Functional morphology of kidneys Clearance

Assoc. Prof. MUDr. Markéta Bébarová, Ph.D.

Department of Physiology

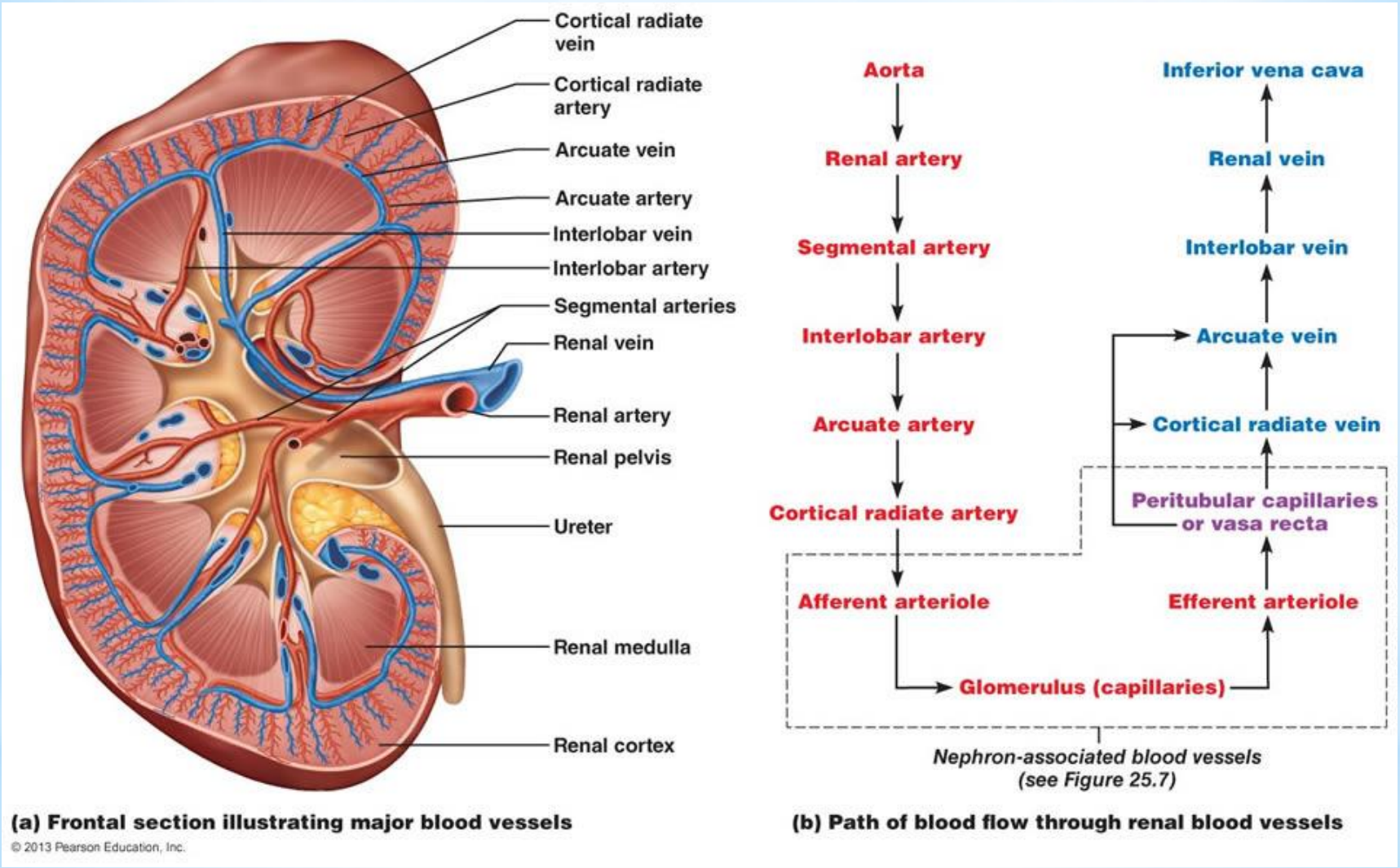
Faculty of Medicine, Masaryk University

This presentation includes only the most important terms and facts. Its content by itself is not a sufficient source of information required to pass the Physiology exam.

Renal Functions

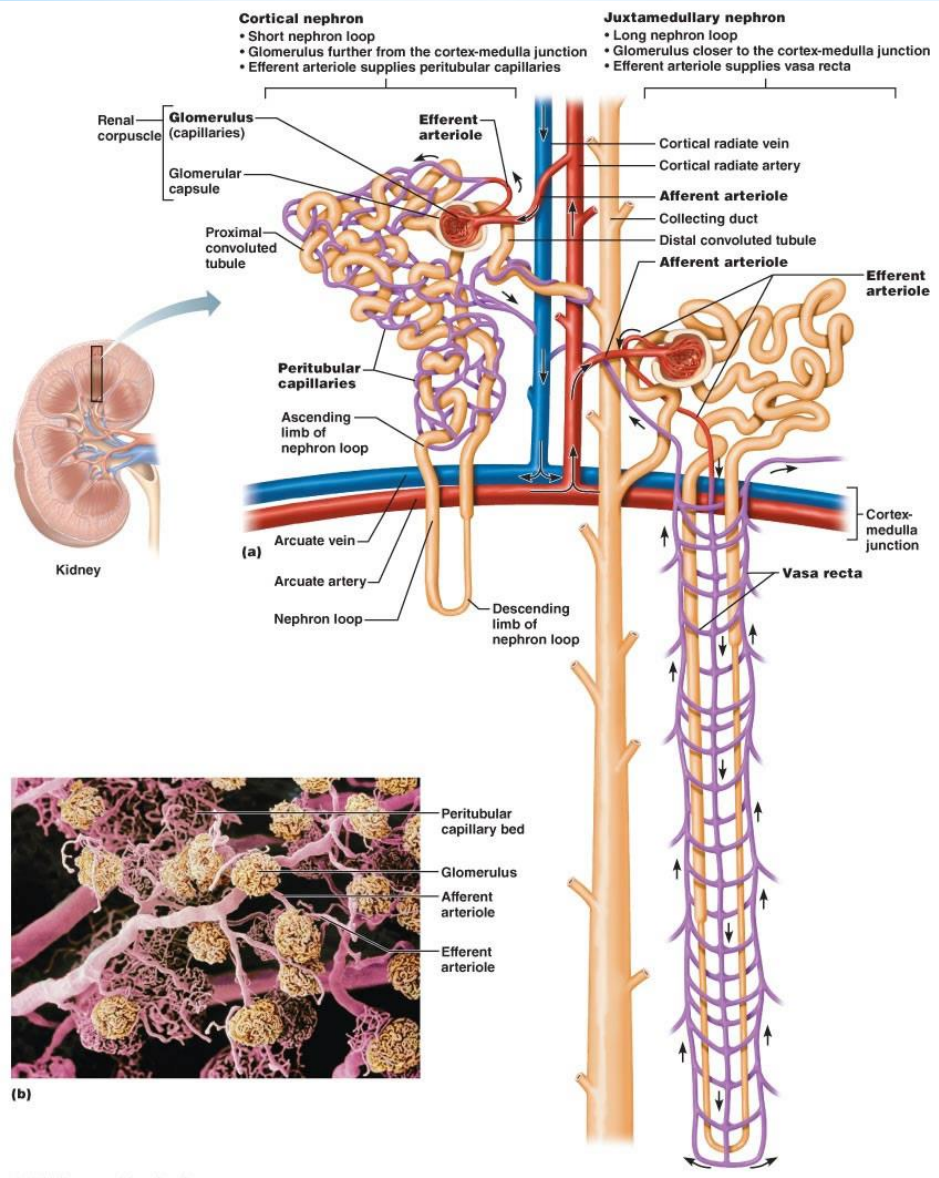
- Excretion of Waste Products and Toxins
- Control of Volume and Composition of Body Fluids, Osmolality
- Regulation of Acid-Base Balance
- Regulation of Blood Pressure
- Secretion, Metabolism and Excretion of Hormones
- Glukoneogenesis

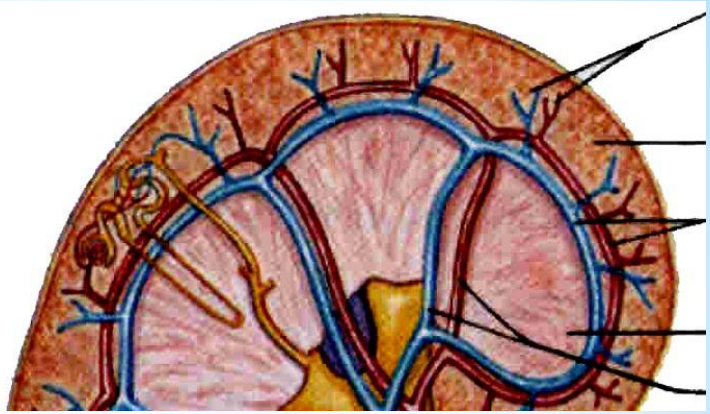
Structure of Kidney



http://classes.midlandstech.edu/carterp/Courses/bio211/chap25/chap25.htm

Structure of Kidney





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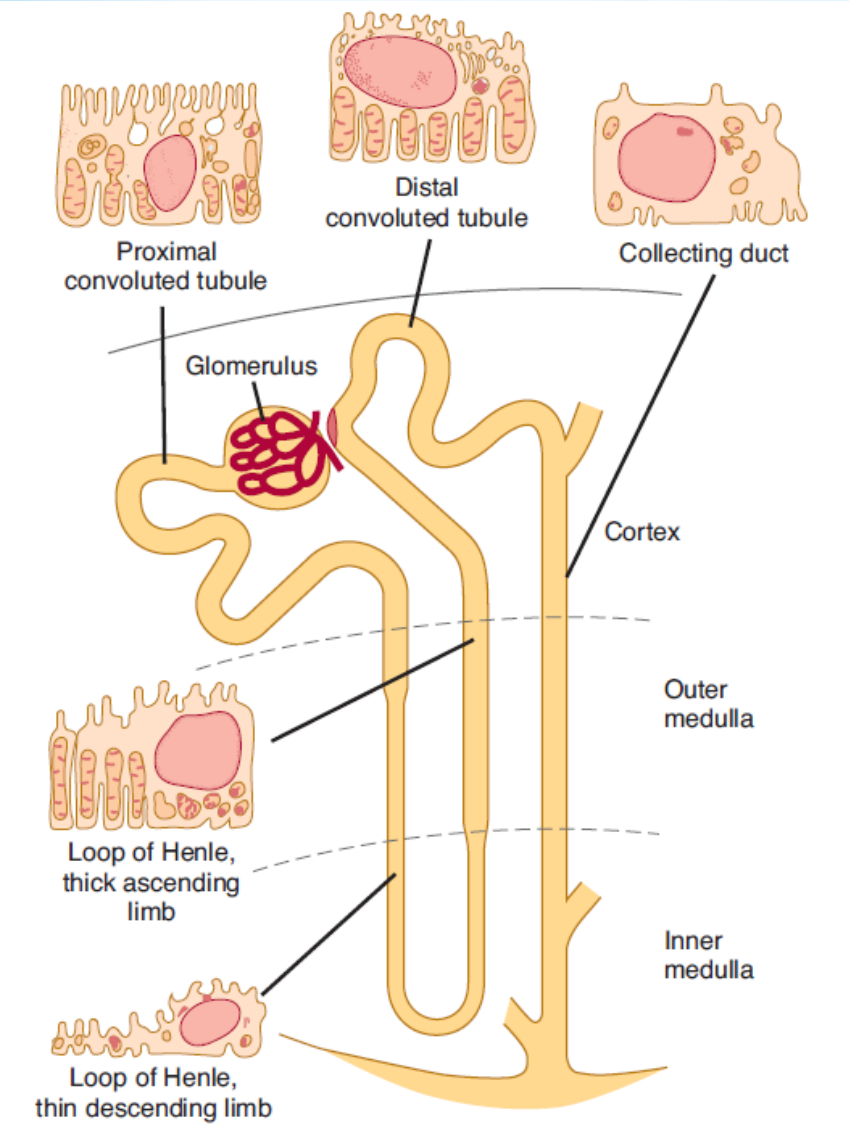
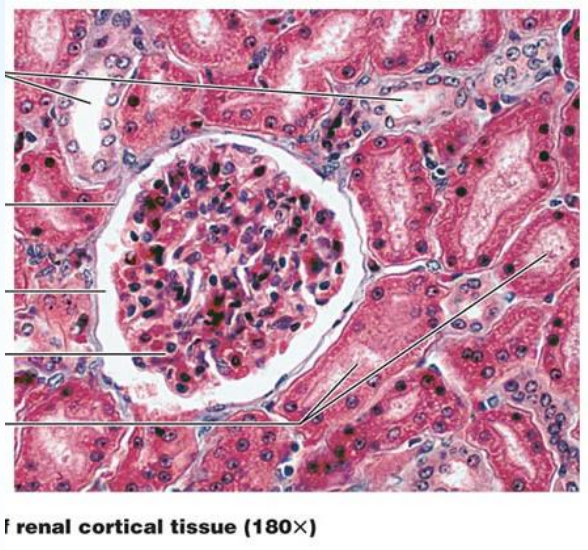
Structure of Nephron





renal cortical tissue (180×)

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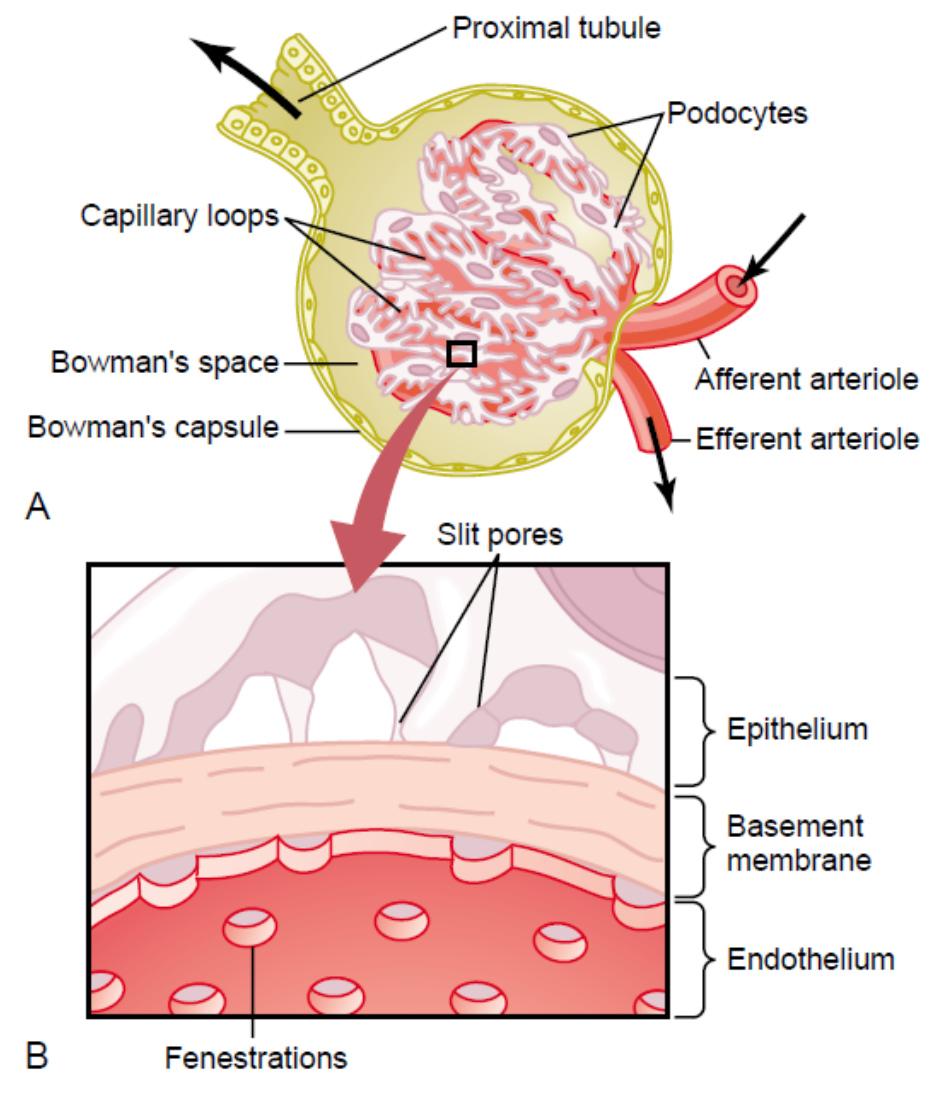
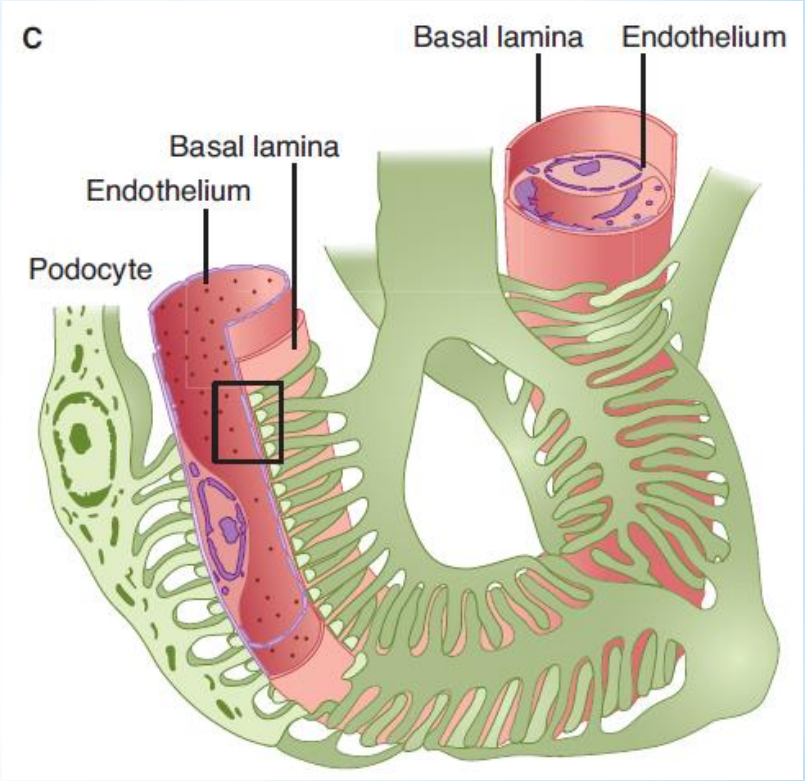
Structure of Nephron - Glomerulus





mesangial cells

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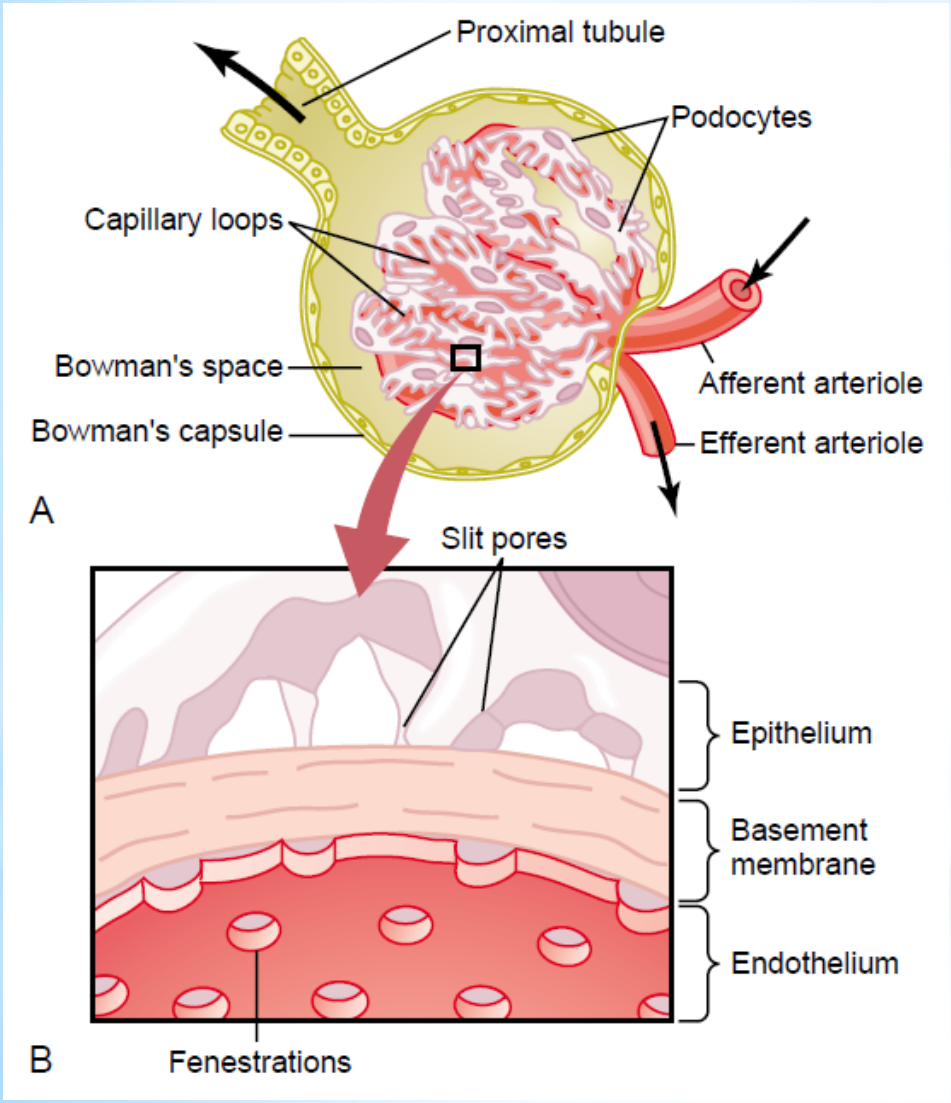
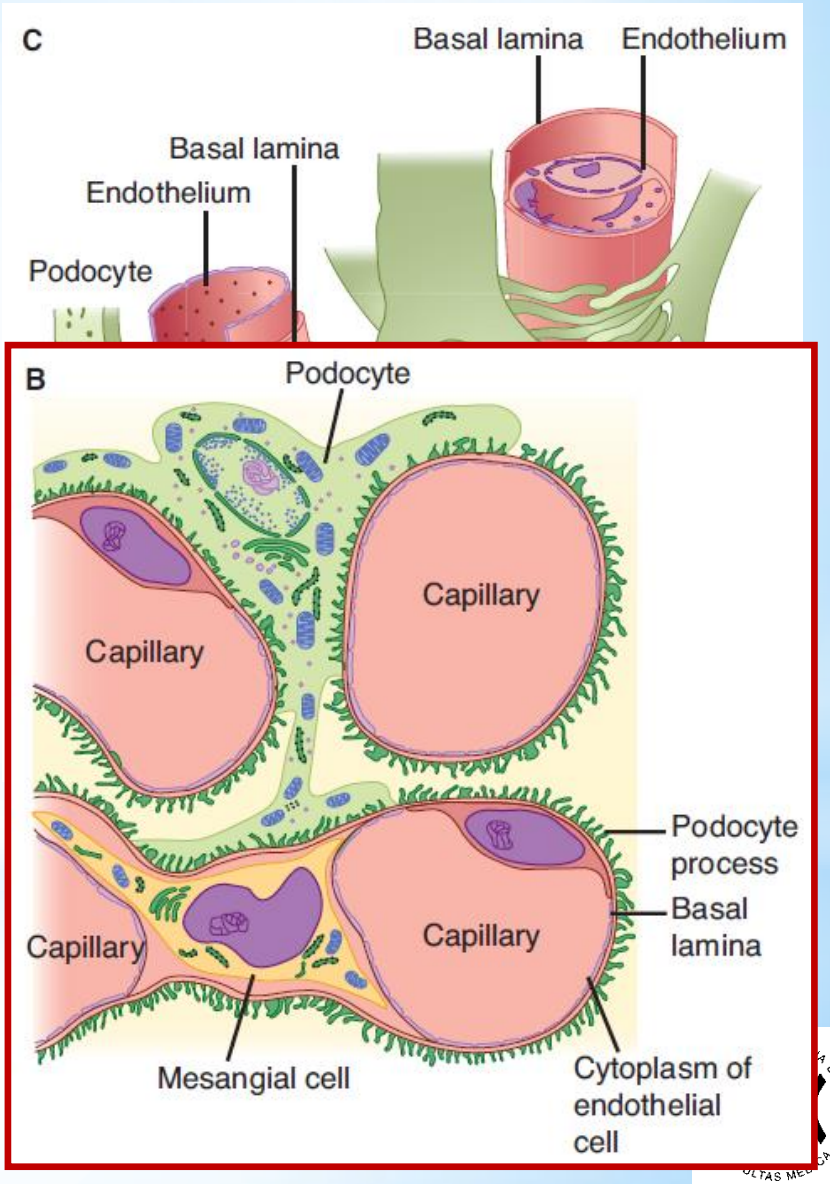
Structure of Nephron - Glomerulus





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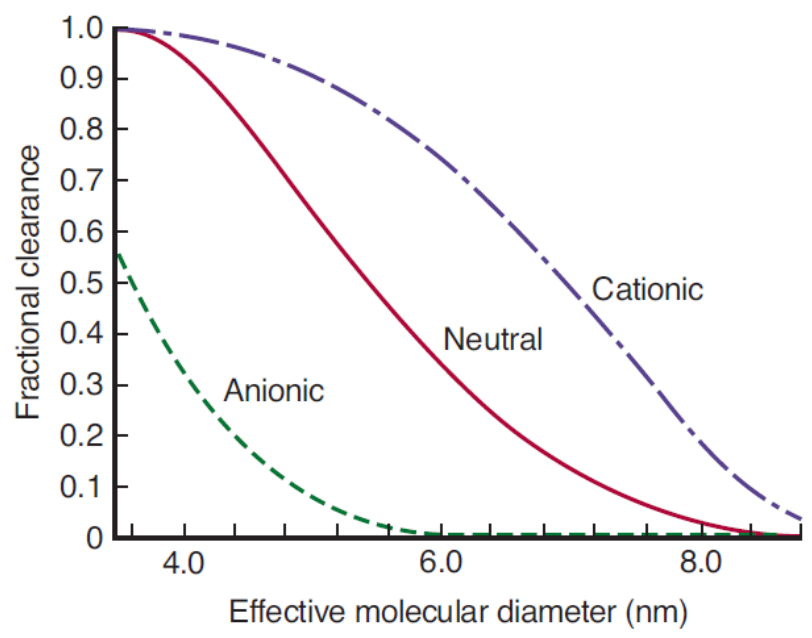
Structure of Nephron - Glomerulus

- High filtration rate in glomeruli
  provided by high permeability of glomerular membrane
- Protein passage barrier
  negative charge of all layers of glomerular membrane



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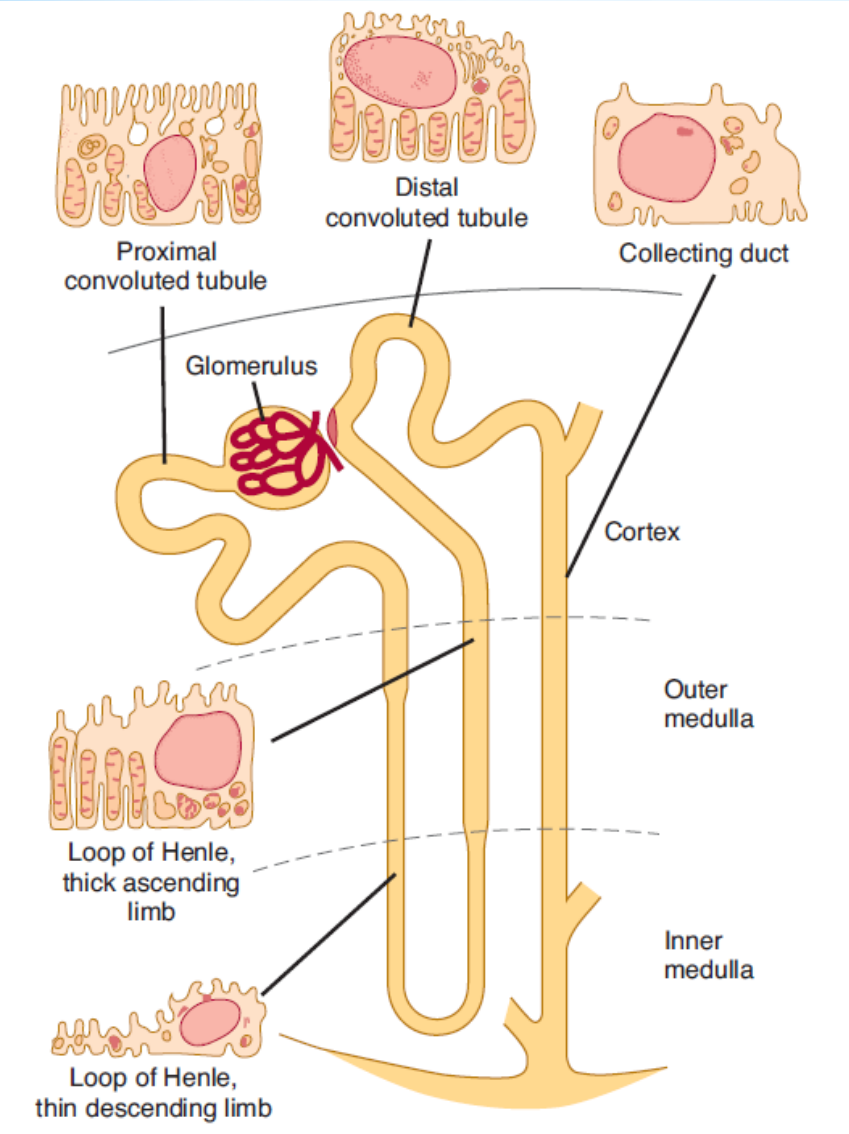
Structure of Nephron - Tubulus



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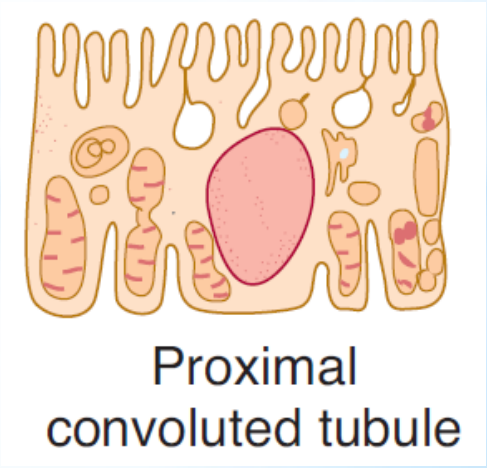
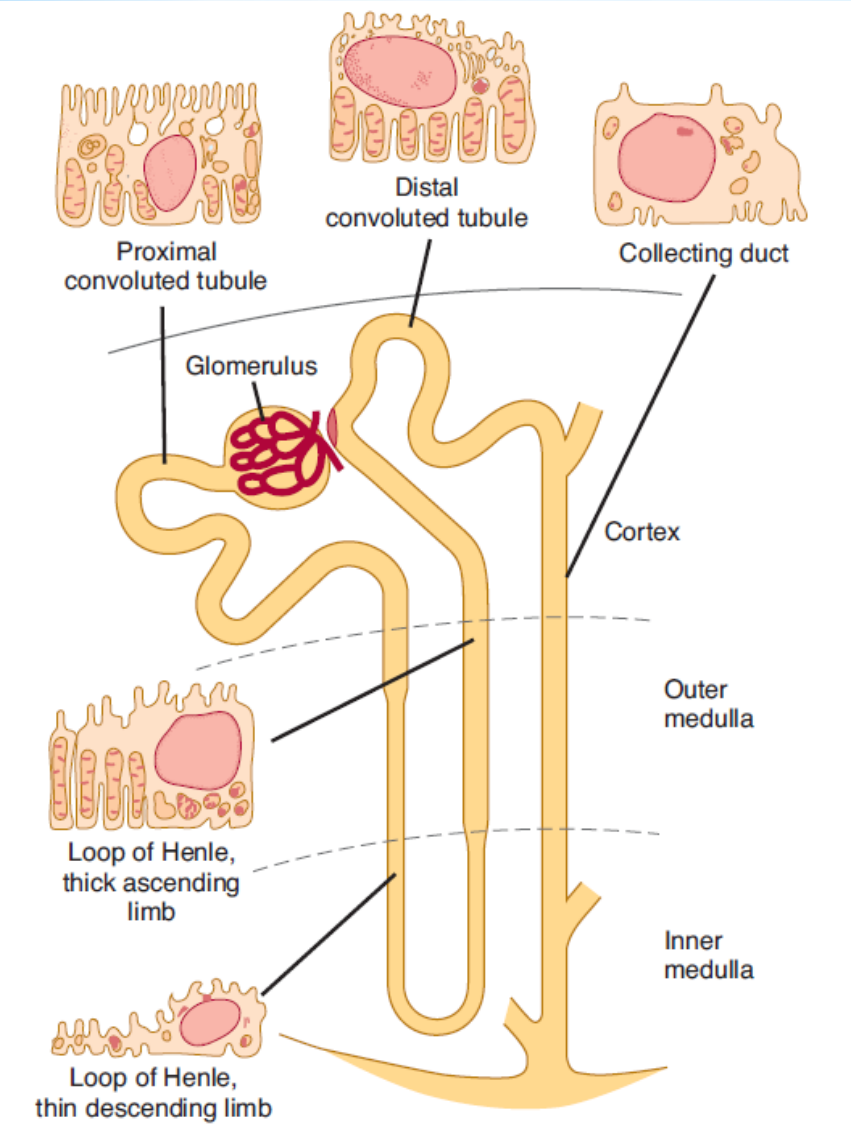
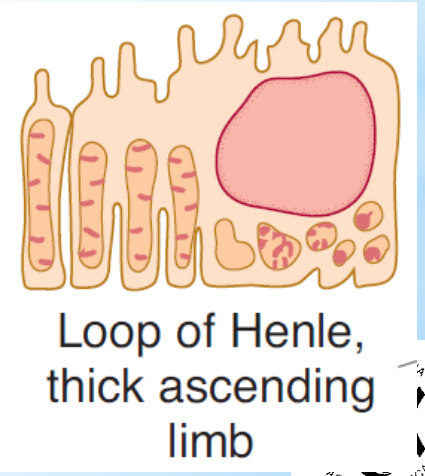
- glomerulus
- proximal convoluted tubule



Structure of Nephron - Tubulus



- glomerulus
- proximal convoluted tubule
- loop of Henle



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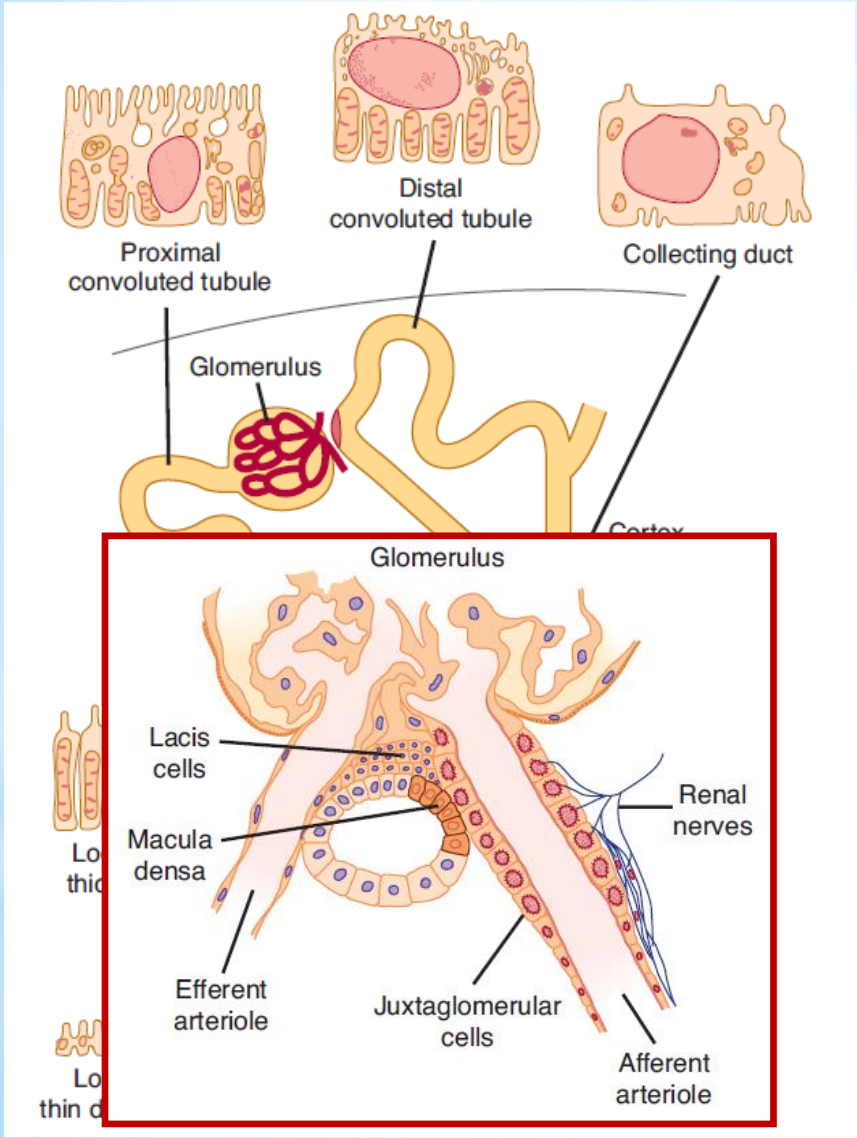
Structure of Nephron - Tubulus



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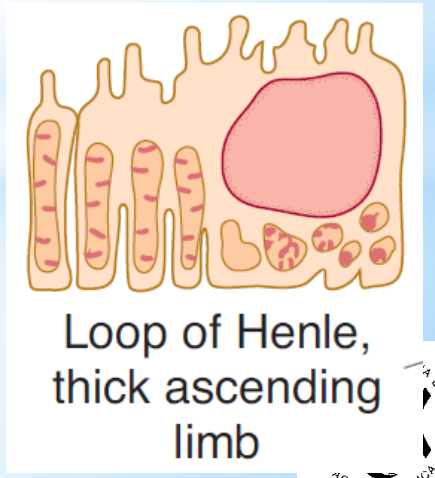

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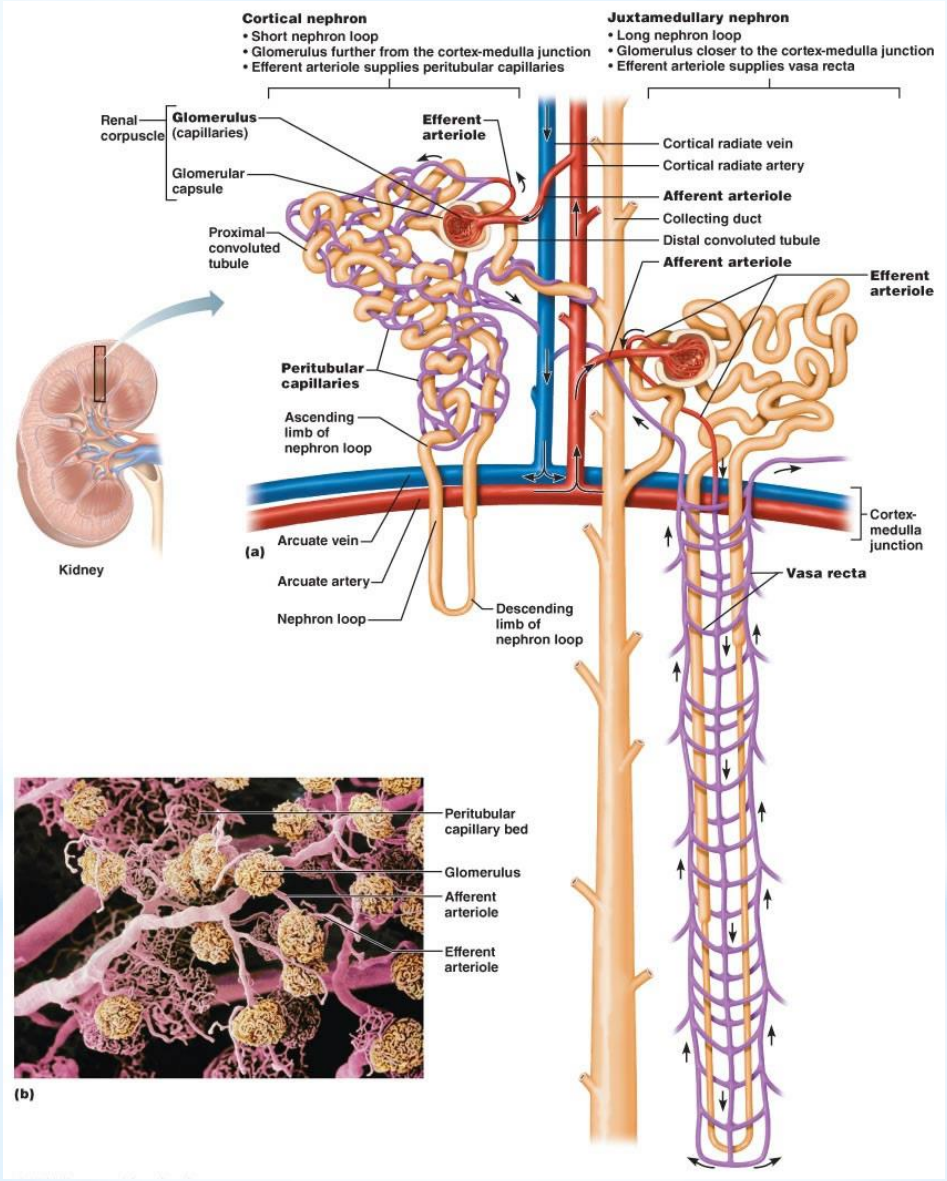

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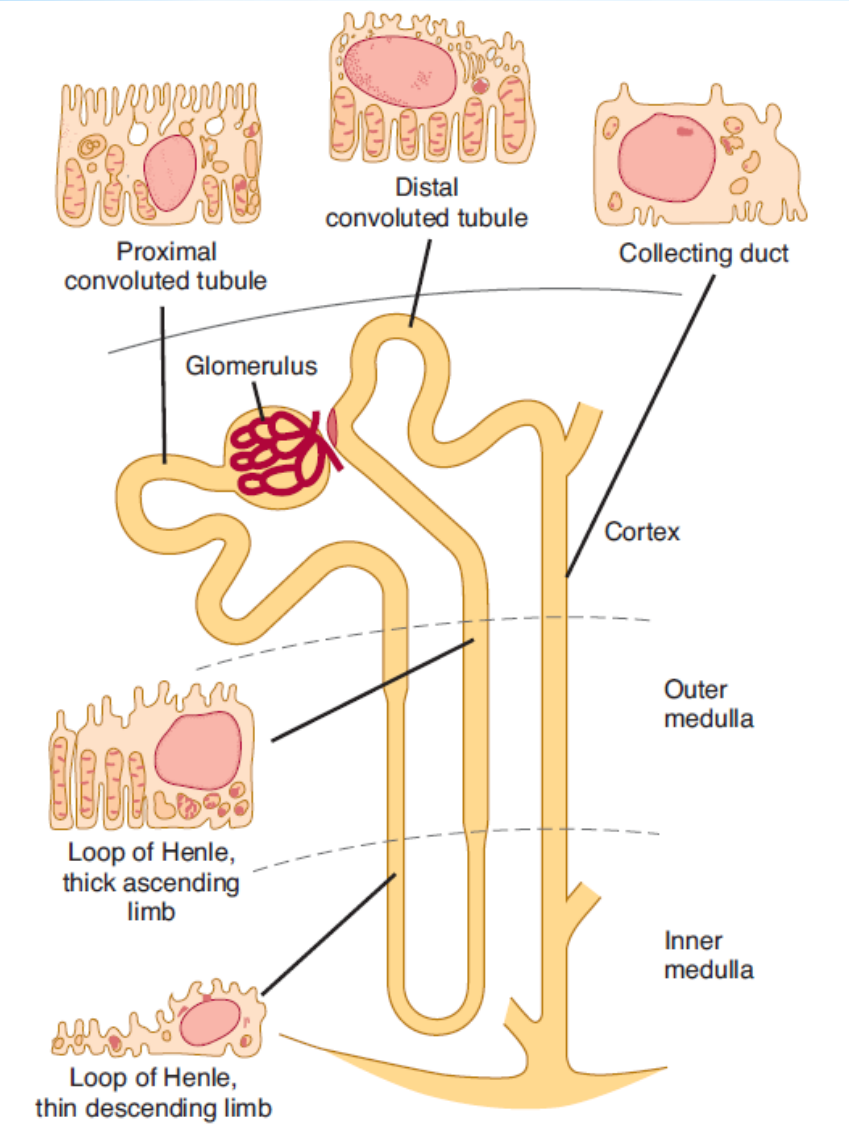
Structure of Nephron - Tubulus



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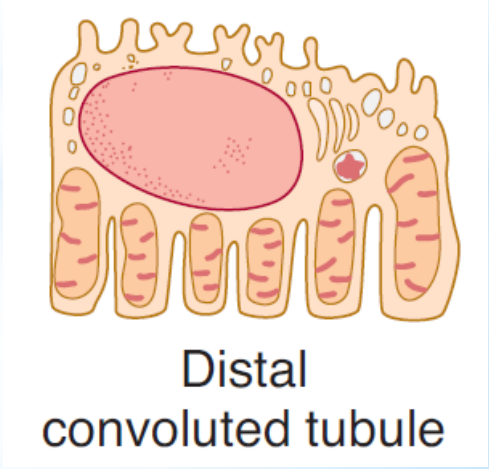
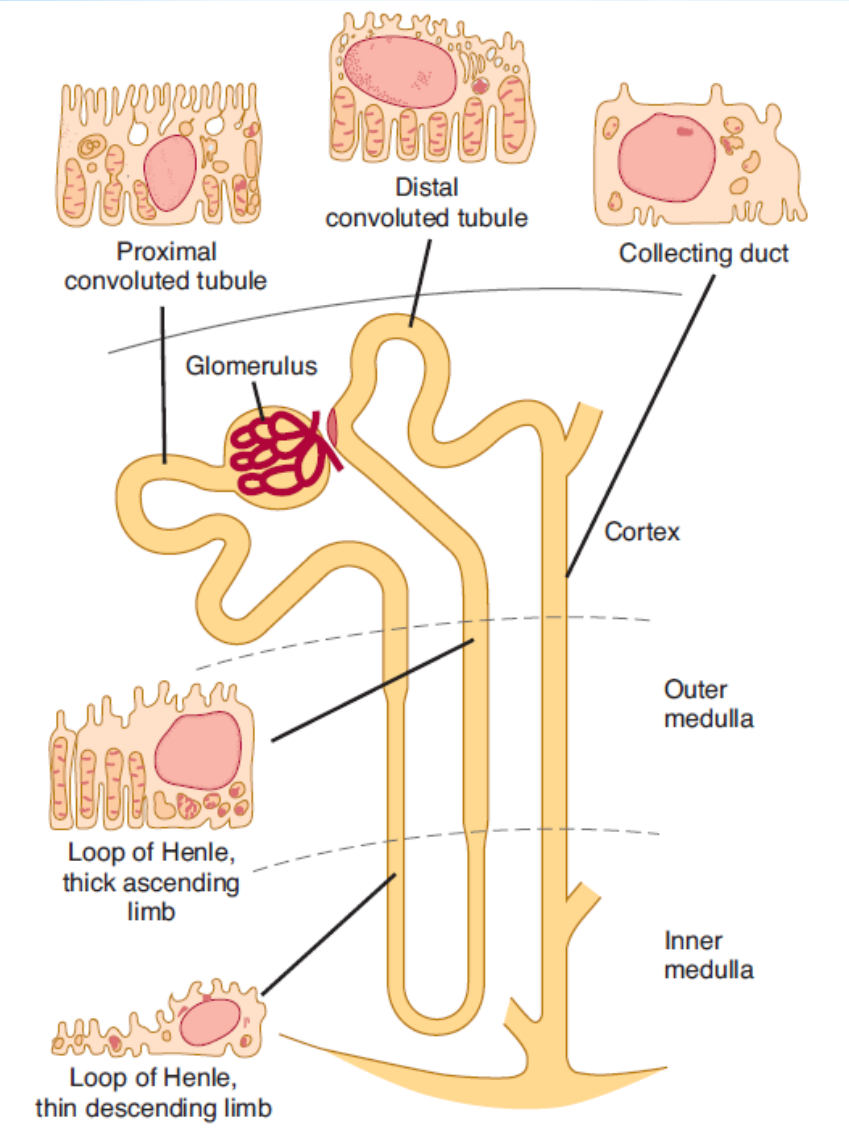
- glomerulus
- proximal convoluted tubule
- loop of Henle
- distal convoluted tubule



Structure of Nephron - Tubulus



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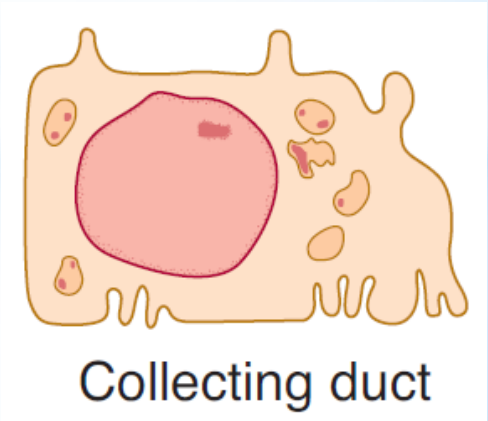
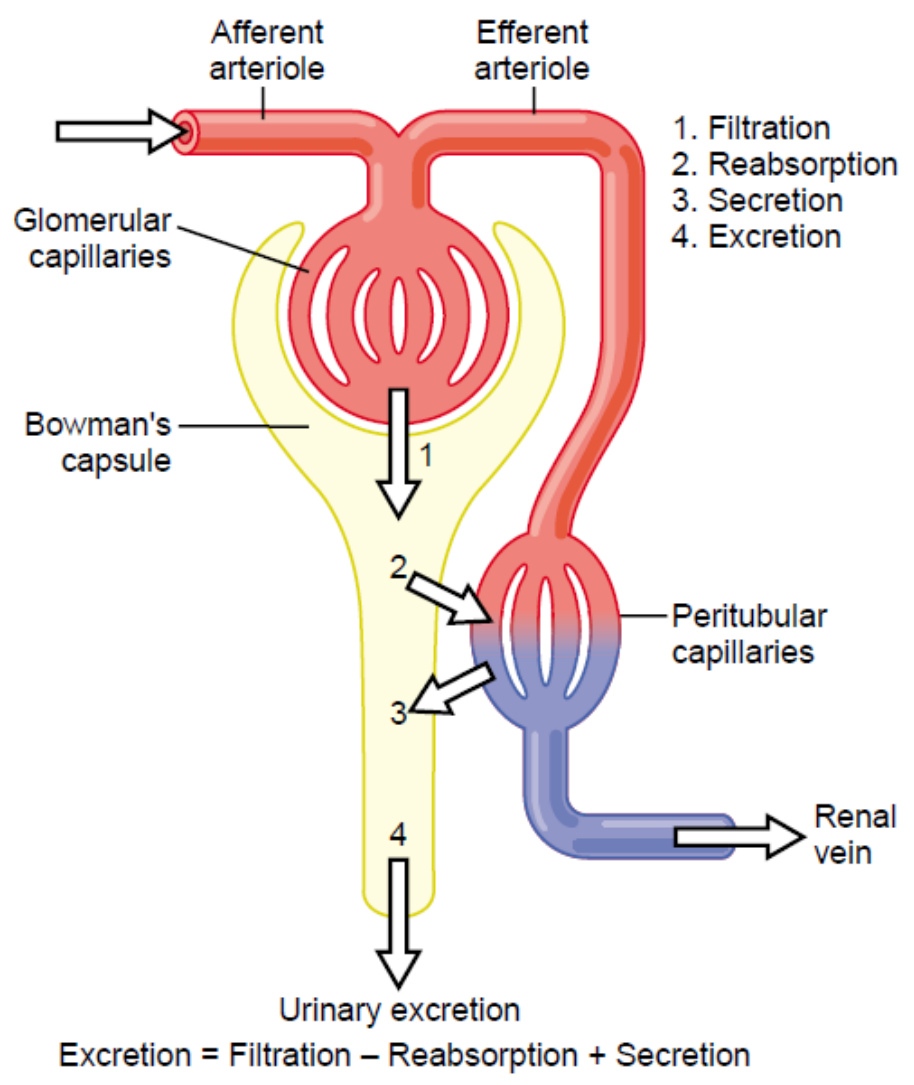
- glomerulus
- proximal convoluted tubule
- loop of Henle
- distal convoluted tubule
- collecting duct



Urine Formation



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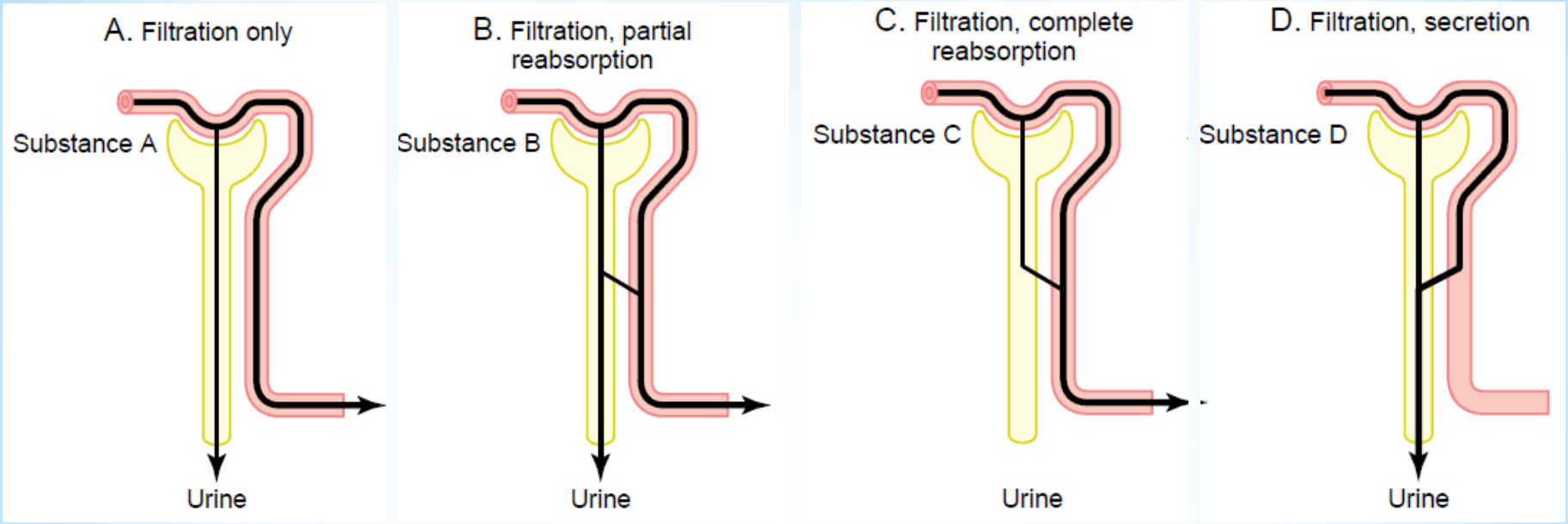
1) Glomerular filtration
2) Tubular reabsorption
3) Tubular secretion
4) Urine excretion

Urine Formation



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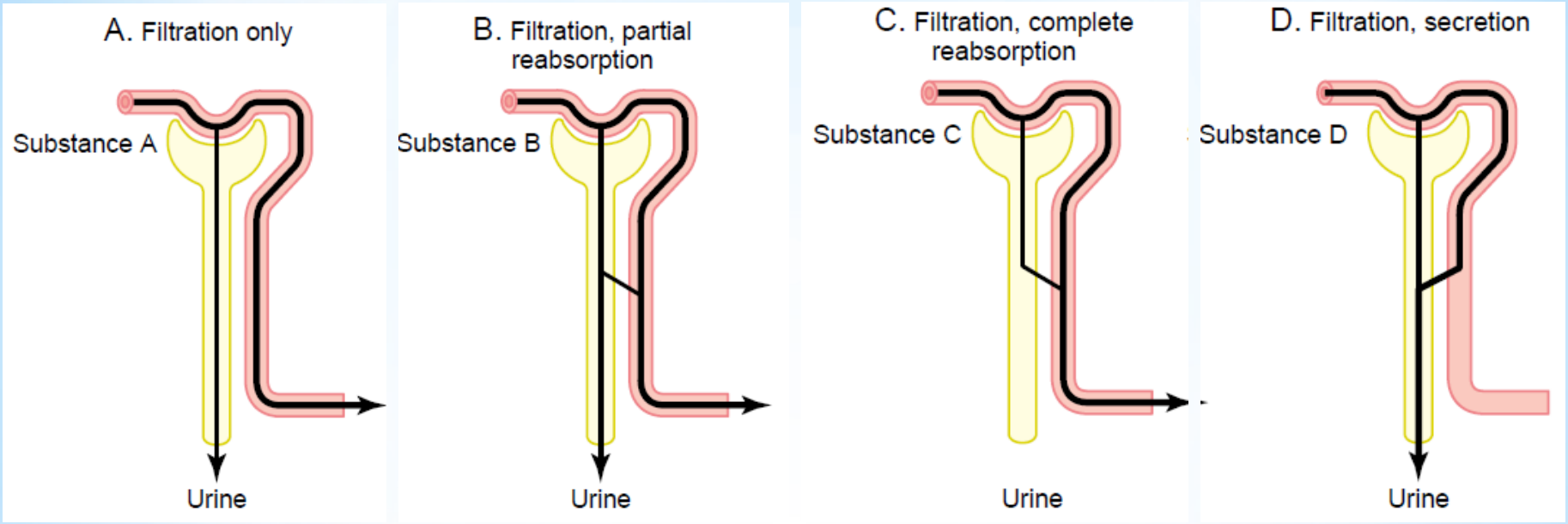
- creatinine
- other waste products
- electrolytes
- amino acids
- glucose
- PAH
- toxins
- organic base and acids

Urine Formation



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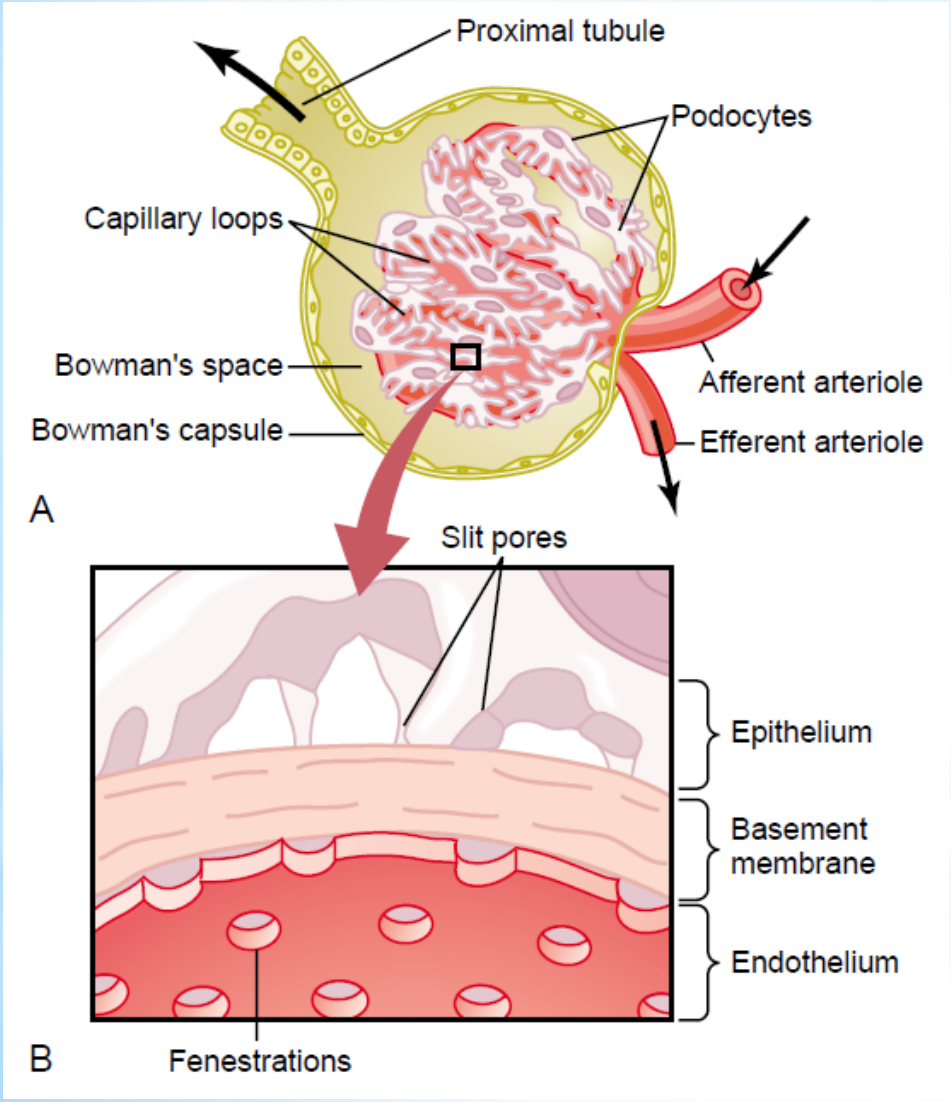
- creatinine
- other waste products

Substance	Concentration in Urine (U)	Concentration in Plasma (P)	U/P Ratio
Glucose (mg/dL)	0	100	0
Na^+ (mEq/L)	90	140	0.6
Urea (mg/dL)	900	15	60
Creatinine (mg/dL)	150	1	150

- PAH
- toxins
- organic base and acids

Urine Formation - Glomerular Filtration



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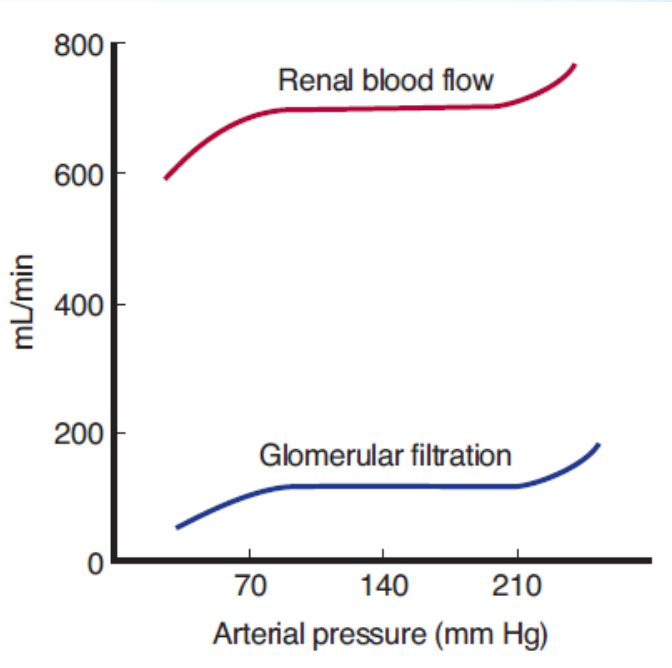
GFR = 125 ml/min = 180 l/day

FF = 0.2

20% of plasma filtered!



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Urine Formation - Glomerular Filtration

Glomerular filtration rate (GFR) depends on:

1) Capillary filtration coefficient K_f
   (permeability and area of glomerular membrane; mesangial cells)

2) Balance of hydrostatic and coloid osmotic forces

$$\text{GFR} = K_f \cdot \text{net filtration pressure}$$

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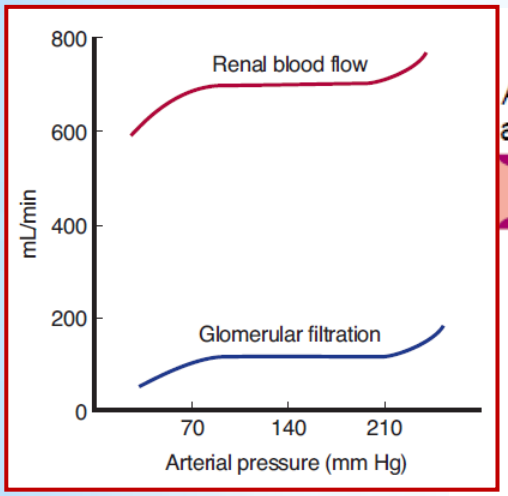
Urine Formation - Glomerular Filtration

GFR = K_f · net filtration pressure



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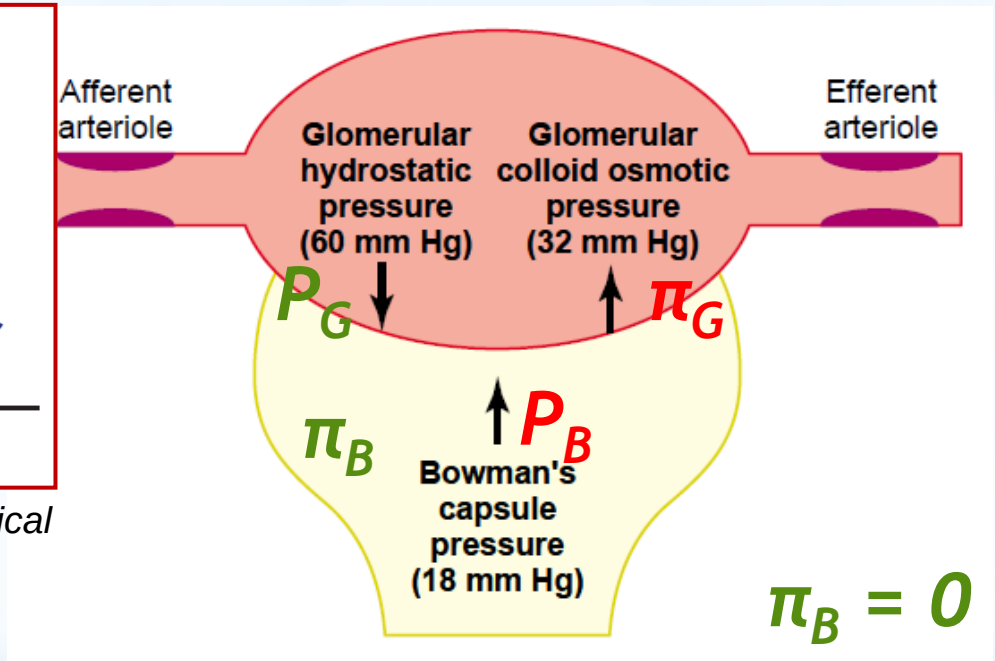

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Under physiological conditions:

net filtration pressure = $P_G + \pi_B - P_B - \pi_G = 60 + 0 - 18 - 32 = 10$ mmHg

$$GFR = K_f \cdot (P_G + \pi_B - P_B - \pi_G)$$

Urine Formation - Glomerular Filtration

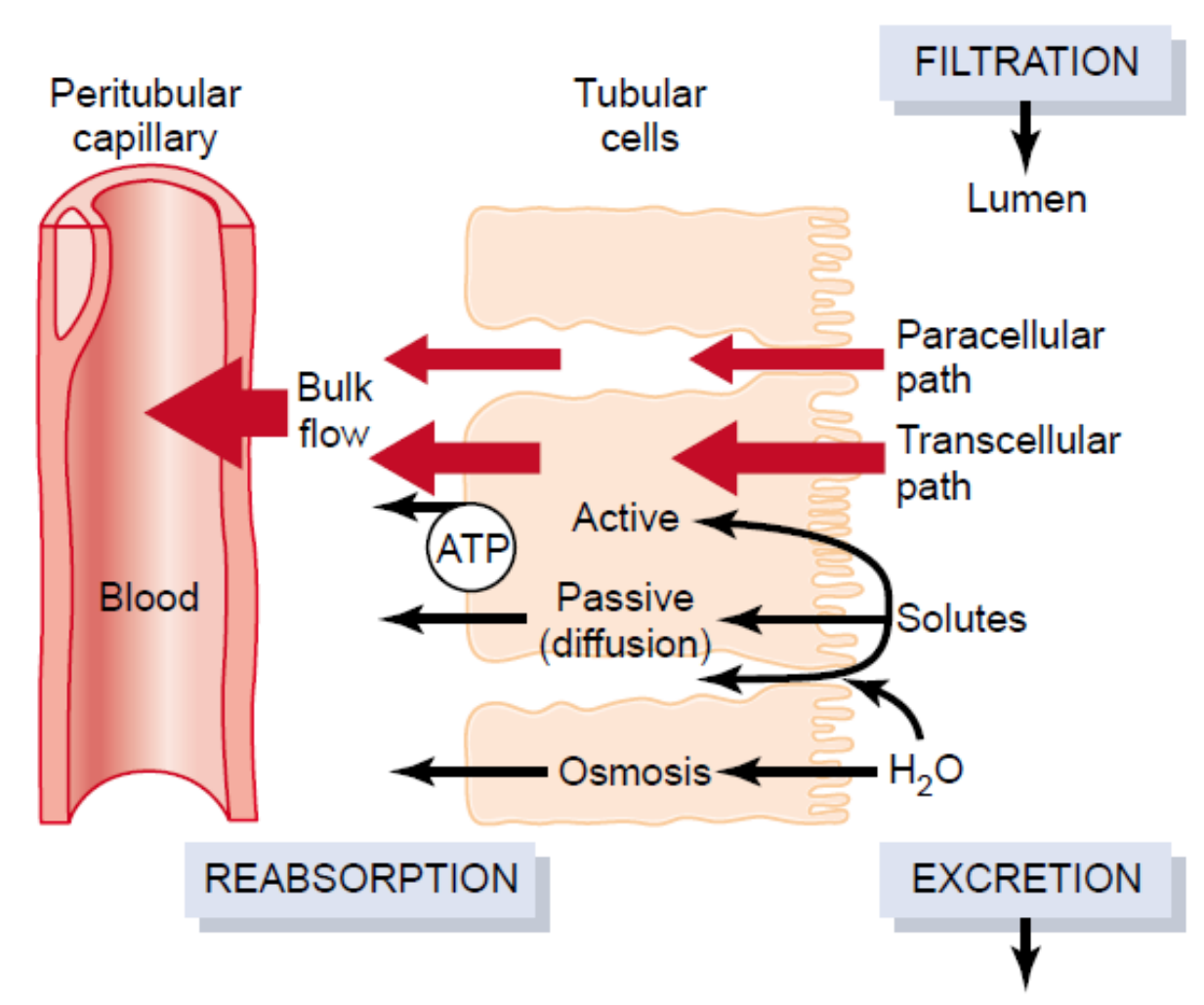
Vas afferens, vas efferens

- input and output of high-pressure glomerular capillary net
- glomerular blood flow = $\frac{P_{v.a.} - P_{v.e.}}{R_{v.a.} + R_{v.e.} + \cancel{R_{g.k.}}}$
- ↑ resistance of *vas aff.* or *vas eff.* → ↓ renal blood flow (if the arterial pressure is stable)
- control the glomerular filtration pressure:

constriction of *vas aff*. → ↓ glomerular pressure → ↓ filtration

constriction of *vas eff*. → ↑ glomerular pressure → ↑ filtration

Urine Formation – Tubular Processes



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Urine Formation – Tubular Processes

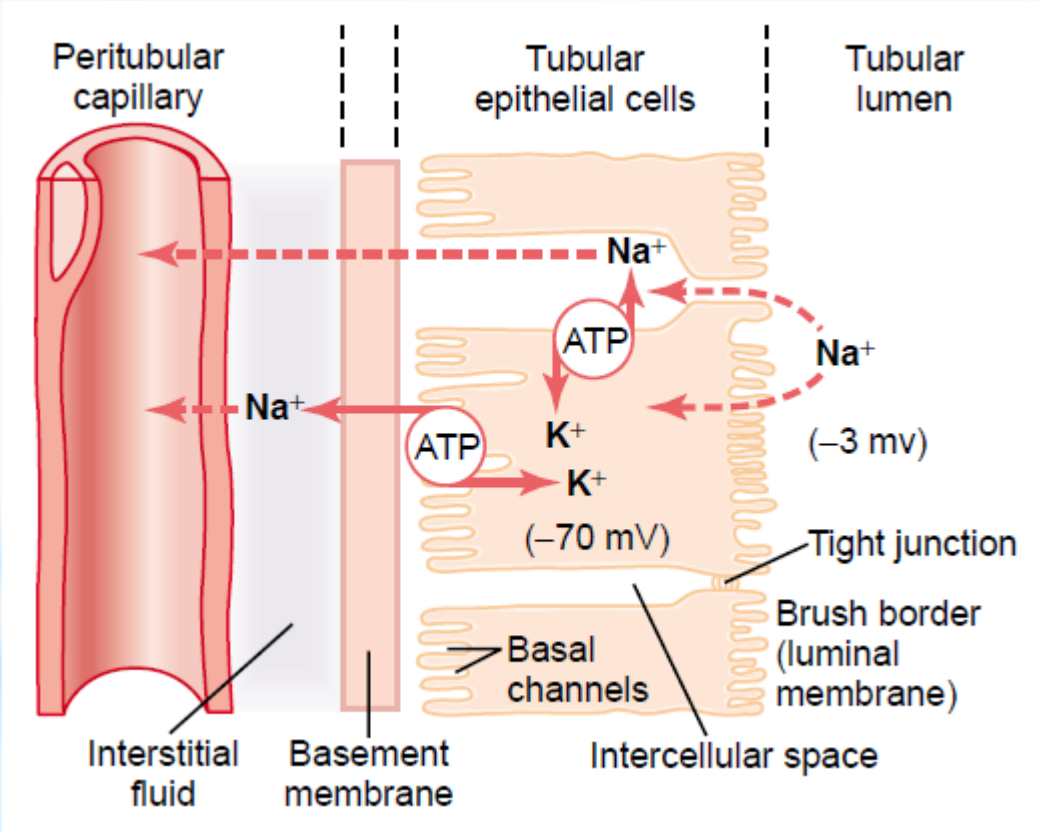
Active Transport Mechanisms

1) Primary active transport
2) Secondary active transport
3) Pinocytosis
   (big molecules, *e.g.* proteins, namely in the proximal tubule)

Urine Formation – Tubular Processes

Active Transport Mechanisms

1) Primary active transport



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Urine Formation – Tubular Processes

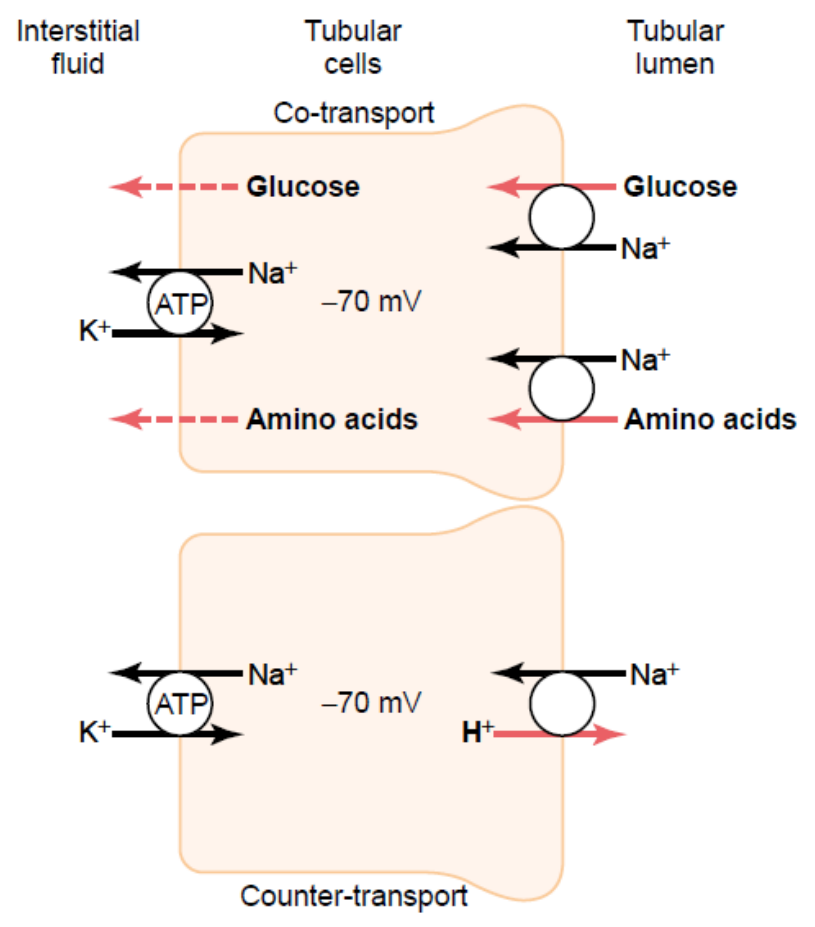
Active Transport Mechanisms

1) Primary active transport
   - Na^+/K^+ ATPase
   - H^+ ATPase
   - Ca^{2+} ATPase

Urine Formation – Tubular Processes

Active Transport Mechanisms

2) Secondary active transport



symport

antiport

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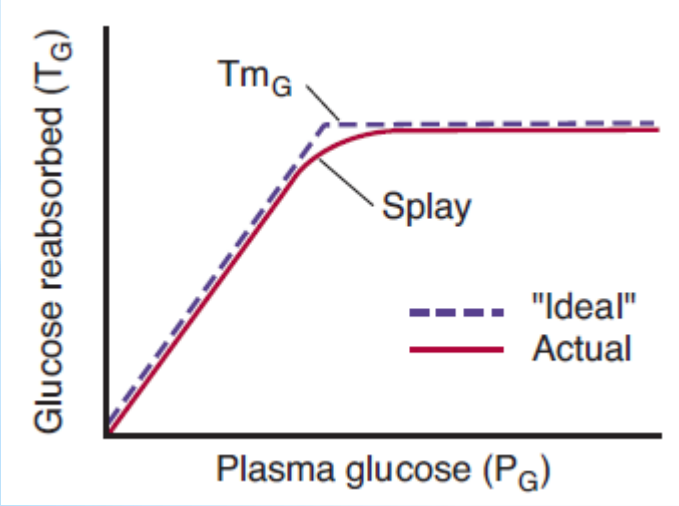
Urine Formation – Tubular Processes

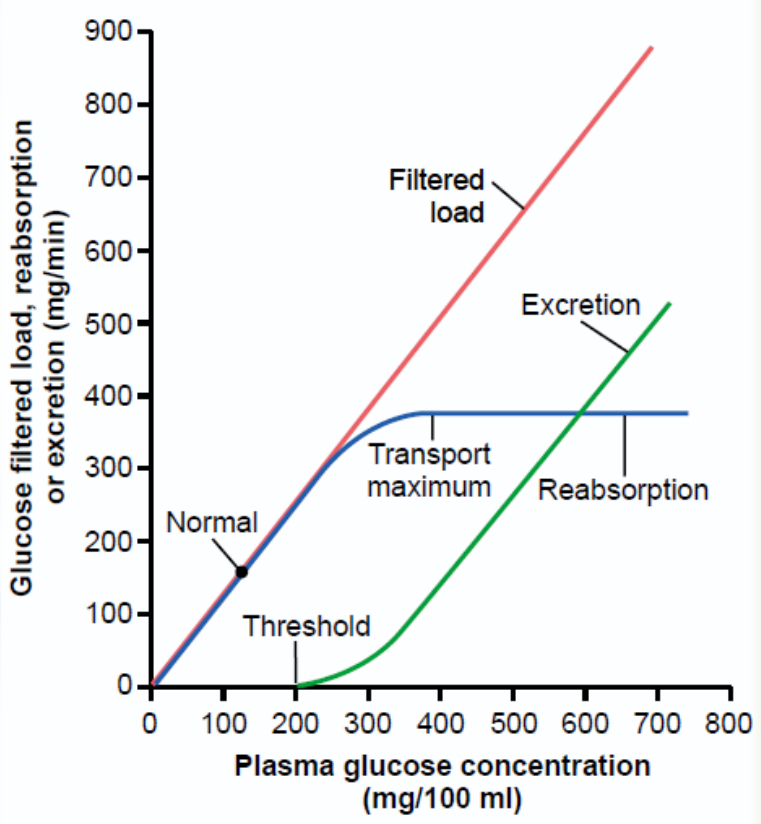
Active Transport Mechanisms

Substances using active transport show the so called transport maximum (given by saturation of the transporter).

for example glucose

transport maximum:
~320 mg/min





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Urine Formation – Tubular Processes

Active Transport Mechanisms

Substances using active transport show the so called transport maximum (given by saturation of the transporter).

reabsorption

Substance	Transport Maximum
Glucose	375 mg/min
Phosphate	0.10 mM/min
Sulfate	0.06 mM/min
Amino acids	1.5 mM/min
Urate	15 mg/min
Lactate	75 mg/min
Plasma protein	30 mg/min

secretion

Substance	Transport Maximum
Creatinine	16 mg/min
Para-aminohippuric acid	80 mg/min

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Urine Formation – Tubular Processes

Active Transport Mechanisms

Substances using active transport without the transport maximum (the gradient-time transport).

- reabsorption of Na^+ in the proximal tubule

⬇

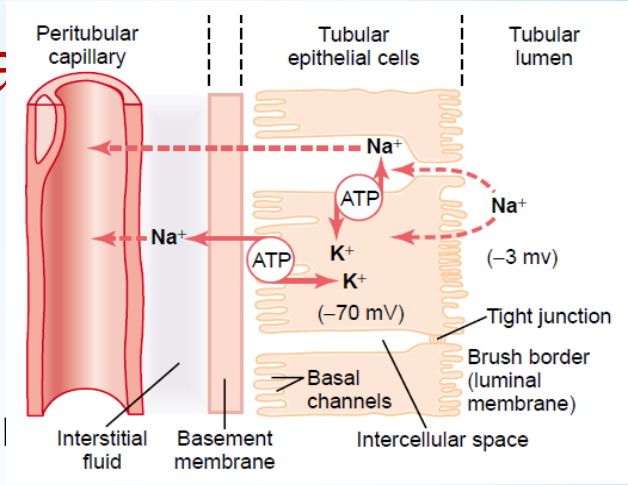
The higher concentration of Na^+ in the proximal tubule, the higher velocity of its reabsorption.

The slower flow of fluid in the proximal tubule, the more Na^+ is reabsorpbed.

In the distal parts of tubule, Na^+ reabsorption shows the transport maximum (non-leaky tight junctions, smaller transport) – may be increased, e.g. by aldosteron.

Urine Formation – Tubular Processes

Active Transport Mecha

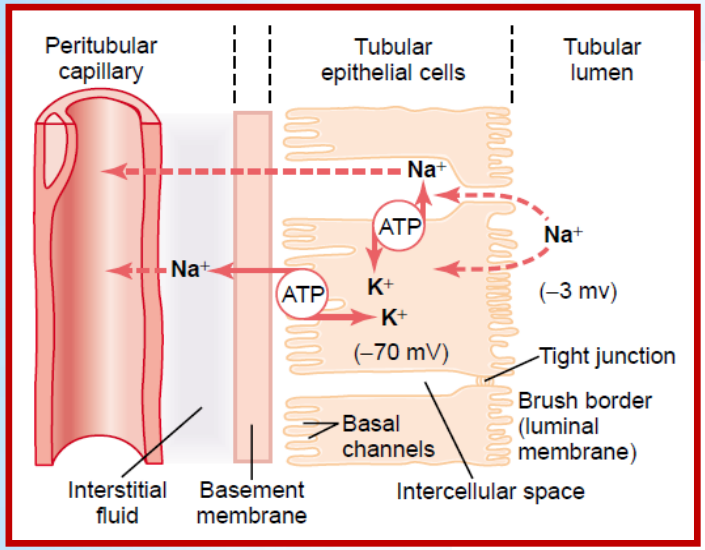


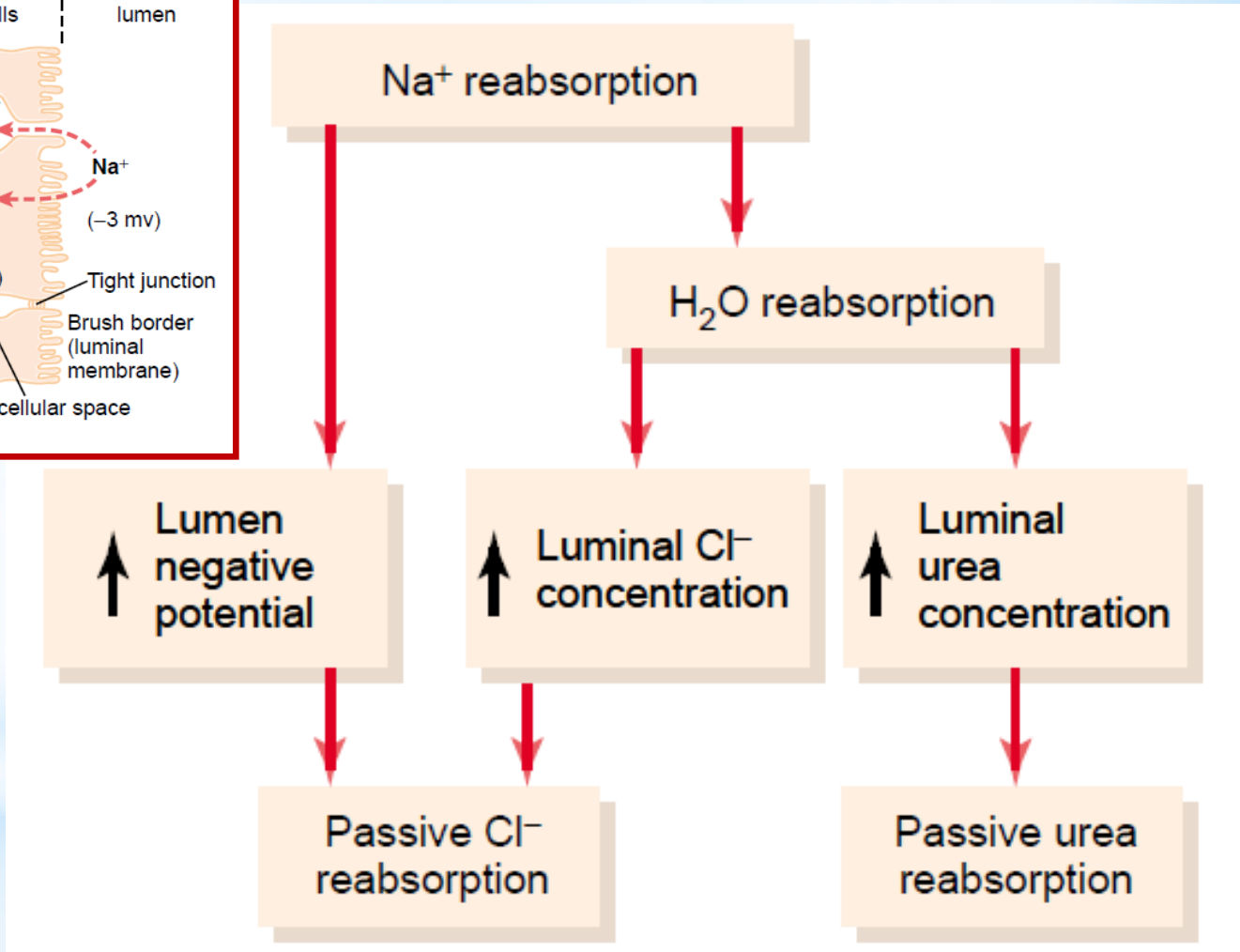
1) Primary active transport
2) Secondary active transport
3) Pinocytosis
   (big molecules, *e.g.* proteins, namely in the p

Passive Transport Mechanisms

1) Reabsorption of H_2O by osmosis
   - in the proximal tubule (highly permeable for H_2O)
   - active reabsorption of solutes → lumen-intersticium concentration gradient → H_2O osmosis into intersticium
2) Reabsorption of solutes by diffusion
   - Cl^- (Na^+ into intersticium, reabsorption of H_2O by osmosis)
   - urea (reabsorption of H_2O by osmosis)

Urine Formation – Tubular Processes





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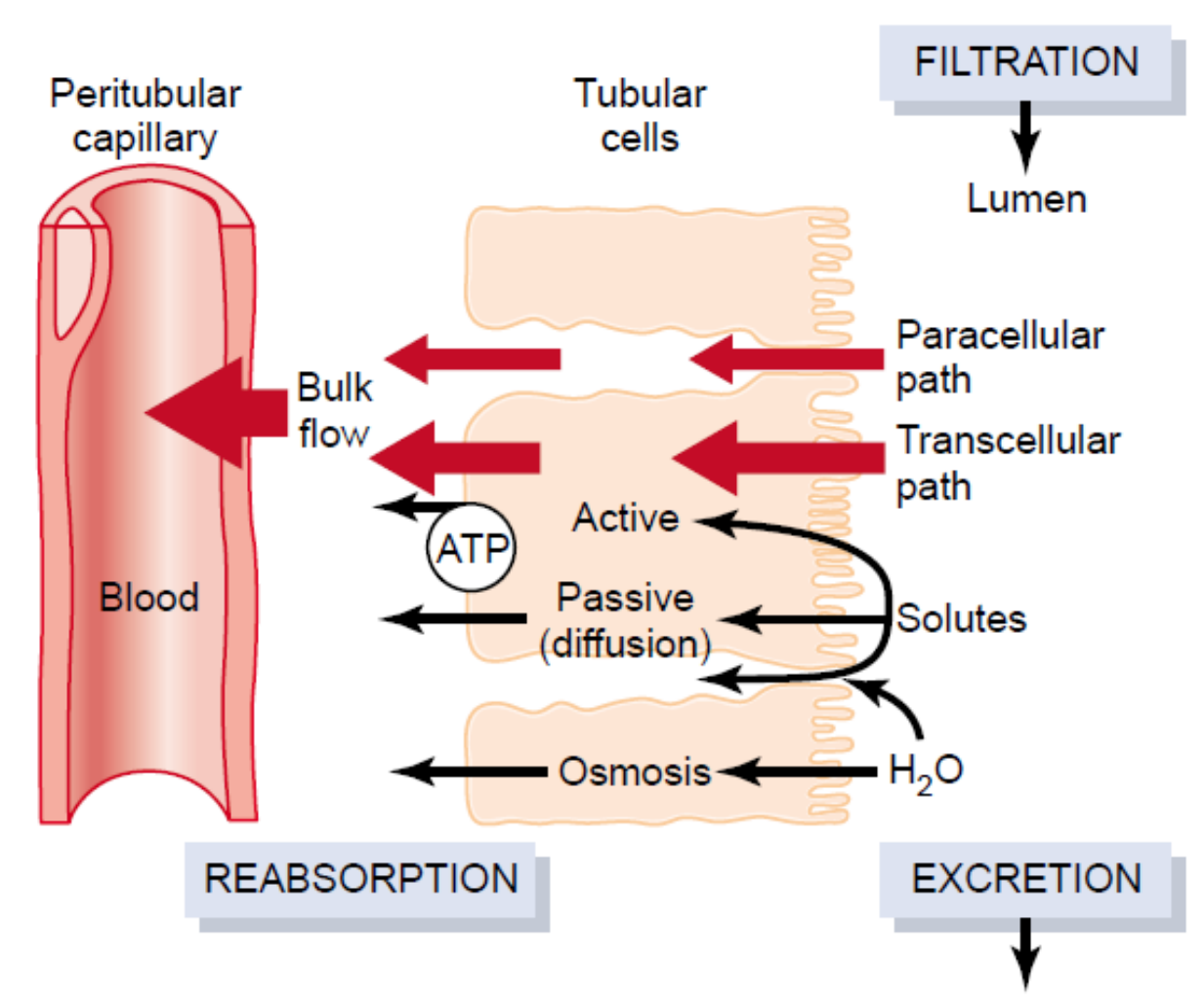
Urine Formation – Tubular Processes



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Urine Formation – Tubular Processes

Physical Forces in Peritubular Capillaries and in Renal Intersticium

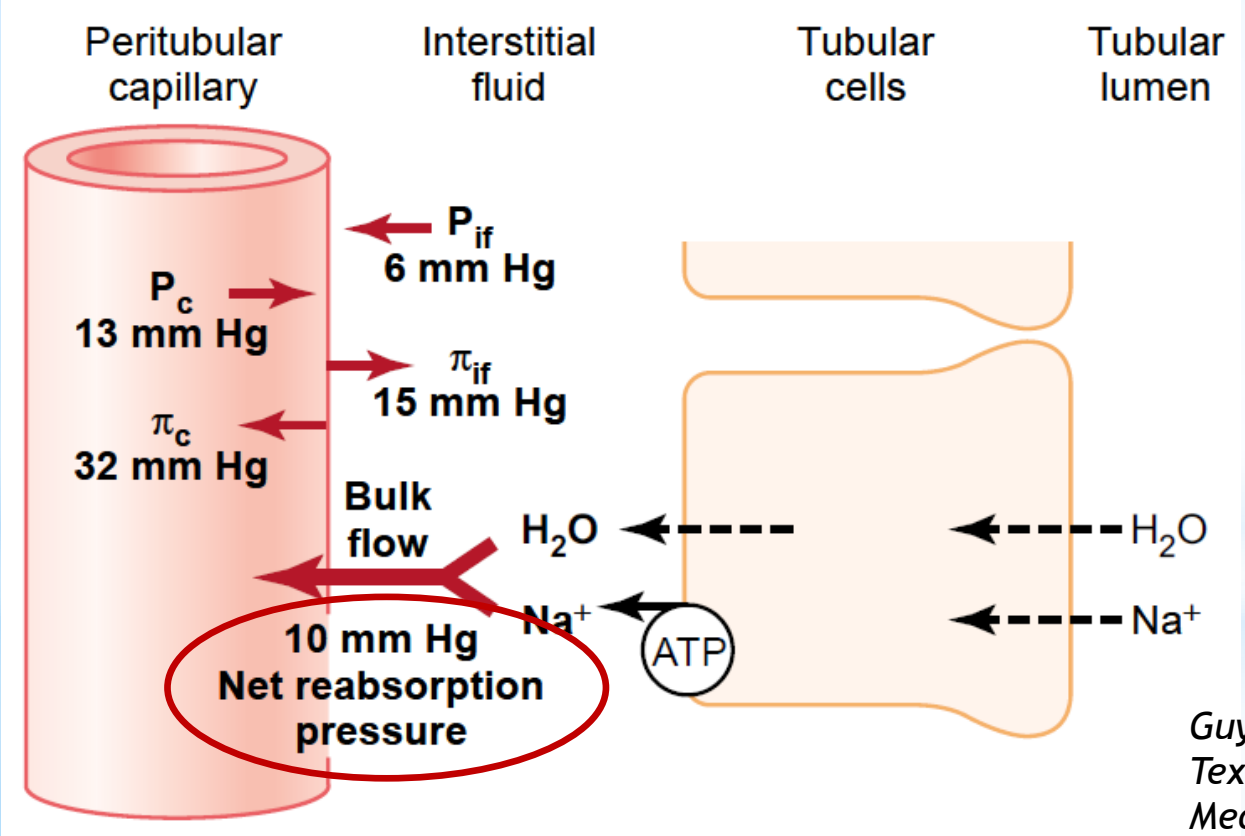
- tubular reabsorption is controlled by hydrostatic and coloid osmotic forces (similary to GFR)

$$GFR = K_f \cdot \text{net filtration pressure}$$

$$TRR = K_f \cdot \text{net reabsorptive force}$$

Urine Formation – Tubular Processes

Physical Forces in Peritubular Capillaries and in Renal Interstitium



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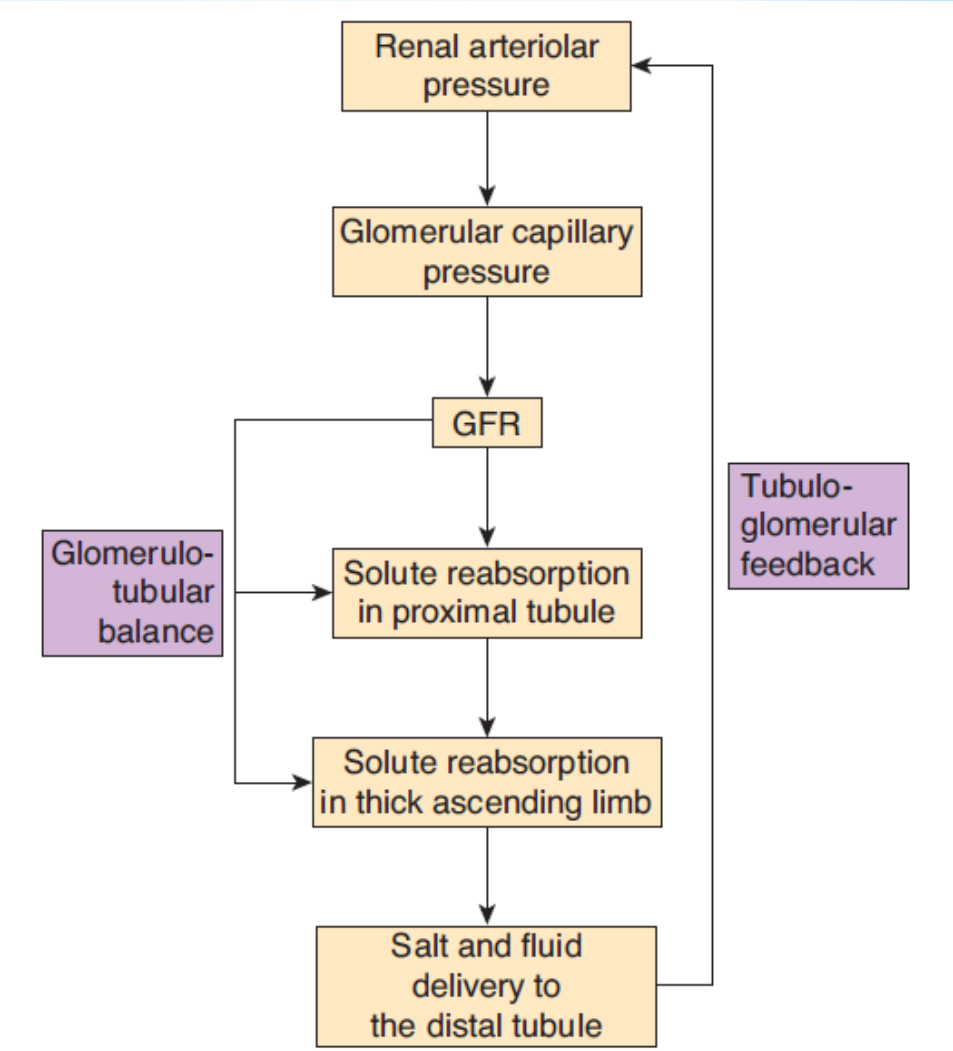
Urine Formation – Tubular Processes

Tubuloglomerular feedback

Glomerulotubular balance



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Urine Formation – Tubular Processes

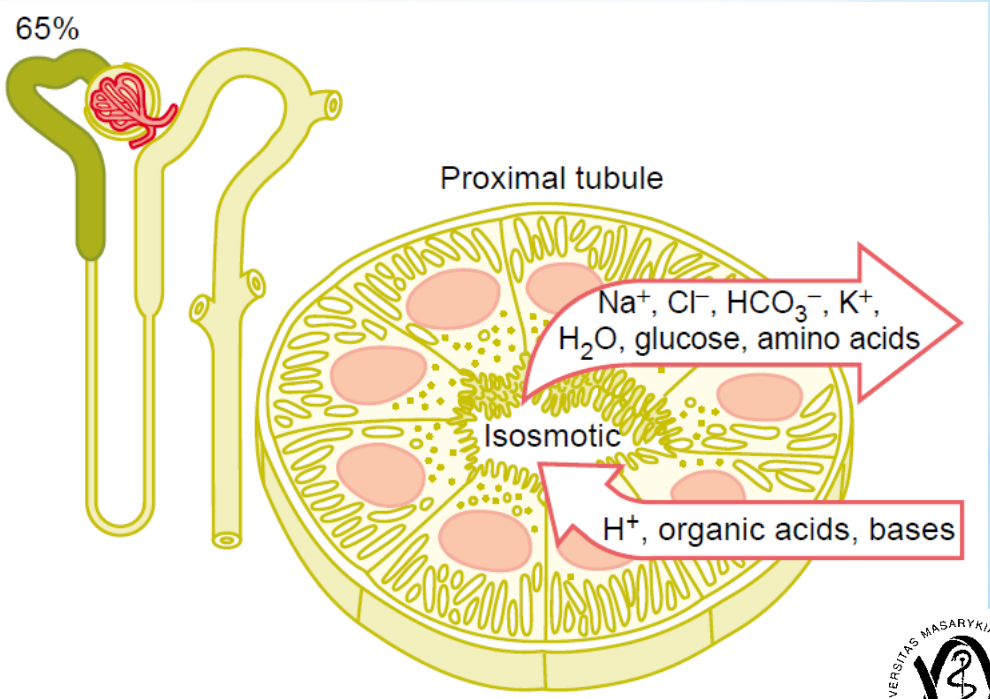
Proximal Tubule

1) complete reabsorption of substances playing key roles for the organism (glucose, amino acids)
2) partial reabsorption of substances important for the organism (ions – Na^+, K^+, Cl^-, *etc.*)
3) reabsorption of water
4) secretion of H^+
5) reabsorption of HCO_3^-

Result:

isoosmotic fluid,

notably decreased volume



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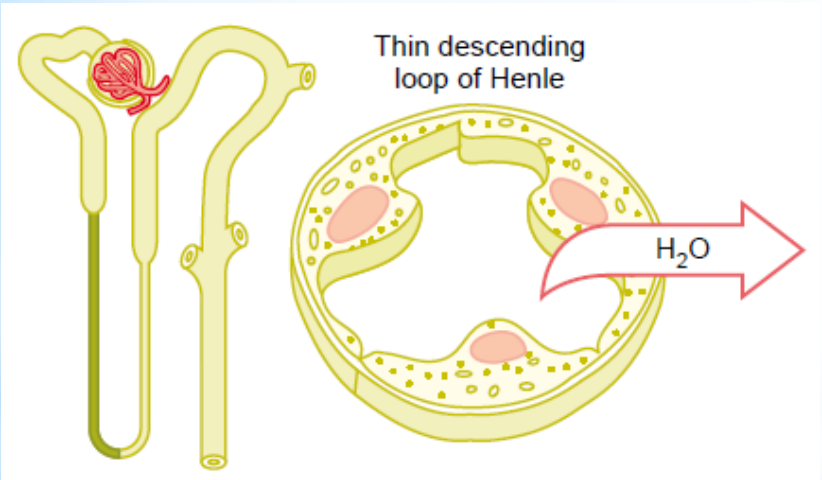
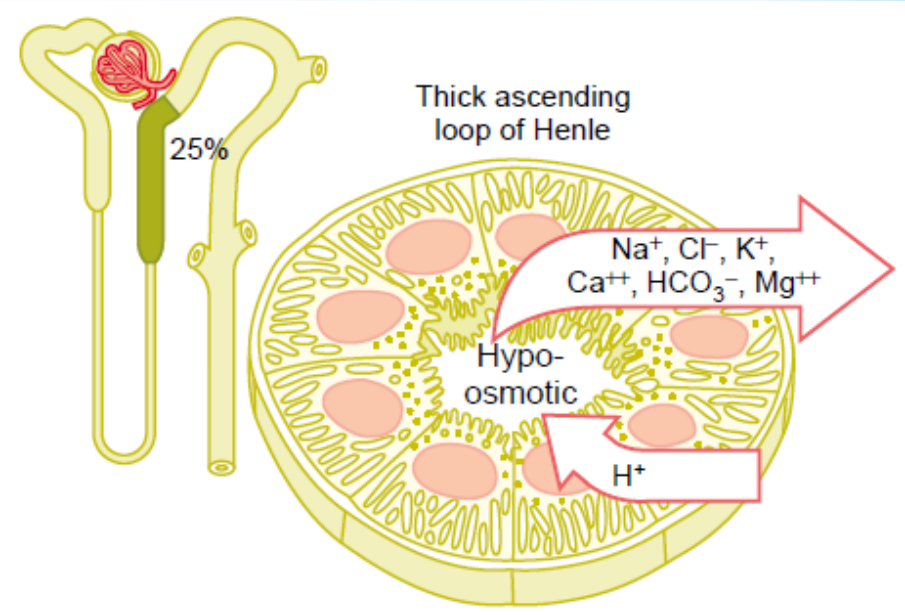
Urine Formation – Tubular Processes

Loop of Henle

1) thin descending part - passive reabsorption of water (osmosis)
2) thick ascending part - active reabsorption of ions ($Na^+/K^+/2Cl^-$ symport), secretion of H^+, reabsorption of HCO_3^-





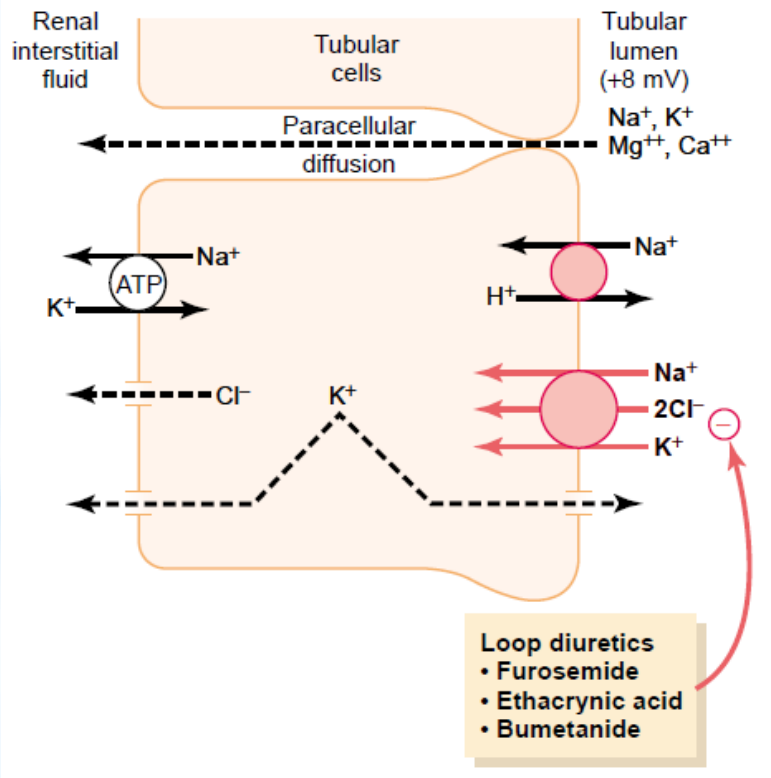
counter-current multiplier

Result: hypotonic fluid, volume further decreased

Urine Formation – Tubular Processes

Loop of Henle

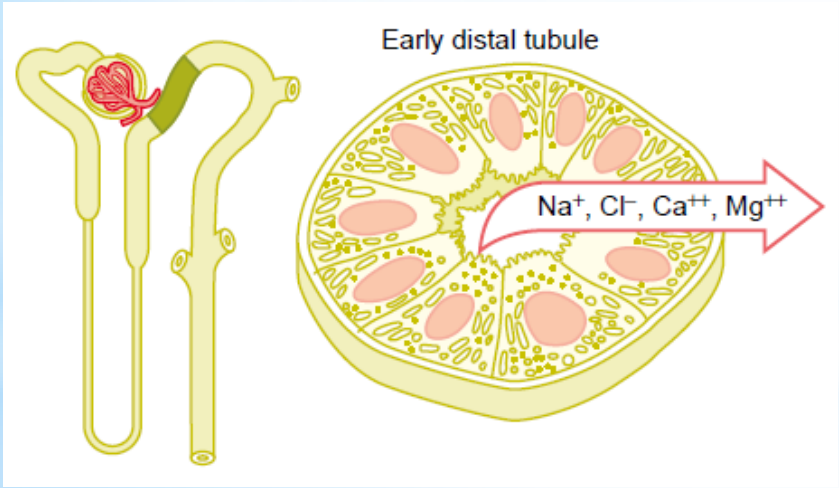
1) thin descending part - passive reabsorption of water (osmosis)
2) thick ascending part - active reabsorption of ions ($Na^+/K^+/2Cl^-$ symport), secretion of H^+, reabsorption of HCO_3^-

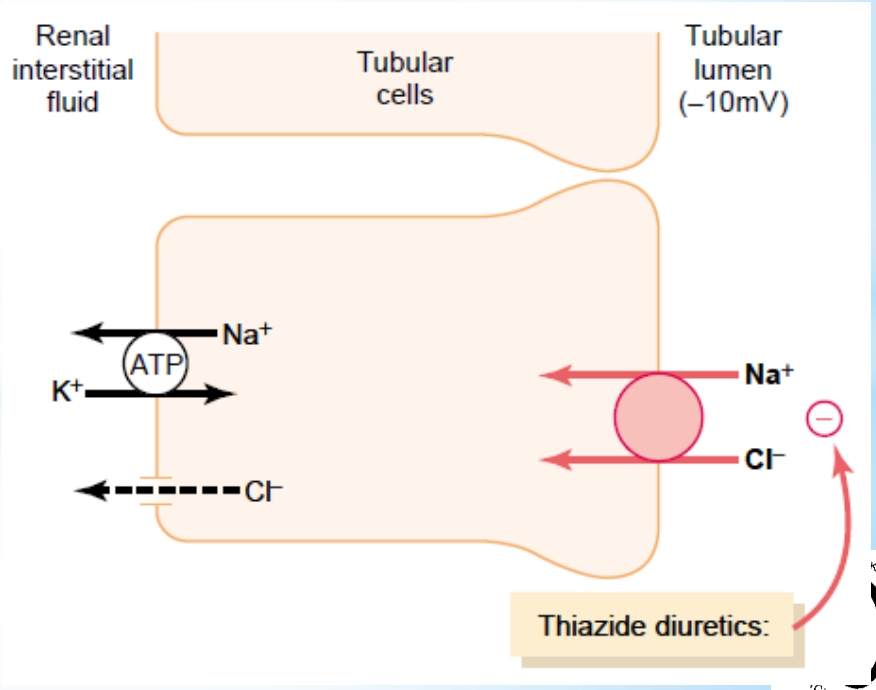


Urine Formation – Tubular Processes

Distal tubule

1) juxtaglomerular apparatus
2) active reabsorption of solutes similar to the thick ascending loop of Henle, also no permeability for urea and water – the so called dilution segment (dilutes the tubular fluid)



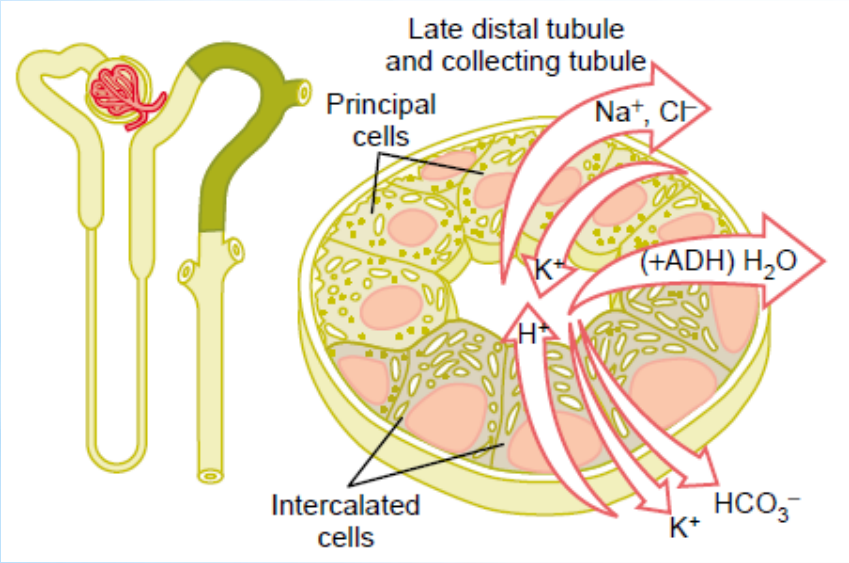


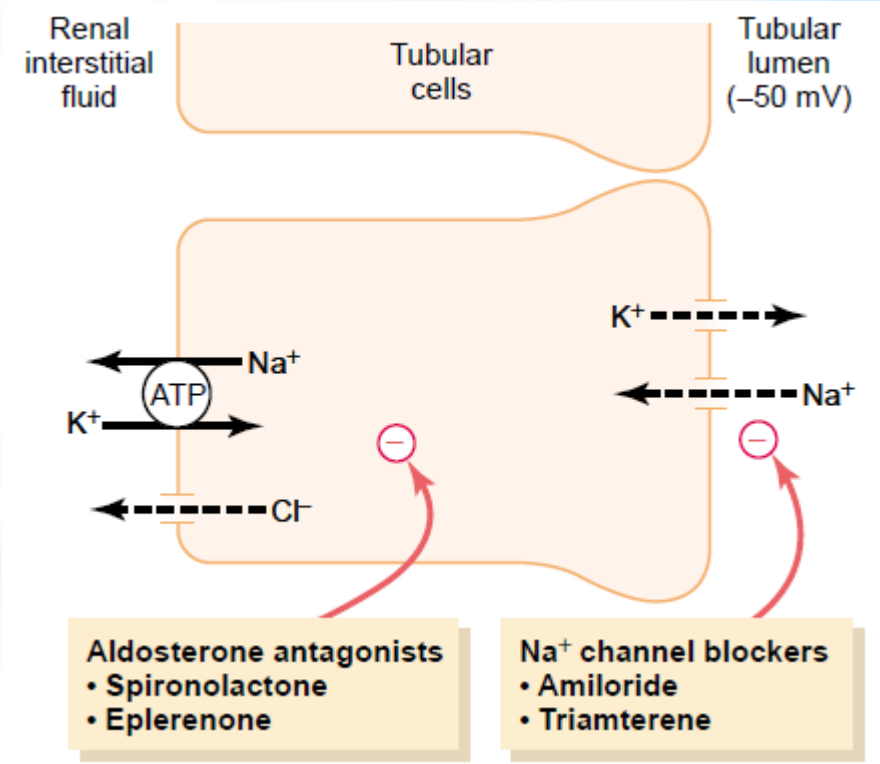
Result: hypotonic fluid

Urine Formation – Tubular Processes

Collecting duct (+ end of distal tubule)

1) principal cells – reabsorption of Na^+ and water (ADH), secretion of K^+

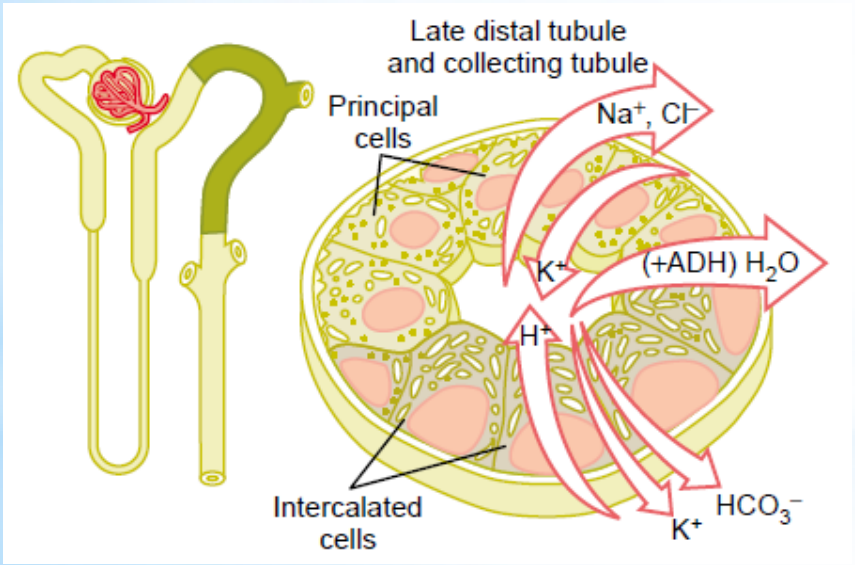


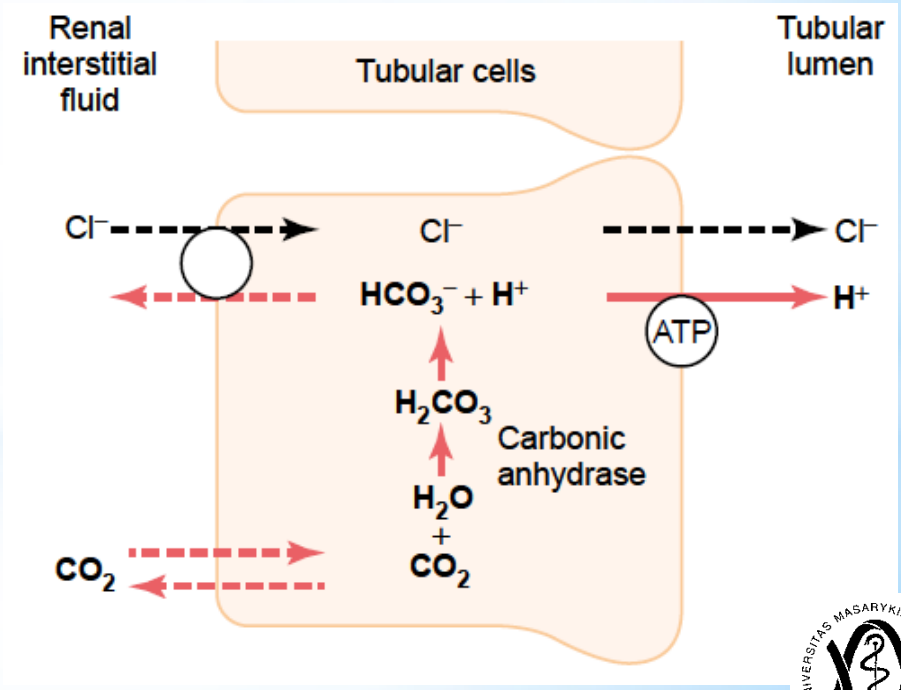


Urine Formation – Tubular Processes

Collecting duct (+ end of distal tubule)

1) principal cells – reabsorption of Na^+ and water (ADH), secretion of K^+
2) intercalated cells – secretion of H^+, reabsorption of HCO_3^- and K^+

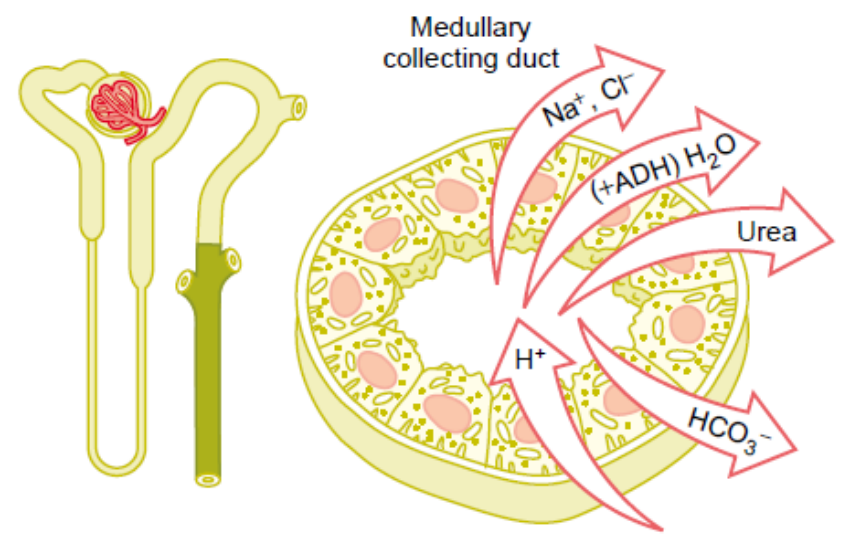




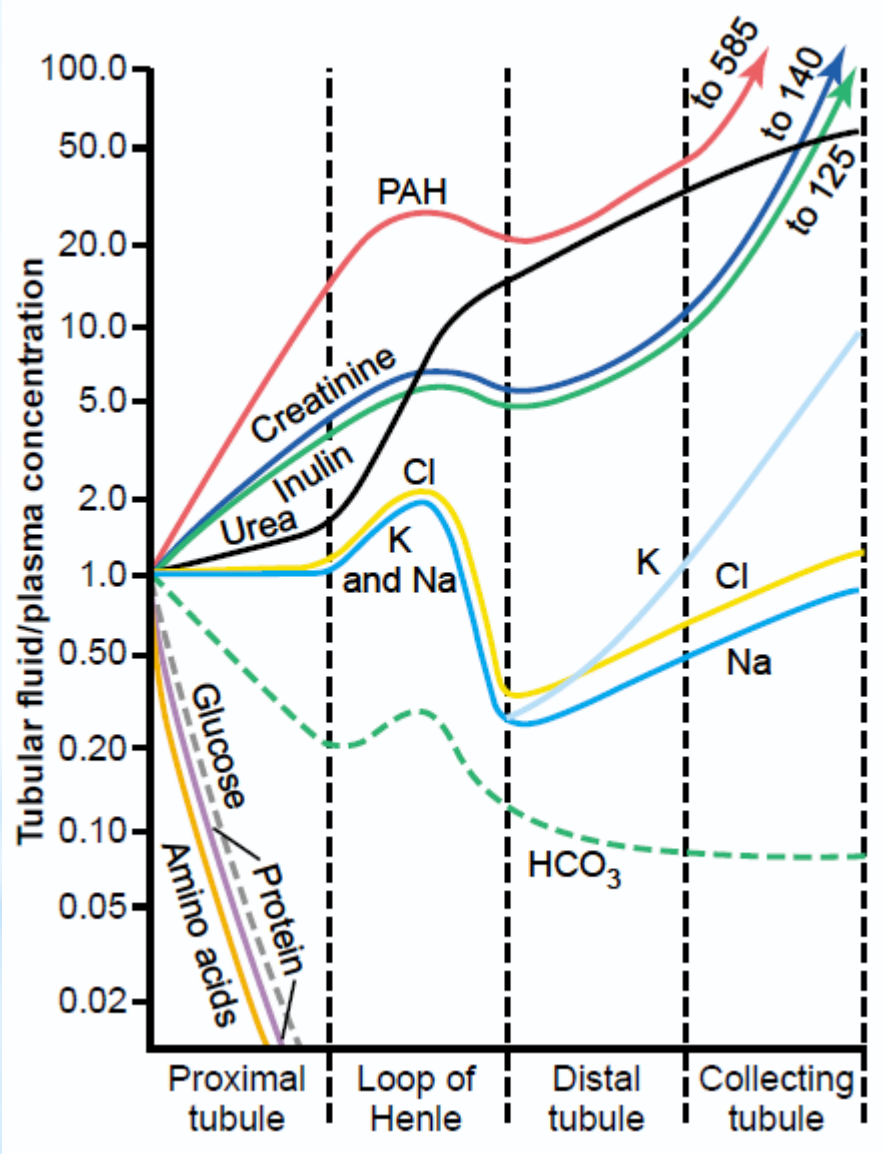
Urine Formation – Tubular Processes

Collecting duct – medullar part

1) reabsorption of Na^+ and Cl^-, water (ADH), urea
2) secretion of H^+, reabsorption of HCO_3^-



Urine Formation – Tubular Processes



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pronounced secretion in comparison with H_2O

pronounced reabsorption in comparison with H_2O

Renal Clearance

= the volume of plasma that is cleared of the substance by kidneys per unit time

Using *clearance*, we can quantified the excretion ability of kidneys, the velocity of renal blood flow and even basic functions of kidneys (GFR, tubular reabsorption and secretion).

$$C_S \cdot P_S = V \cdot U_S \longrightarrow C_S = \frac{V \cdot U_S}{P_S}$$

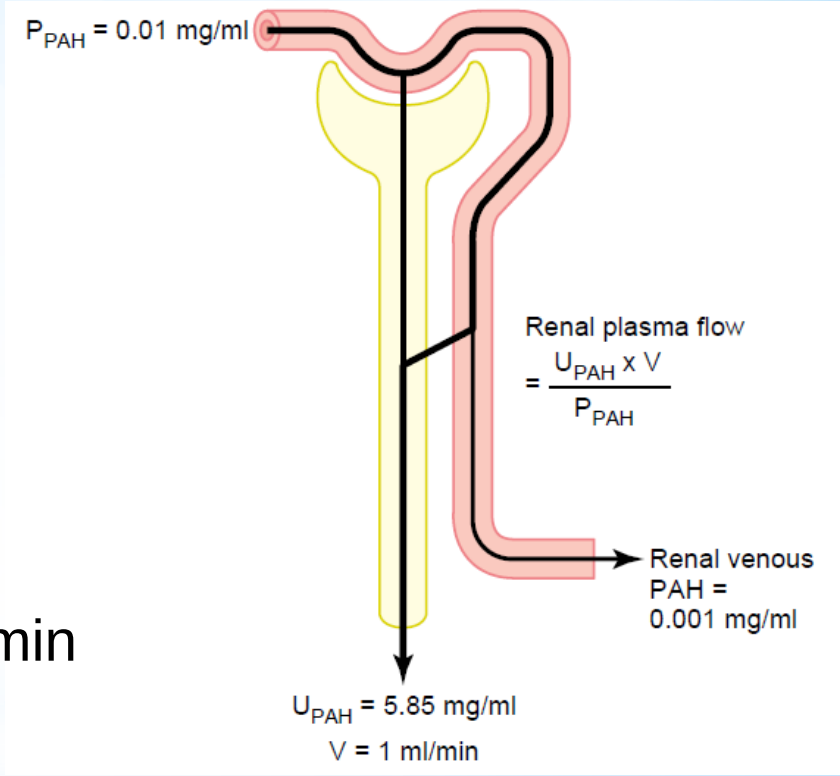
[ml/min]

Renal Clearance

Determination of renal plasma flow velocity (RPF)

Clearance of a substance that is fully cleared from plasma in glomerulotubular apparatus.

PAH (paraaminohippuric acid) cleared by 90%



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$$RPF = \frac{5.85 \times 1 \text{ mg/min}}{0.01 \text{ mg/ml}} = 585 \text{ ml/min}$$

Correction to the extraction ratio of PAH (E_{PAH}):

$$E_{PAH} = \frac{P_{PAH} - V_{PAH}}{P_{PAH}} = 0.9 \longrightarrow RPF = \frac{585 \text{ ml/min}}{0.9} = 650 \text{ ml/min}$$

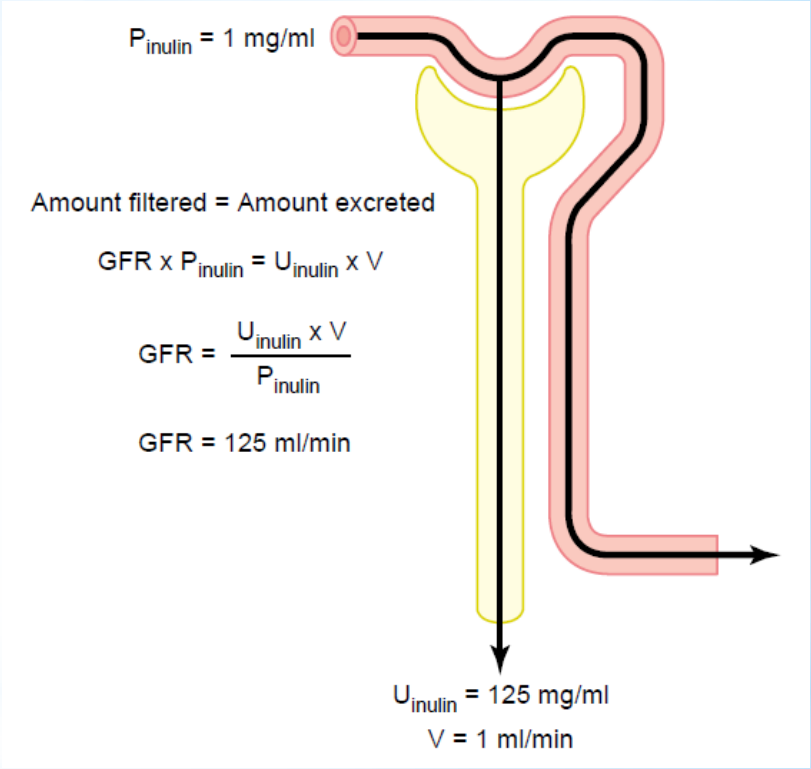
Renal Clearance

Determination of glomerular filtration rate (GFR)

Clearance of a substance that is fully filtered in the glomerulus and is not reabsorbed/secreted in tubules.

Inulin

Creatinine



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Renal Clearance

Calculation of Filtration Fraction (FF)

FF is the fraction of plasma filtered through the glomerular membrane.

$$FF = \frac{GFR}{RPF} = \frac{125\ ml/min}{650\ ml/min} = 0.19$$ → ~20% of plasma is filtered in the glomerulus

Calculation of Tubular Reabsorption/Secretion

A. $GFR \cdot P_S > V \cdot U_S$ substance reabsorbed

B. $GFR \cdot P_S < V \cdot U_S$ substance secreted