Functional morphology of kidneys
Clearance

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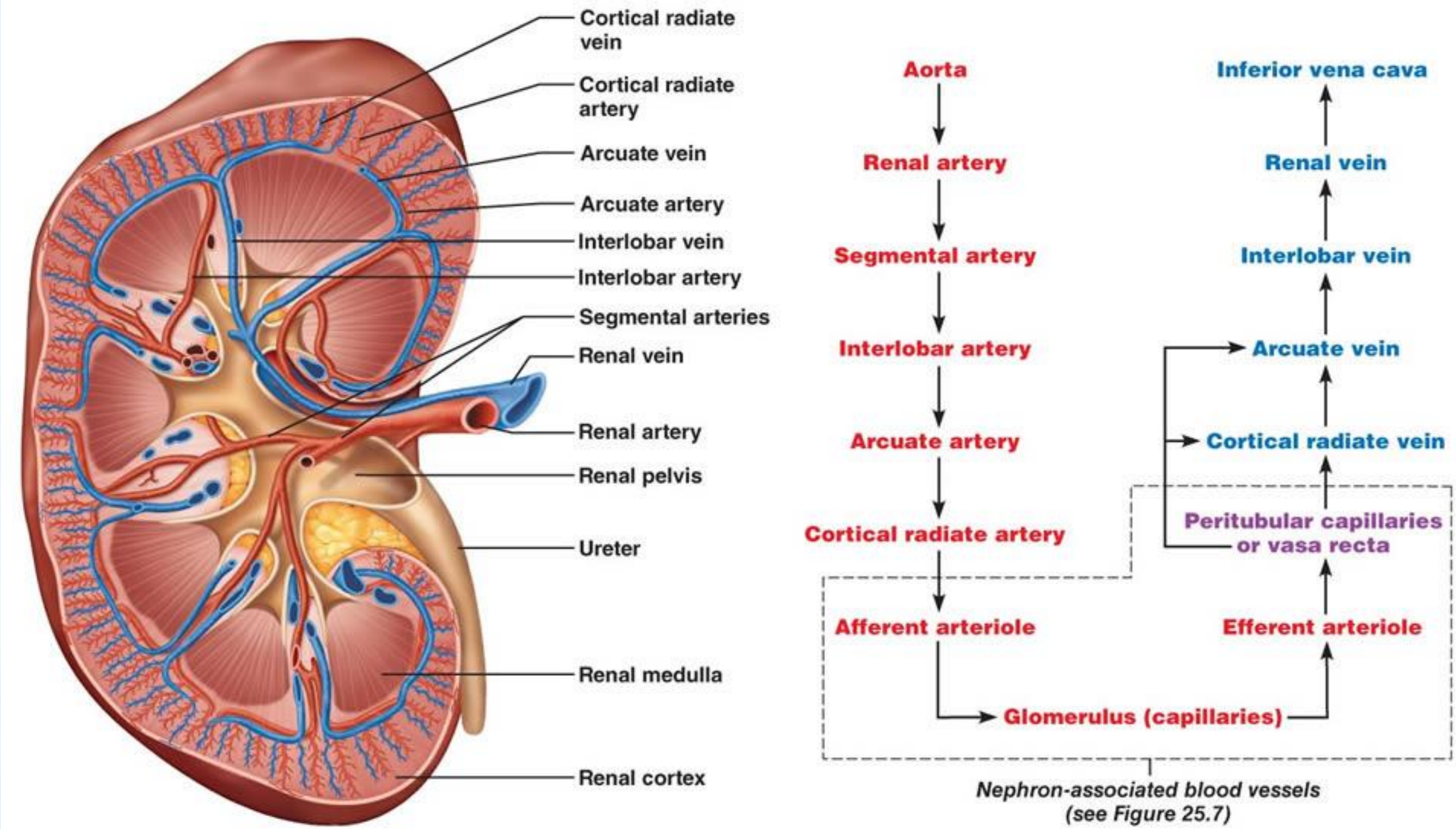
This presentation includes only the most important terms and facts. Its content by itself is not a sufficient source of information required to pass the Physiology exam.

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

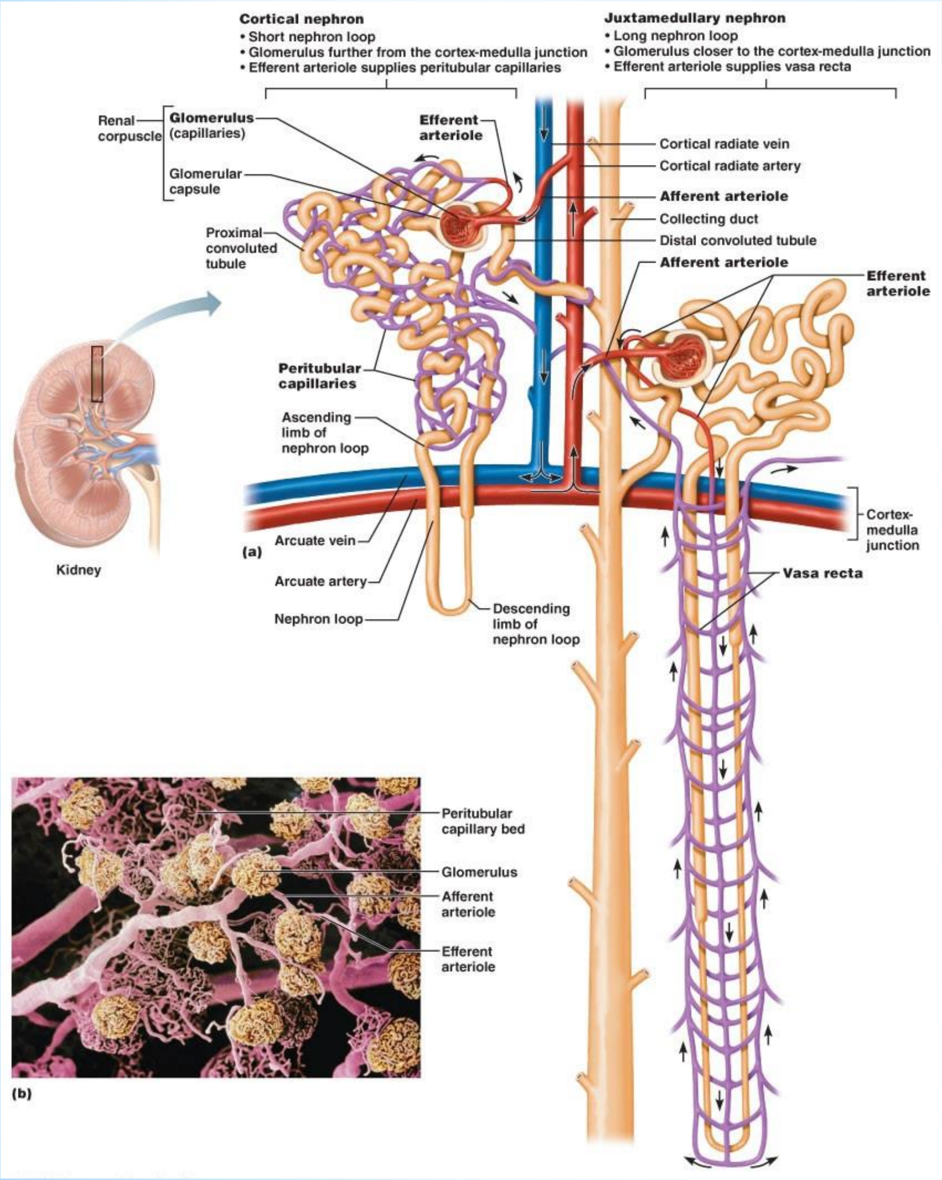


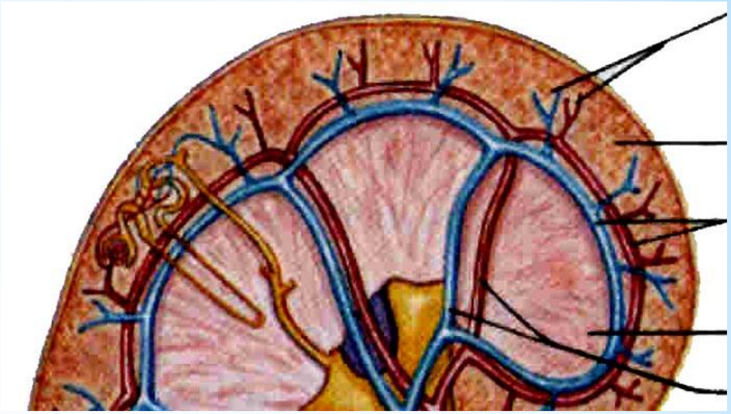
(a) Frontal section illustrating major blood vessels

(b) Path of blood flow through renal blood vessels

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

Structure of Kidney





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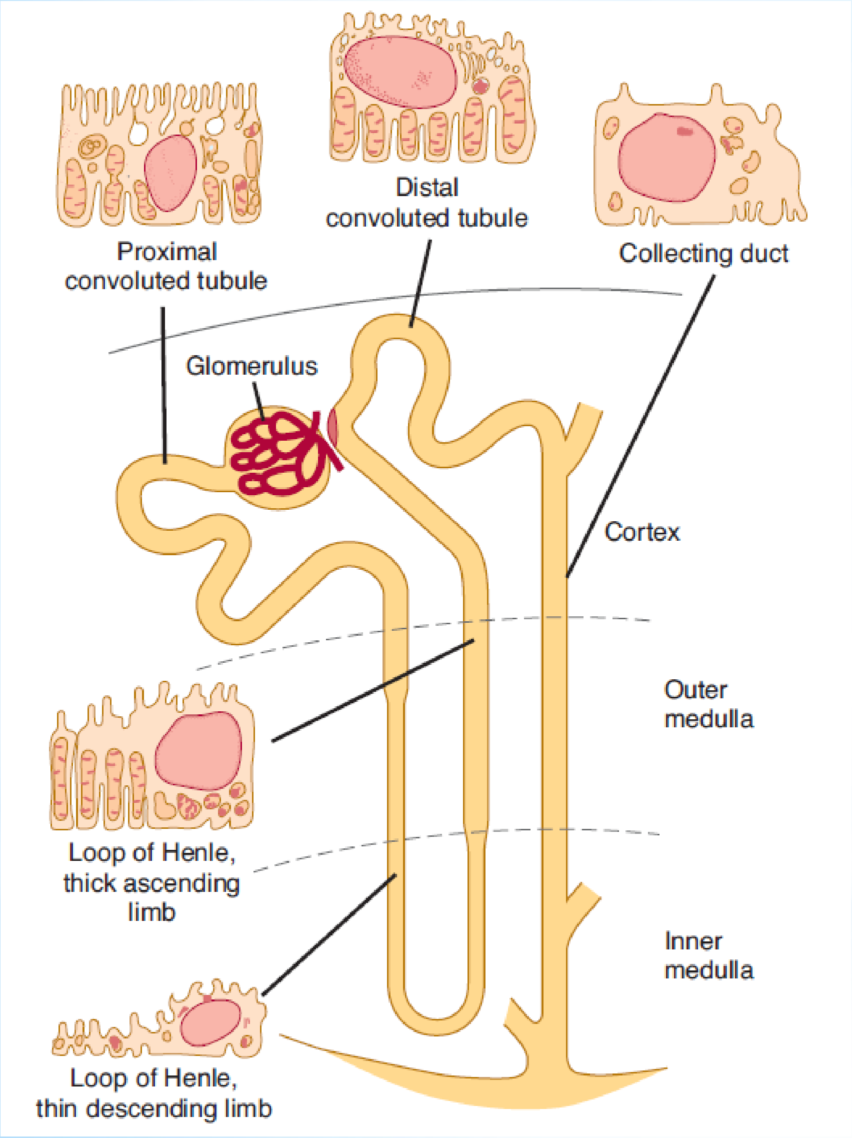
Structure of Nephron



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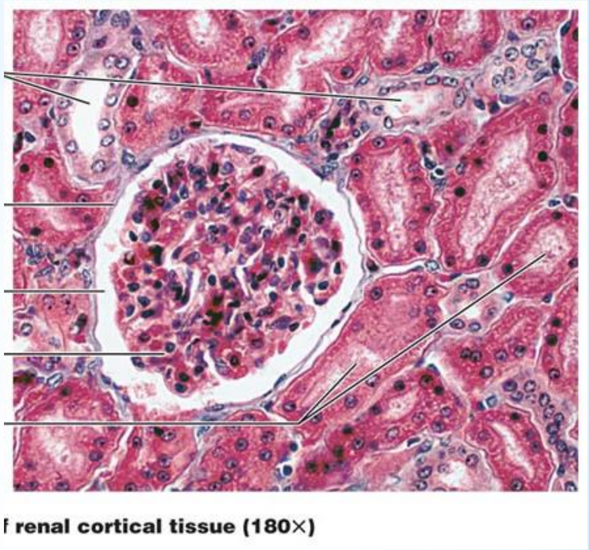
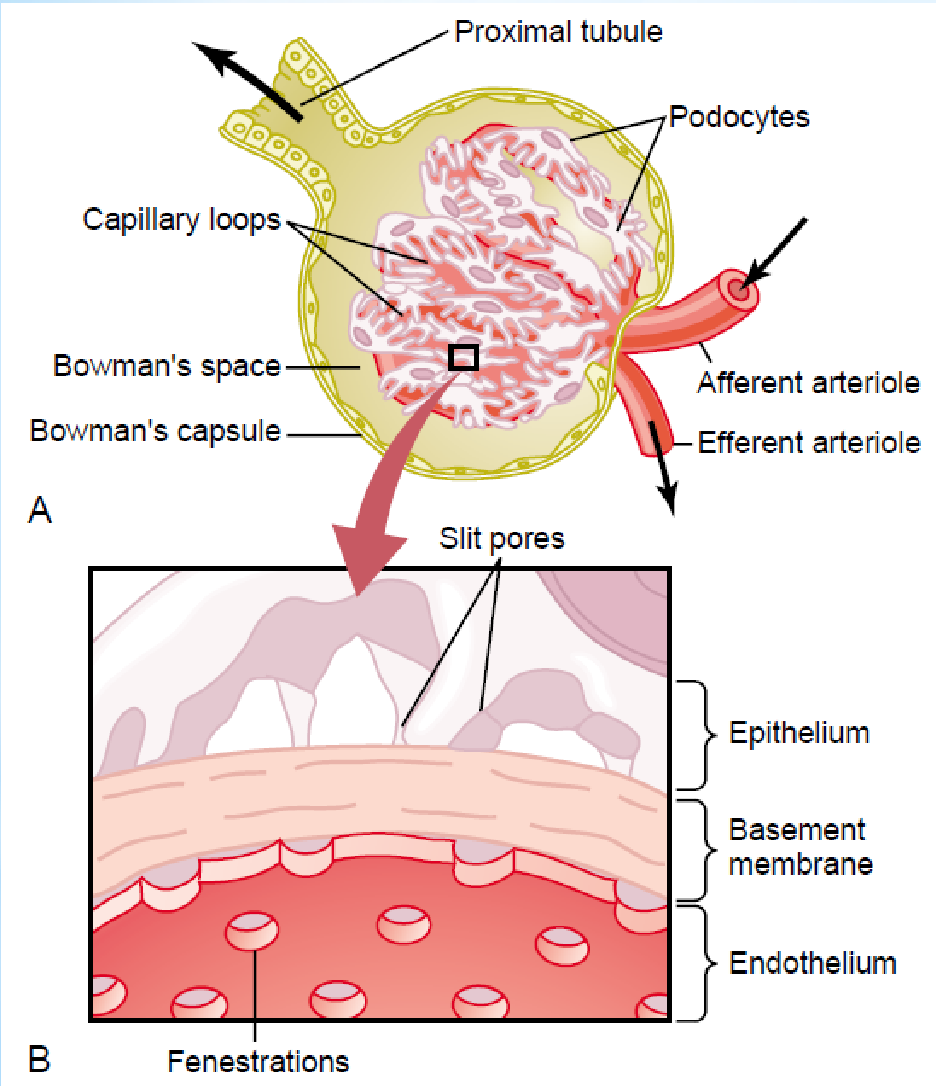
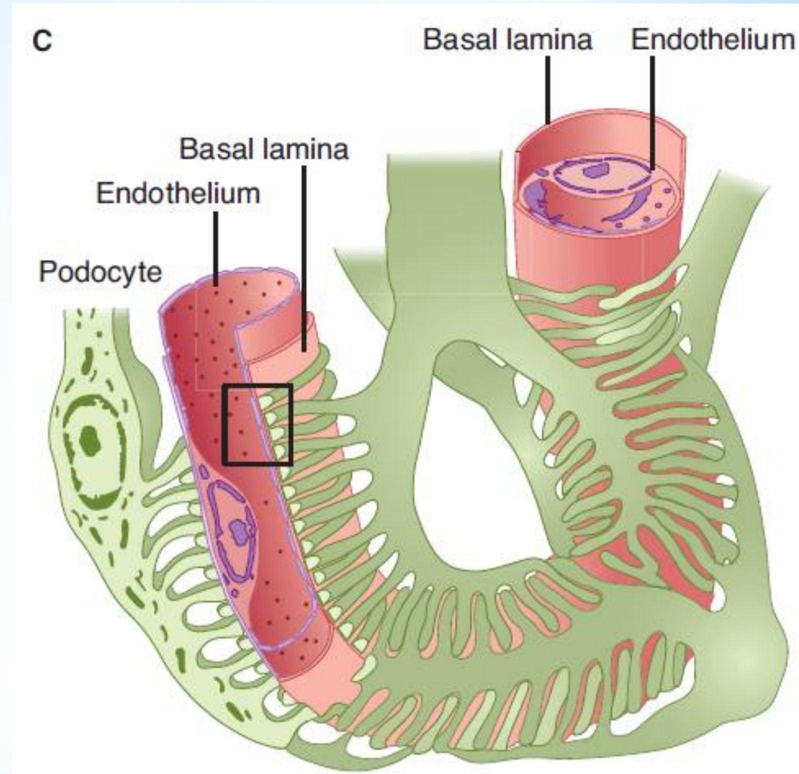


Structure of Nephron - Glomerulus





mesangial cells

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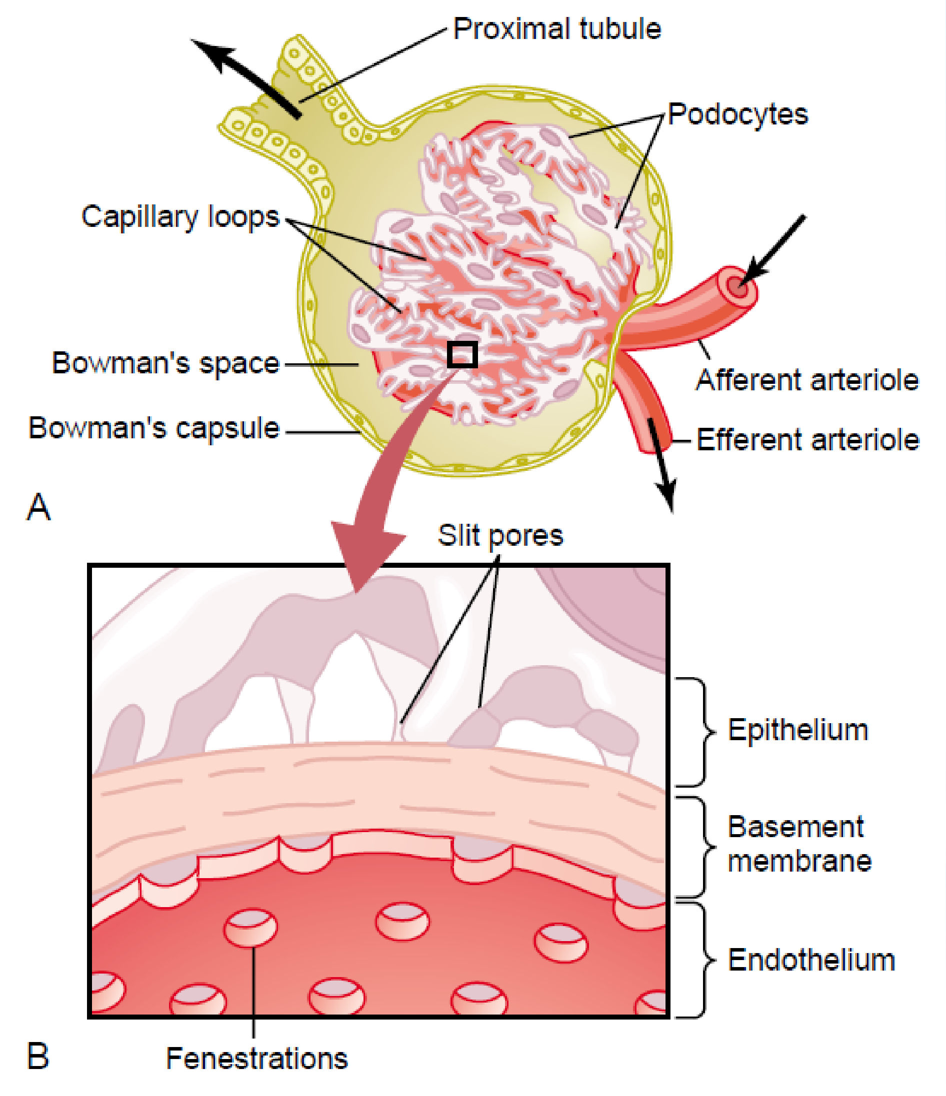
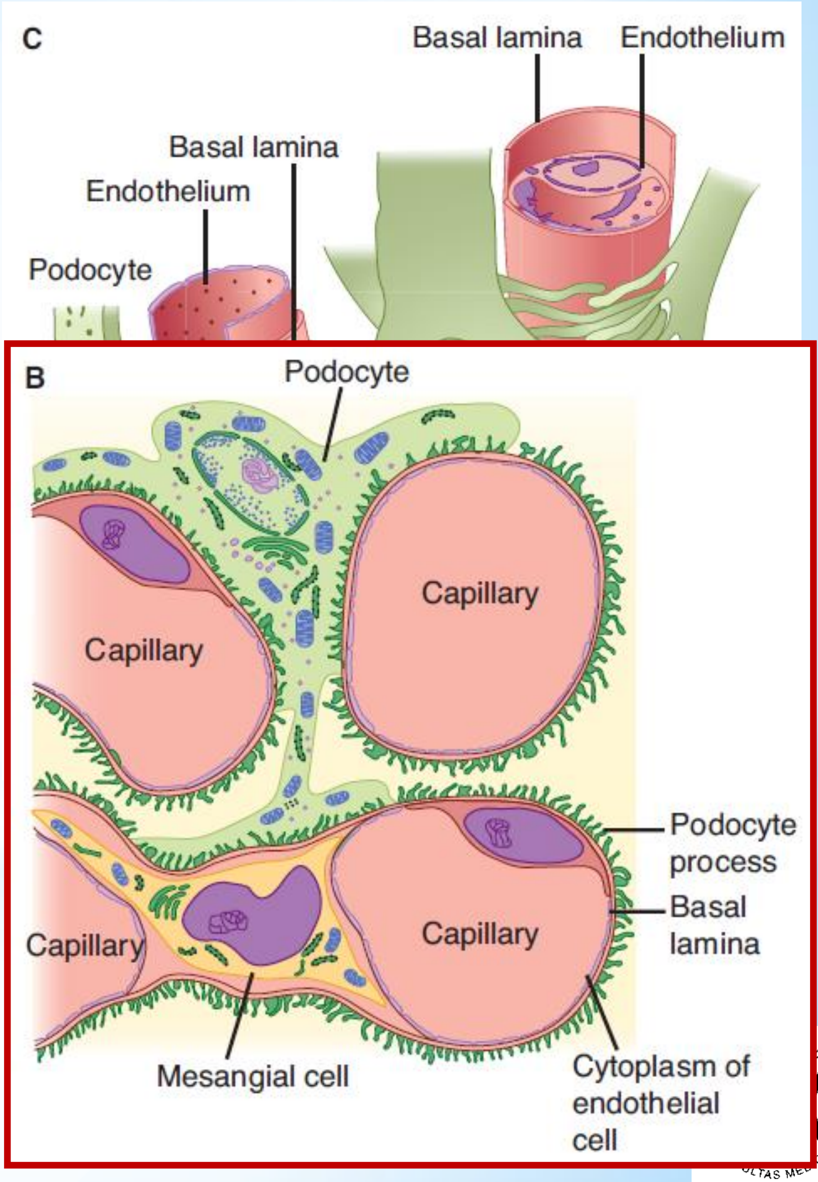
Structure of Nephron - Glomerulus





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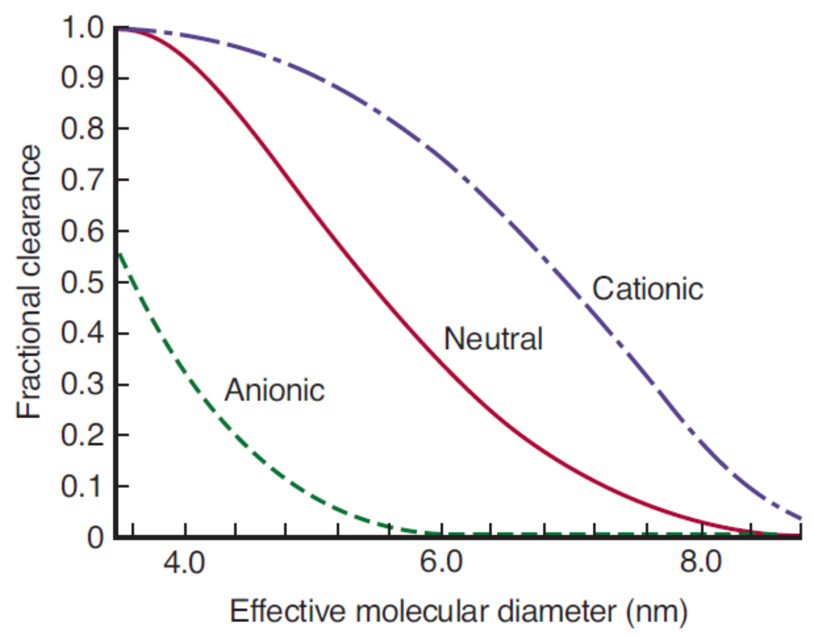
Structure of Nephron - Glomerulus

- 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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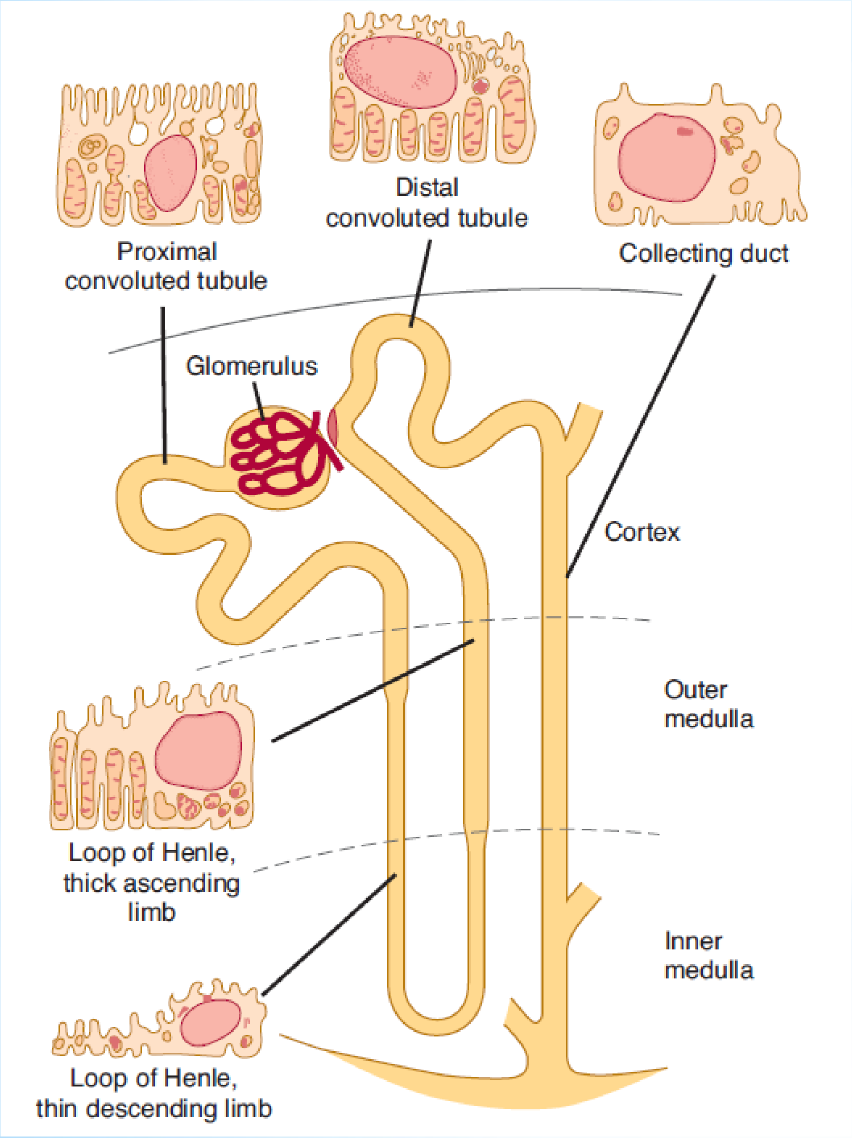
Structure of Nephron - Tubulus



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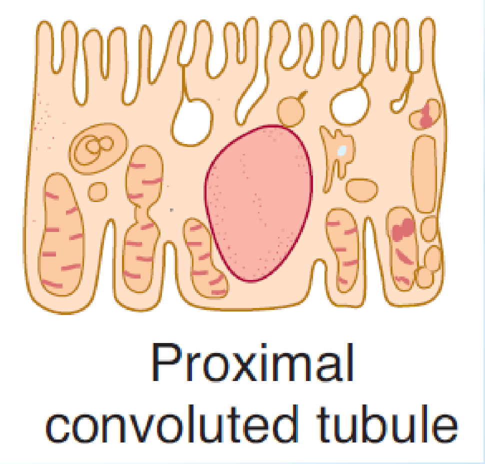
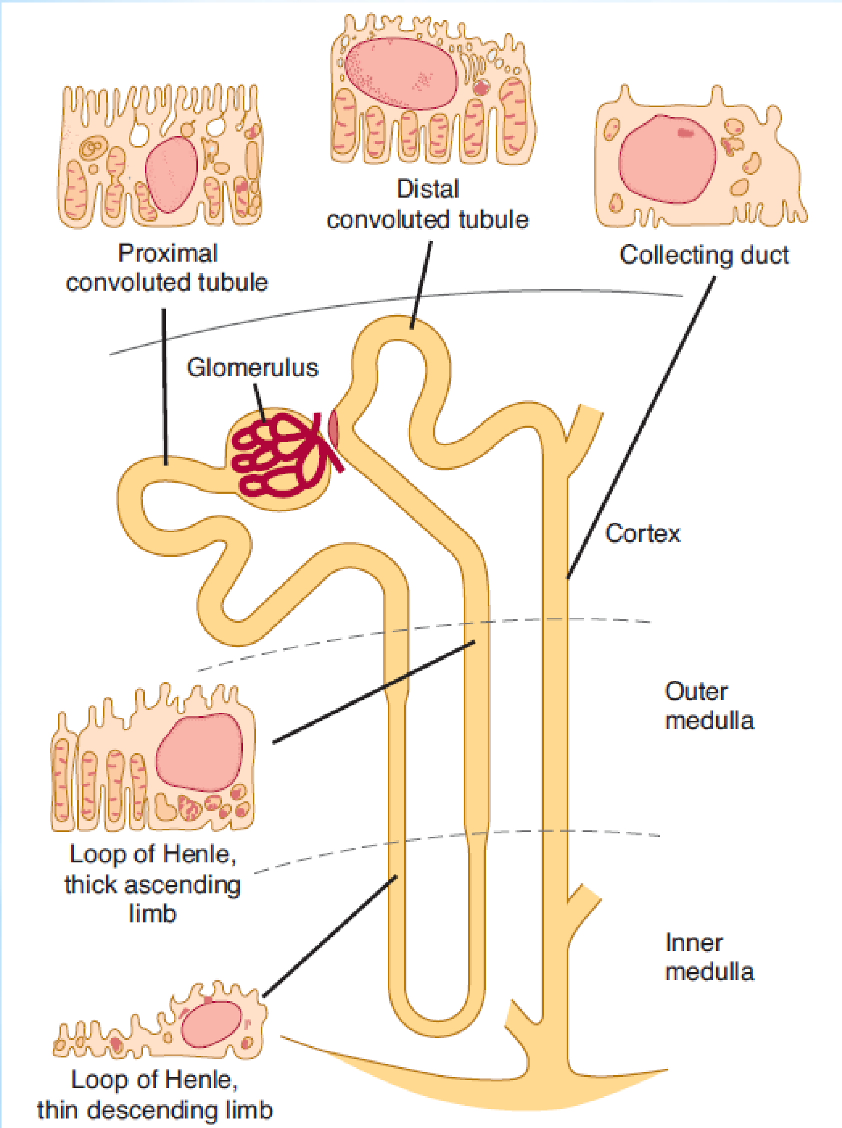
- glomerulus
- proximal convoluted tubule



Structure of Nephron - Tubulus



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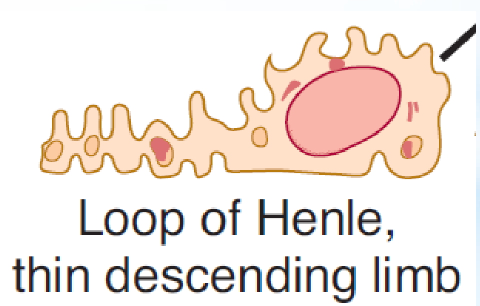
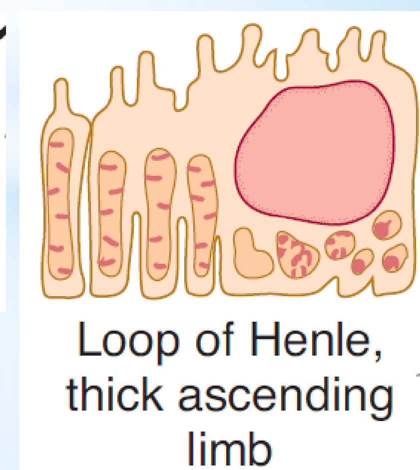
- glomerulus
- proximal convoluted tubule
- loop of Henle





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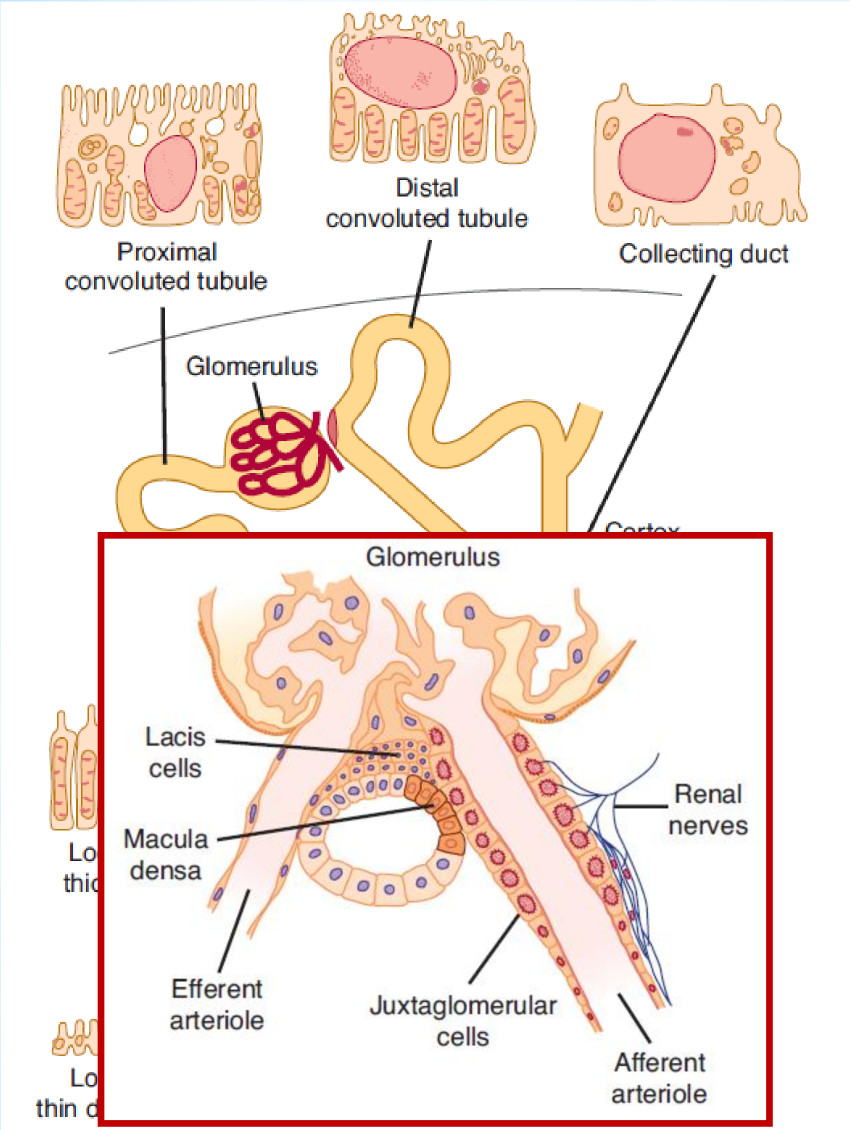

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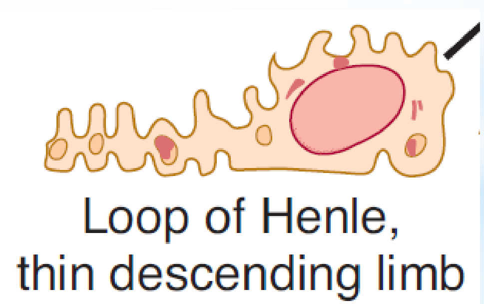

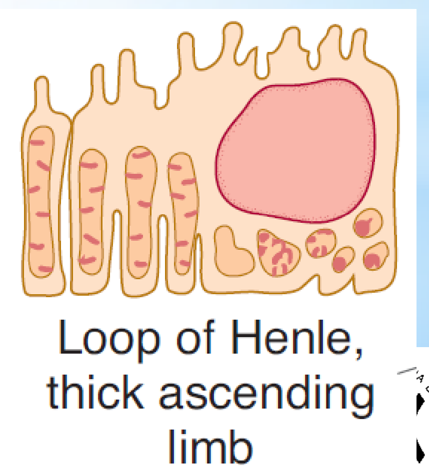

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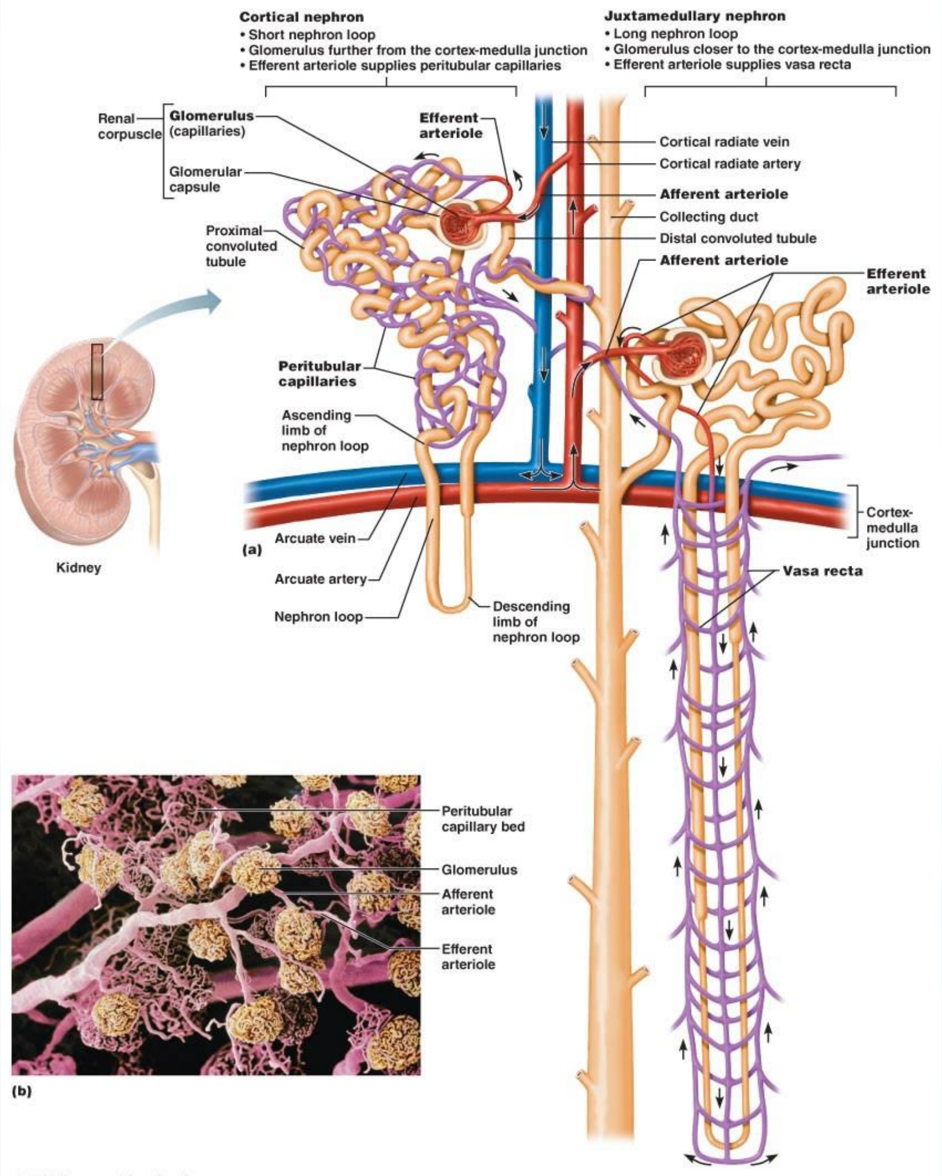

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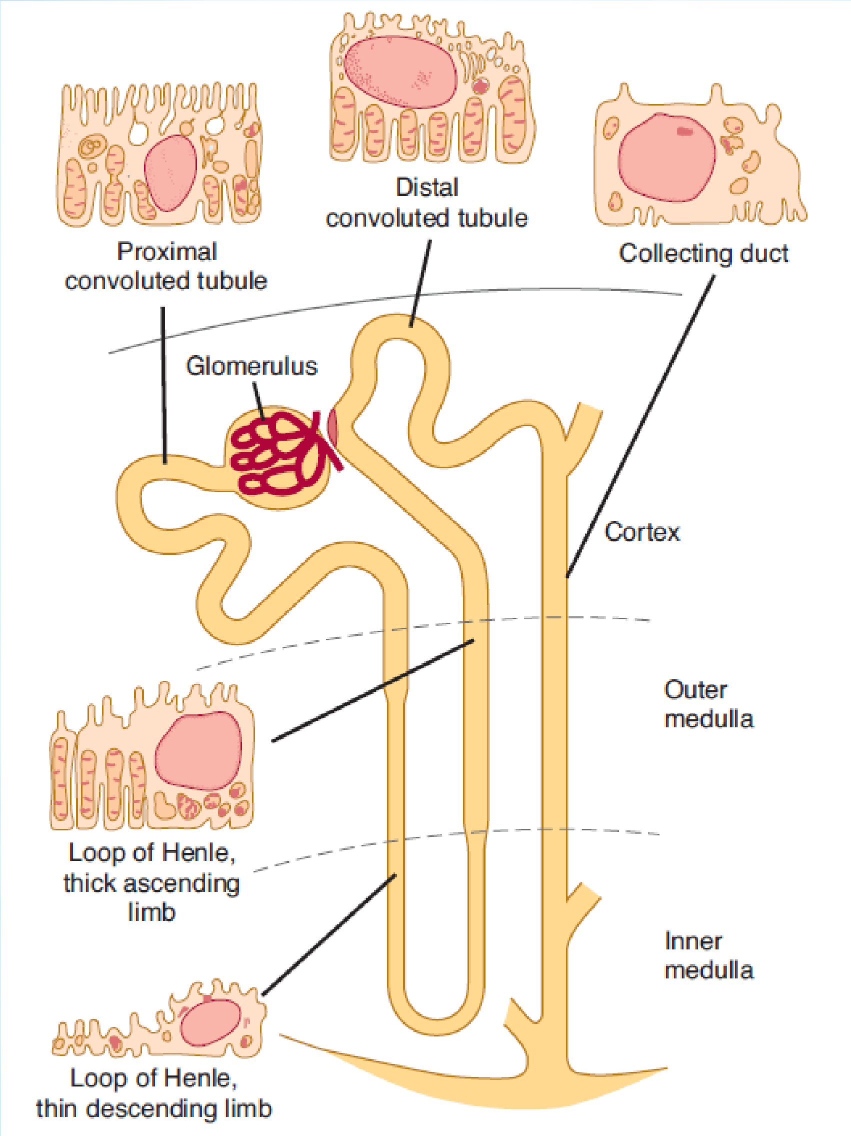
Structure of Nephron - Tubulus



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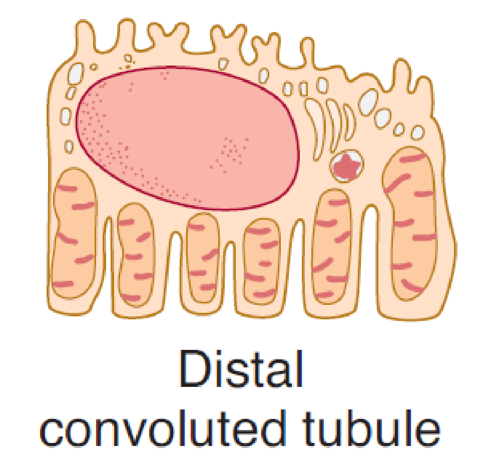
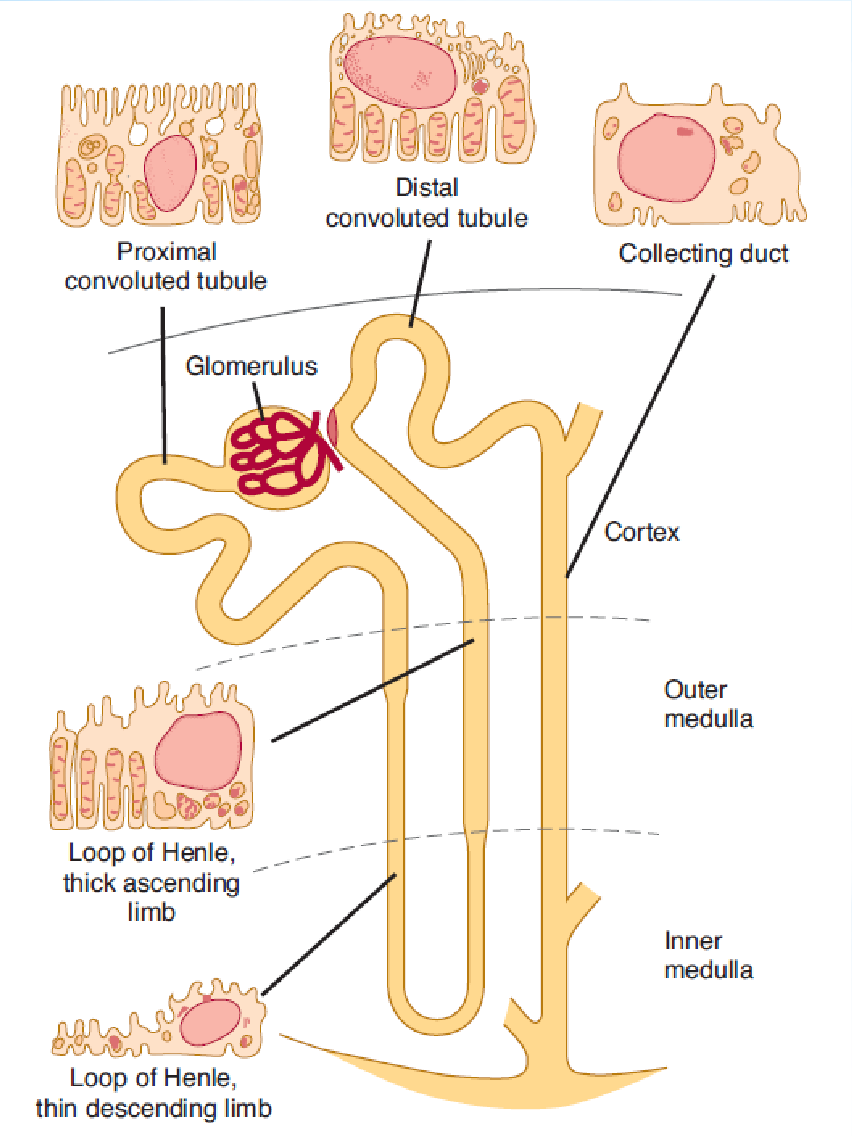
- glomerulus
- proximal convoluted tubule
- loop of Henle
- distal convoluted tubule



Structure of Nephron - Tubulus



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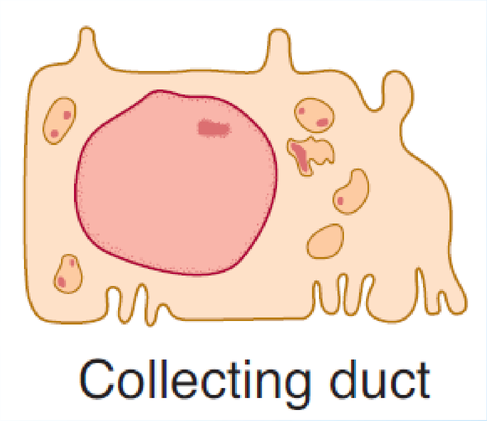
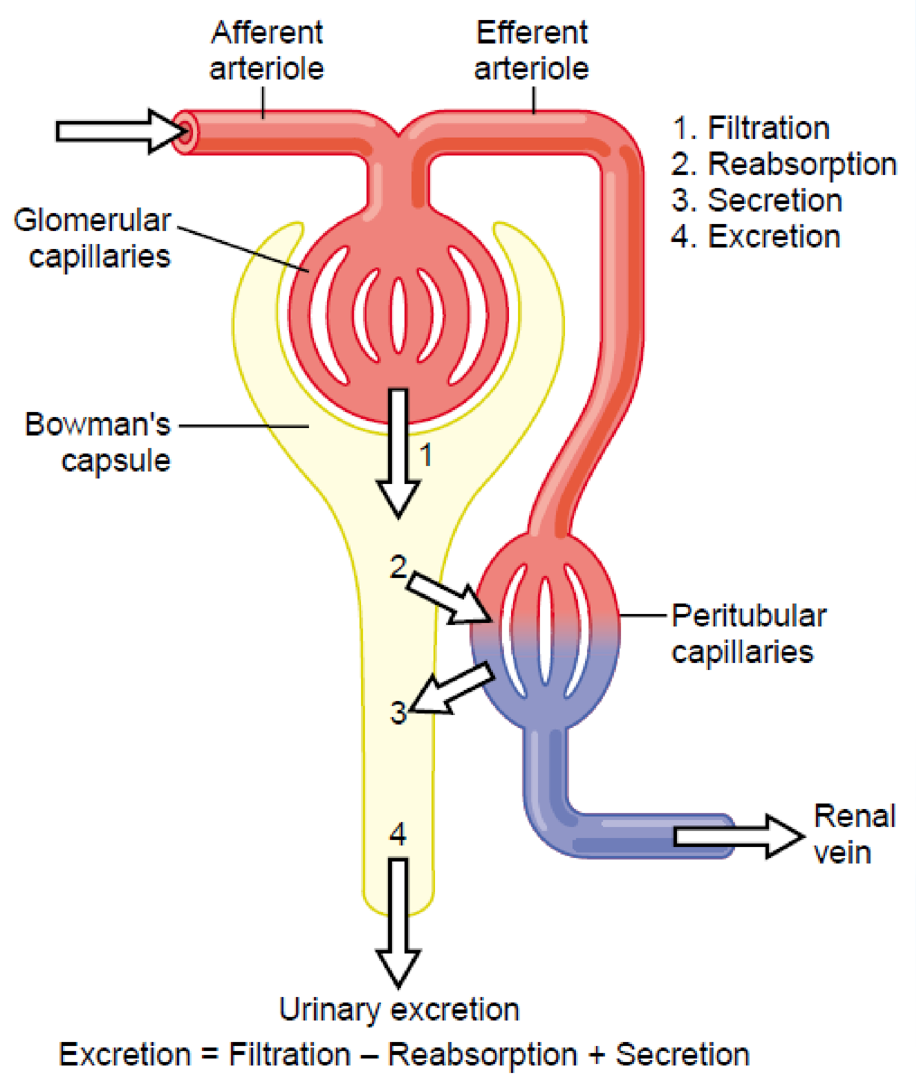
- glomerulus
- proximal convoluted tubule
- loop of Henle
- distal convoluted tubule
- collecting duct



Urine Formation



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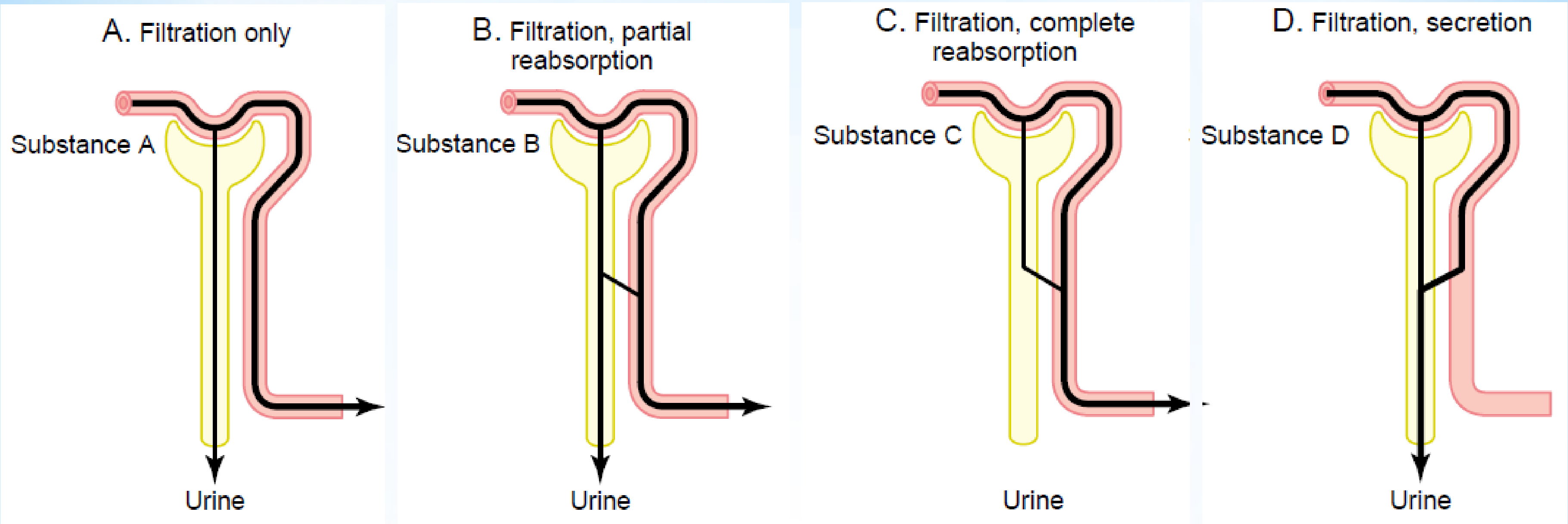
1) Glomerular filtration
2) Tubular reabsorption
3) Tubular secretion
4) Urine excretion

Urine Formation



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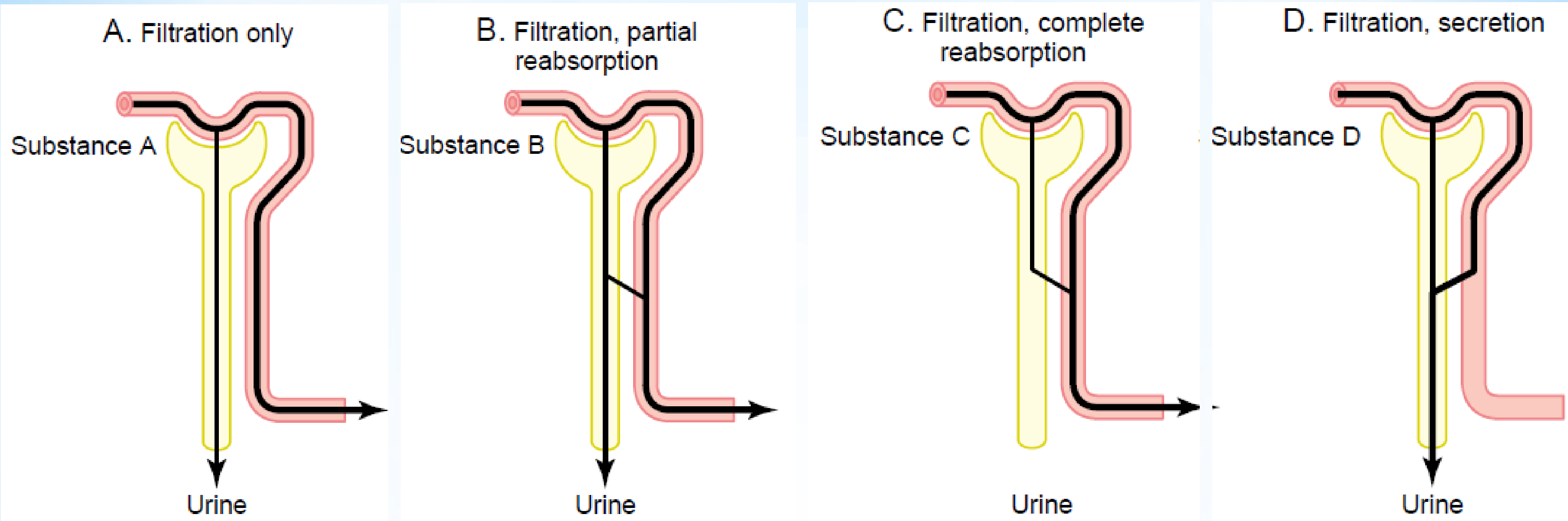
- creatinine
- other waste products

- electrolytes

- amino acids
- glucose

- PAH
- toxins
- organic base and acids

Urine Formation



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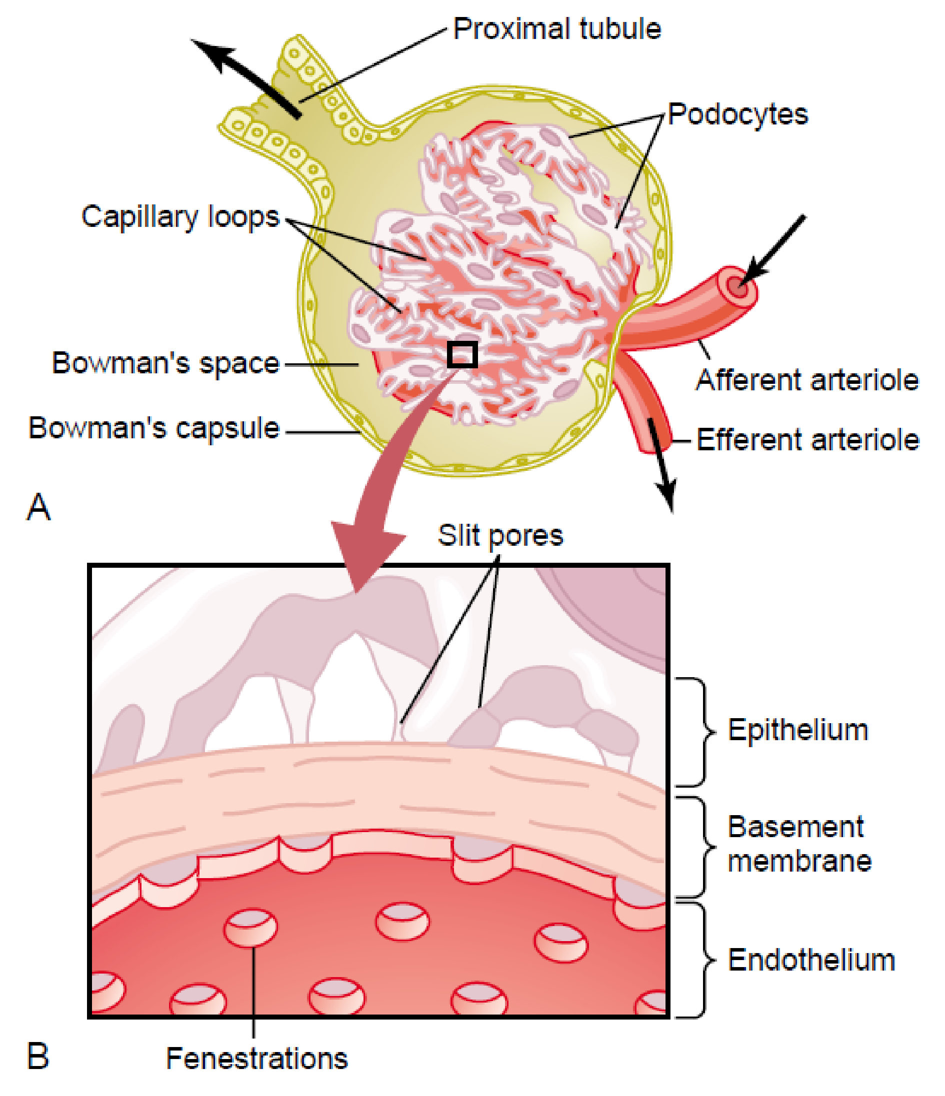
- creatinine
- other waste products

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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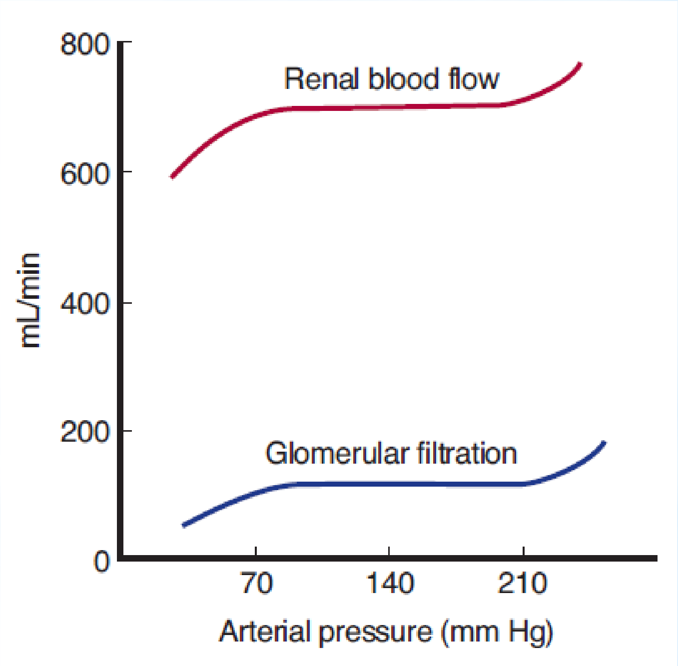
GFR = 125 ml/min = 180 l/day

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

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

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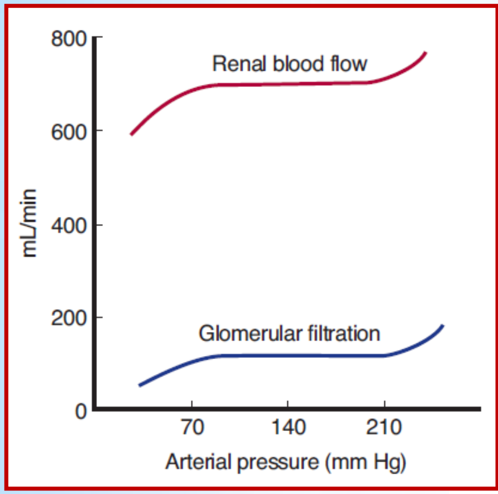
Urine Formation - Glomerular Filtration

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



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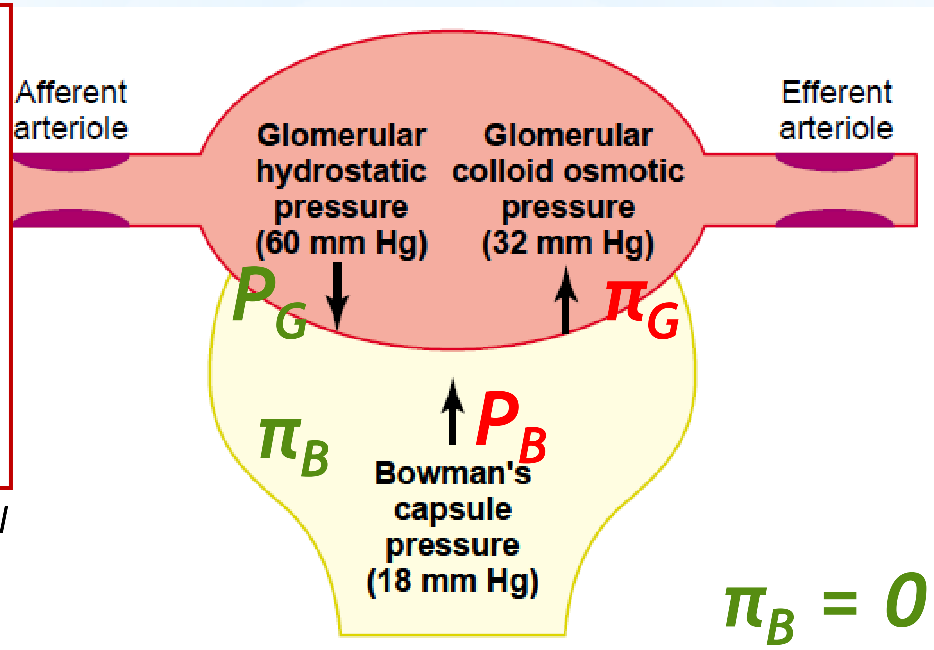

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Under physiological conditions:

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

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

Urine Formation - Glomerular Filtration

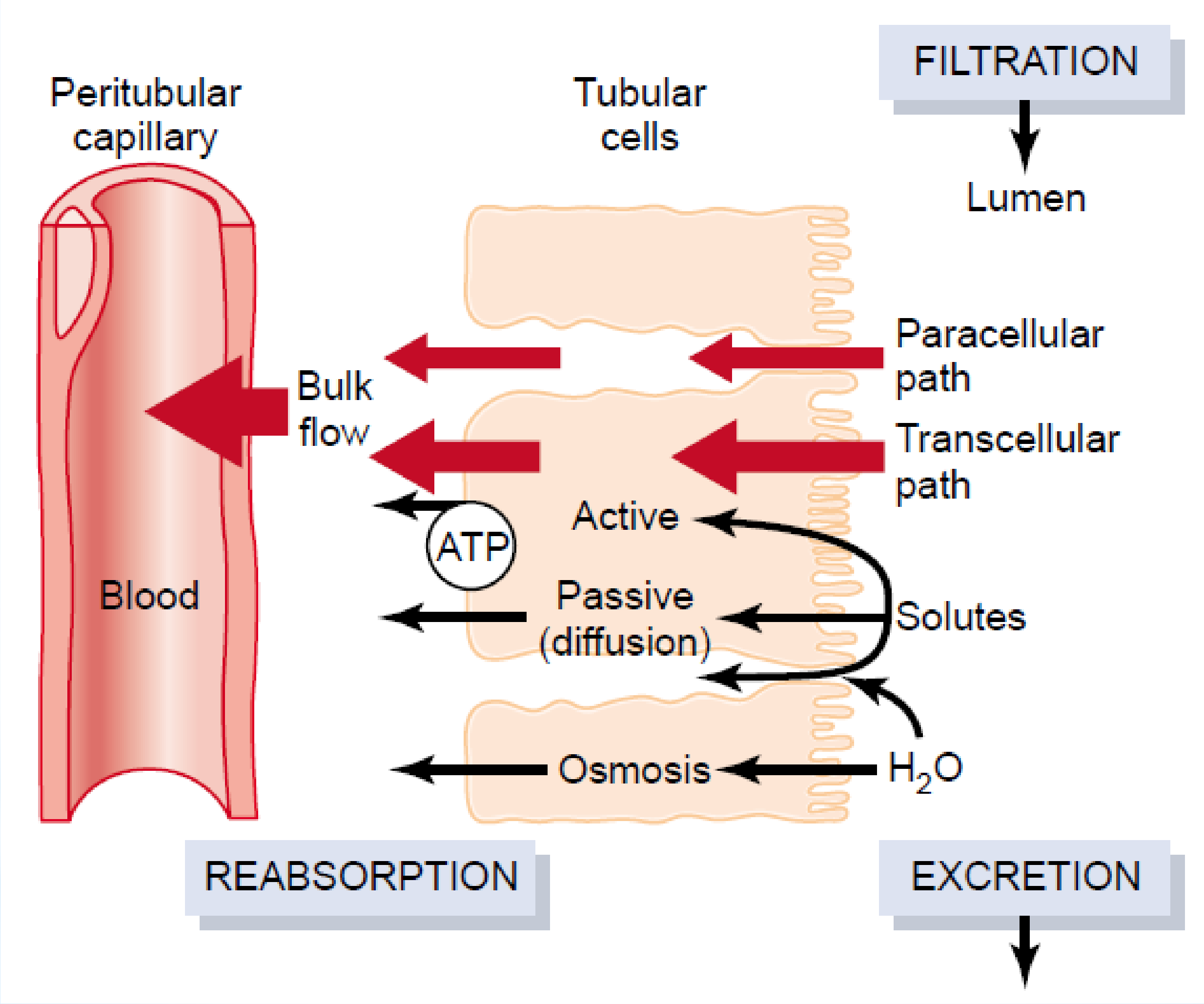
Vas afferens, vas efferens

- input and output of high-pressure glomerular capillary net
- glomerular blood flow = $\dfrac{P_{v.a.} - P_{v.e.}}{R_{v.a.} + R_{v.e.} + \cancel{R_{g.k.}}}$
- ↑ 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

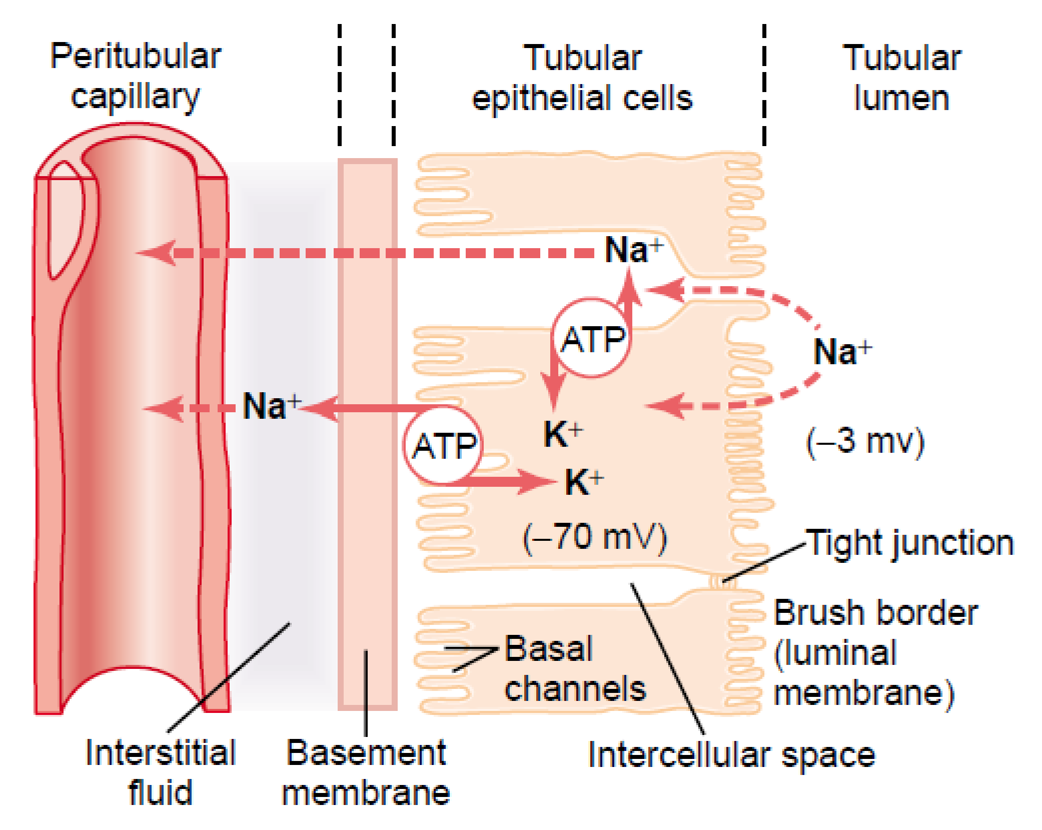
Active Transport Mechanisms

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

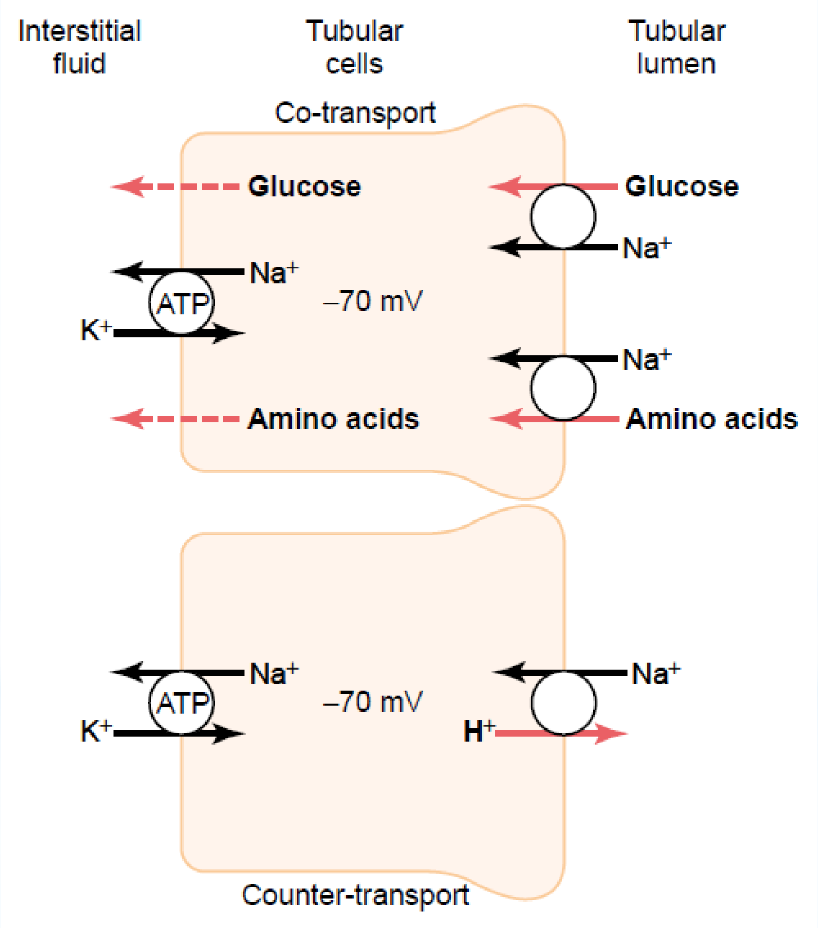
Active Transport Mechanisms

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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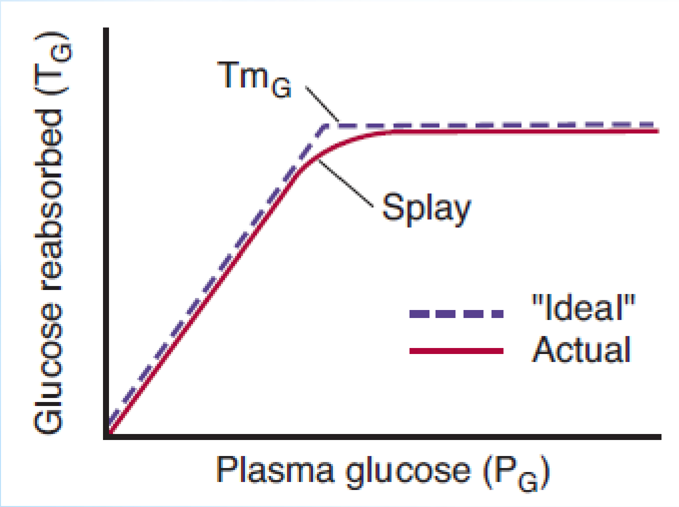
Urine Formation – Tubular Processes

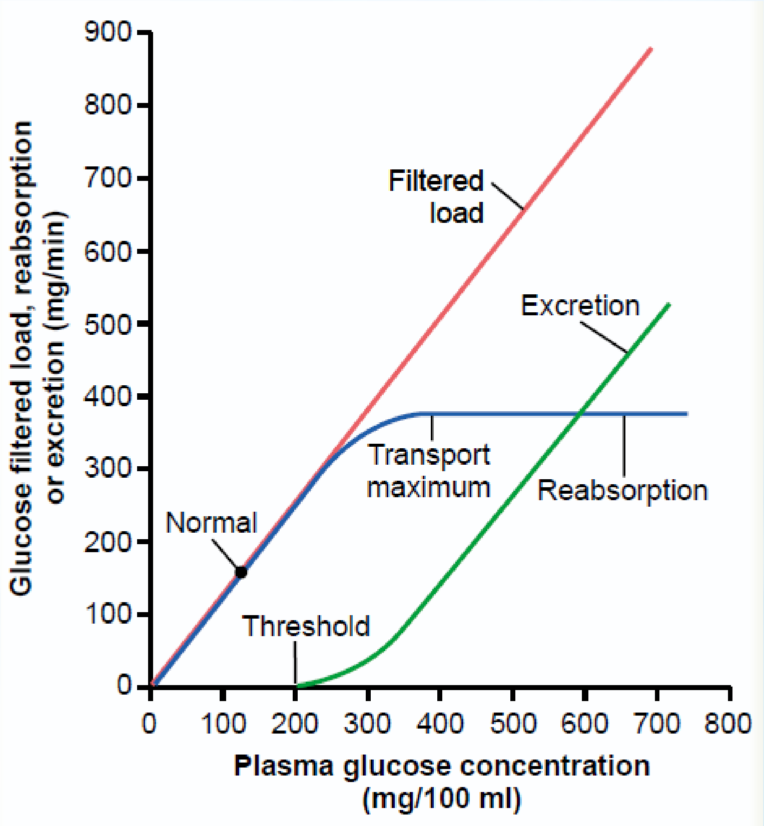
Active Transport Mechanisms

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

⬇

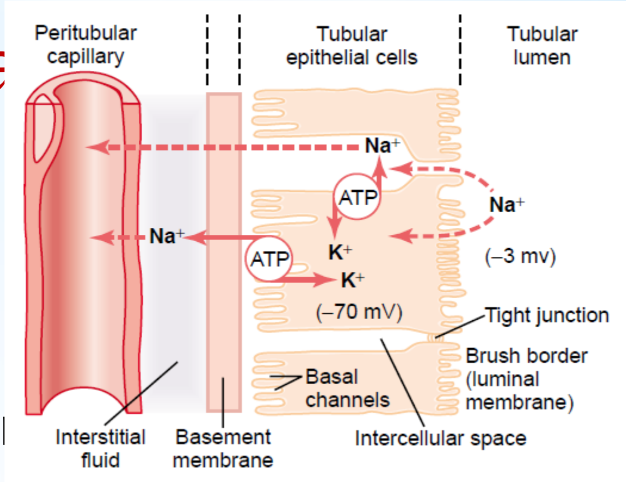
The higher concentration of Na^+ in the proximal tubule, the higher velocity of its reabsorption.

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

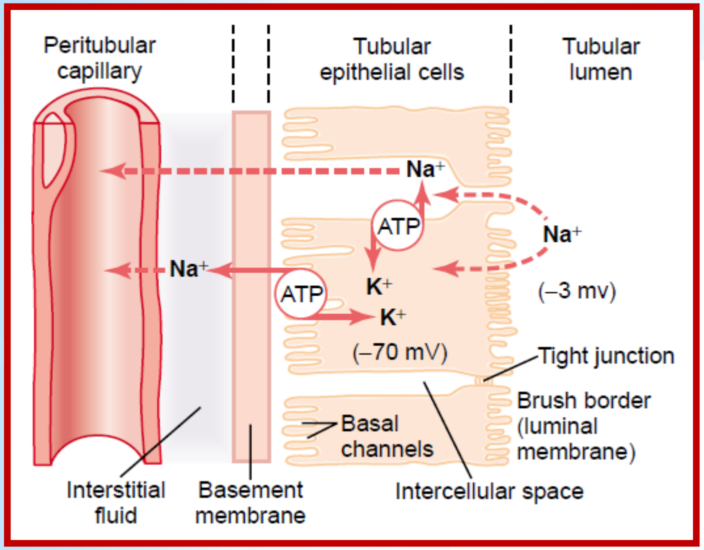


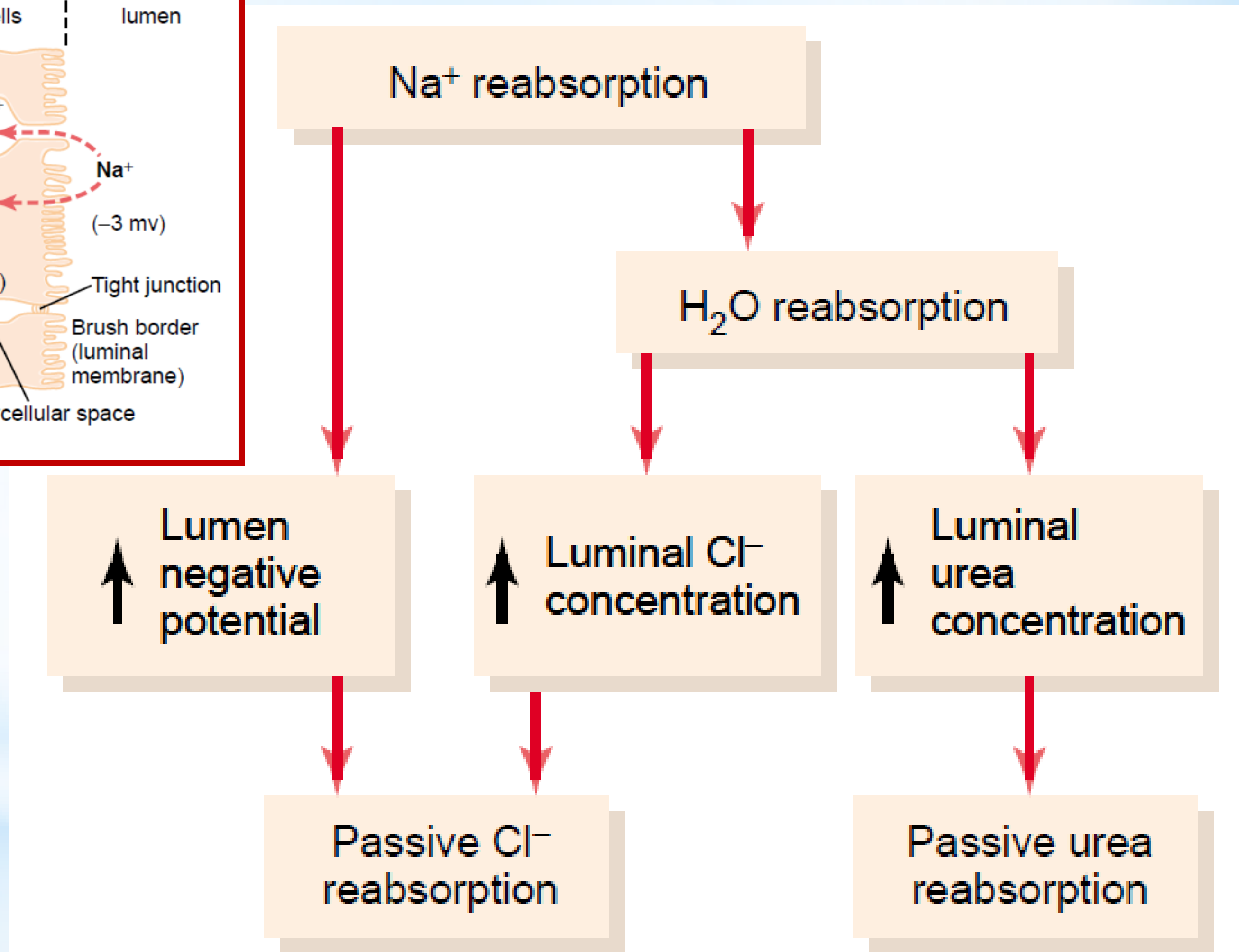
1) Primary active transport
2) Secondary active transport
3) Pinocytosis
   (big molecules, *e.g.* proteins, namely in the pr

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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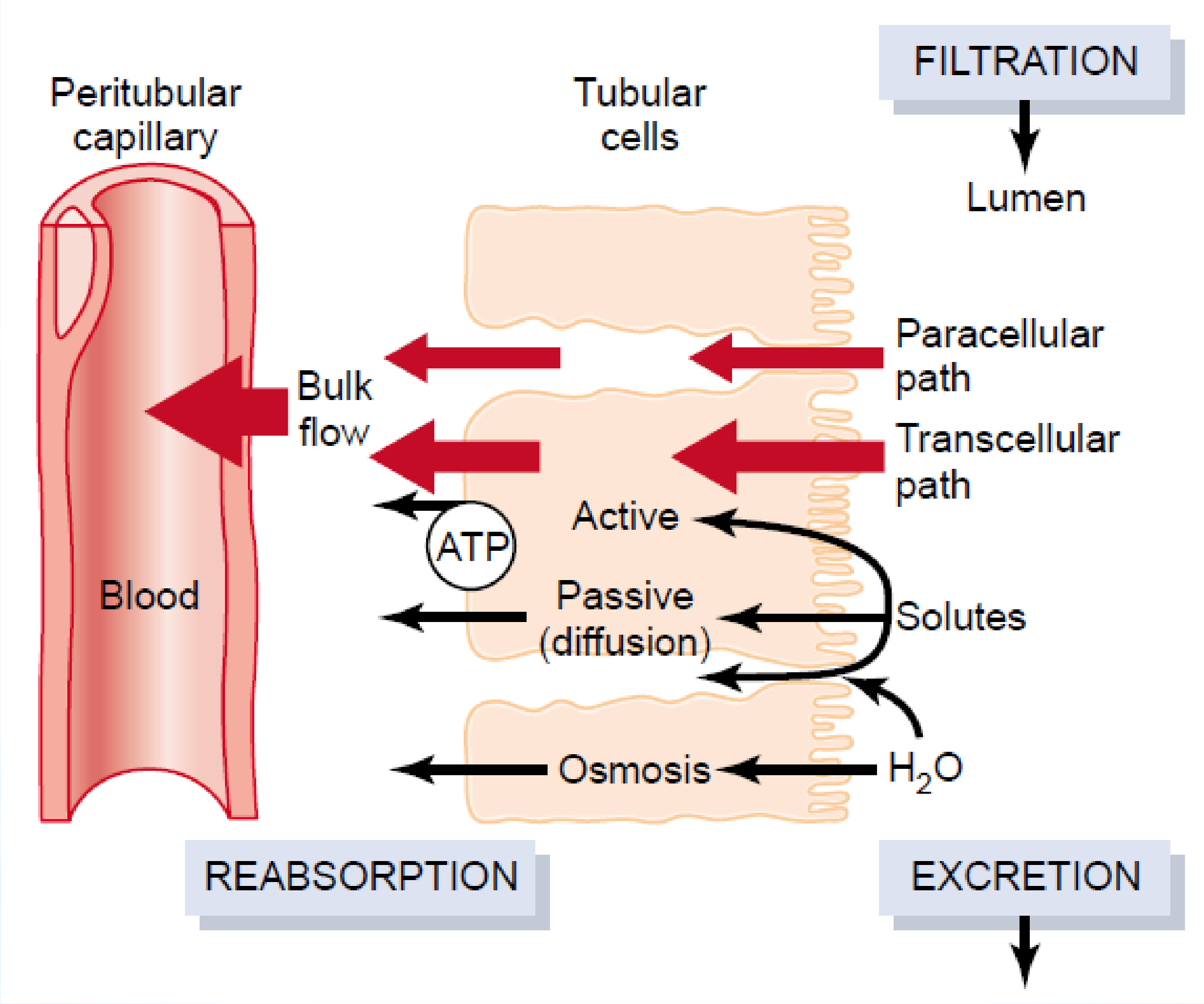
Urine Formation – Tubular Processes



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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)

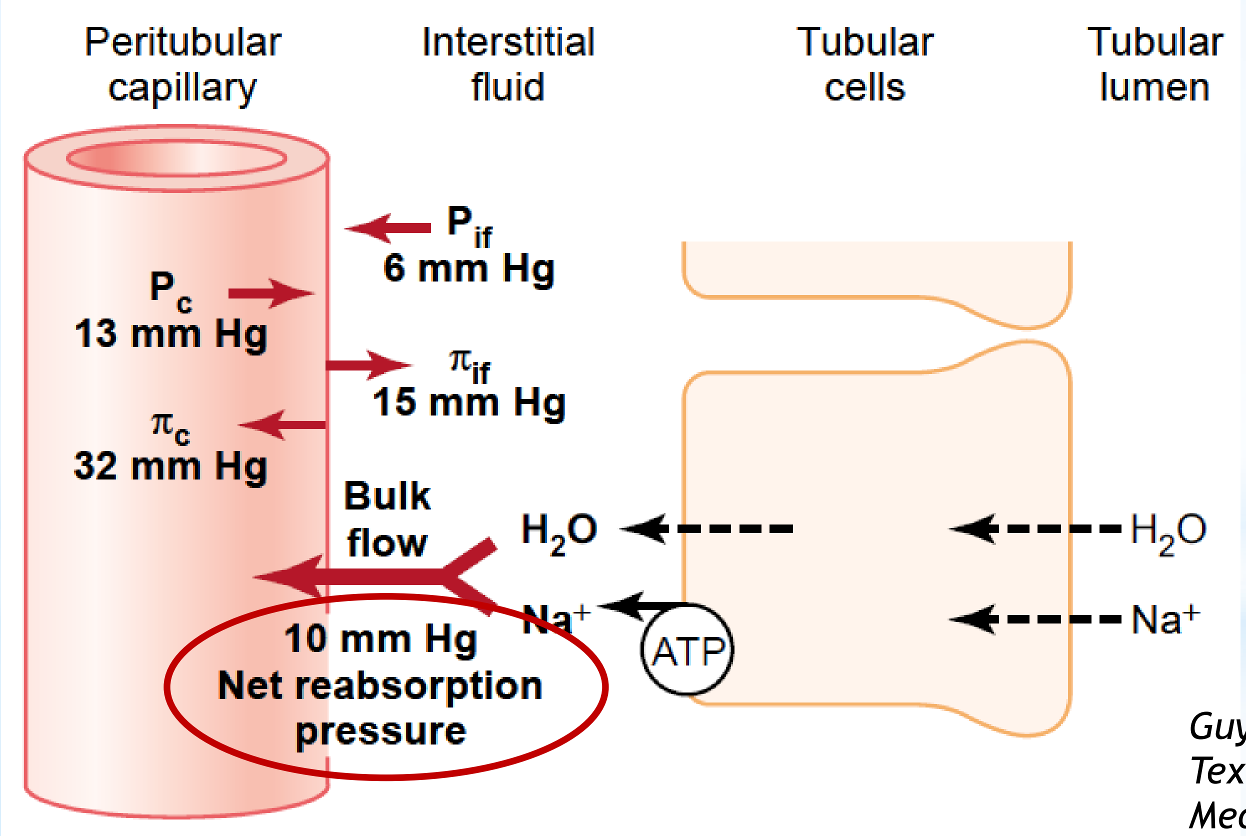
$$GFR = K_f \cdot \text{net filtration pressure}$$

↓

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

Urine Formation – Tubular Processes

Physical Forces in Peritubular Capillaries and in Renal Intersticium



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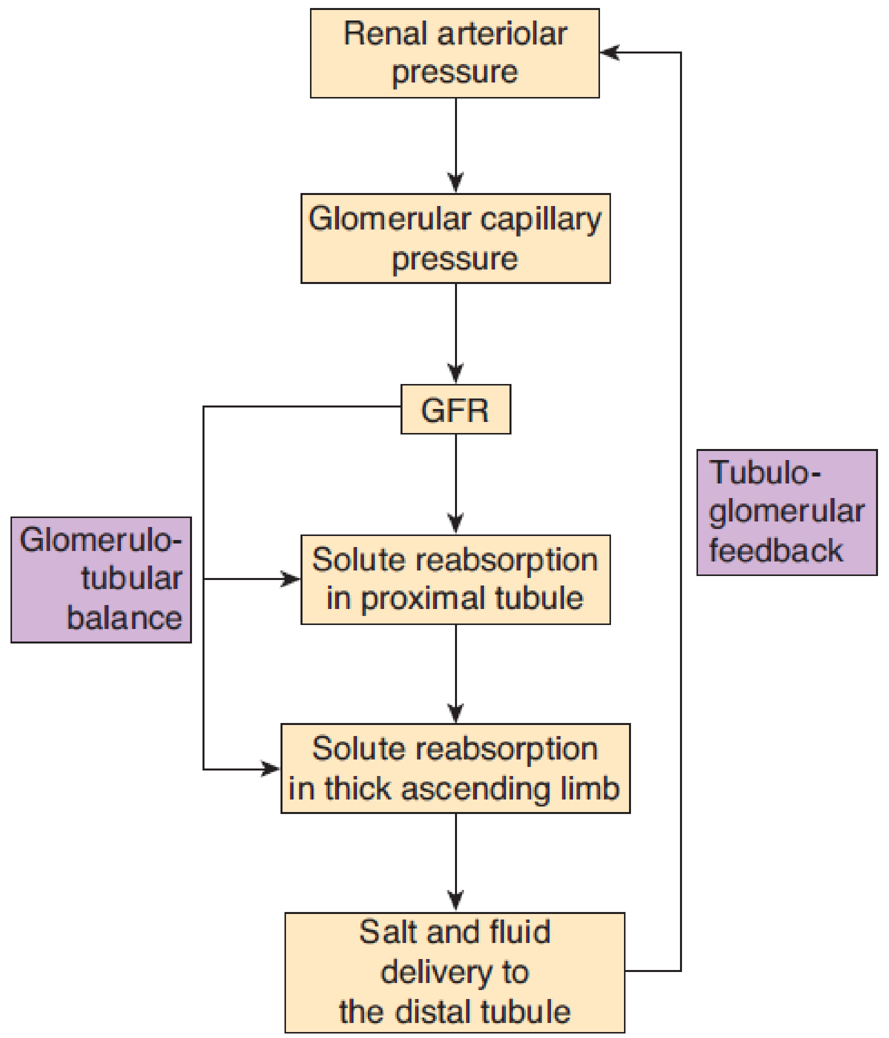
Urine Formation – Tubular Processes

Tubuloglomerular feedback

Glomerulotubular balance



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Urine Formation – Tubular Processes

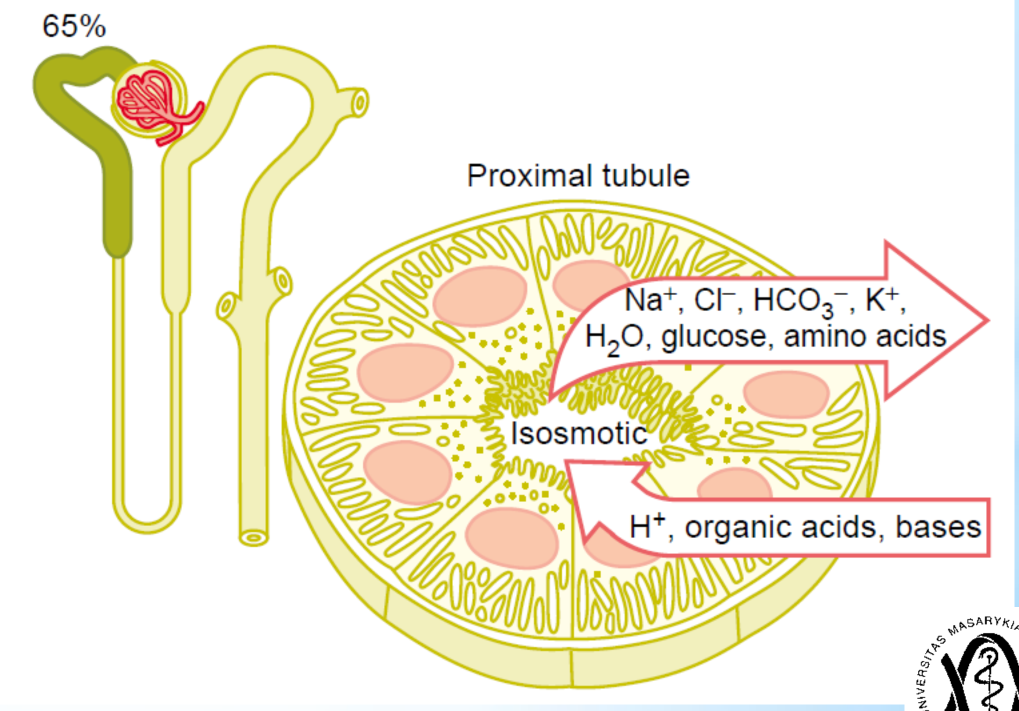
Proximal Tubule

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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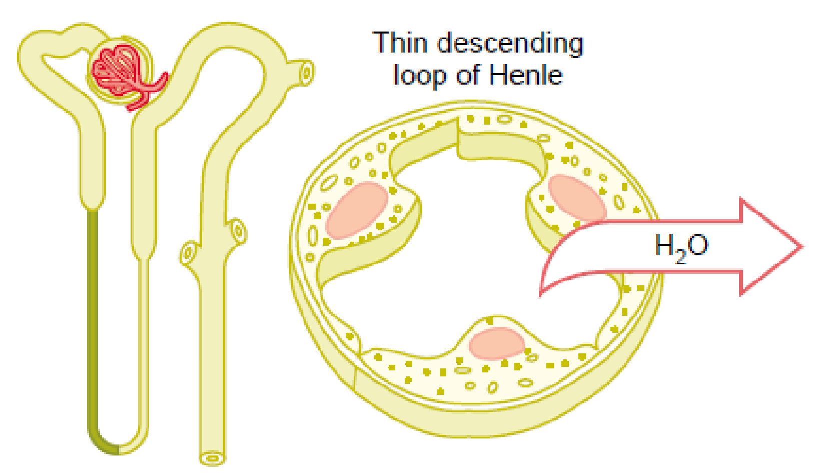
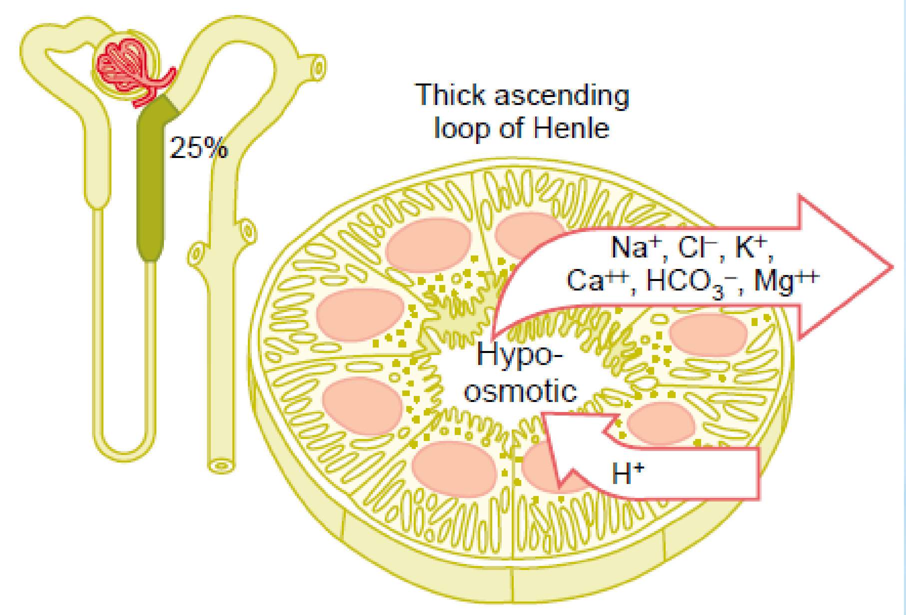
Urine Formation – Tubular Processes

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^-





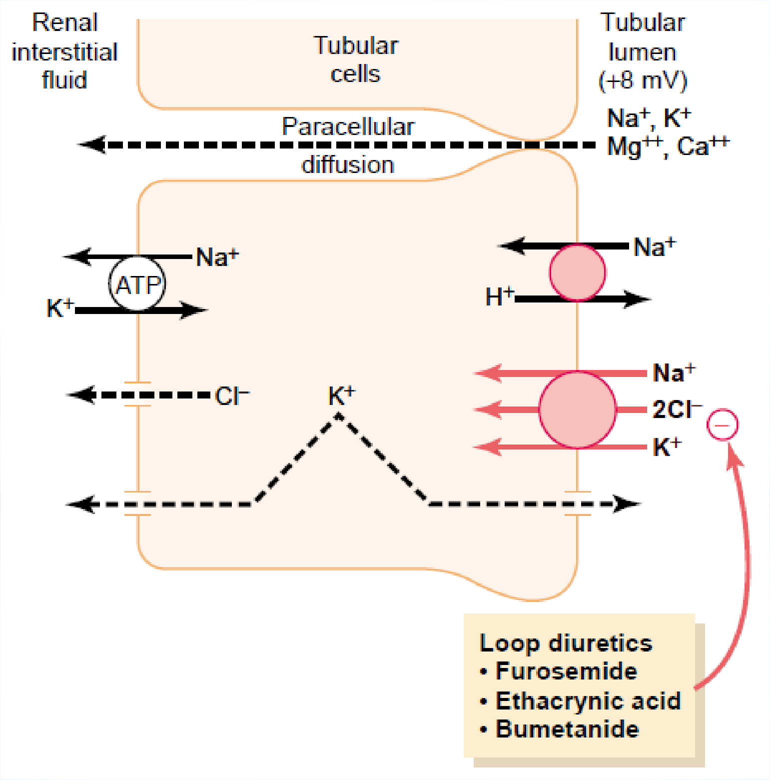
counter-current multiplier

Result: hypotonic fluid, volume further decreased

Urine Formation – Tubular Processes

Loop of Henle

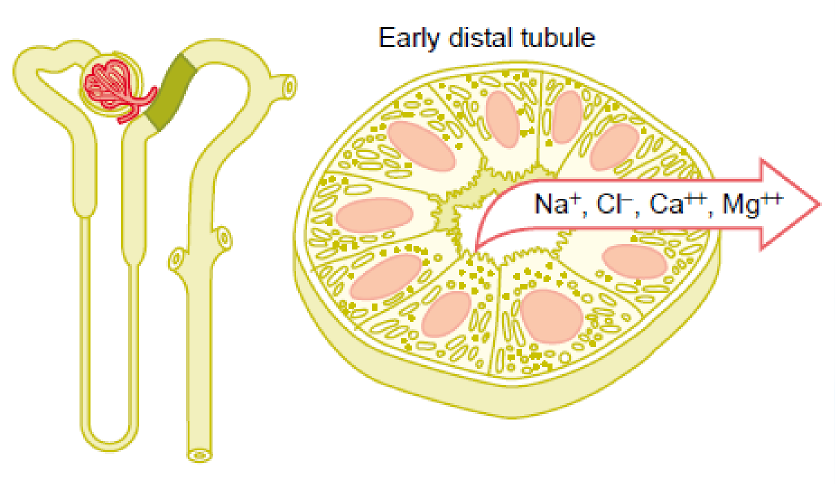
1) thin descending part - passive reabsorption of water (osmosis)
2) thick ascending part - active reabsorption of ions ($Na^+/K^+/2Cl^-$ symport), secretion of H^+, reabsorption of HCO_3^-

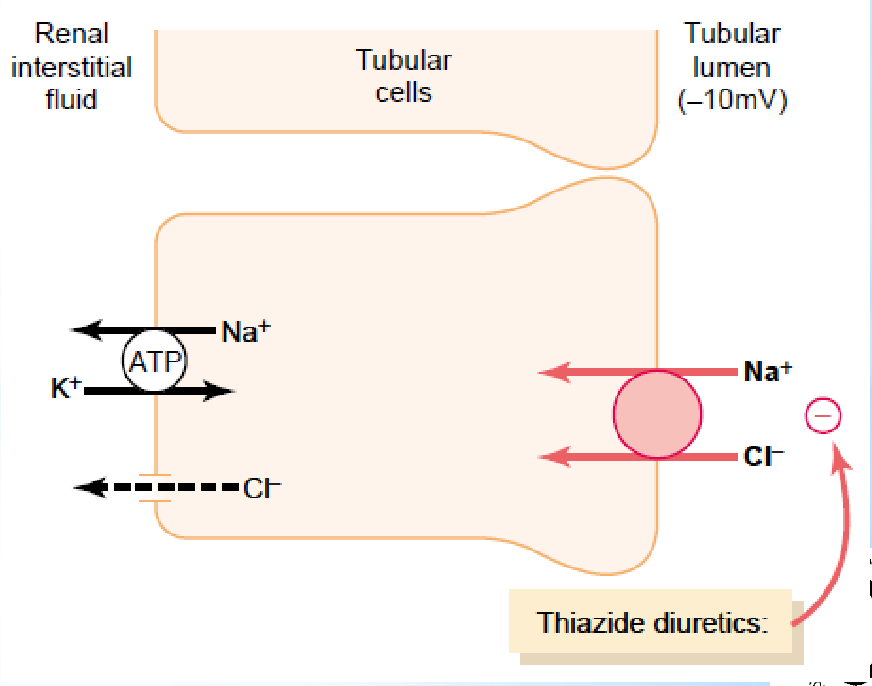


Urine Formation – Tubular Processes

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)



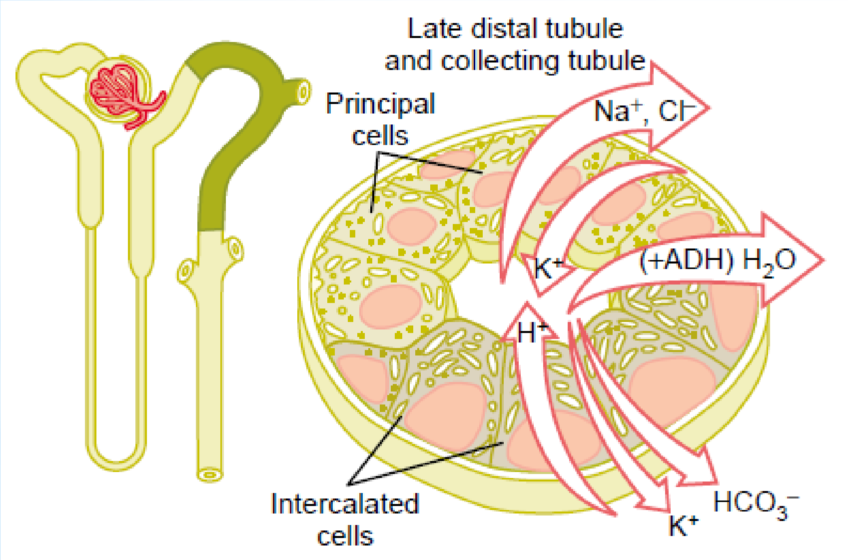


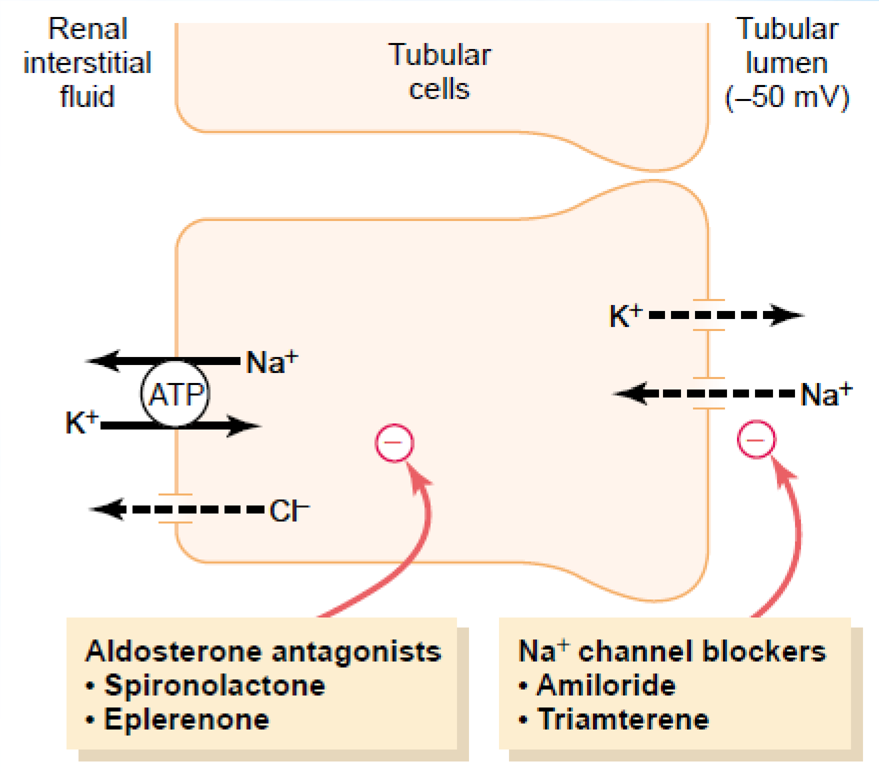
Result: hypotonic fluid

Urine Formation – Tubular Processes

Collecting duct (+ end of distal tubule)

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

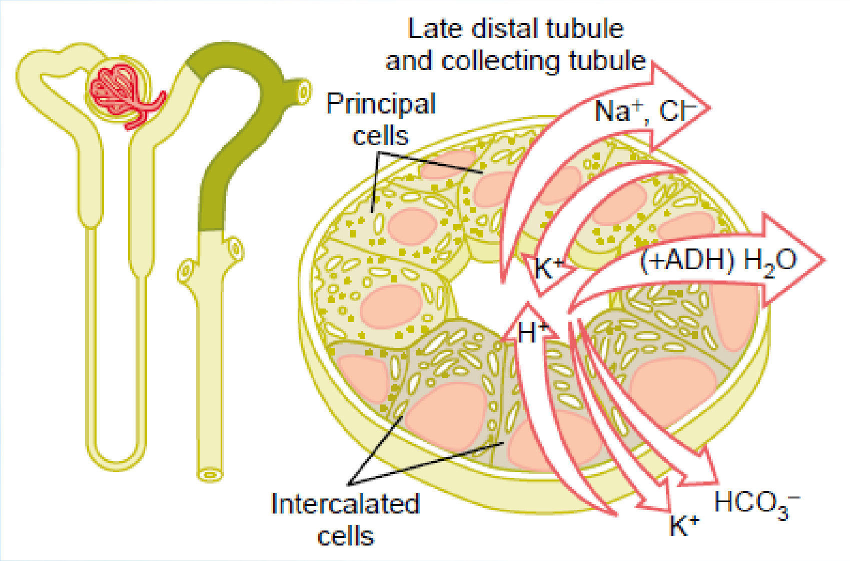


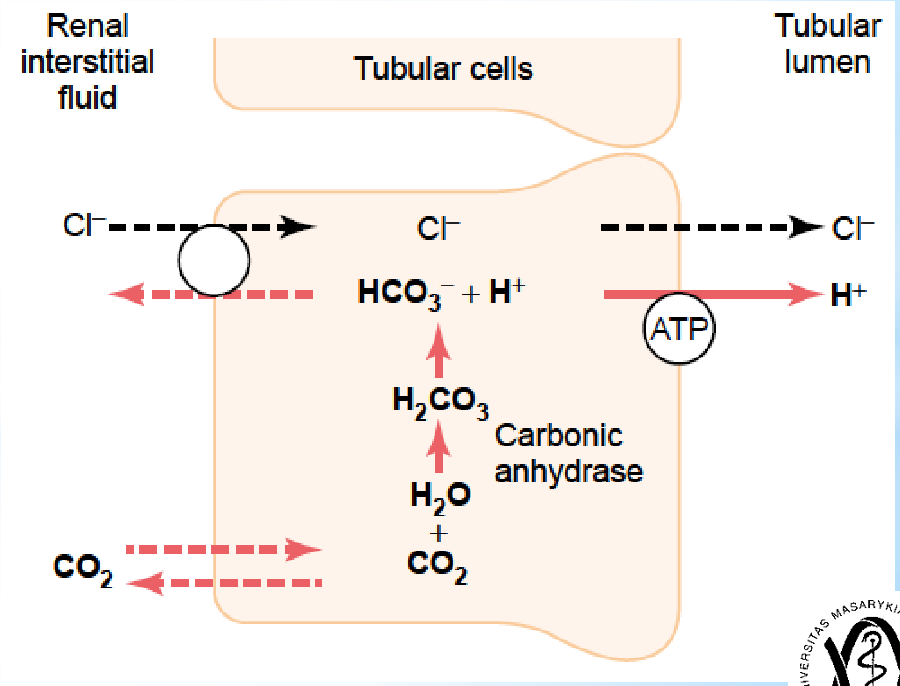


Urine Formation – Tubular Processes

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^+

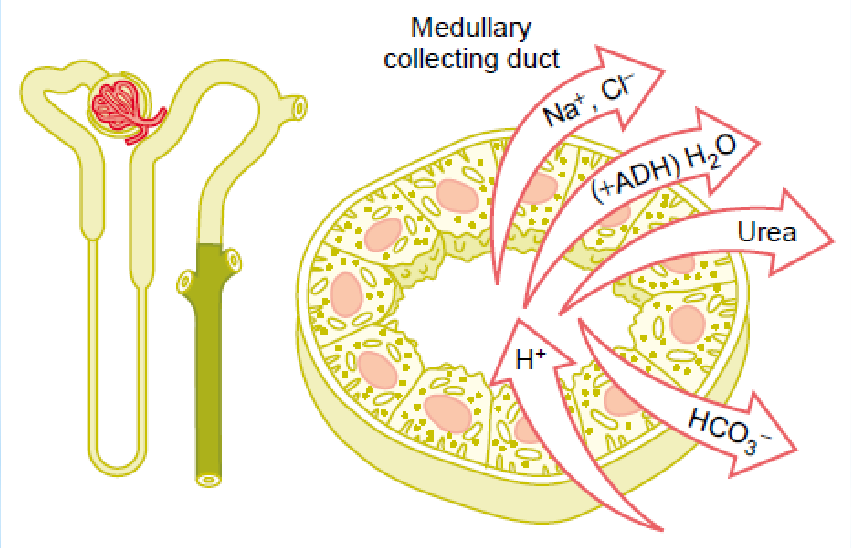




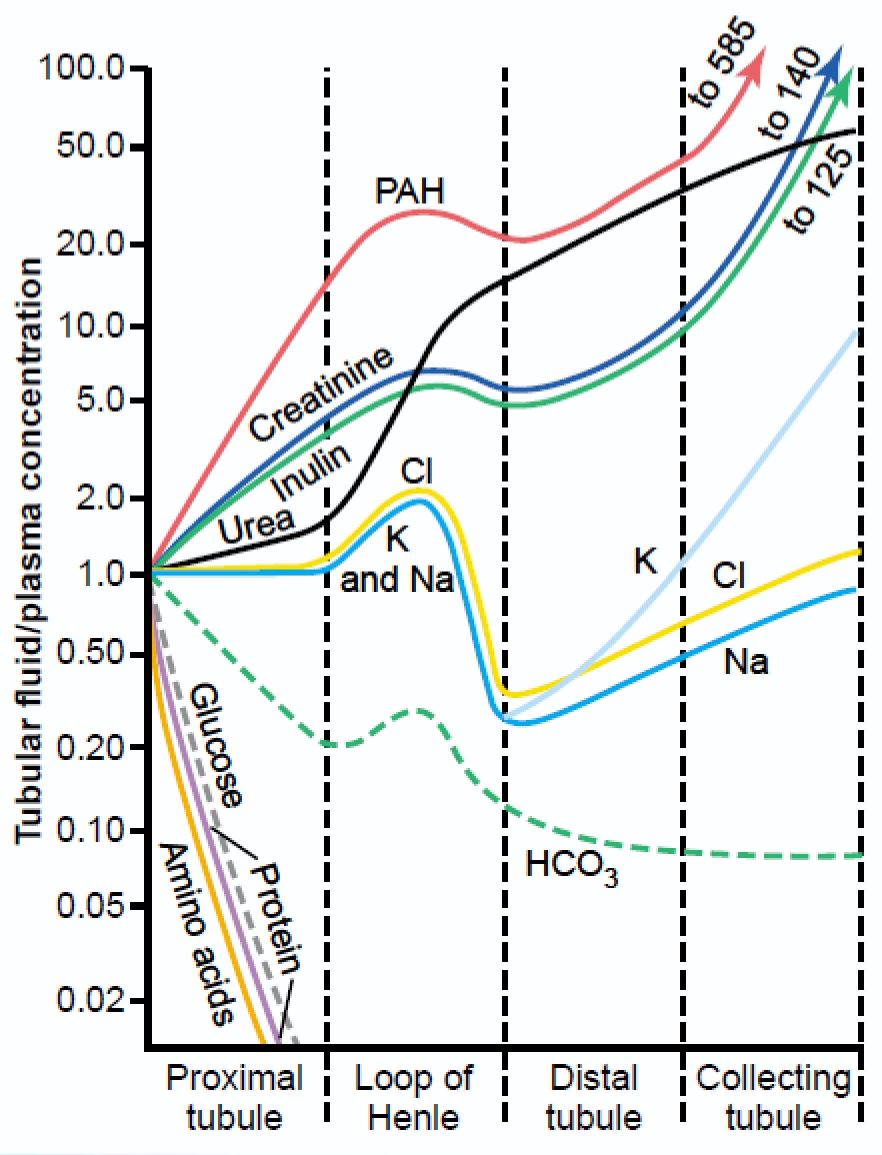
Urine Formation – Tubular Processes

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

Examination of renal function

- Renal clearance
- Examination of function of renal tubules

a) Examination of concentration ability of kidneys

- Concentration test using thirstiness
  (very unpleasant; 12 hours of thirstiness, urine sample every 4 hours – urine density and osmolality; also a blood sample)
- Adiuretin test
  (more pleasant for patient; no drinks and food during night, ADH application in the morning through the nasal mucosa – urine density and osmolality)

a) Examination of dilution ability of kidneys

(test of reaction on increased water intake – decreased ADH production + increased diuresis in healthy people)

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).

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

C_S [ml/min]

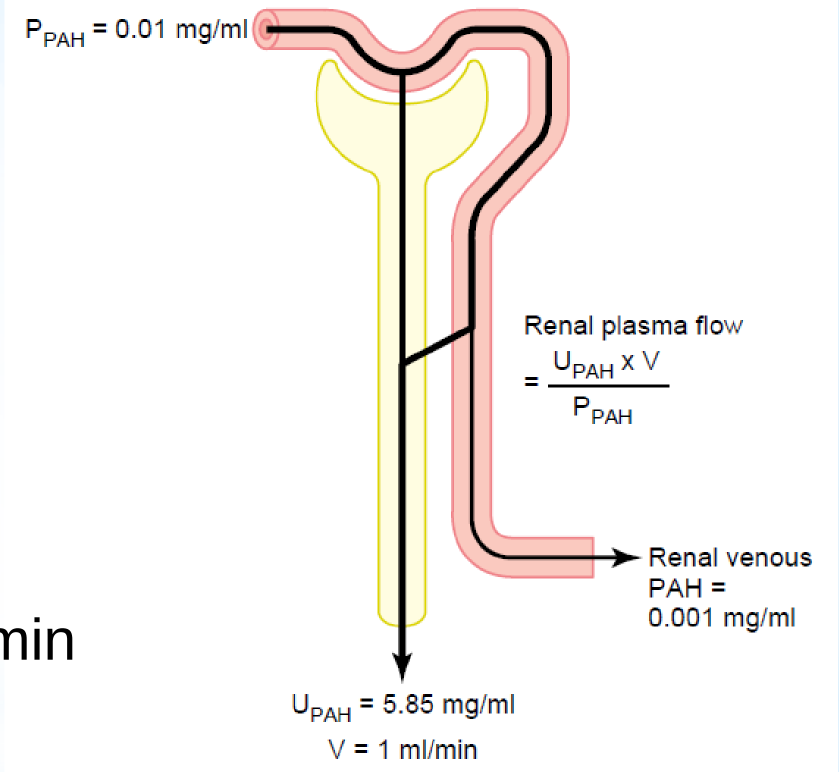
Renal Clearance

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%

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



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

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

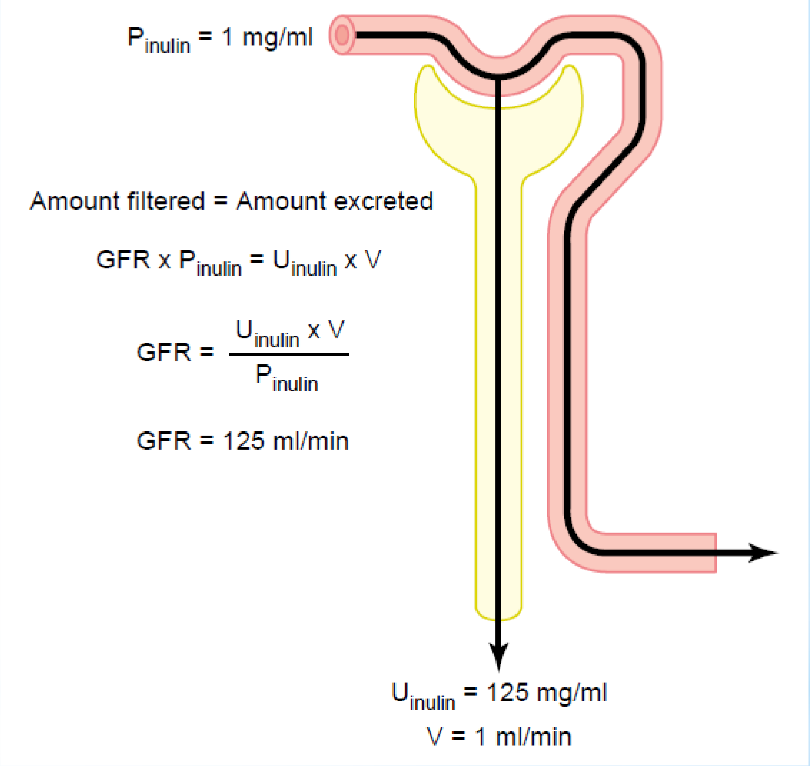
Renal Clearance

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.

$$FF = \frac{GFR}{RPF} = \frac{125 \text{ ml/min}}{650 \text{ ml/min}} = 0.19 \longrightarrow$$

~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