LIST OF CONTACTS for solving technical and organisation problems

Before sending an email, please, read carefully all information and instructions in this document.

Contact person	email	Responsibility
MUDr. Zuzana Nováková, Ph.D.	znovak@med.muni.cz	Practices
Mgr. Monika Řezníčková	mnemec@med.muni.cz	Seminars
Prof. MUDr. Marie Nováková, Ph.D., guarantor	majka@med.muni.cz	Rules, exceptions, lectures
Dr. Xenie Budínská, Ph.D.	409542@mail.muni.cz	Organisation of examination

Above listed contact persons will answer your questions according to their time possibilities, no later than during 5 working days. Emails addressed to other teachers of the Physiology department (regarding the above-mentioned agenda) will not be considered.

Functional morphology of kidneys Clearance

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

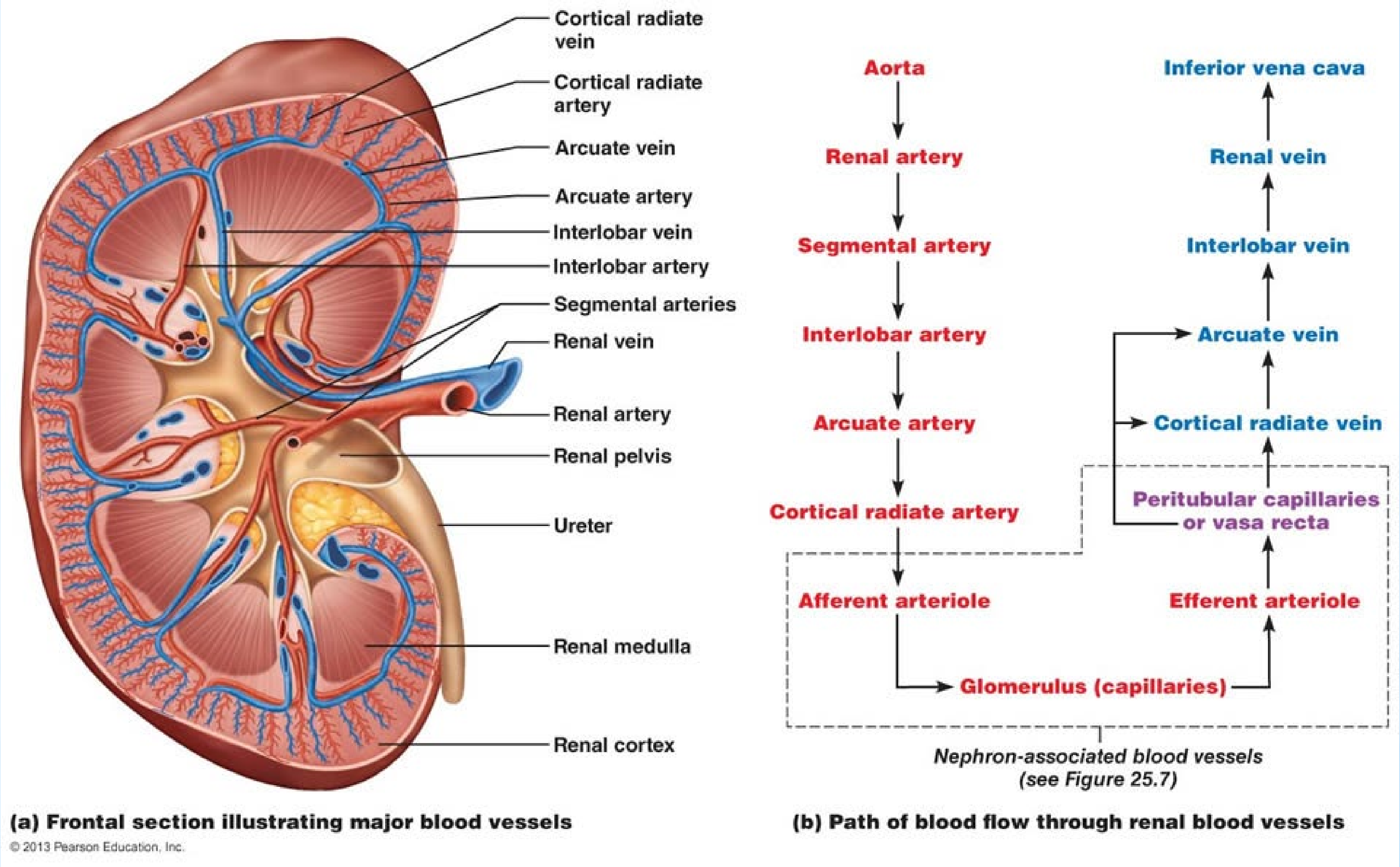
Department of Physiology

Faculty of Medicine, Masaryk University

Renal Functions

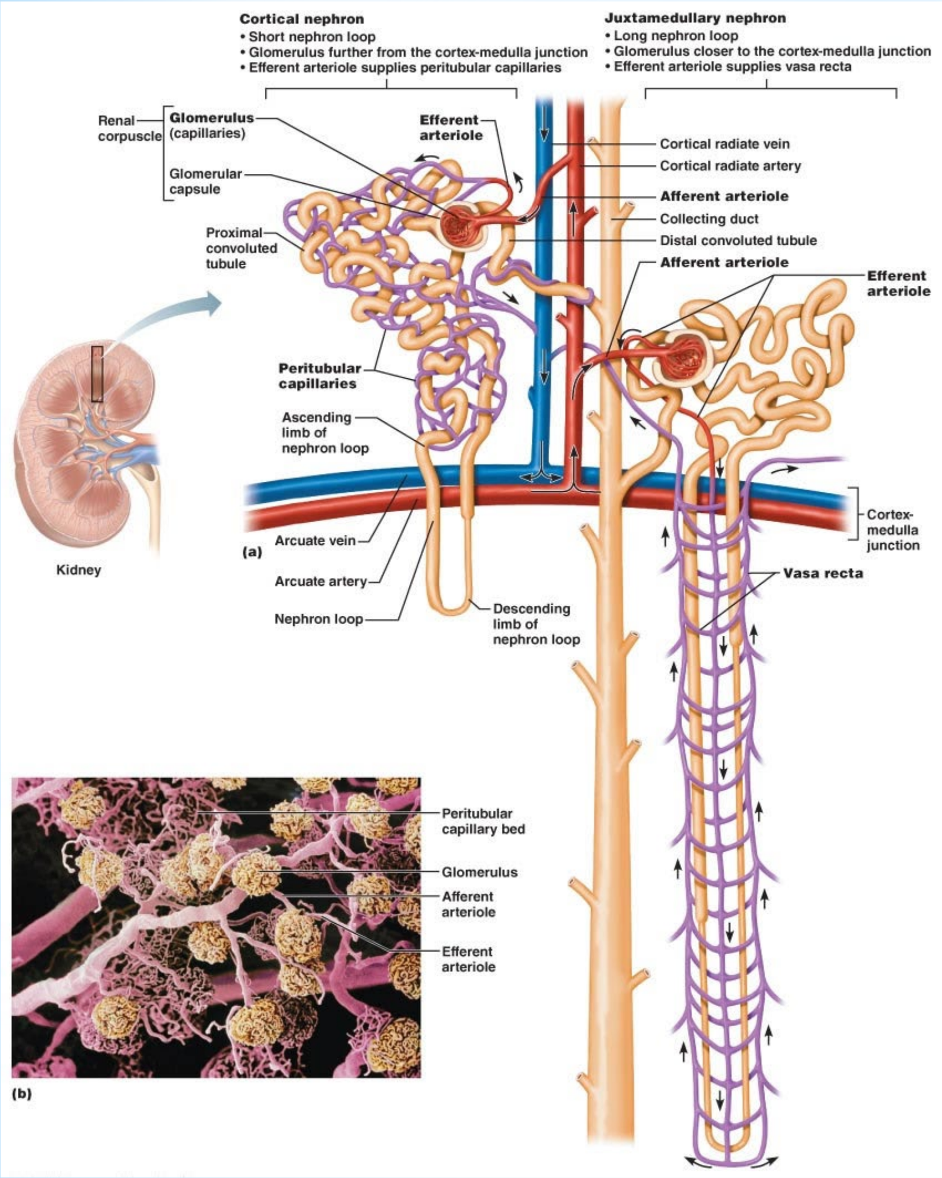
- Excretion of Waste Products and Toxins
  (entry from the external environment or production in the course of metabolic events)
- Control of Volume and Composition of Body Fluids, Osmolality
- Regulation of Acid-Base Balance
- Regulation of Blood Pressure
- Secretion, Metabolism and Excretion of Hormones
  (renin, erythropoetin, kinins, prostaglandins, 1,25-diOHcholekalciferol)
- Glukoneogenesis

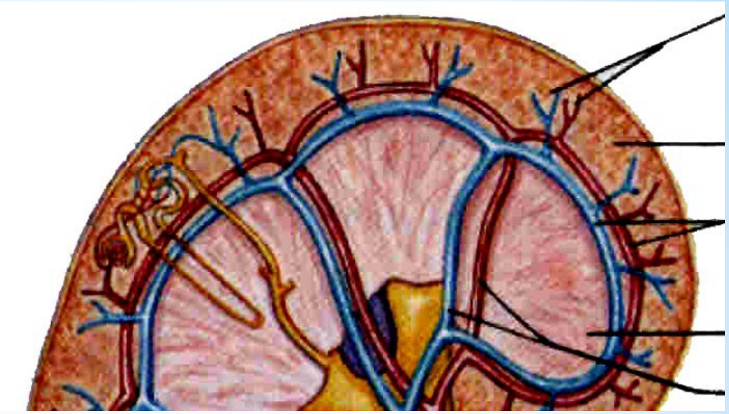
Structure of Kidney



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

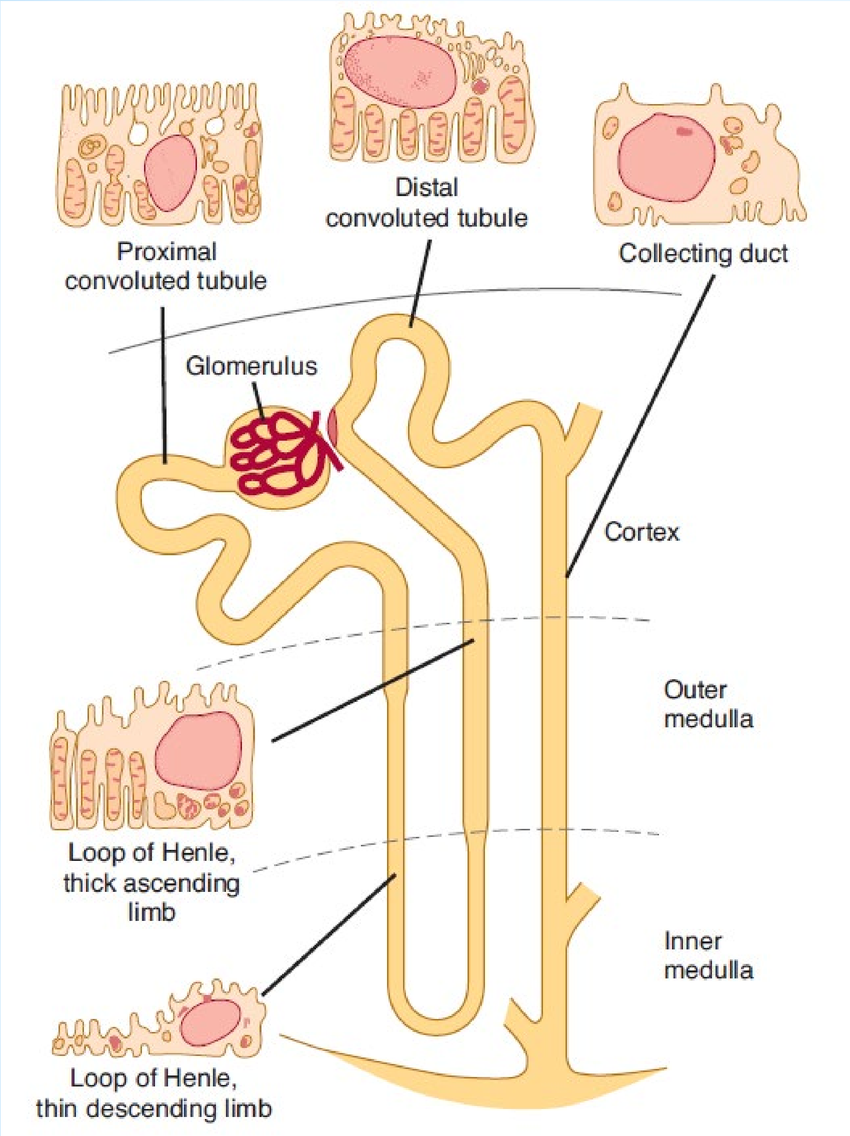
Structure of Kidney





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

Structure of Nephron



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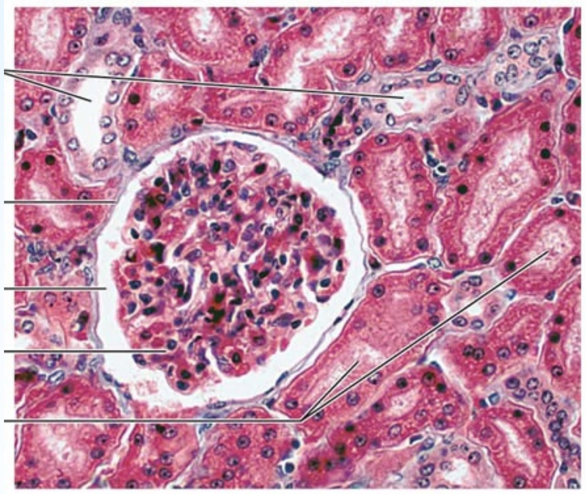
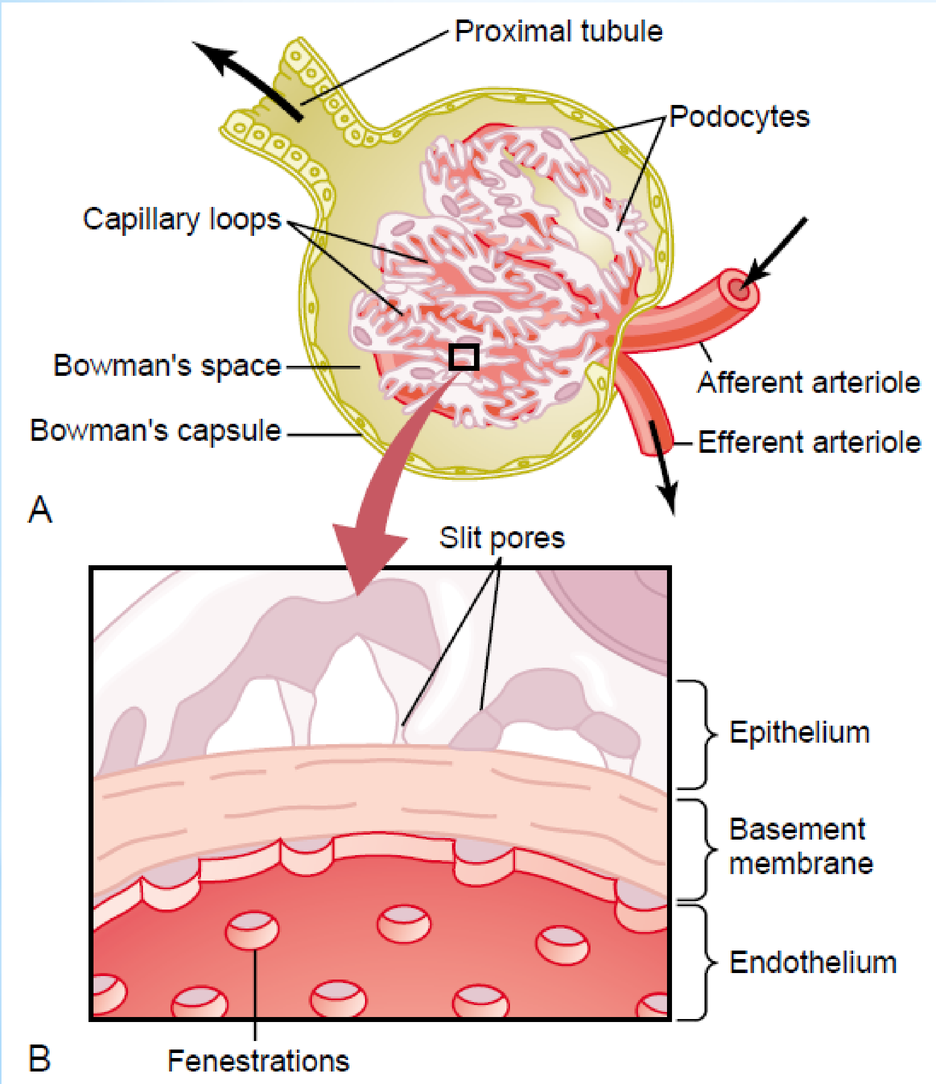
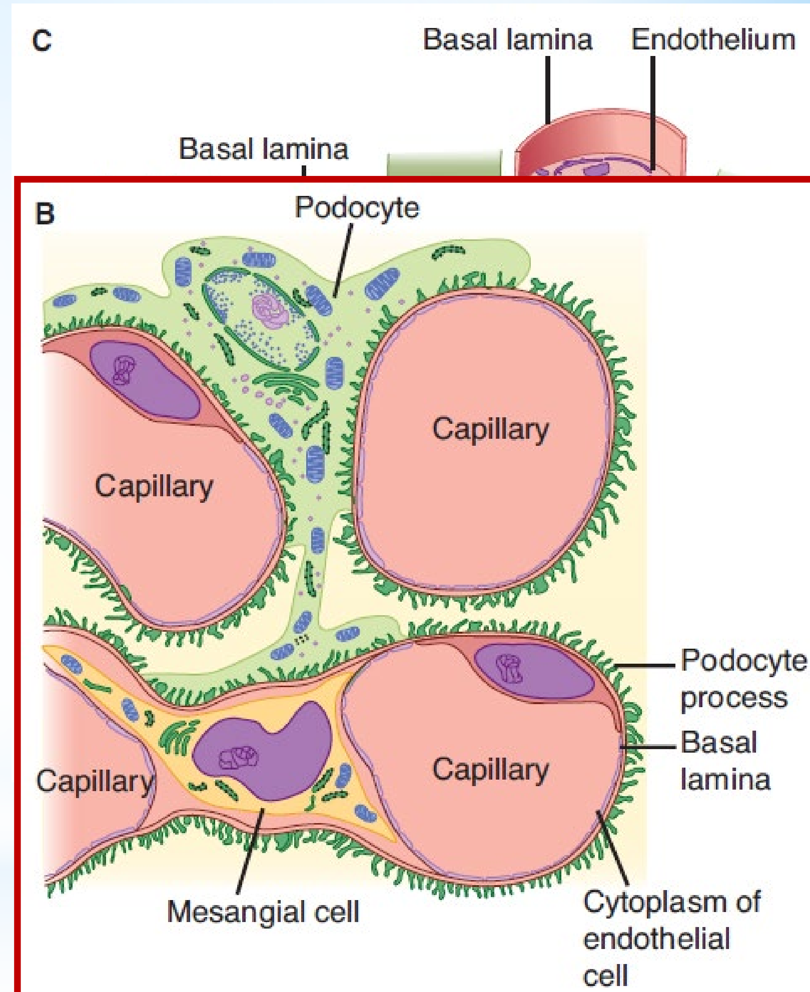


f renal cortical tissue (180×)

Structure of Nephron - Glomerulus





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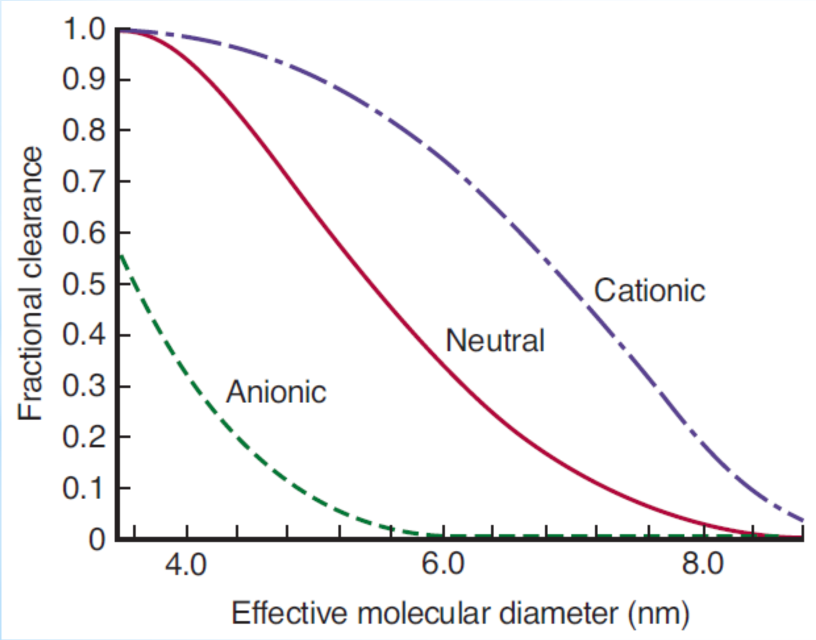
Structure of Nephron - Glomerulus

- **High filtration rate in glomeruli**
  provided by high permeability of glomerular membrane (structure of glomerular membrane - fenestrations, slit pores)

- **Protein passage barrier**
  negative charge of all layers of glomerular membrane



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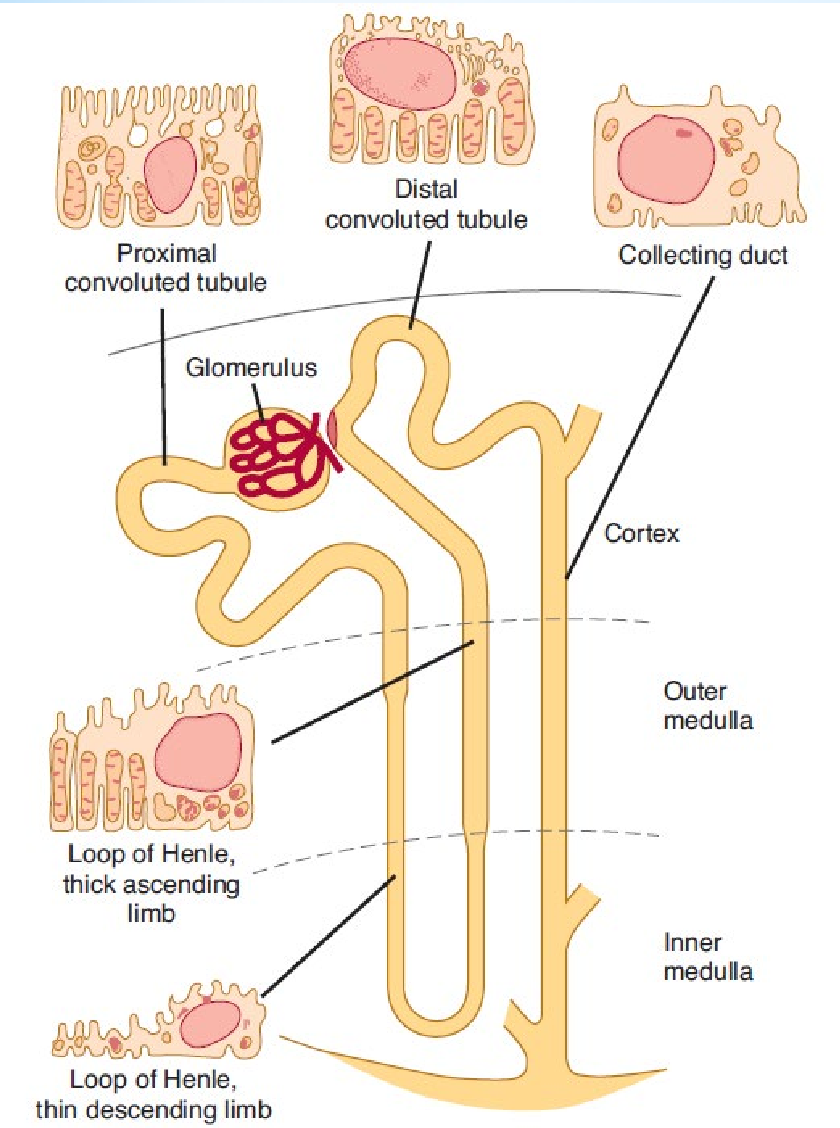
Structure of Nephron - Tubulus



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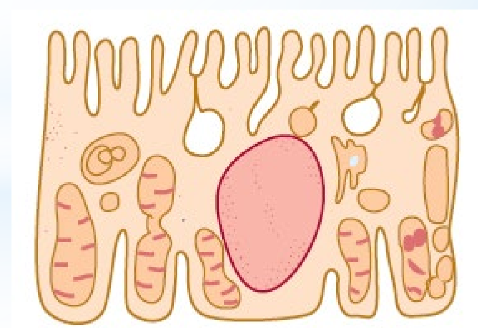
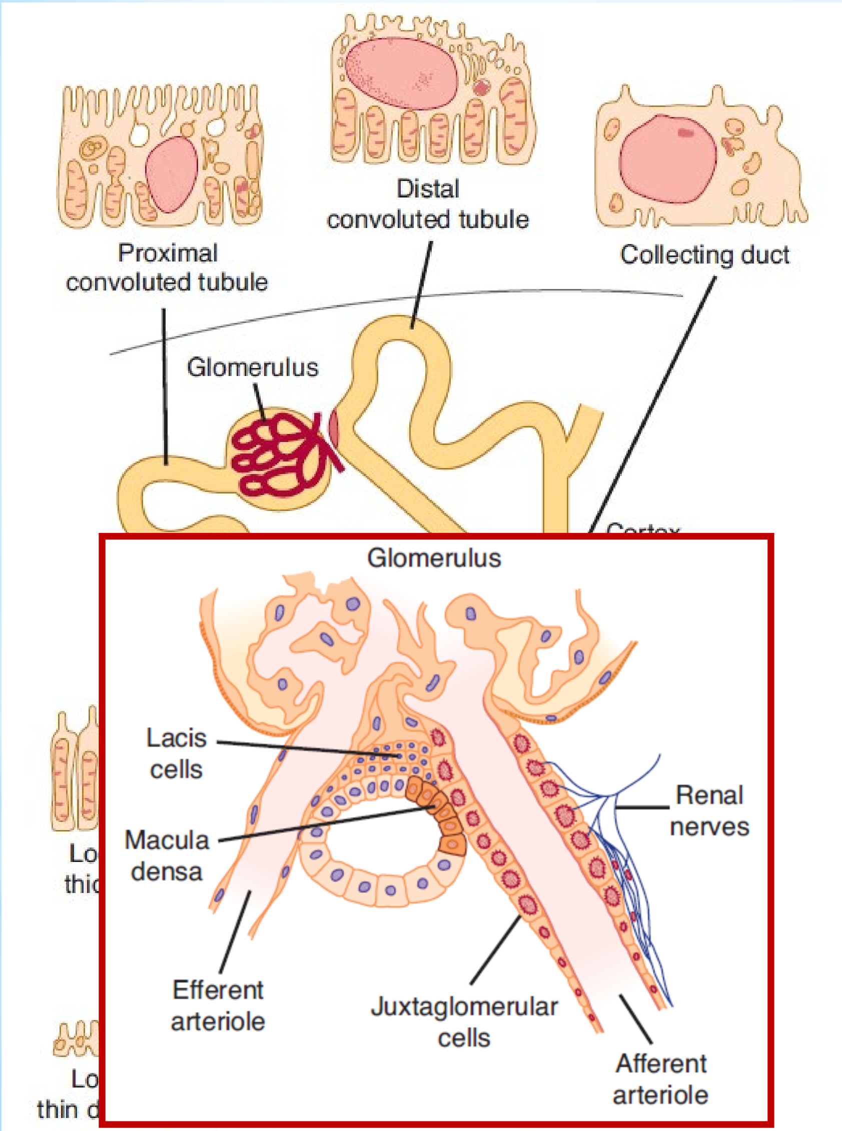
- glomerulus
- proximal convoluted tubule



Structure of Nephron - Tubulus



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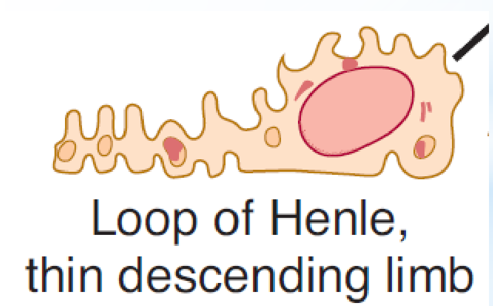
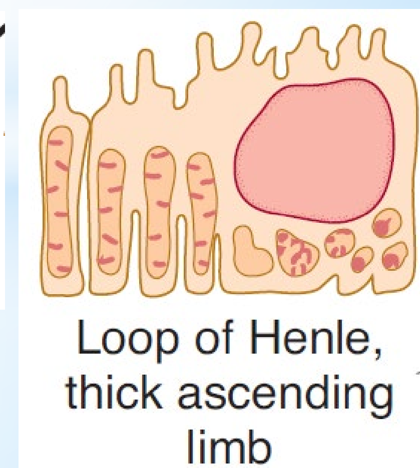
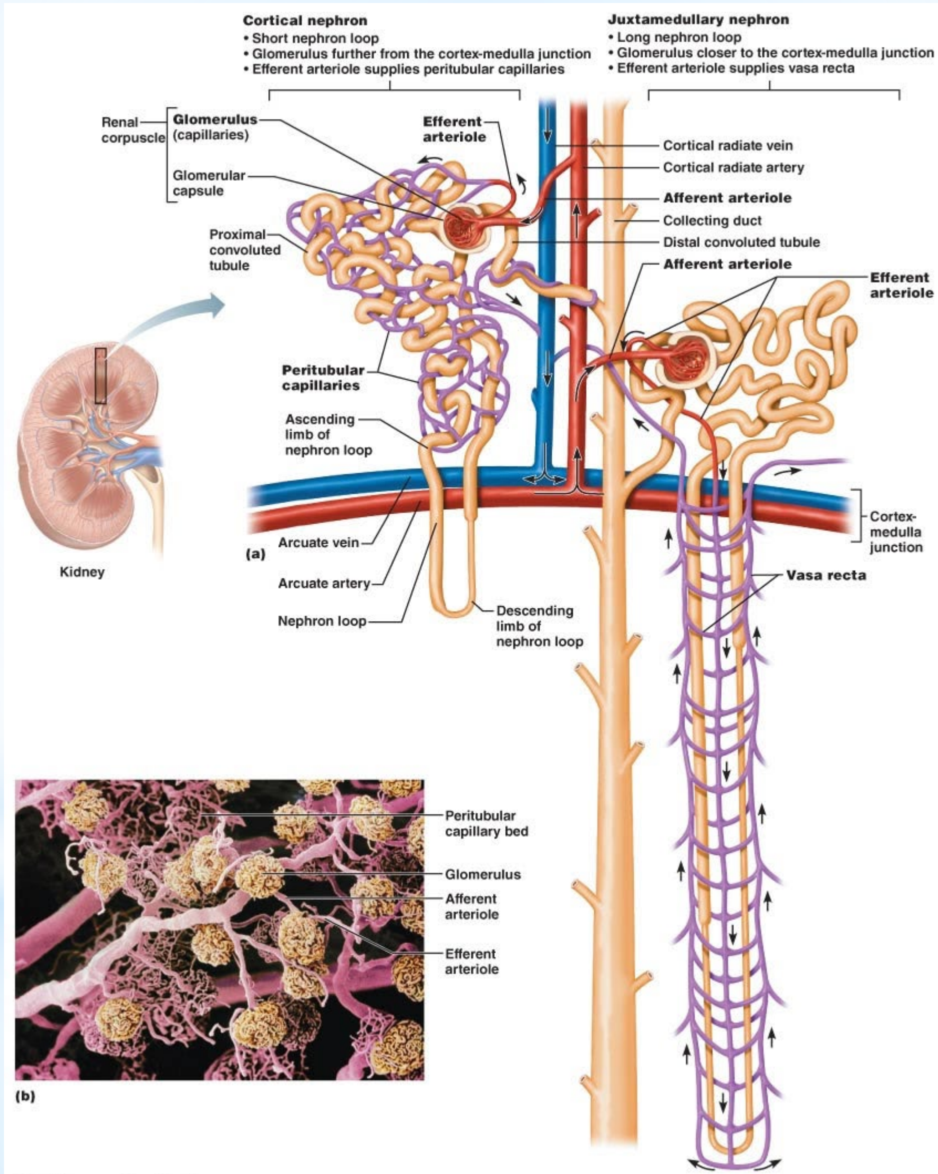
- glomerulus
- proximal convoluted tubule
- loop of Henle





Structure of Nephron - Tubulus



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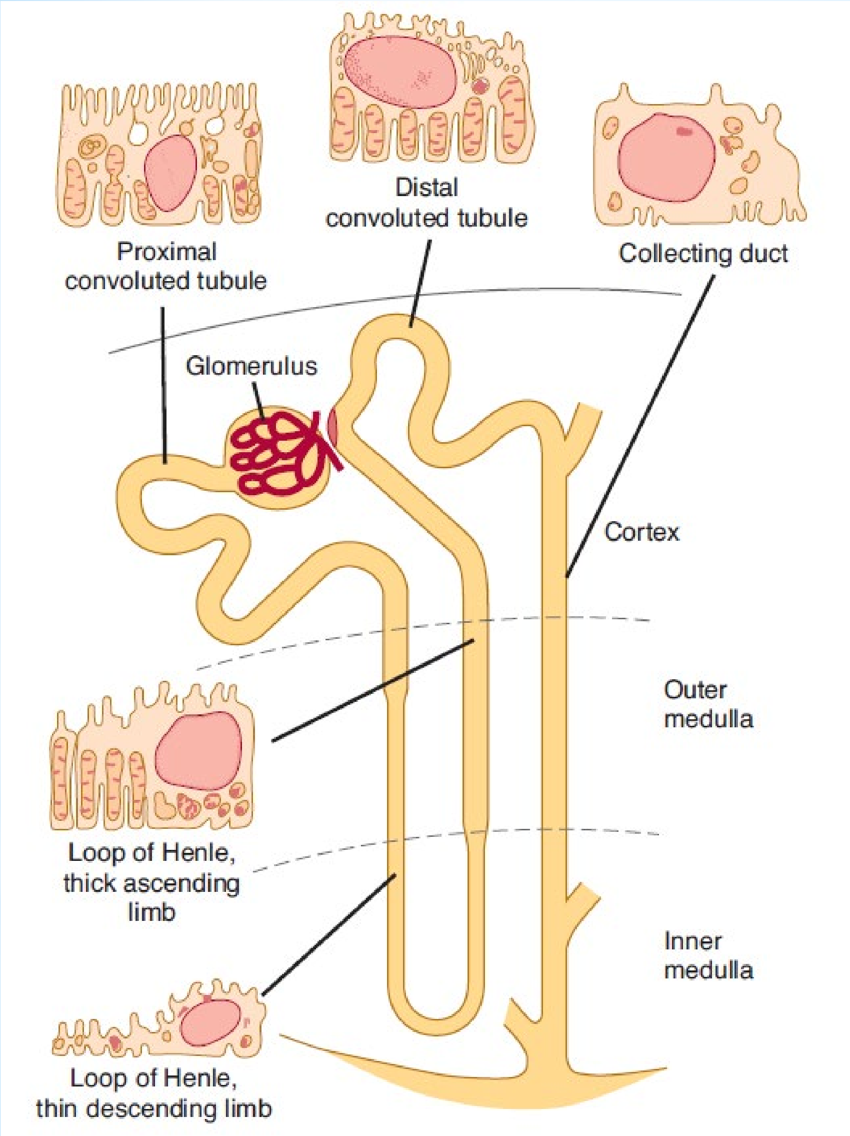
Structure of Nephron - Tubulus



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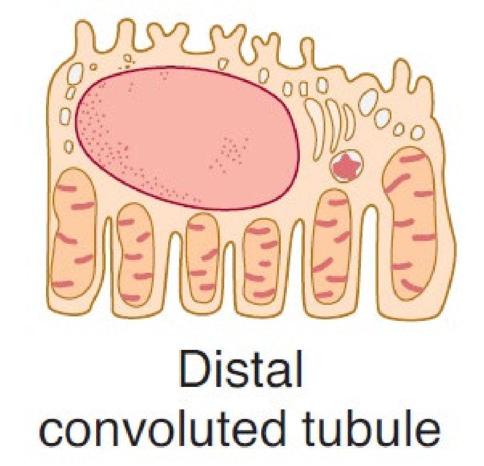
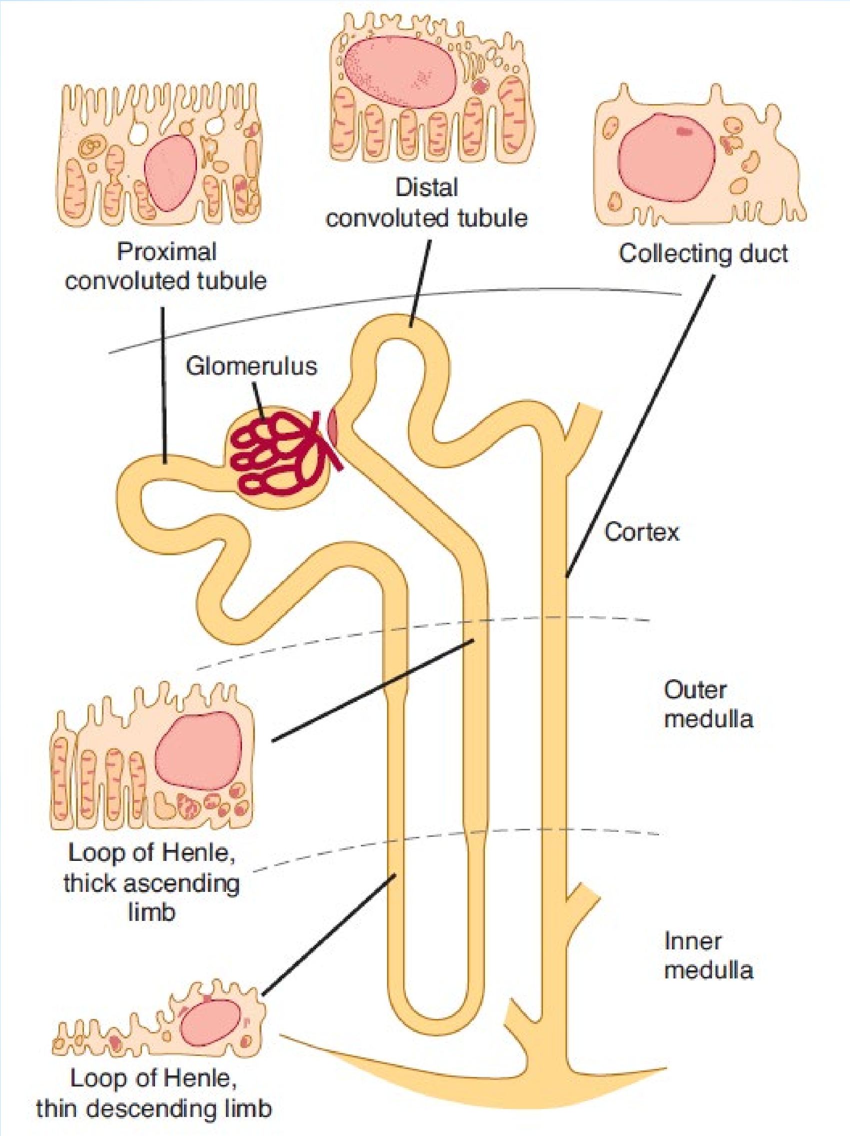
- glomerulus
- proximal convoluted tubule
- loop of Henle
- distal convoluted tubule



Structure of Nephron - Tubulus



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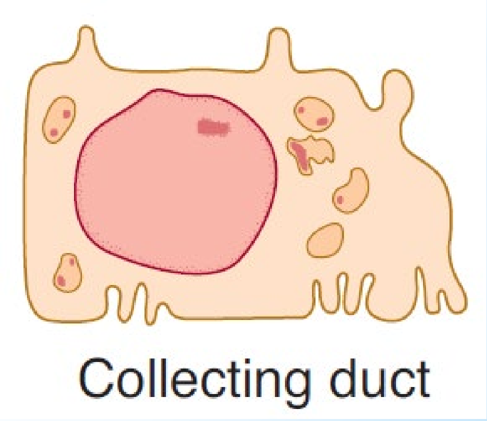
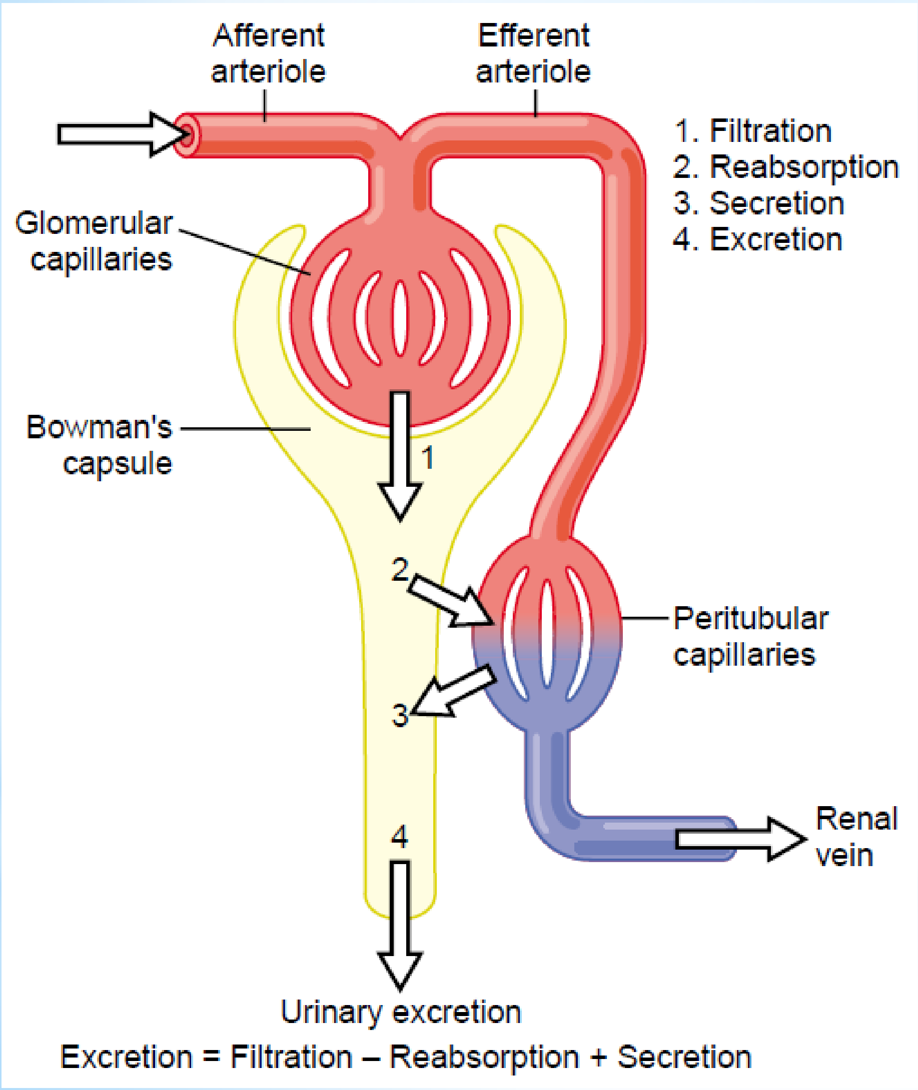
- glomerulus
- proximal convoluted tubule
- loop of Henle
- distal convoluted tubule
- collecting duct



Urine Formation



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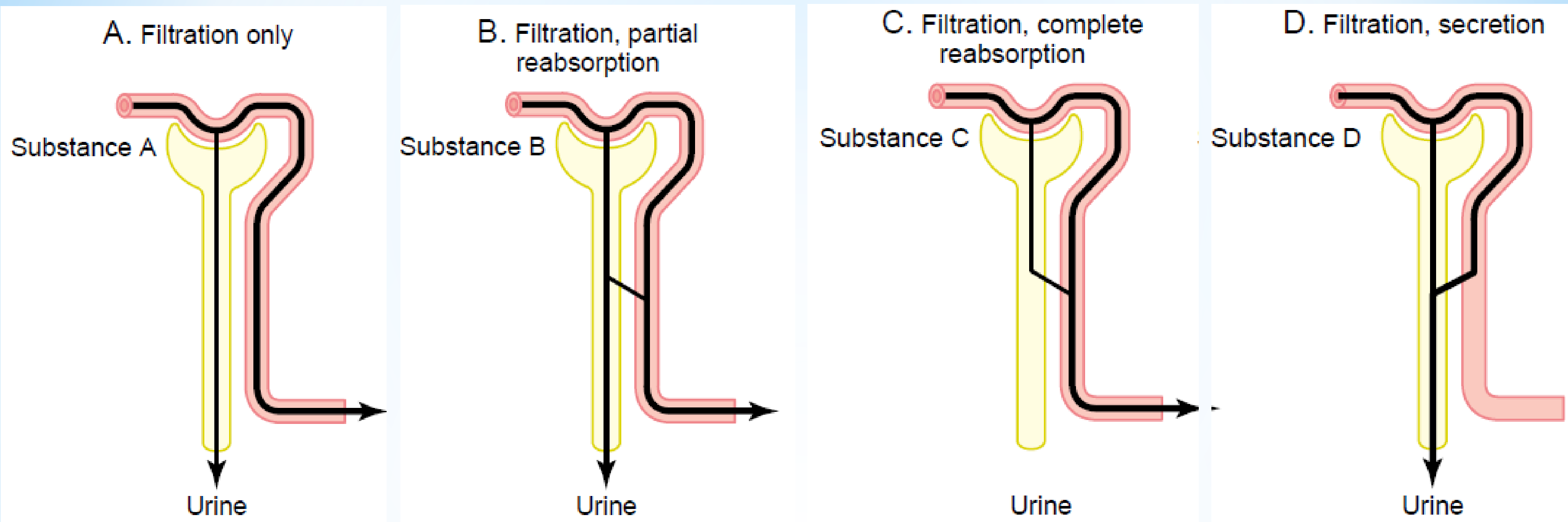
1) Glomerular filtration
2) Tubular reabsorption
3) Tubular secretion
4) Urine excretion

Urine Formation



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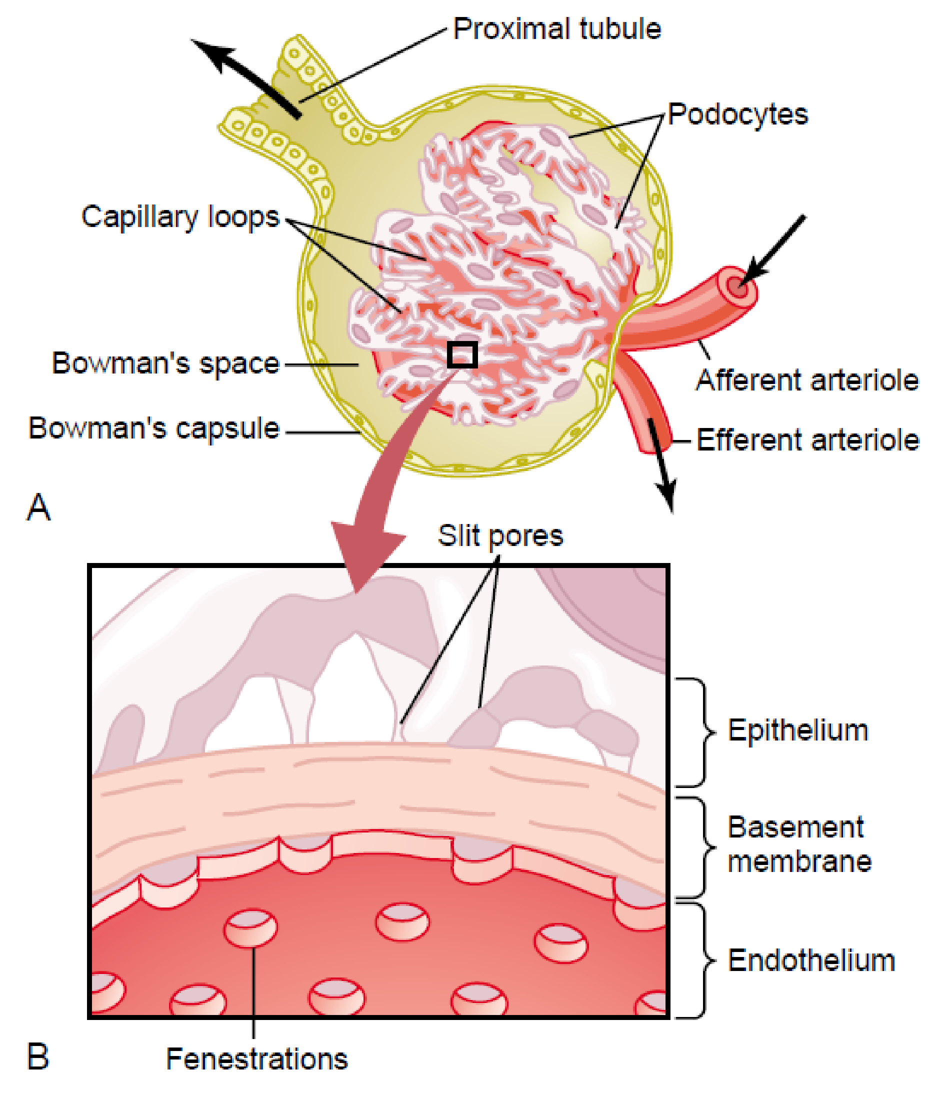
- creatinine
- other waste products

Substance	Concentration in		U/P Ratio
	Urine (U)	Plasma (P)	
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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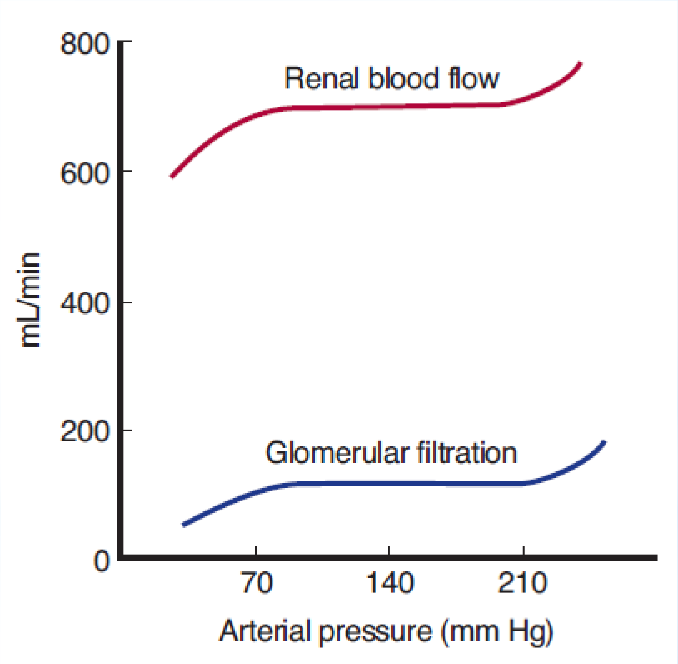
GFR = 125 ml/min = 180 l/day

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)

2) Balance of hydrostatic and coloid osmotic forces

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

Urine Formation - Glomerular Filtration

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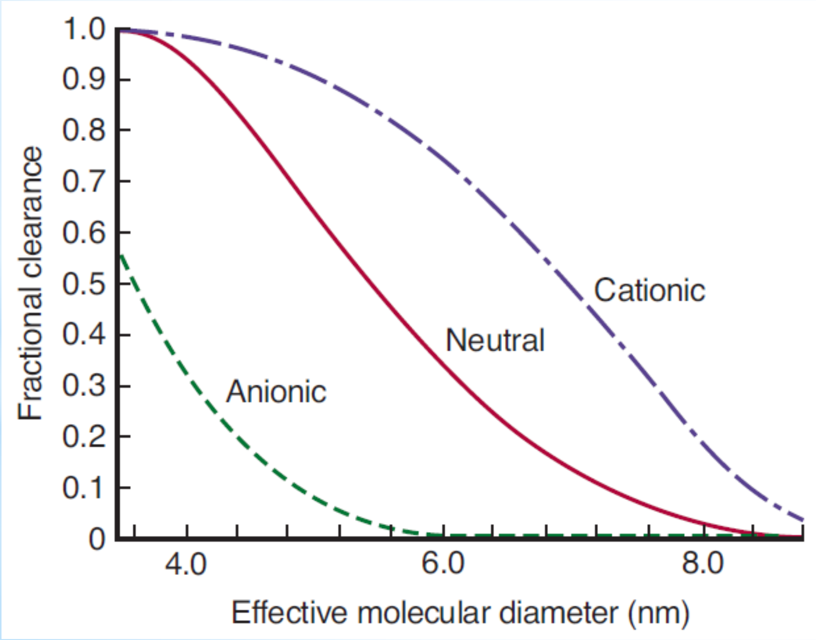
Permeability



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albumin: diameter ~7 nm

loss of negative membrane charge

↓

proteinuria (albuminuria)

Urine Formation - Glomerular Filtration

Glomerular filtration rate (GFR) depends on:

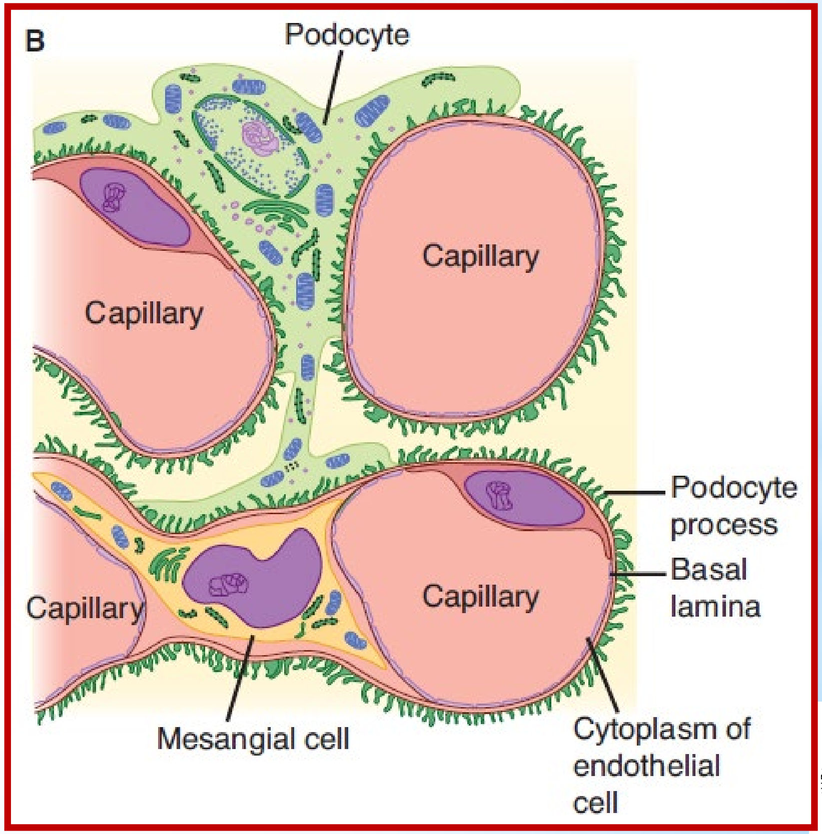
1) Capillary filtration coefficient K_f
(permeability and area of glomerular membrane)

Permeability

Area of capillary bed

mesangial cells:

contraction → reduction of filtration area → ↓ K_f → ↓ GFR



Urine Formation - Glomerular Filtration

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(permeability and area of glomerular membrane)

Permeability

Area of capillary bed

mesangial cells:

contraction → reductic
of filtration area → ↓ K
→ ↓ GFR

Contraction	Relaxation
Endothelins	ANP
Angiotensin II	Dopamine
Vasopressin	PGE_2
Norepinephrine	cAMP
Platelet-activating factor	
Platelet-derived growth factor	
Thromboxane A_2	
PGF_2	
Leukotrienes C_4 and D_4	
Histamine	

Urine Formation - Glomerular Filtration

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Urine Formation - Glomerular Filtration

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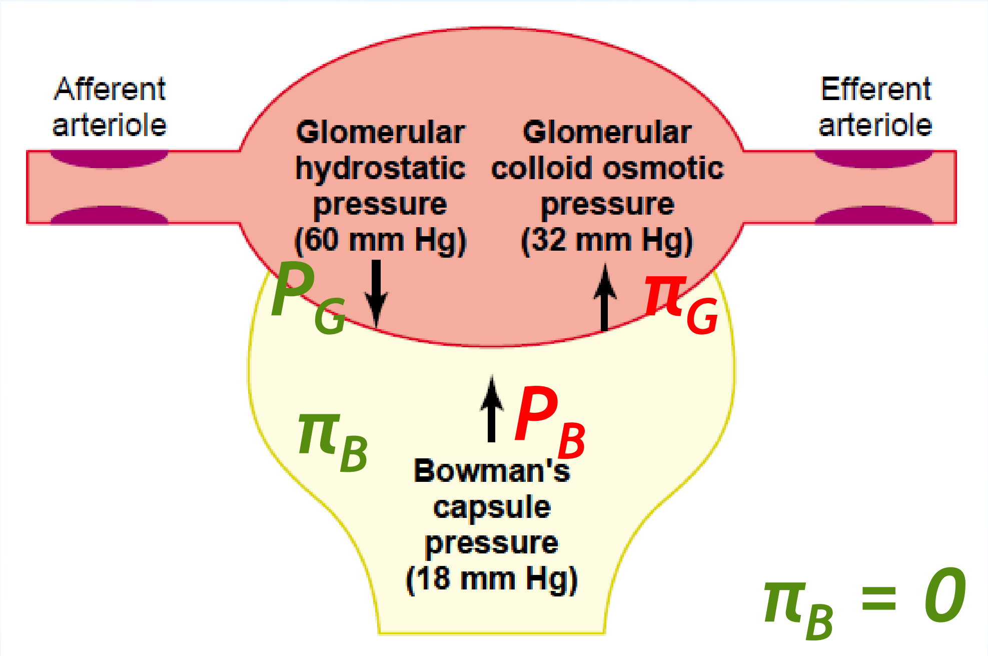

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Under physiological conditions:

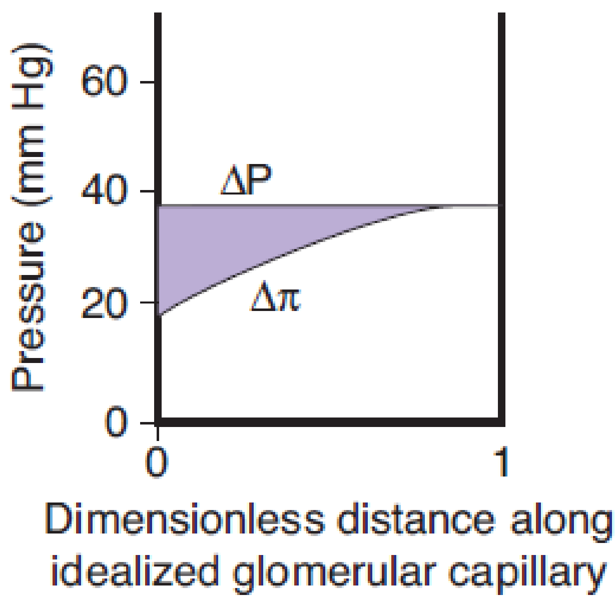
net filtration pressure = $P_G + \pi_B – P_B - \pi_G$ = 60 + 0 – 18 - 32 = 10 mmHg

Urine Formation - Glomerular Filtration

(mm Hg)

	Afferent end	Efferent end
P_{GC}	45	45
P_T	10	10
π_{GC}	20	35
P_{UF}	15	0

$$P_{UF} = P_{GC} - P_T - \pi_{GC}$$



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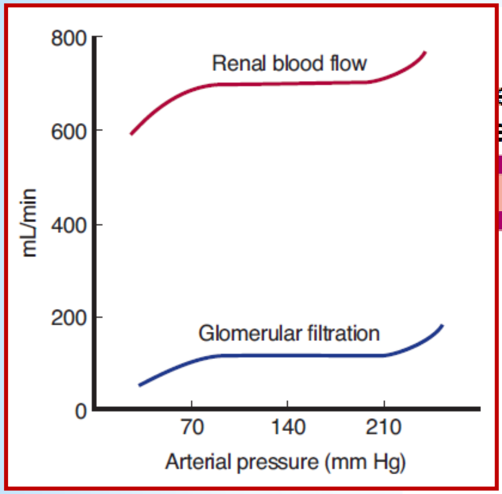
Urine Formation - Glomerular Filtration

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



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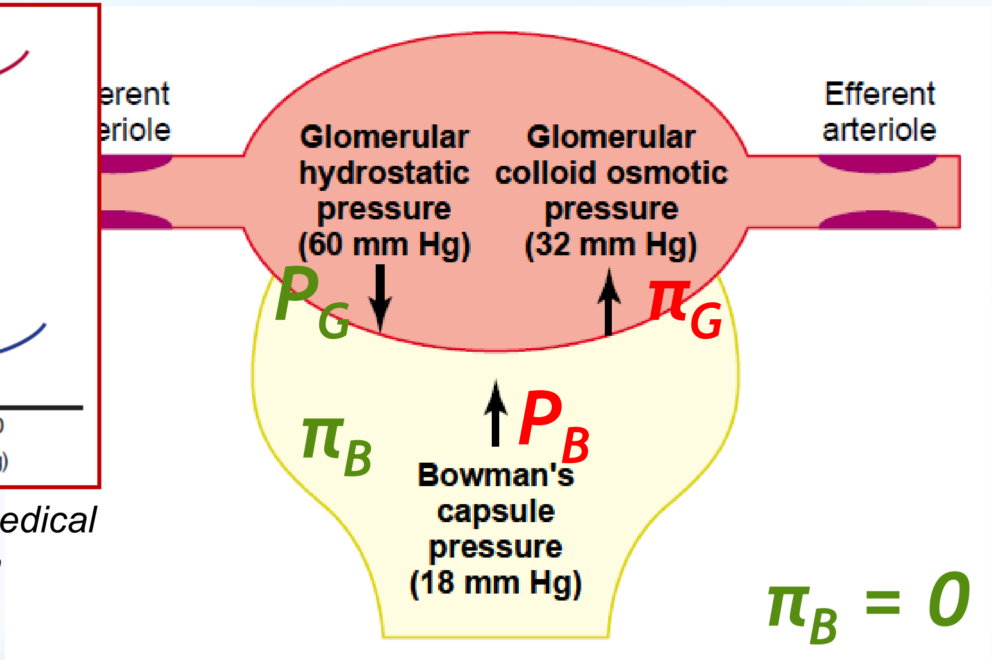

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Under physiological conditions:

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

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

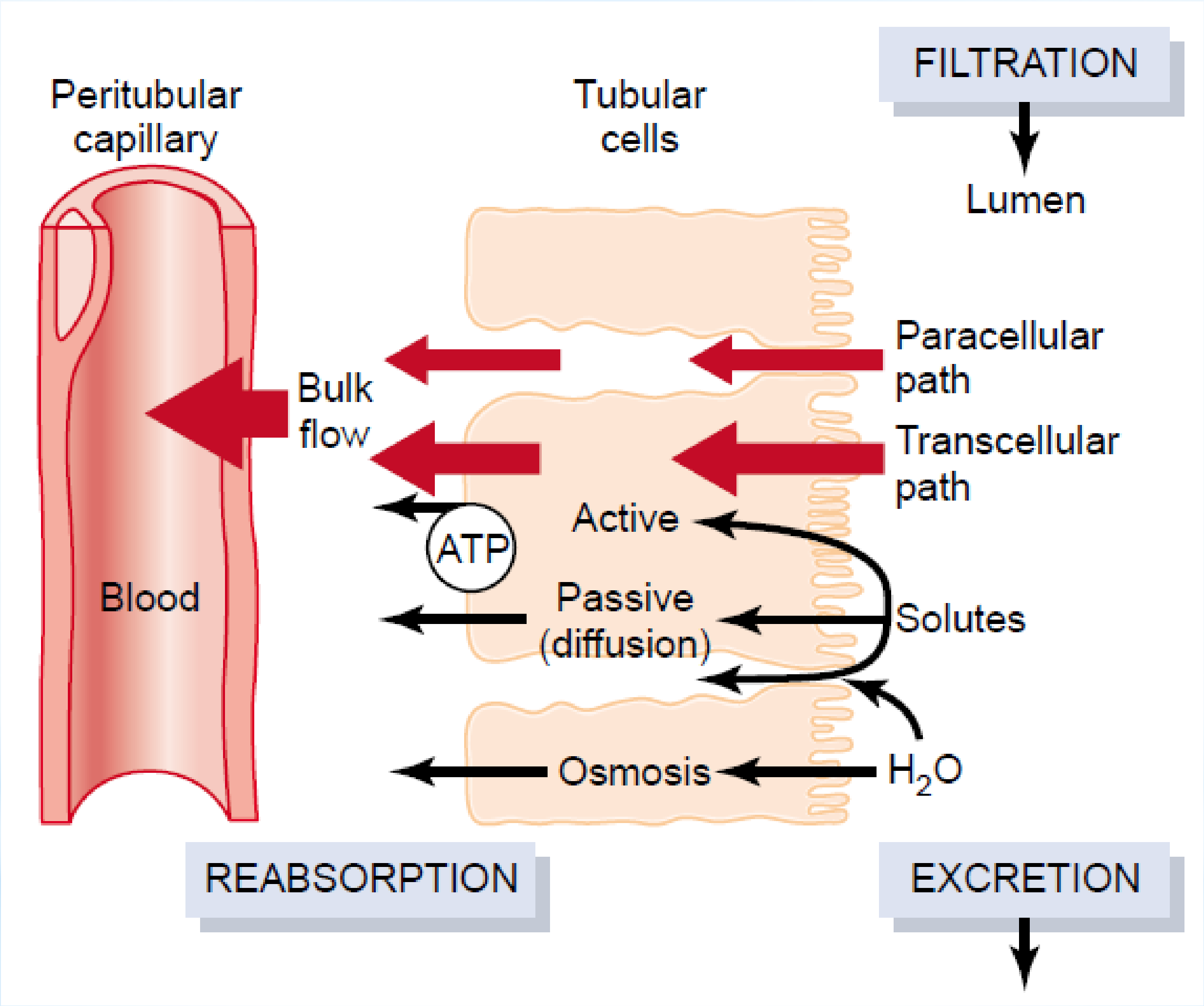
Urine Formation - Glomerular Filtration

Vas afferens, vas efferens

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

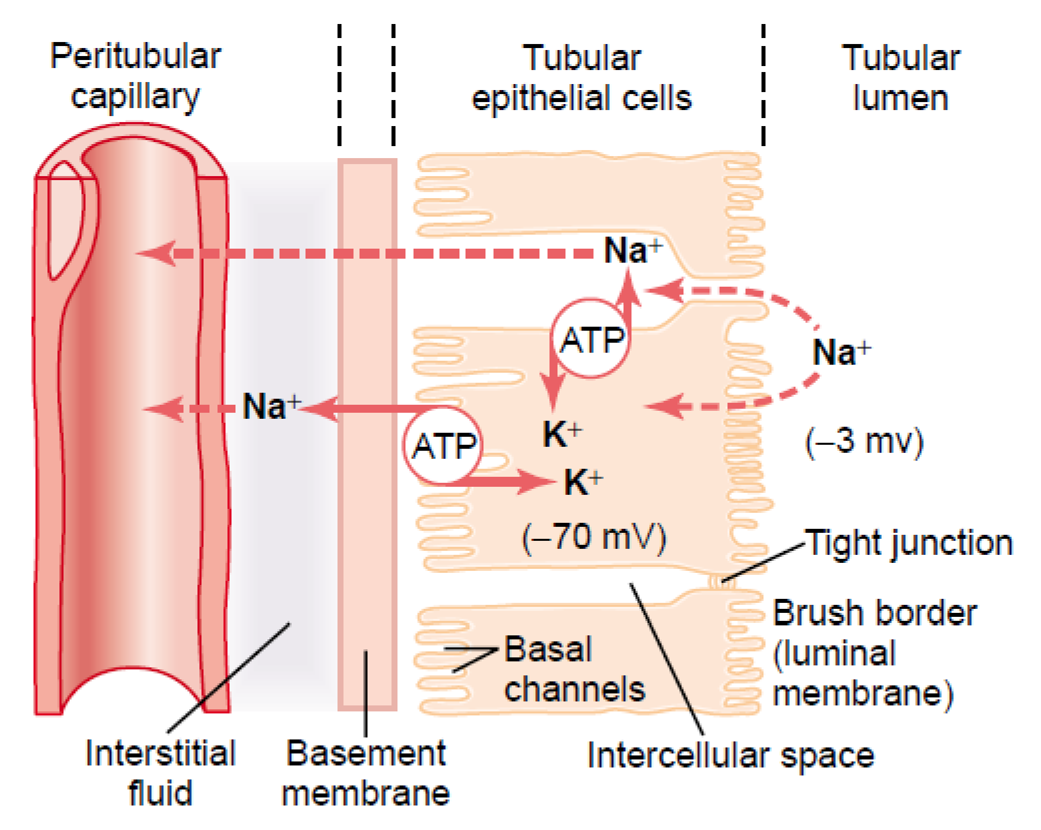
Active Transport Mechanisms

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

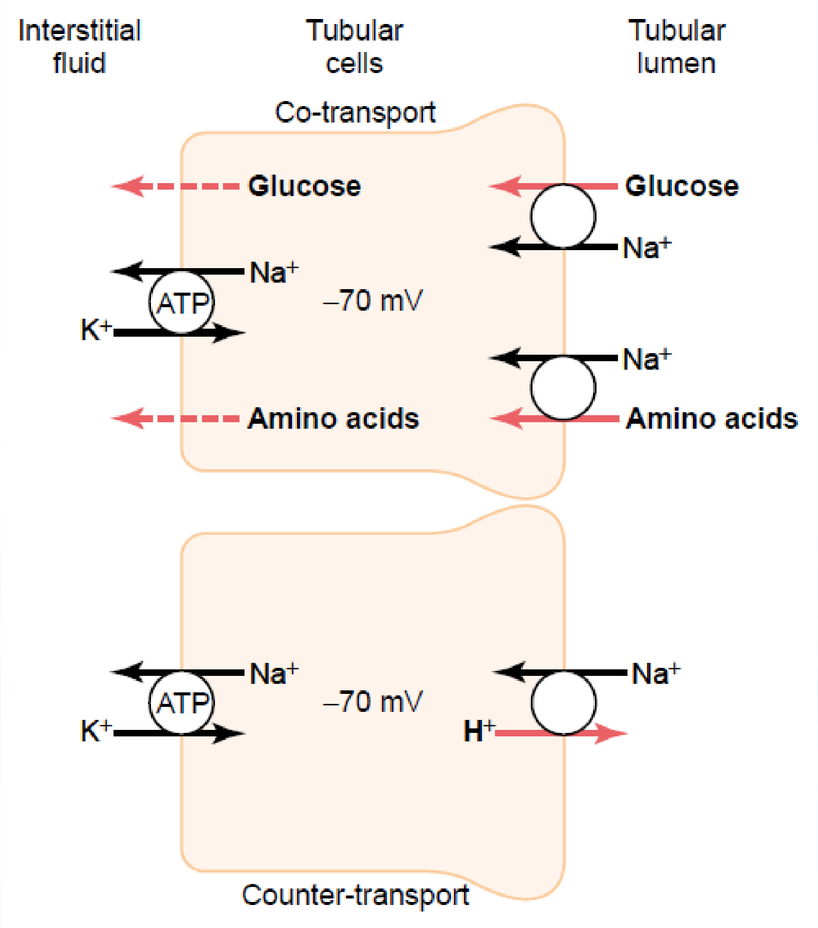
Active Transport Mechanisms

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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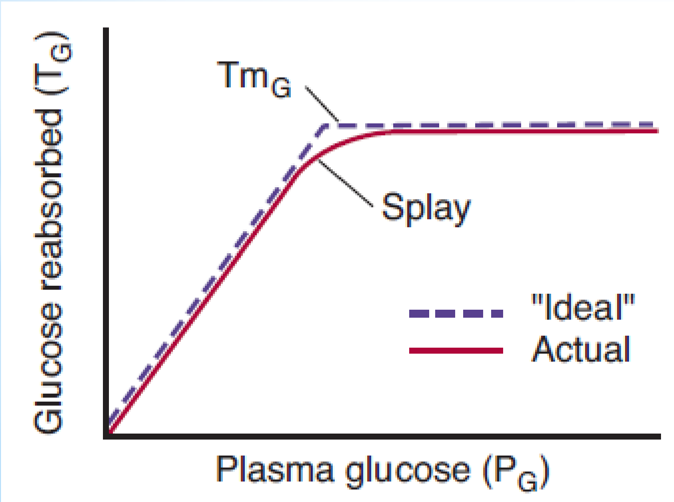
Urine Formation – Tubular Processes

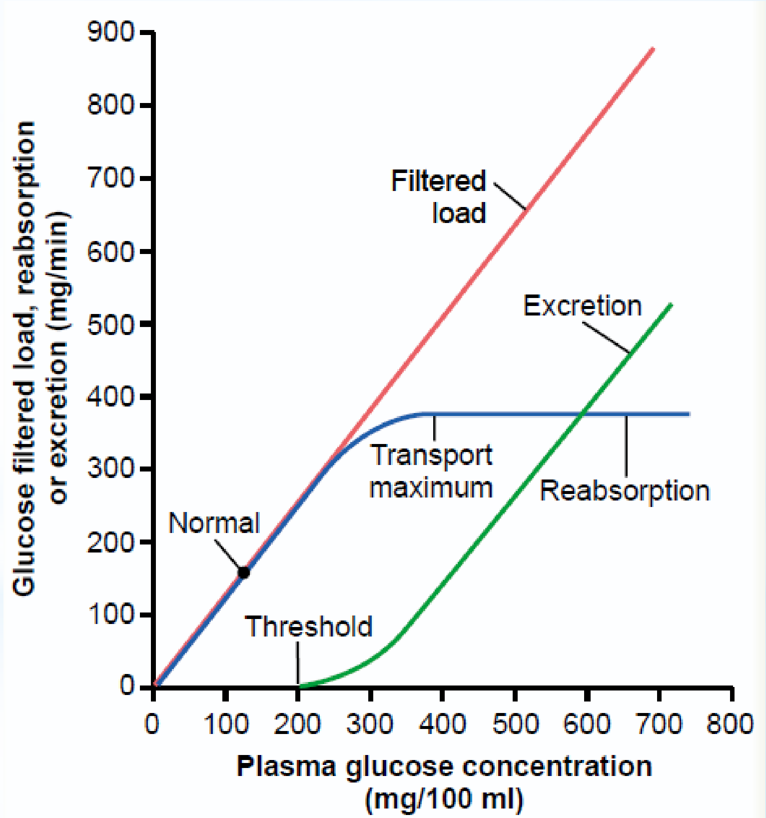
Active Transport Mechanisms

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.

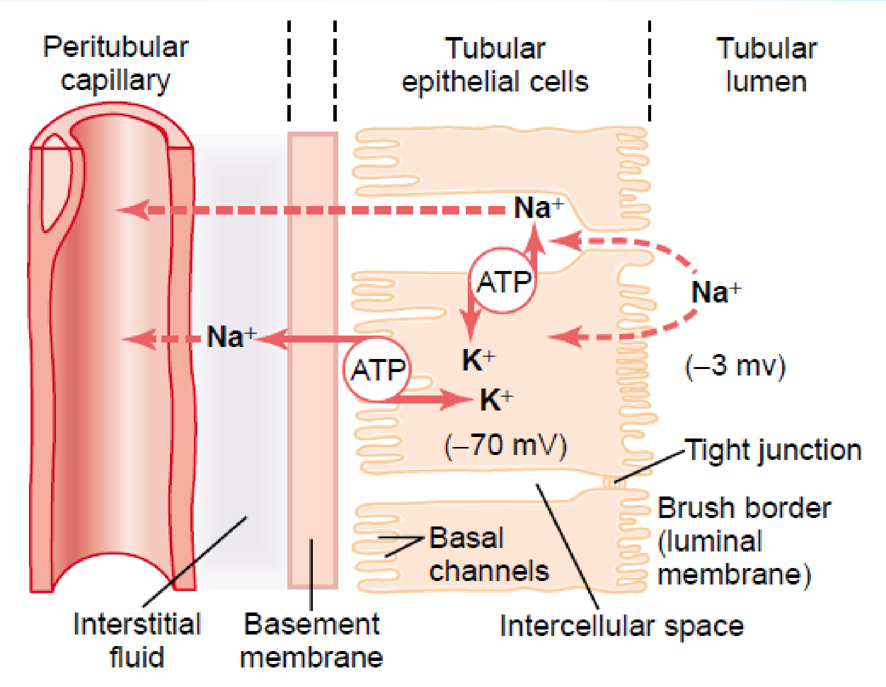
The slower flow of fluid in the proximal tubule, the more Na^+ is reabsorpbed.

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 Transpo

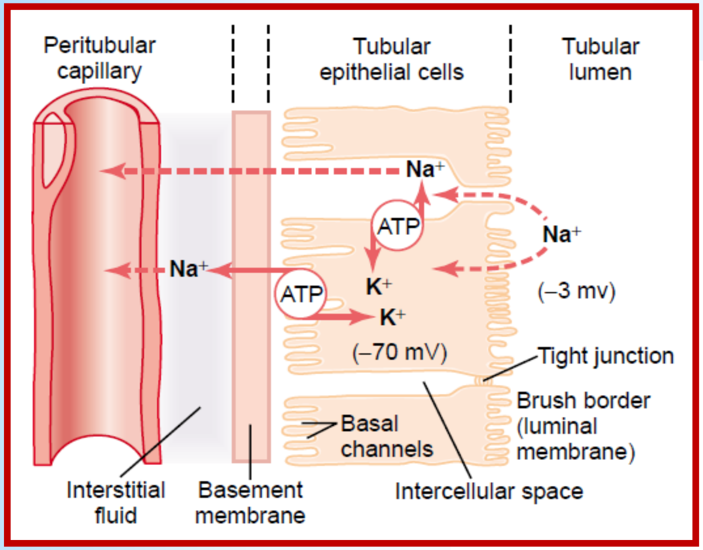
1) Primary active transport
2) Secondary active transport
3) Pinocytosis
   (big molecules, *e.g.* proteins, nam

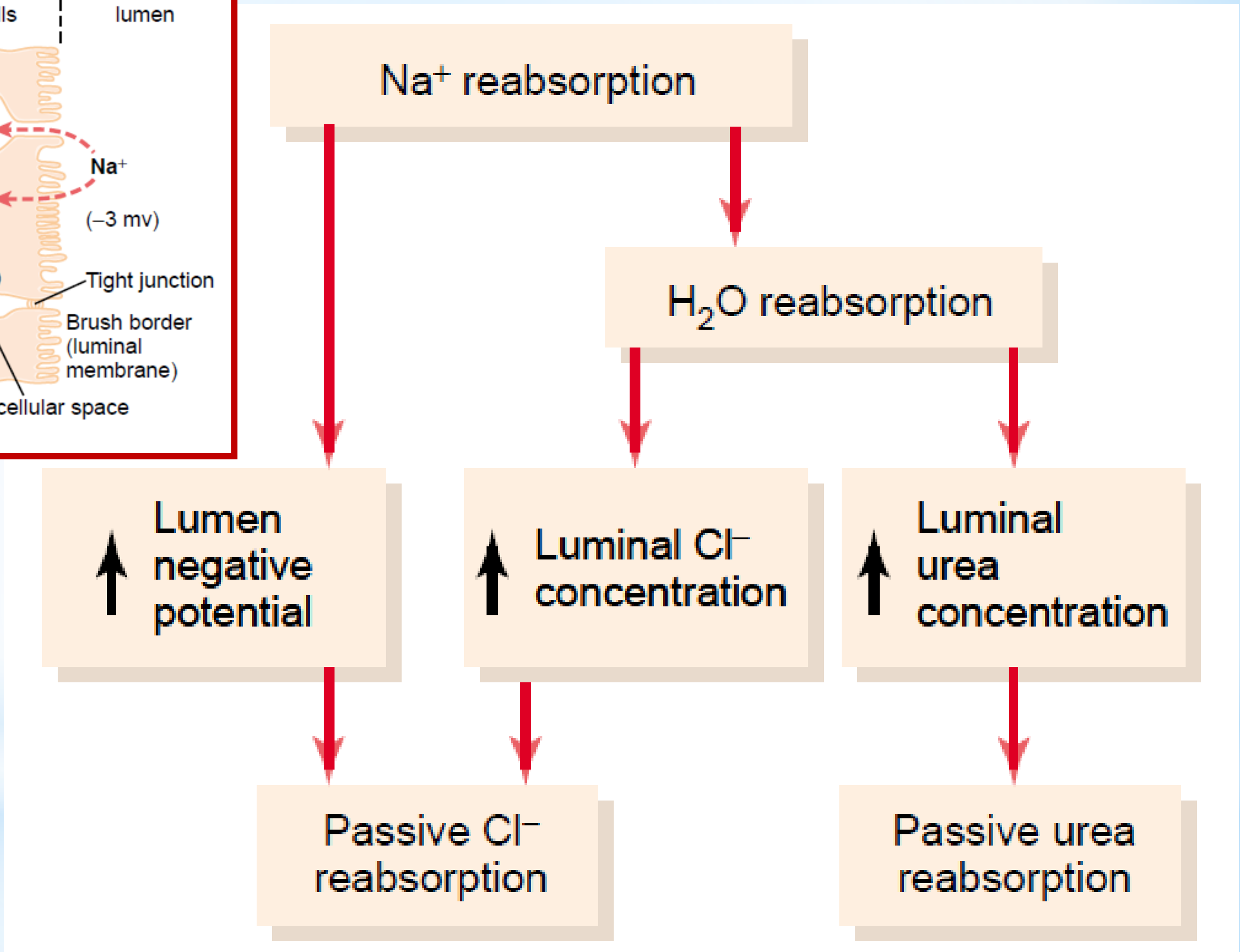


Passive Transpo

1) Reabsorption of H_2O by osm
   - 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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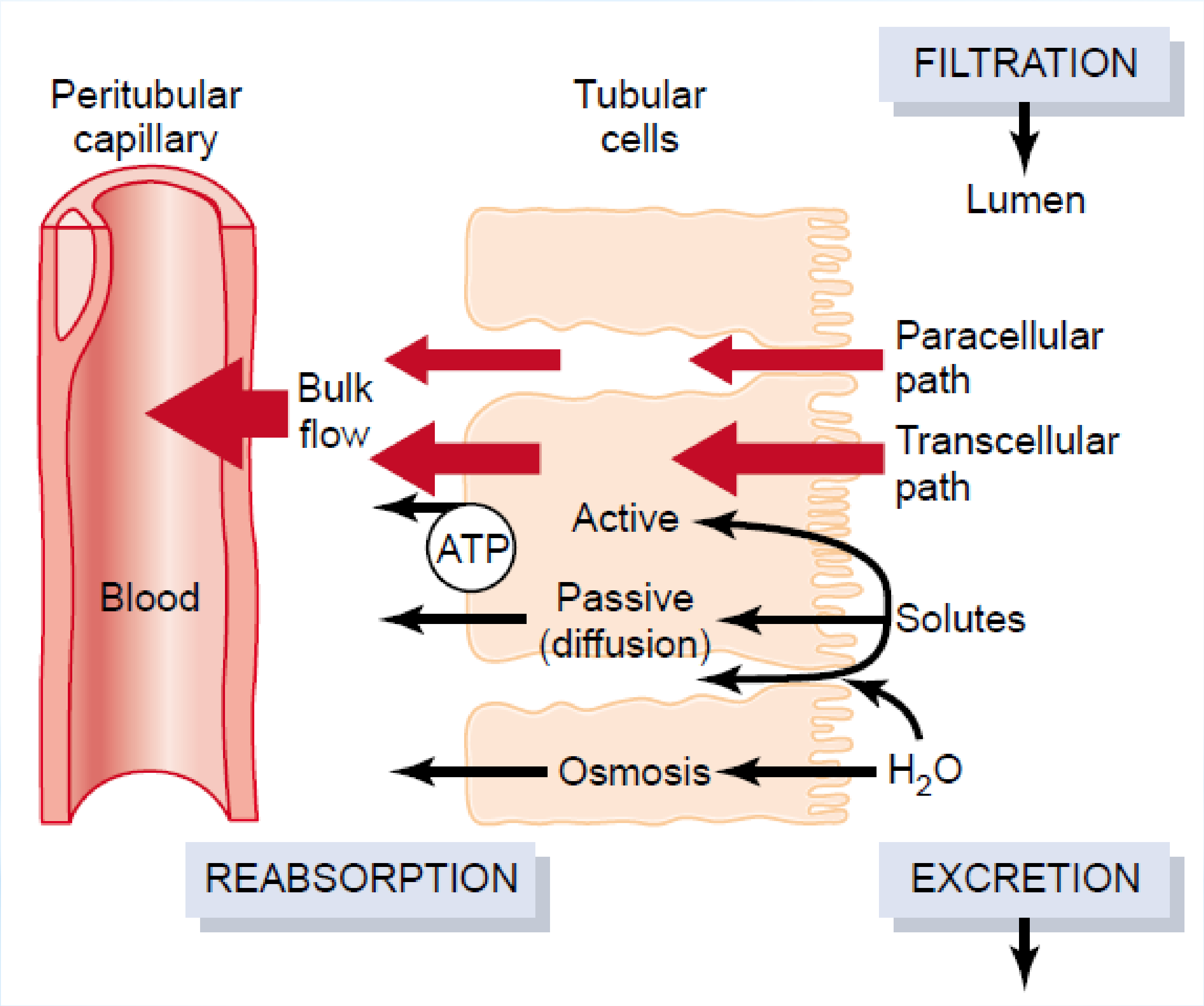
Urine Formation – Tubular Processes



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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)

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

$$\downarrow$$

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

Urine Formation – Tubular Processes

Physical Forces in Peritubular Capillaries and in Renal Intersticium

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↓

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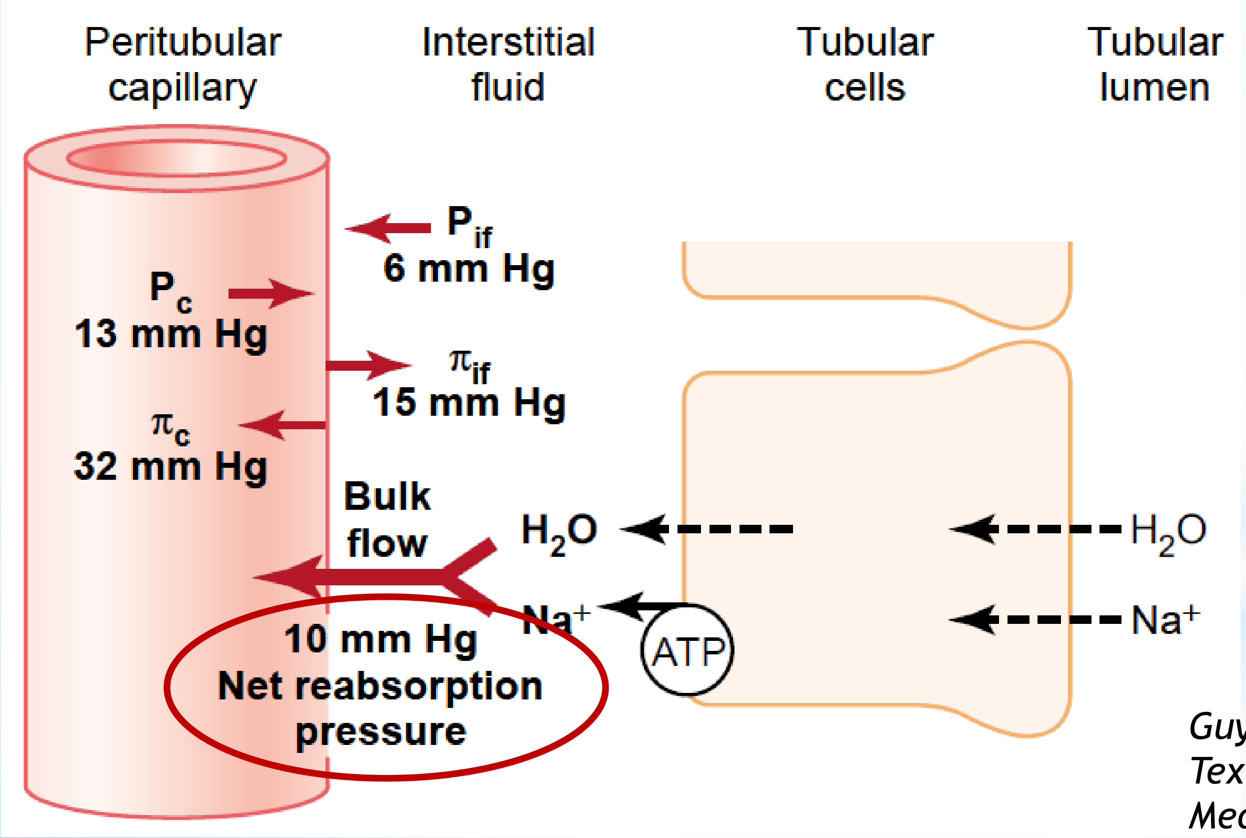
Urine Formation – Tubular Processes

Physical Forces in Peritubular Capillaries and in Renal Intersticium



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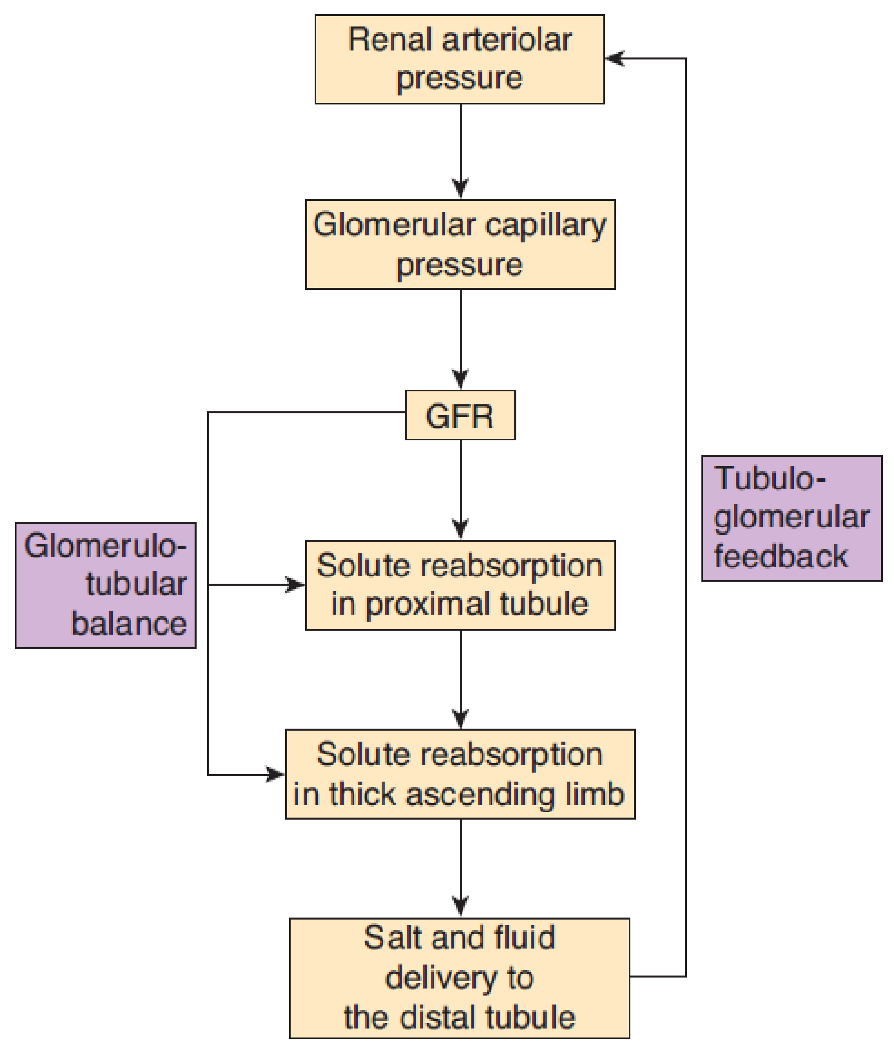
Urine Formation – Tubular Processes

Tubuloglomerular feedback

↑ GFR → ↑ flow of water ans solutes to macula densa → constriction of aff. arteriole (tromboxane A2 ?) → ↓ GFR

Glomerulotubular balance

↑ GFR → ↑ oncotic pressure in peritubular capillaries → ↑ reabsorption in tubules



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Urine Formation – Tubular Processes

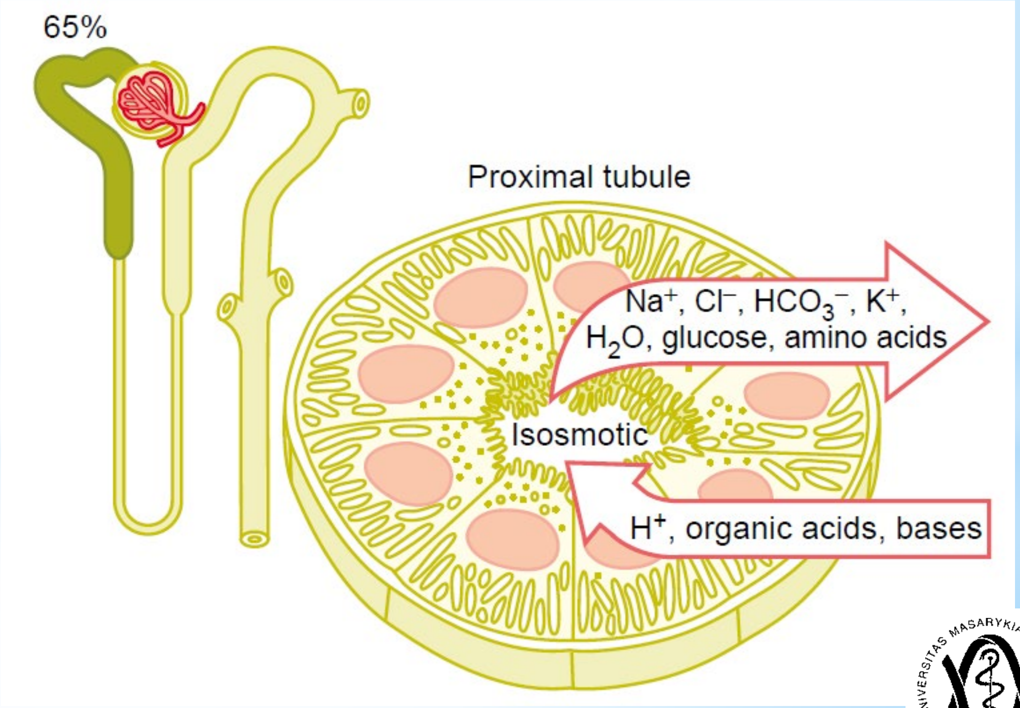
Proximal Tubule

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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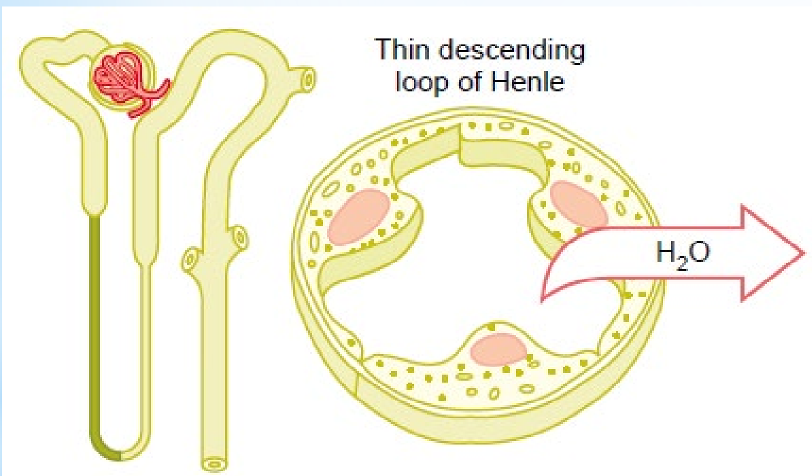
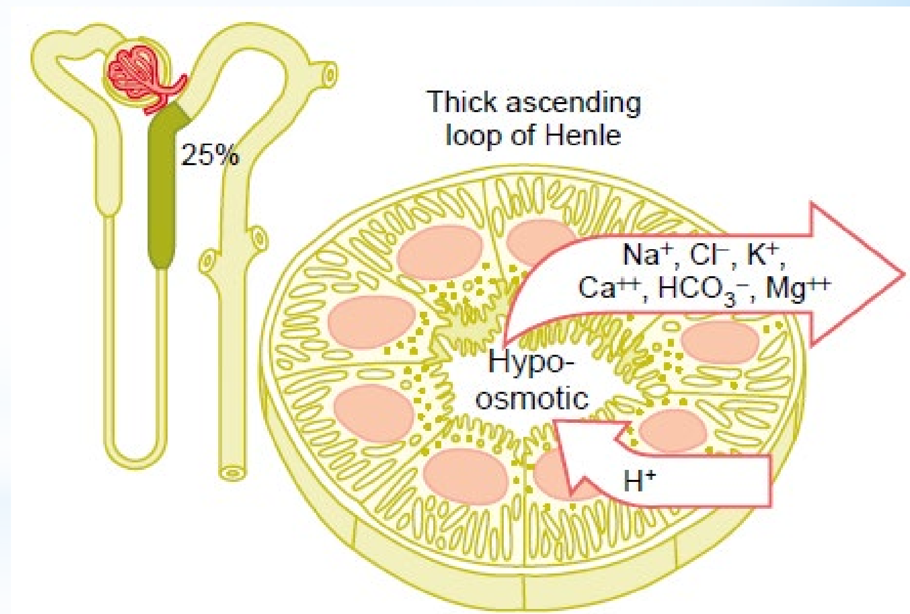
Urine Formation – Tubular Processes

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

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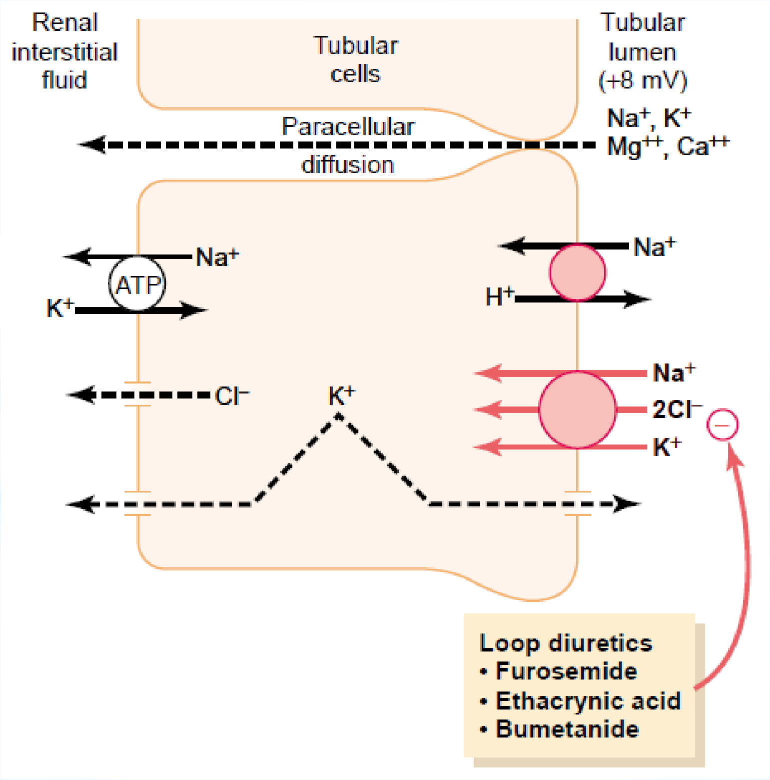
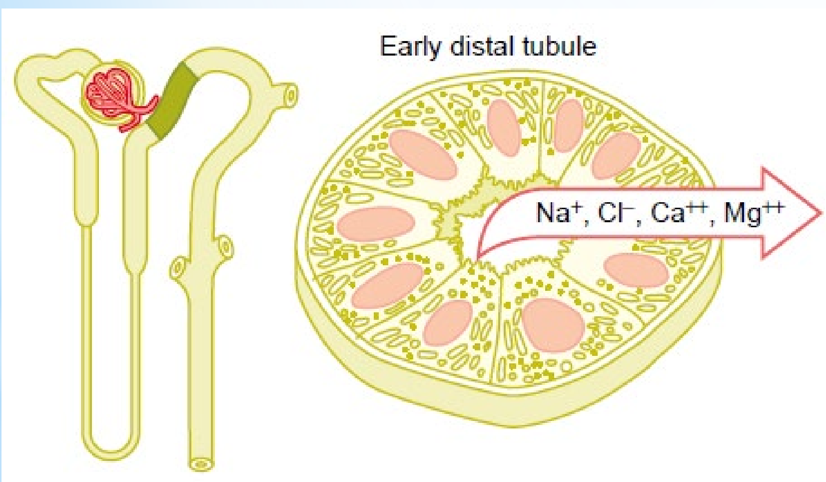
2) thick ascending part - active reabsorption of ions ($Na^+/K^+/2Cl^-$ symport), secretion of H^+, reabsorption of HCO_3^-

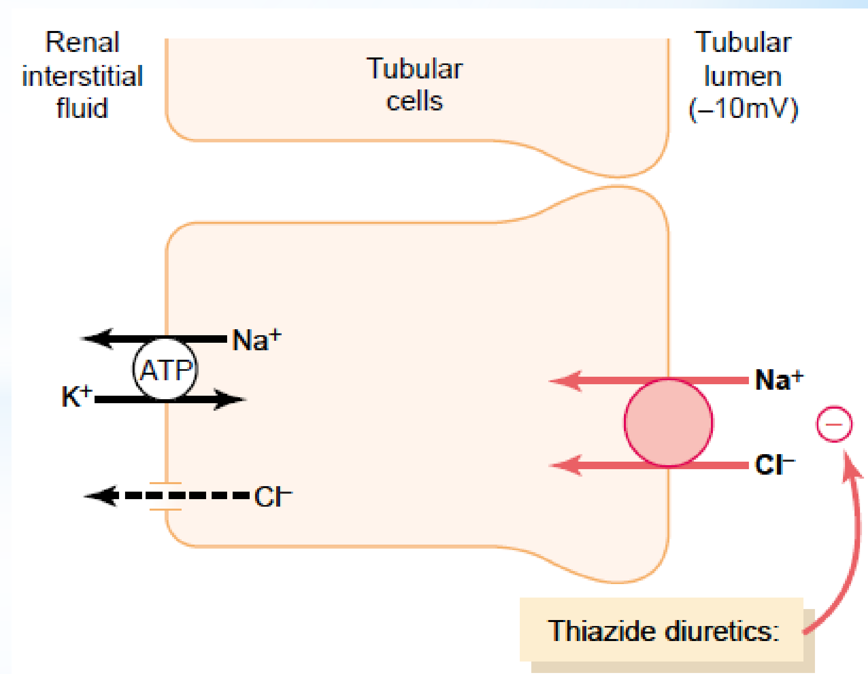


Urine Formation – Tubular Processes

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)



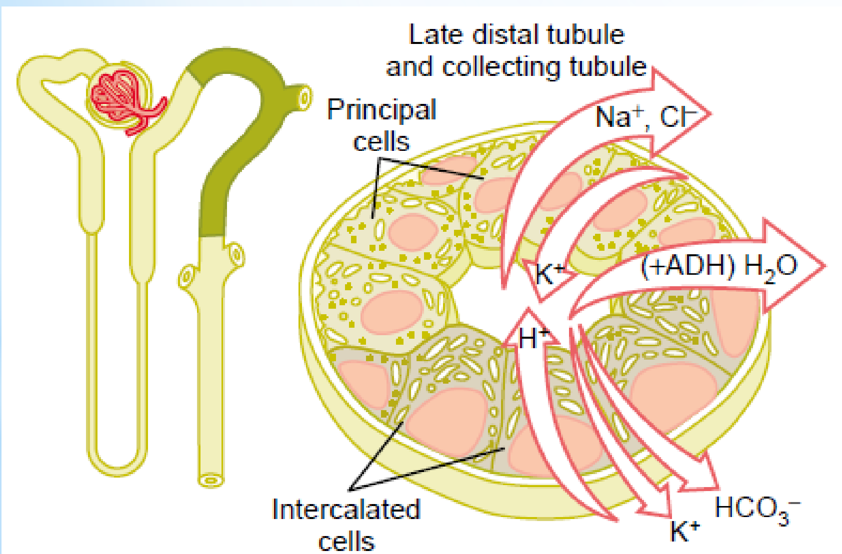


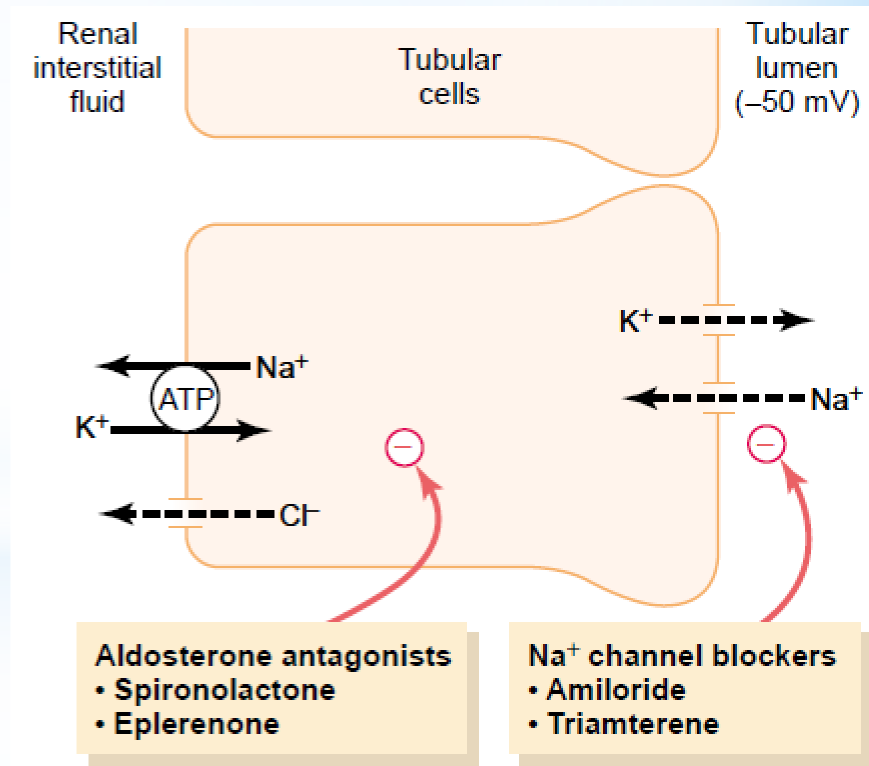
Result: hypotonic fluid

Urine Formation – Tubular Processes

Collecting duct (+ end of distal tubule)

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

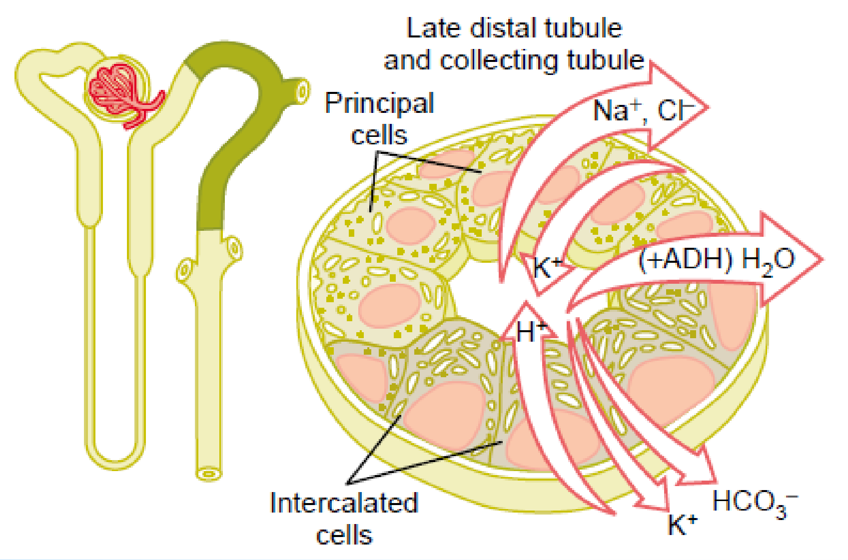


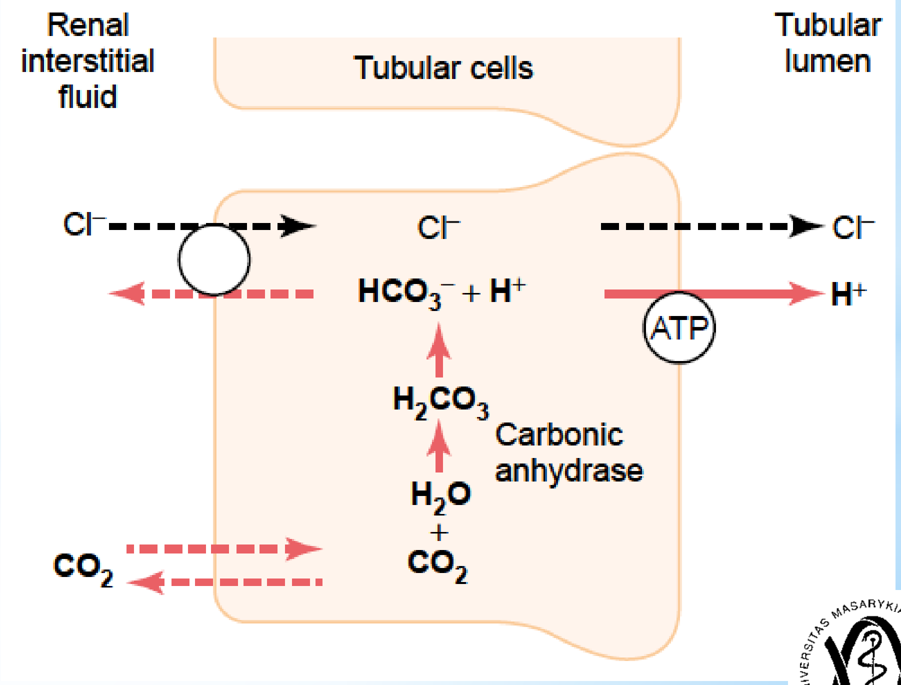


Urine Formation – Tubular Processes

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^+

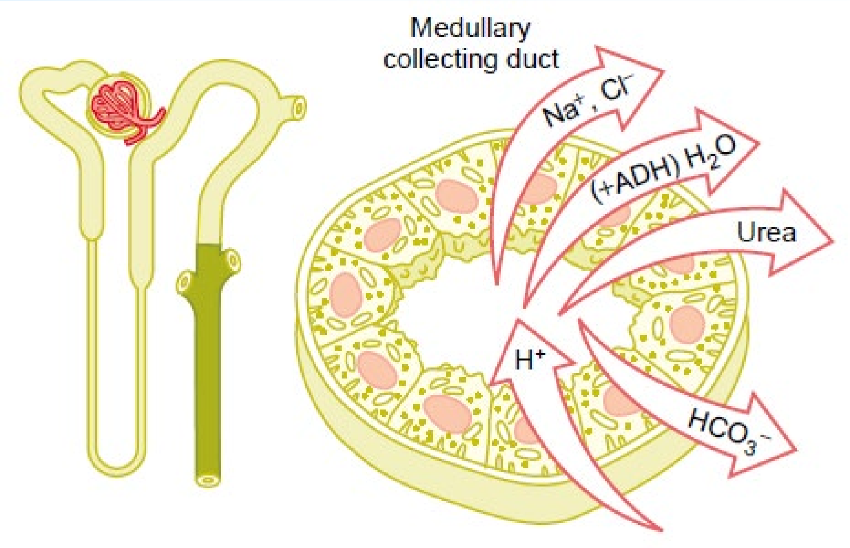




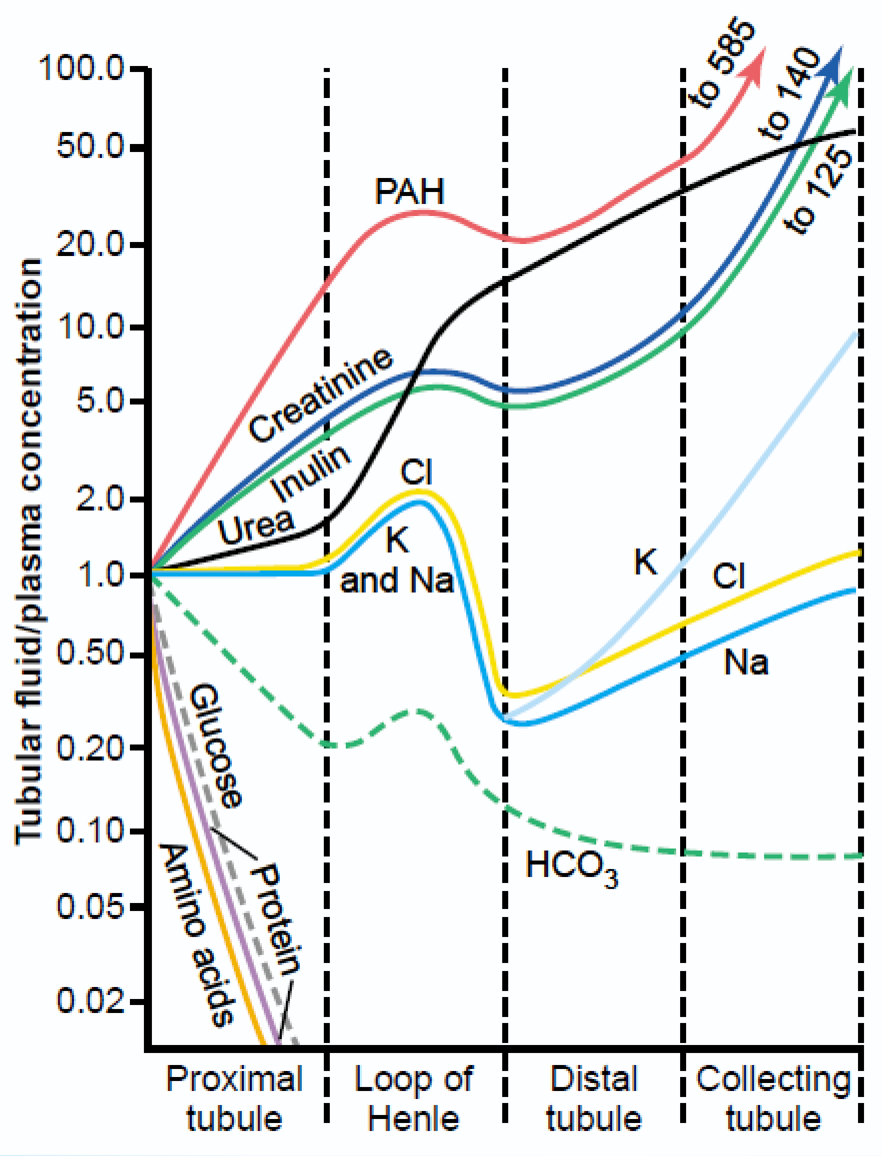
Urine Formation – Tubular Processes

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).

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

[ml/min]

C_S – *clearance* of the substance S

P_S – plasma concentration of the substance S

V – velocity of urine formation

U_S – urine concentrace of the substance S

($V \cdot U_S$ – velocity of urine excretion of the substance S)

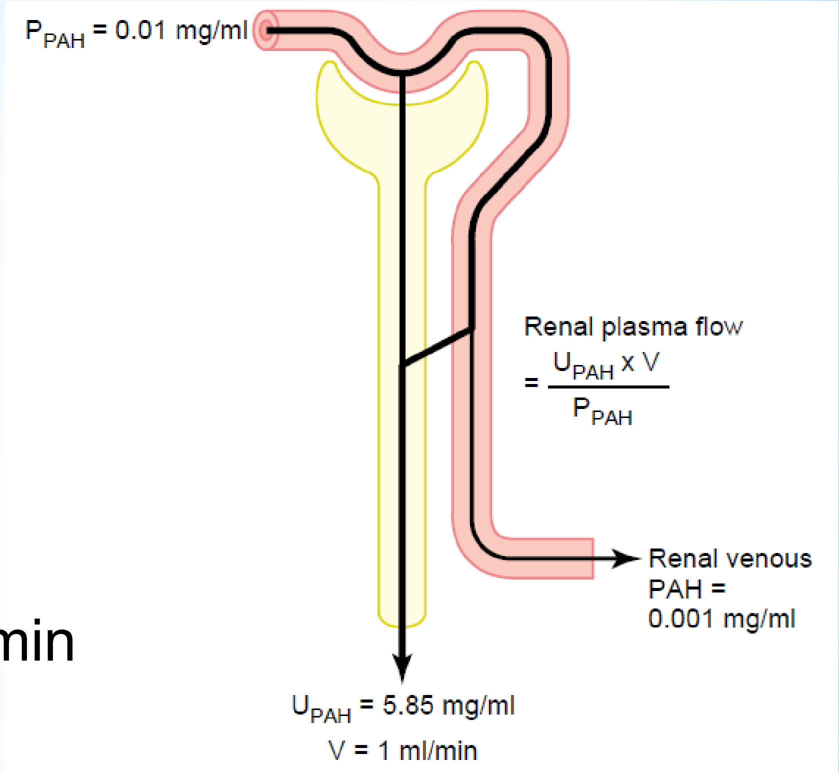
Renal Clearance

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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(in juxtamedullar nephrons, *vasa recta* additionally originate from *v. efferens* – not in contact with proximal and distal tubuli → no excretion of substances

Renal Clearance

Determination of renal plasma flow velocity (RPF)

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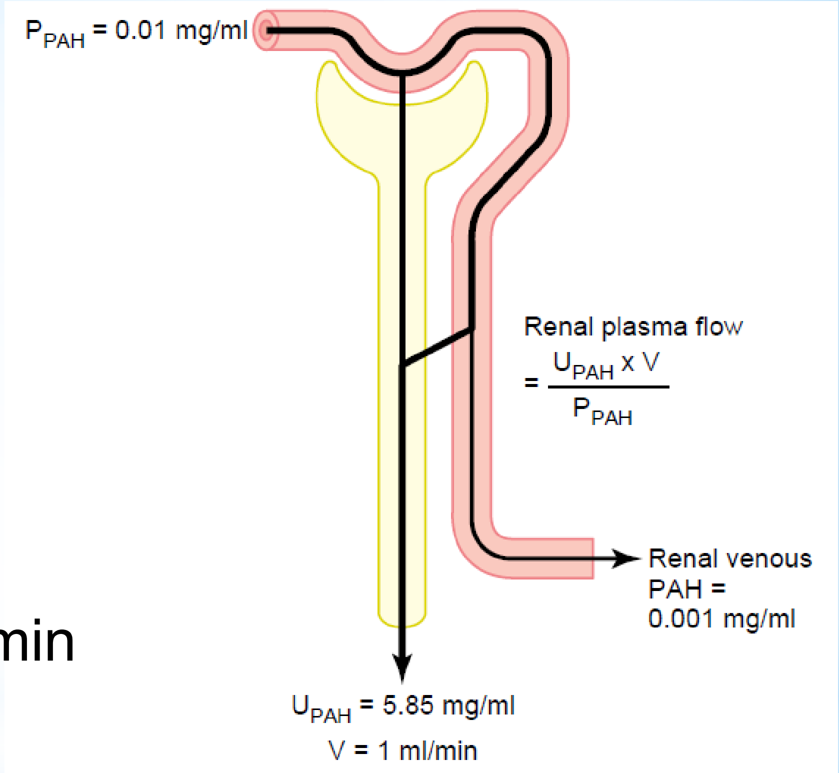

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Correction to the extraction ratio of PAH (E_{PAH}):

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

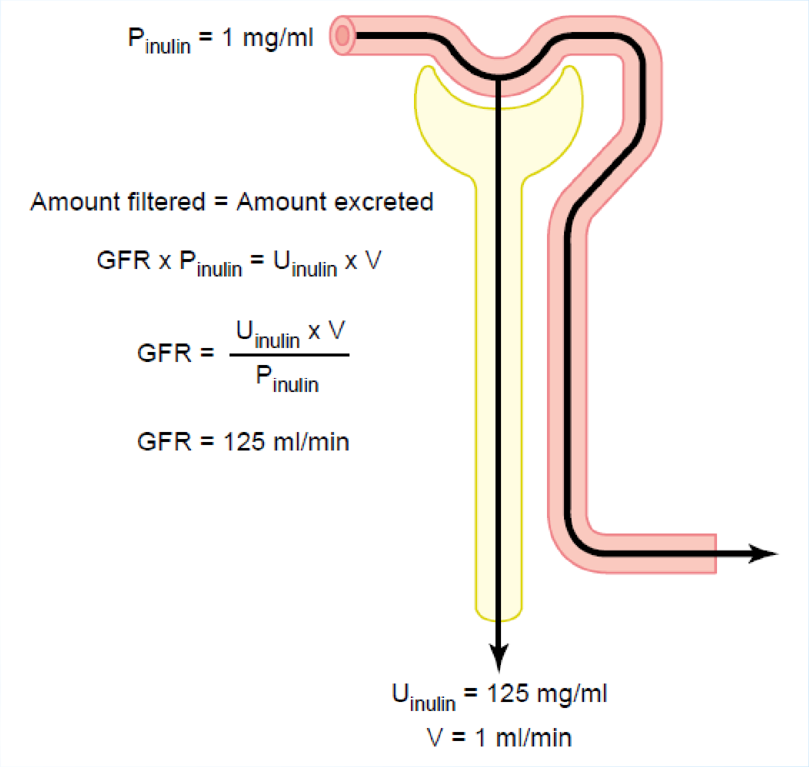
Renal Clearance

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 – polysaccharide that is not formed in the body, i.v. application (is present in roots of some plants)

Creatinine – waste product of muscle metabolism, in approximately constant amount in plasma (not necessary to apply i.v.)



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The most often estimation of GFR in the clinical practise!

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. $GFR \cdot P_S > V \cdot U_S$ velocity of filtration of the substance > its urine excretion ⇒ substance reabsorbed

B. $GFR \cdot P_S < V \cdot U_S$ velocity of filtration of the substance < its urine excretion ⇒ substance secreted