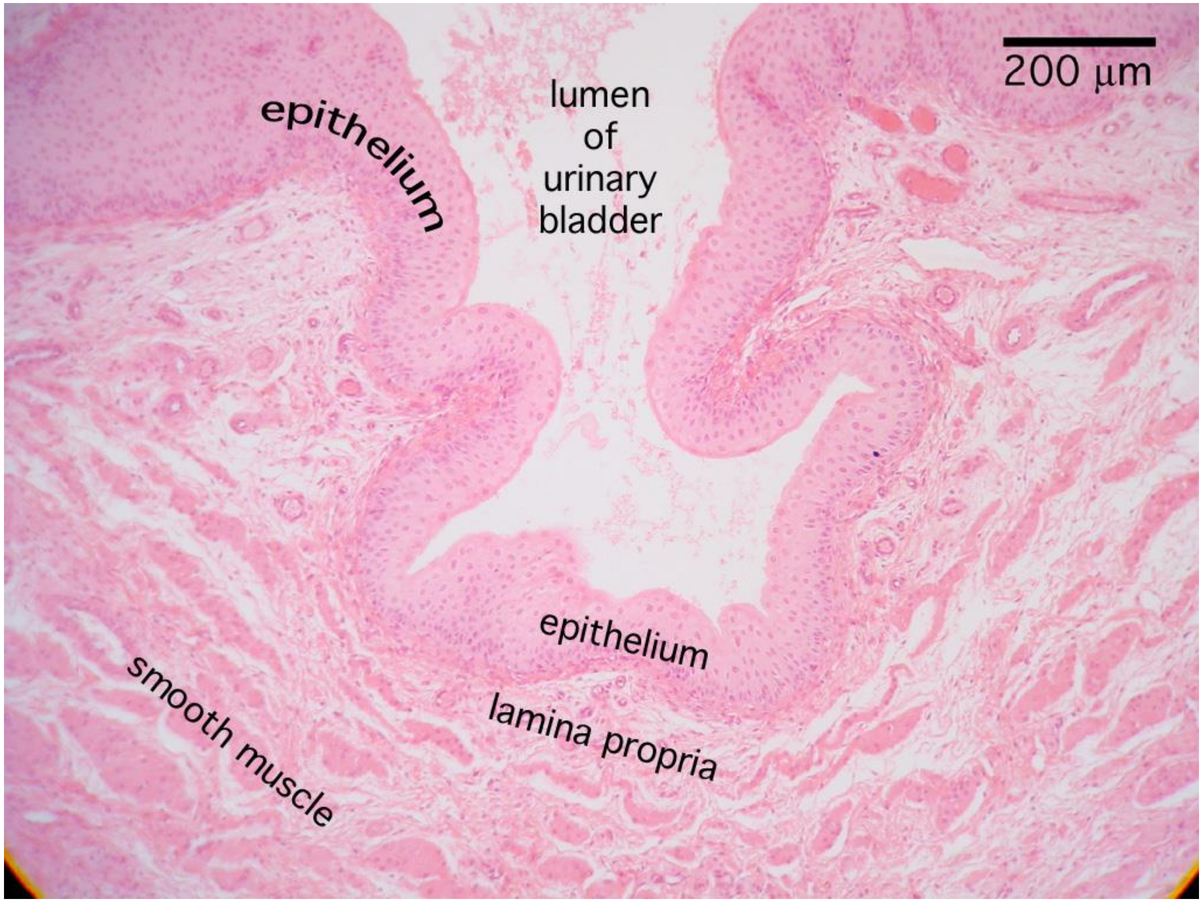
- a mucosa (**transitional epithelium** and lamina propria)
- the muscularis





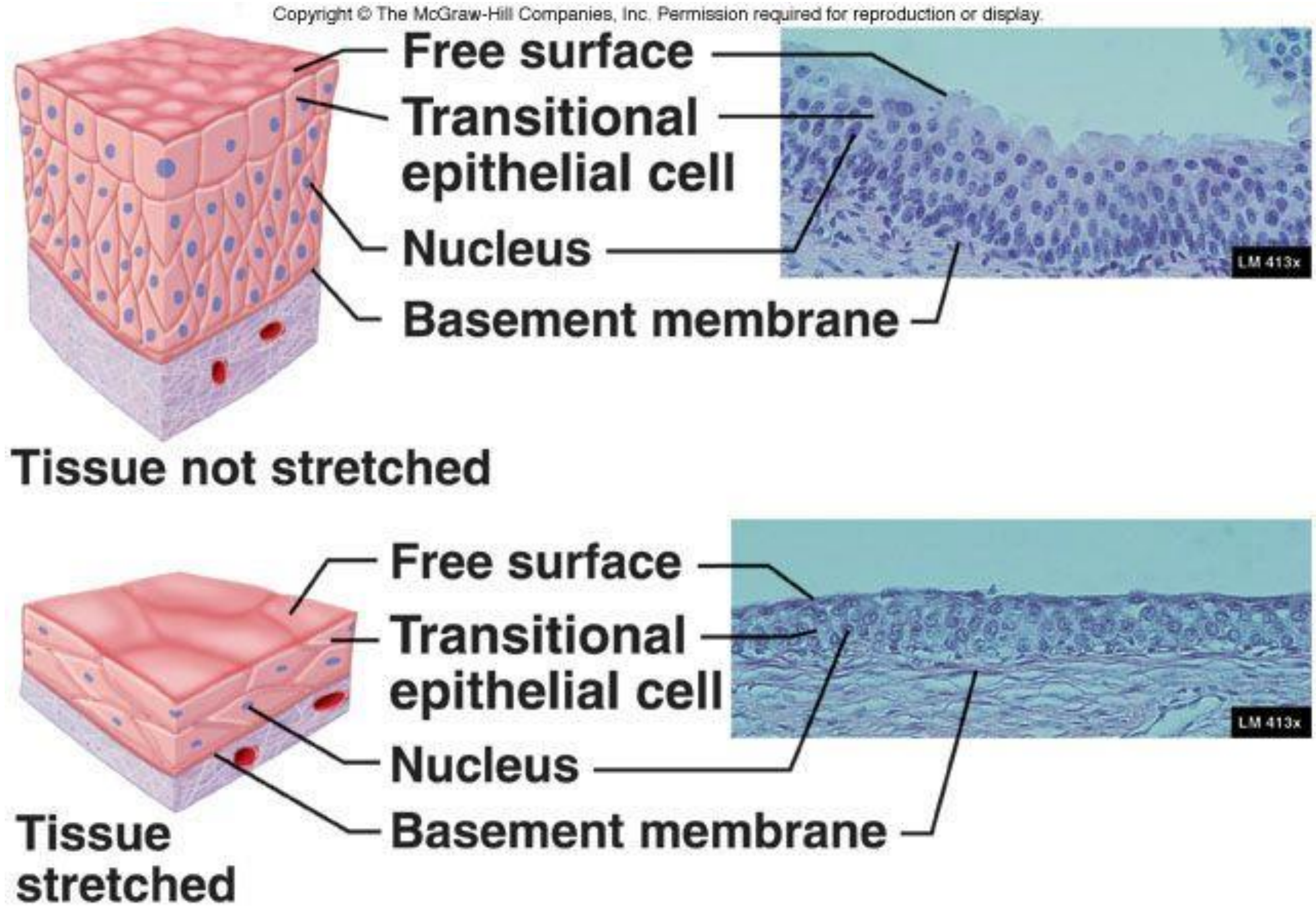
The mucosa of the ureter forms folds which project into the lumen when the ureter is empty

Urinary bladder - is the organ that collects urine excreted by the kidneys



Folds of mucosa are present in empty bladder

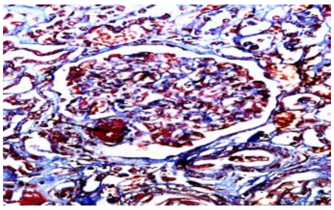
Transitional epithelium



(h) Transitional epithelium

Seminar: Relationship between nephrons and blood vessels.
Practical class: Urinary system.

- **kidney (no. 63),**
- **urinary bladder (no. 67),**
- **ureter (no. 66),**



kidney

- **elements of filtration slits in kidney glomerulus text & photo. # 93**

ureter

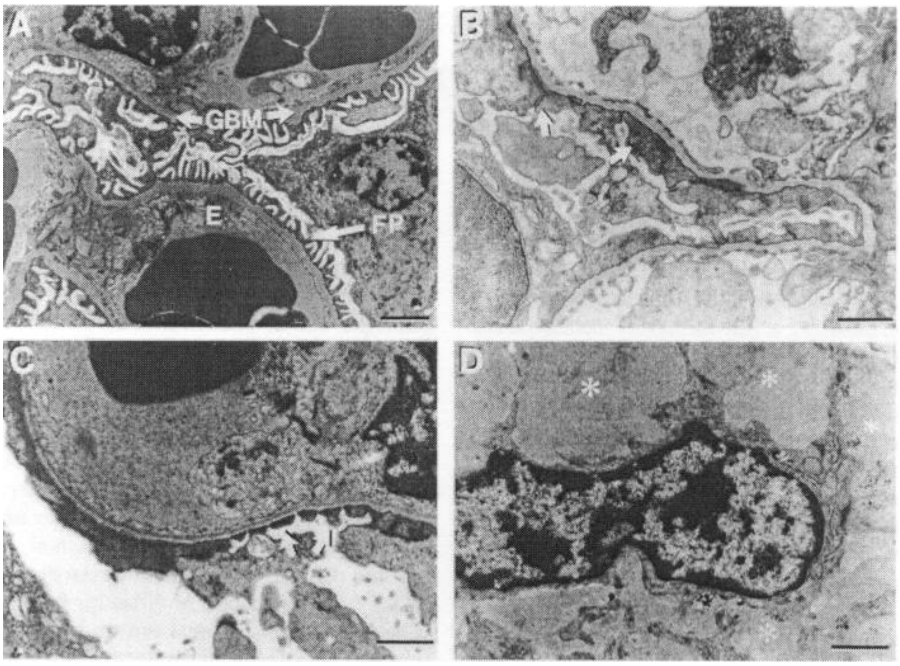
Text and phot. # 93

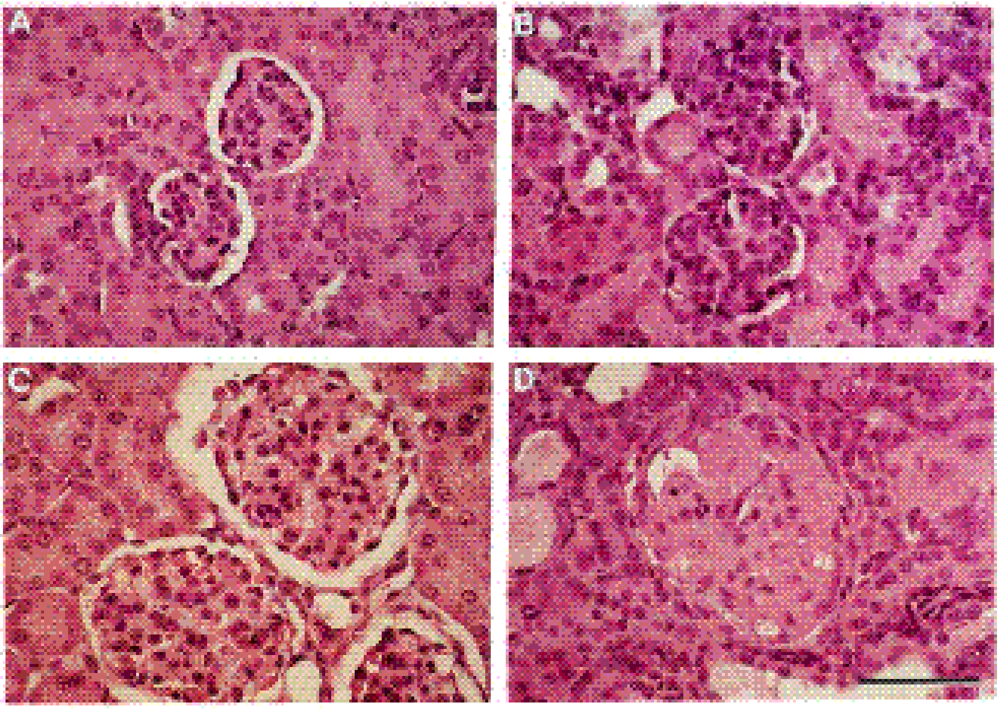
Elements of filtration slits in kidney glomerulus

Filtration of blood plasma in kidney glomerulus goes through a filter composed of endothelial cells of kidney glomerulus, basement membrane and filtration slits and their membranes (filtration slit membranes) located between podocyte extensions (secondary foot processes). Molecules in this membrane have zipperlike formation. They form an ultimate barrier that prevents proteins from leaking into urine. Recently, two proteins, nephrin and CD2AP involved in glomerular filtration were found.

Nephrin is present in filtration slits while CD2AP anchors nephrin to the adjacent cells. Mutation of the nephrin gene leads to the congenital disease called congenital nephrotic syndrome. It is manifested by escape of serum proteins into urine and kidney insufficiency. At present, the only treatment available is kidney transplantation. Mice with knocked down CD2AP gene died after 6- 7 week with symptoms of kidney insufficiency. In their kidneys podocyte extensions were abnormal, mesangial cells proliferated and produced excessive amount of matrix leading to fibrotic changes in kidney glomeruli.

A. EM of a filtration barrier in kidney from 7-day-old normal mouse. GBM- glomerular filtration barrier, FP- podocyte foot.
B. EM of a filtration barrier in kidney from 7-day-old mouse without CD2AP gene. Podocyte extensions are deformed. The rest of a kidney has correct structure.





A. Kidney of 7-day-old normal mouse. H. E.
B. Kidney of 7-day-old mouse without CD2AP gene. Increased number of cells in kidney glomerulus. H.E.
C. Kidney of 14-day-old mouse without CD2AP gene. Increased number of cells and intercellular matrix in glomeruli. H .E.
D. Kidney of 28-old-mouse without CD2AP gene. Fibrotic changes in glomeruli. H. E.

<u>Congenital nephrotic syndrome</u>

Clinical case

Seven-day-old neonate was admitted to the Nephrological Clinic with edema (body swelling caused by excessive fluid accumulation), proteinuria (presence of protein in urine), low albumin concentration in plasma and anemia. The child was born from first pregnancy, at term, by cesarean section. Physical examination disclosed moderate edema of the body and eyelids. Family data:

- mother- in 38 week of pregnancy untreated infection of upper respiratory tract - grandmother (on the mother side) kidney stones, cirrhotic kidney (cirrhosis - fibrous changes leading to a complete destruction of organ parenchyma) - father- arterial hypertension, urography disclosed that he has only one kidney excreting urine.

Laboratory examination:

Marked proteinuria (protein in urine) and anemia. There were no symptoms of renal insufficiency (concentration of urea and creatinine in blood remained normal).

Kidney biopsy: light microscopy disclosed irregular thickening of glomerular basement membranes and in some glomeruli increased number of mesangial cells. EM examination revealed swollen podocytes with abnormal "fused" extensions.

Treatment:

Infusion of 20% albumin solution Furosemide (diuretic drug; drug increasing urine excretion) Encorton (steroid hormone) for 8 weeks Blood transfusion

The treatment did not decrease proteinuria. In view of the protein loss the kidney was destroyed pharmacologically by administration of Captopril (Ca^{2+} antagonist) and indomethacin (non-steroid antyinflammatory drug). The child will by subjected to peritoneal dialysis and kidney transplantation.

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