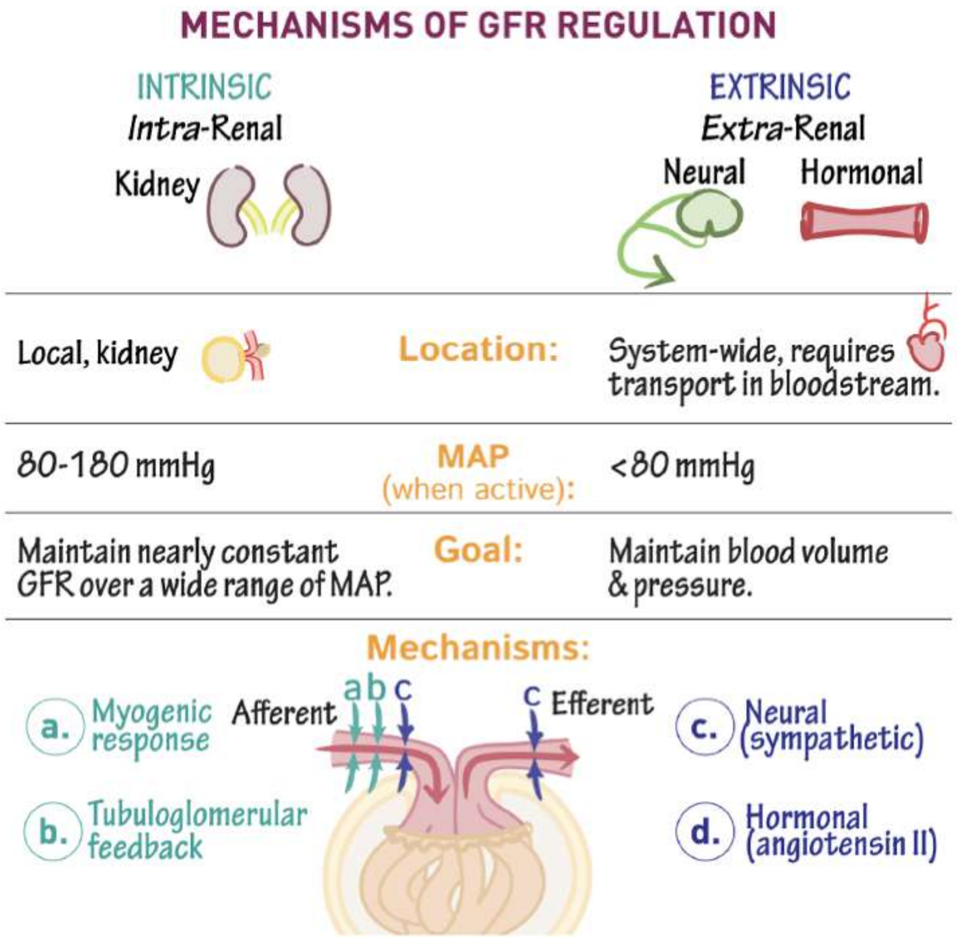
Lecture 2- Renal physiology

Control of GFR and RBF



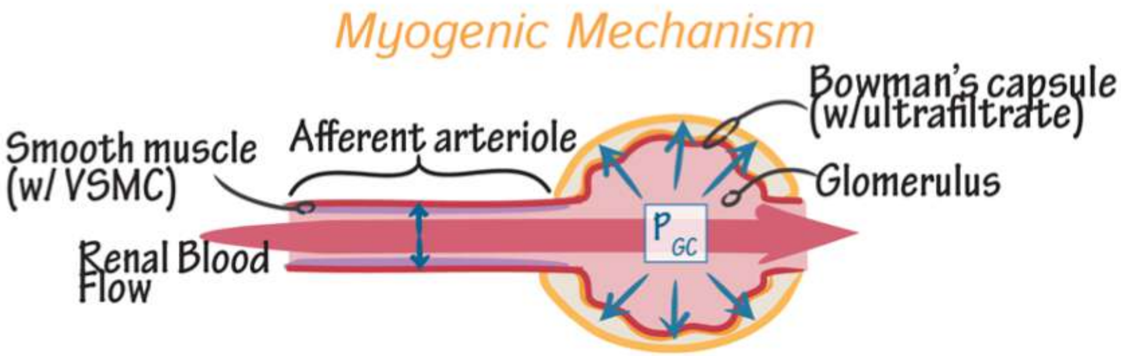
Autoregulation

Intrinsic ability of kidneys to regulate its own **blood flow** **to maintain constant GFR**

Autoregulation → constant RBF & GFR over P changes 80-170 mmHg

Two mechanisms involved in renal autoregulation:
1. Myogenic response
2. Tubuloglomerular feedback

Myogenic response



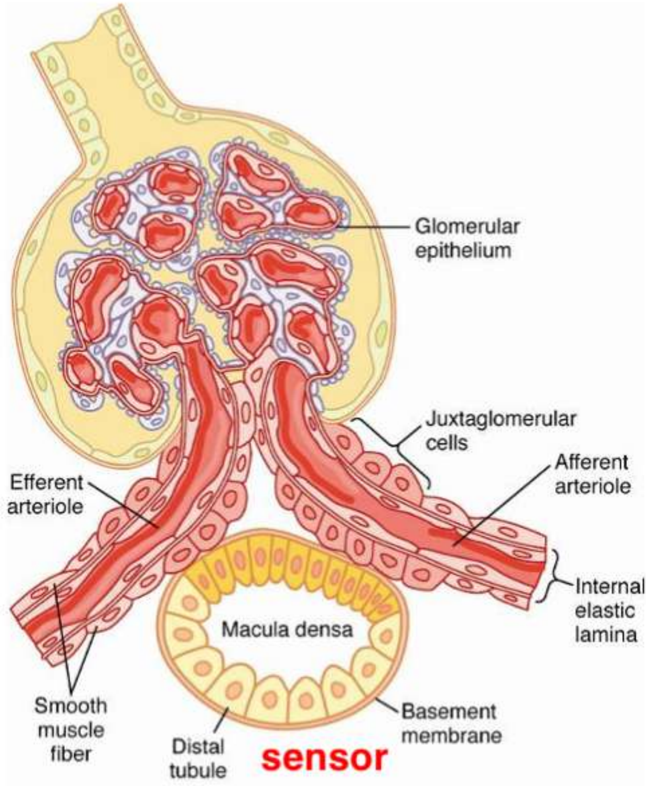
1. ↑RBF = ↑Hydrostatic pressure against the walls of the afferent arteriole.

↑flow of Ca from ECF into cells

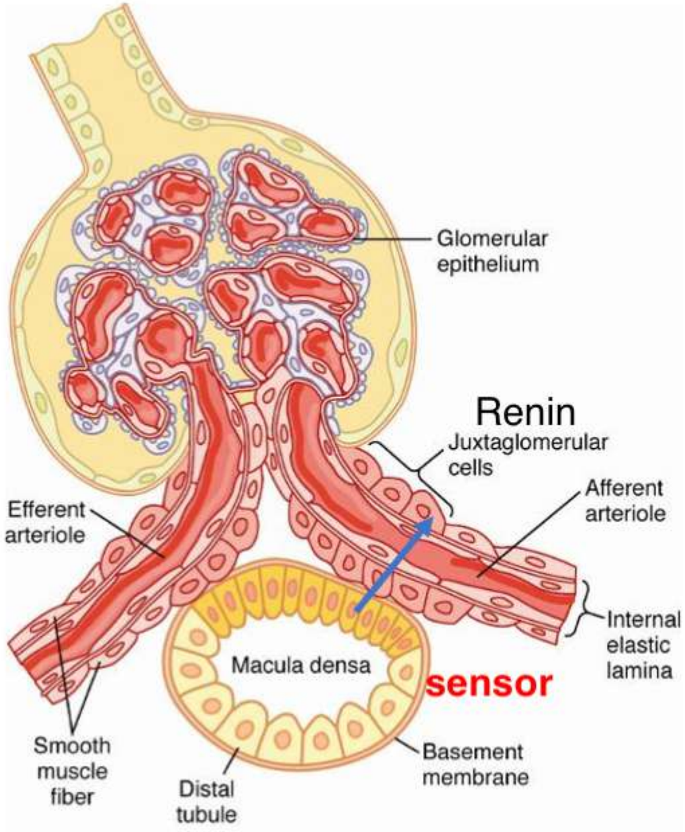
2. Stretch receptors in VSMC initiate VASOCONSTRICTION.

Juxtaglomerular apparatus

- The juxta-glomerular apparatus is a specialized structure formed by the **distal convoluted tubule and the glomerular afferent arteriole**
- Its main function is to **regulate blood pressure** and **GFR**
- It's made up of **juxtaglomerular cells and the macula densa**
- The macula densa is a collection of specialized epithelial cells in the *distal convoluted tubule* that **detect Na concentration** of the fluid in the tubule



Juxtaglomerular apparatus

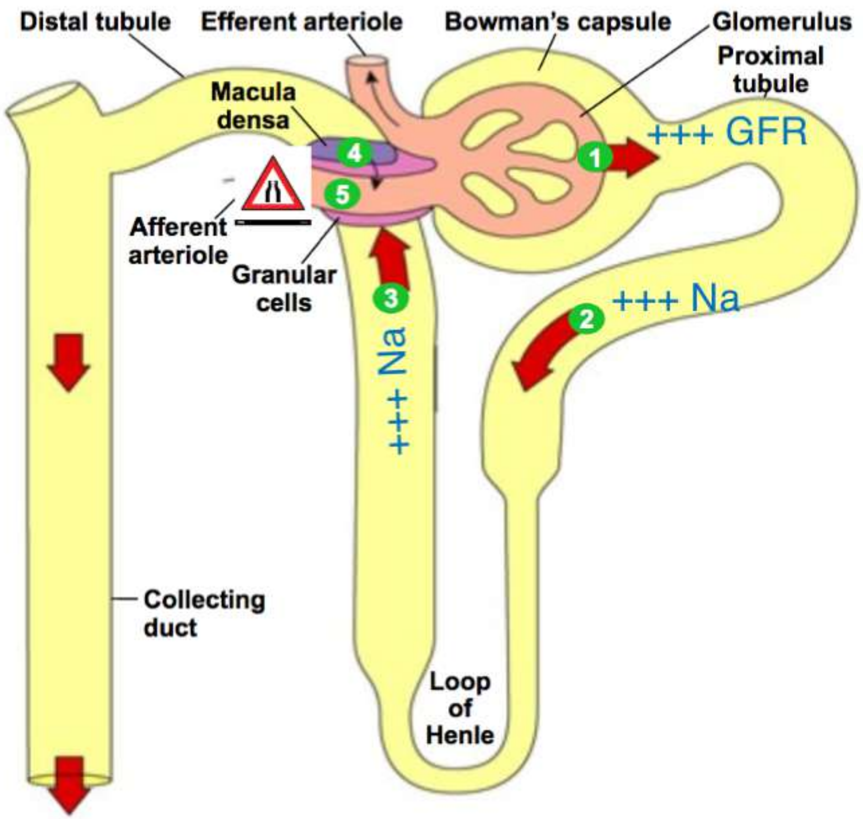


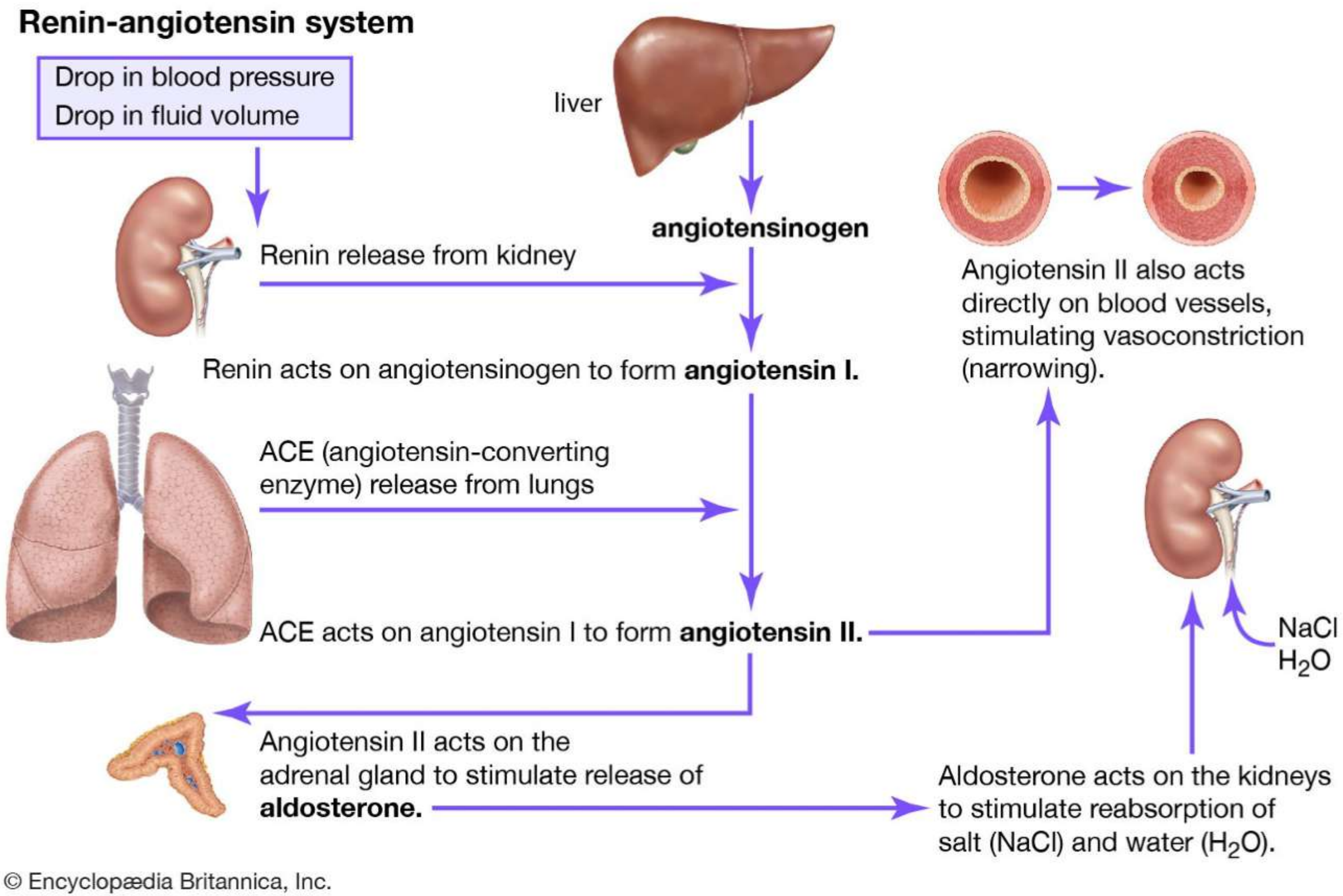
Tubuloglomerular feedback

High Na→
↑ adenosin→ VC of A } ↓↓ GFR

Low Na→
↑ NO & PG→ VD of A
↑ Renin—angio II→
VC of E & Aldosterone secretion } +++ GFR

Tubuloglomerular feedback




Renin-angiotensin system
Drop in blood pressure
Drop in fluid volume
liver
angiotensinogen
Renin release from kidney
Renin acts on angiotensinogen to form **angiotensin I.**
ACE (angiotensin-converting enzyme) release from lungs
ACE acts on angiotensin I to form **angiotensin II.**
Angiotensin II also acts directly on blood vessels, stimulating vasoconstriction (narrowing).
NaCl
H_2O
Angiotensin II acts on the adrenal gland to stimulate release of **aldosterone.**
Aldosterone acts on the kidneys to stimulate reabsorption of salt (NaCl) and water (H_2O).
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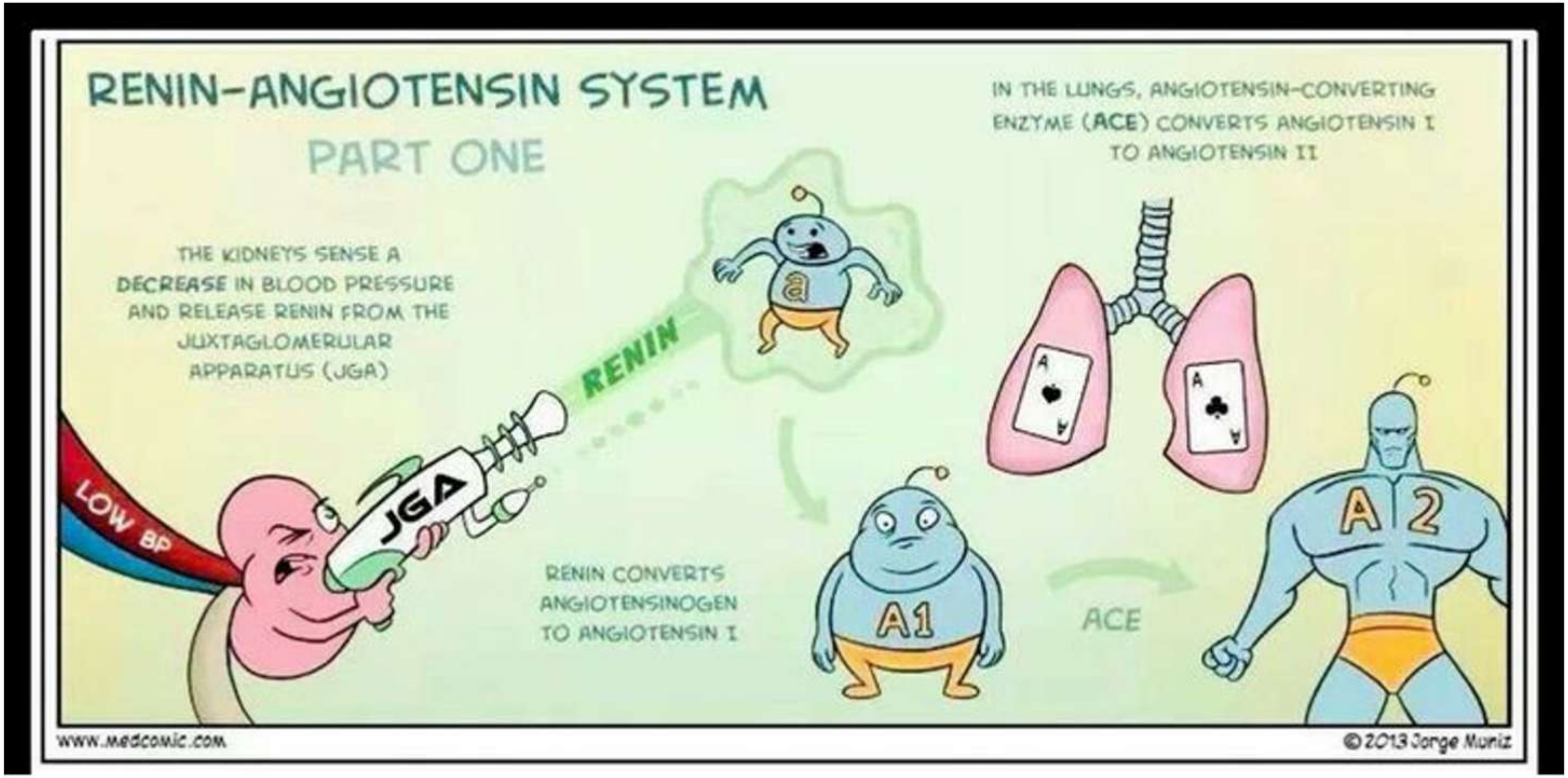
RENIN-ANGIOTENSIN SYSTEM
PART ONE
THE KIDNEYS SENSE A DECREASE IN BLOOD PRESSURE AND RELEASE RENIN FROM THE JUXTAGLOMERULAR APPARATUS (JGA)
LOW BP
JGA
RENIN
a
RENIN CONVERTS ANGIOTENSINOGEN TO ANGIOTENSIN I
A1
IN THE LUNGS, ANGIOTENSIN-CONVERTING ENZYME (ACE) CONVERTS ANGIOTENSIN I TO ANGIOTENSIN II
ACE
A2
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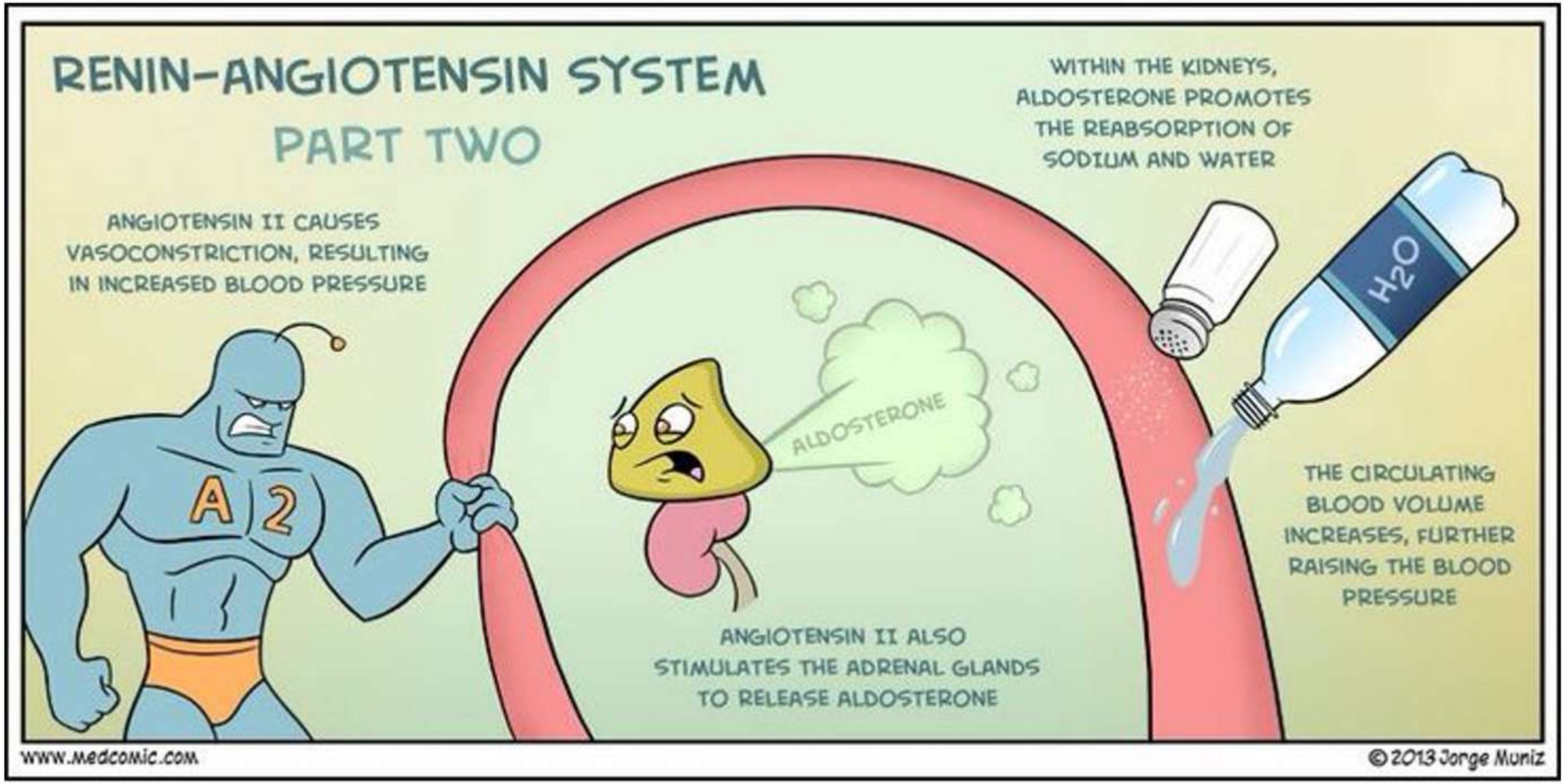
RENIN-ANGIOTENSIN SYSTEM
PART TWO
ANGIOTENSIN II CAUSES VASOCONSTRICTION, RESULTING IN INCREASED BLOOD PRESSURE
A2
ANGIOTENSIN II ALSO STIMULATES THE ADRENAL GLANDS TO RELEASE ALDOSTERONE
ALDOSTERONE
WITHIN THE KIDNEYS, ALDOSTERONE PROMOTES THE REABSORPTION OF SODIUM AND WATER
H2O
THE CIRCULATING BLOOD VOLUME INCREASES, FURTHER RAISING THE BLOOD PRESSURE
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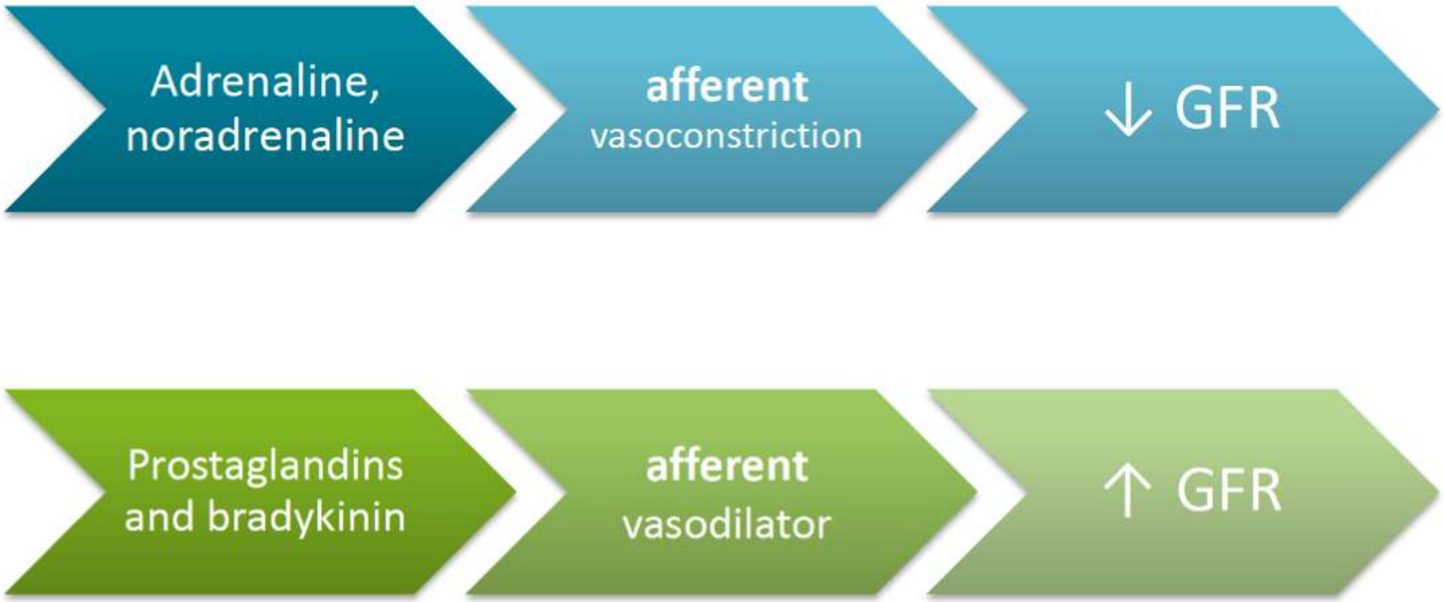
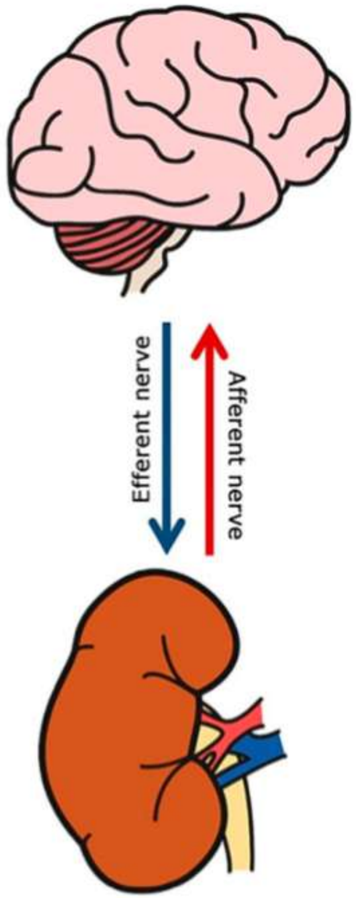
Other Hormonal regulation of GFR



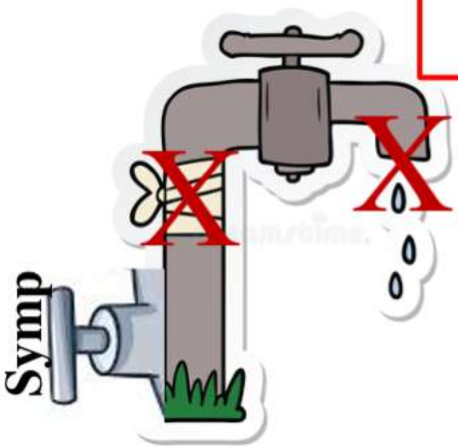
Nervous regulation of GFR and RBF

Moderate sympathetic stimulation→ little effect
Sympathetic have **little** influence on RBF (↓RBF).

Strong sympathetic stimulation→ vasoconstriction (Afferent) →↓GFR
Sympathetic stimulation→ ↑ Renin



Sympathetic is important in acute disturbances (e.g. defense reaction, brain ischemia, or severe haemorrhage)



Clearance

- Volume of plasma completely cleared of a substance by both kidneys per unit time.

- Clearance measures how fast theis substance is removed from bloodstream and excreted in urine.

- High clearance → quick removal, Low clearance → slow removal

- To quantify renal function (RBF, GFR, reabsorption & secretion)

Clearance Technique

$$Cs \times Ps = Us \times V$$

$$Cs = \frac{Us \times V}{Ps} = \frac{\text{urine excretion rate}}{\text{Plasma conc.}}$$

Where : Cs = clearance of substance S
Ps = plasma conc. of substance S
Us = urine conc. of substance S
V = urine flow rate

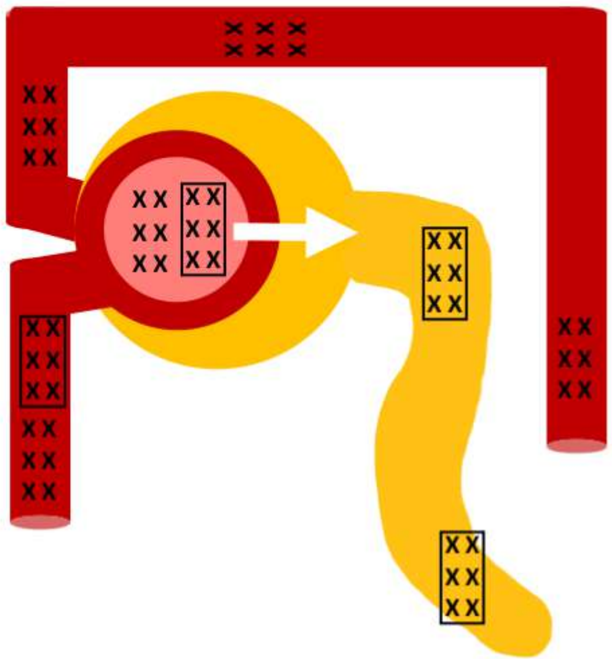
Use of clearance to measure GFR

For a substance that is freely filtered, but <u>not</u> reabsorbed or secreted (inulin, ^{125}I-iothalamate, creatinine), renal clearance is <u>equal</u> to GFR

Amount filtered = Amount excreted

$$GFR \times P_{in} = U_{in} \times V$$

$$GFR = \frac{U_{in} \times V}{P_{in}}$$



Creatinine clearance to estimate GFR

Advantages:

- Cleared from the body fluids *almost entirely* by glomerular filtration
- Not require intravenous infusion

Disadvantages

- not perfect marker of GFR because a small amount of it is **secreted** by the tubules→ amount of creatinine excreted > amount filtered→ a slight error in measuring plasma creatinine

Use of clearance to estimate RPF

Theoretically, if a substance is <u>completely</u> cleared from plasma→ its clearance rate =<u>renal plasma flow (RPF)</u>

Amount of substance delivered to kidneys in blood= Amount excreted in urine

$$(RPF \times Ps) = (Us \times V)$$

$$RPF = Us \times V / Ps$$

$$\mathbf{Cx = RPF}$$

Use of PAH clearance to estimate renal plasma flow

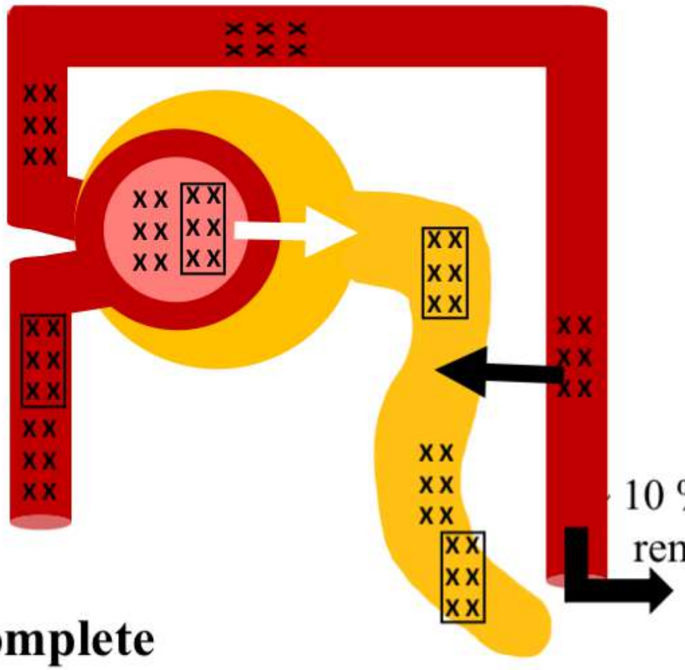
Paraminohippuric acid (PAH) is 90% filtered and secreted and is almost completely cleared from the renal plasma

amount entered ≅ amount excreted

$$RPF \times P_{pah} = U_{PAH} \times V$$

$$RPF = \frac{U_{PAH} \times V}{P_{PAH}}$$

RPF = Clearance PAH



To calculate <u>actual</u> RPF , one must correct for incomplete extraction of PAH

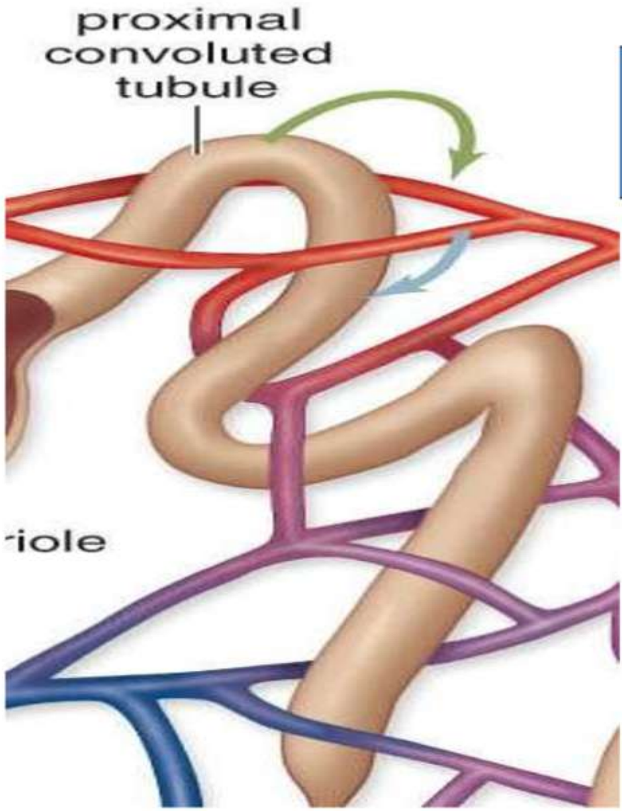
Calculation of tubular reabsorption/excretion

- If the rates of **glomerular filtration** and **renal excretion** of a substance are known, one can *calculate whether there is a net reabsorption or a net secretion* of that substance by the renal tubules.

- If the rate of **excretion** of the substance (Us x V) < the **filtered load** of the substance (GFR x Ps), then some of the substance must have been **reabsorbed** from the renal tubules.

- If the **excretion rate** of the substance > **filtered load**, then the rate of excretion= **sum of the rate of glomerular filtration plus tubular secretion.**

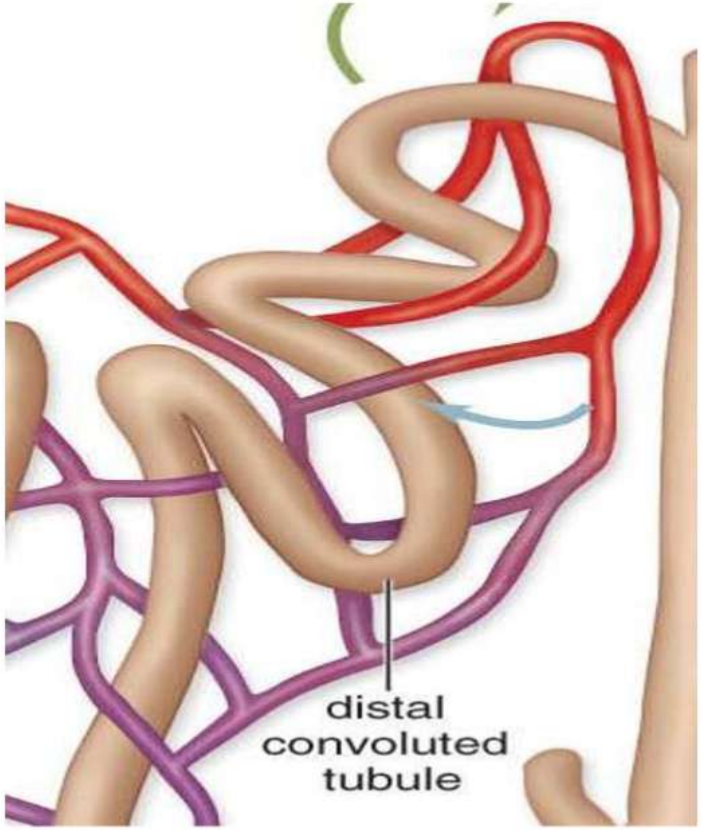
Tubular Reabsorption



return of filtrates from tubules through diffusion & active transport

- Selective
- Most electrolytes (e.g. Na^+, K^+, HCO_3^-, Cl^-), nutritional substances (e.g. glucose) are almost completely reabsorbed
- Most waste products (e.g. urea, creatinine, uric acid, urates) poorly reabsorbed

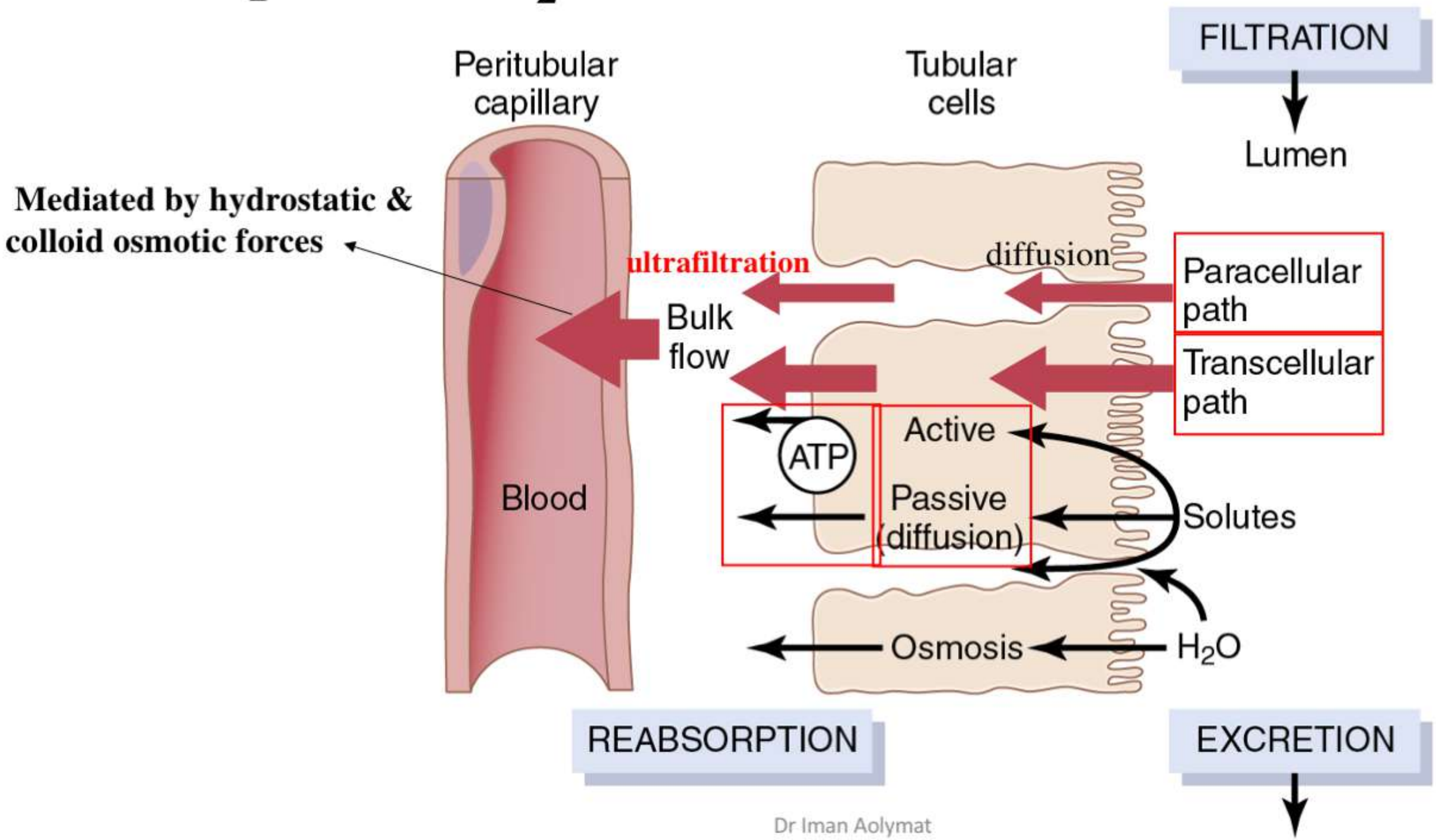
3. Tubular Secretion



Movement of molecules from blood into tubule

Excretion of waste products (e.g. H+, drugs and toxins).

Reabsorption of H_2O and solutes

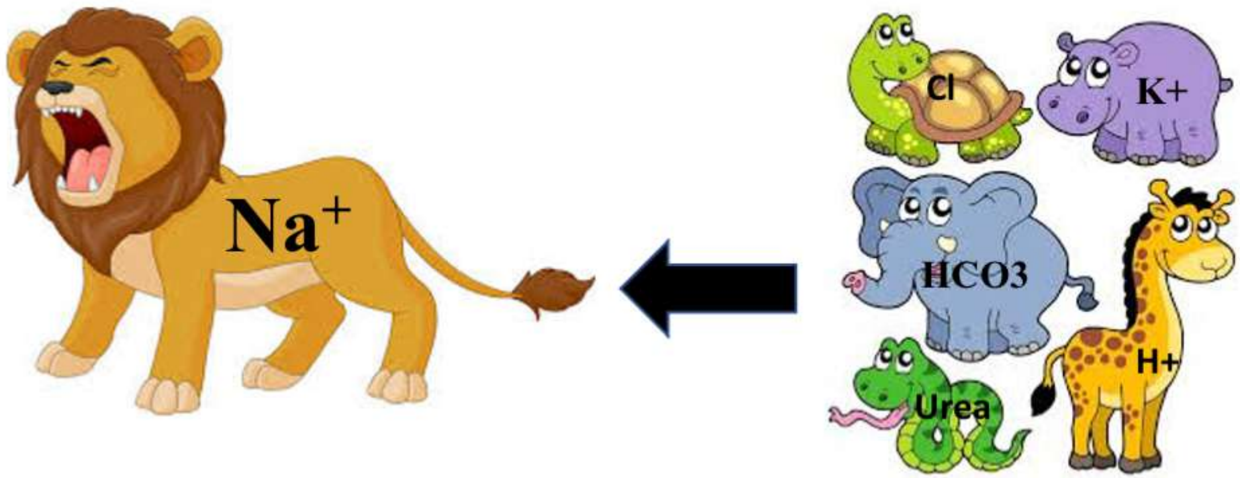


ACTIVE TRANSPORT

- Moved against electrochemical gradient
- ATP-dependent

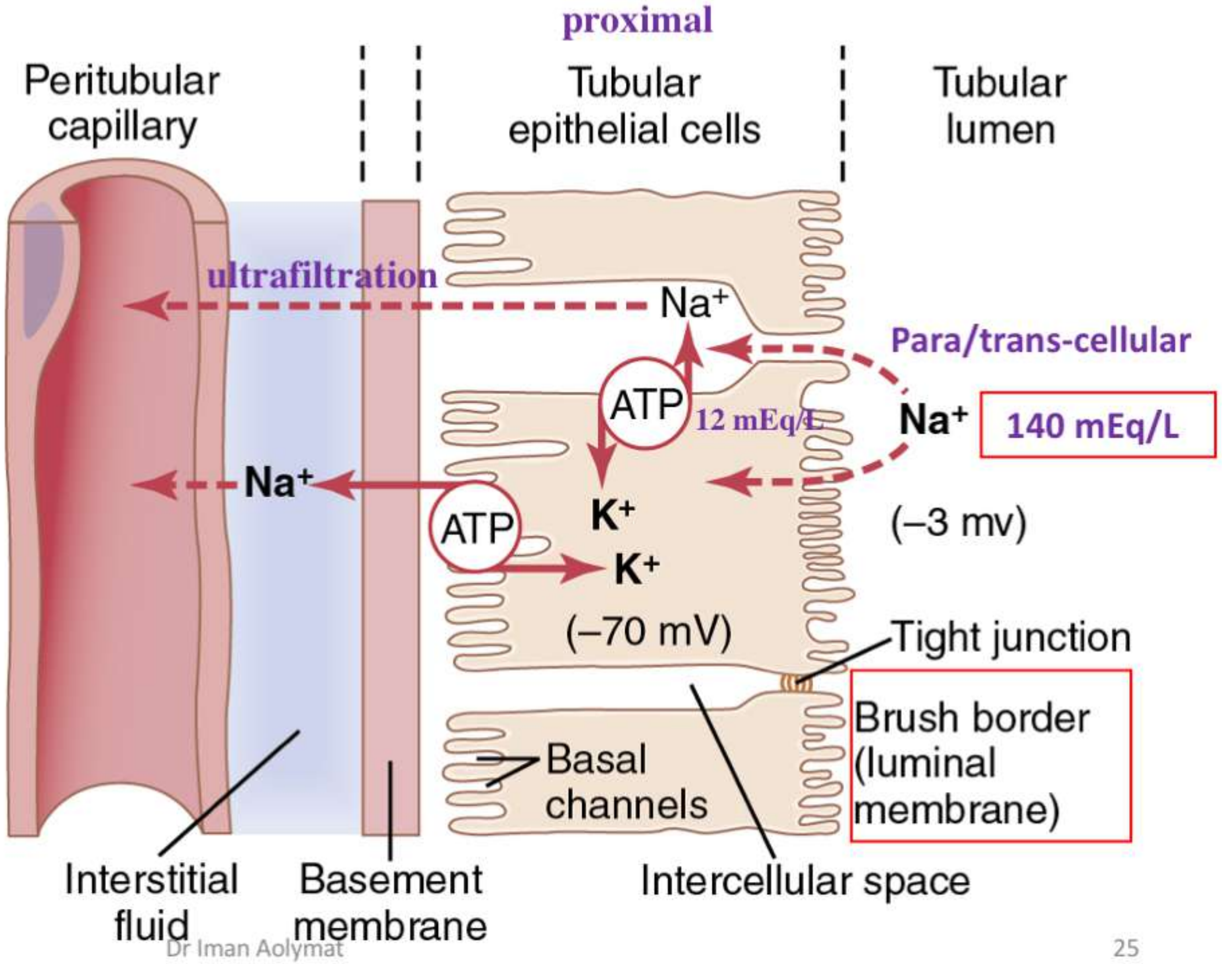
- Primary active transporters in kidneys:
- Na^+ -K^+ ATPase
- H^+ ATPase
- H^+ -K^+ ATPase
- Ca+ ATPase

Reabsorption of H_2O & solutes is coupled to Na^+ reabsorption

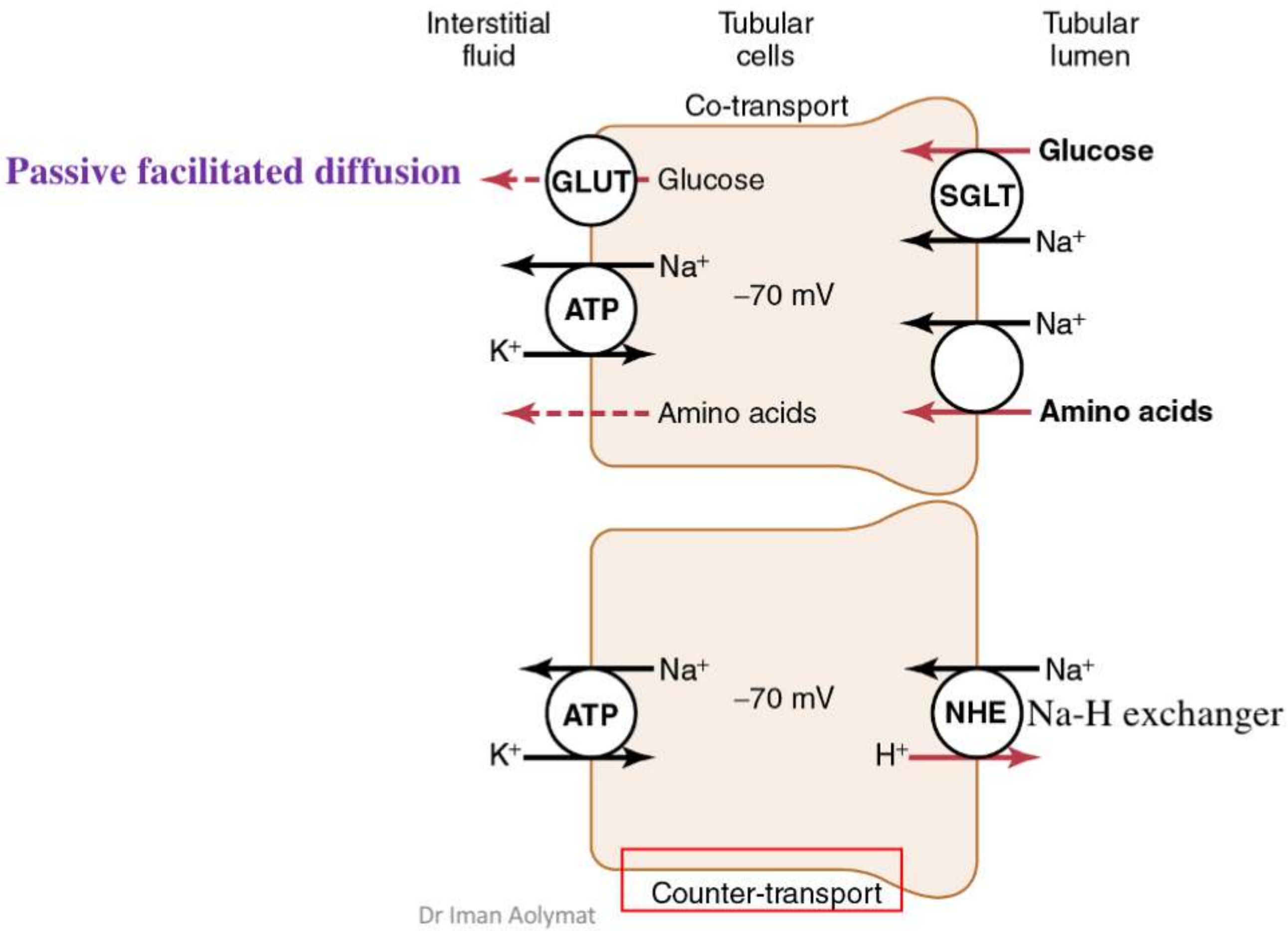


Primary active transport of Na^+

Passive diffusion of Na
1) Concentration gradient difference
2) -70 mV intracellular potential attracts positive Na



Mechanisms of secondary active transport.



Reabsorption of H_2O & solutes is coupled to Na^+ reabsorption

- H_2O is absorbed by **osmosis** through aquaporins/tight junctions
- Proximal tubules are **highly permeable** to H_2O
- H_2O osmosis drag other solutes (Na, Cl, K, Ca & Mg) mainly in *proximal T.*

Reabsorption of Cl & urea

- <u>Cl reabsorption</u>

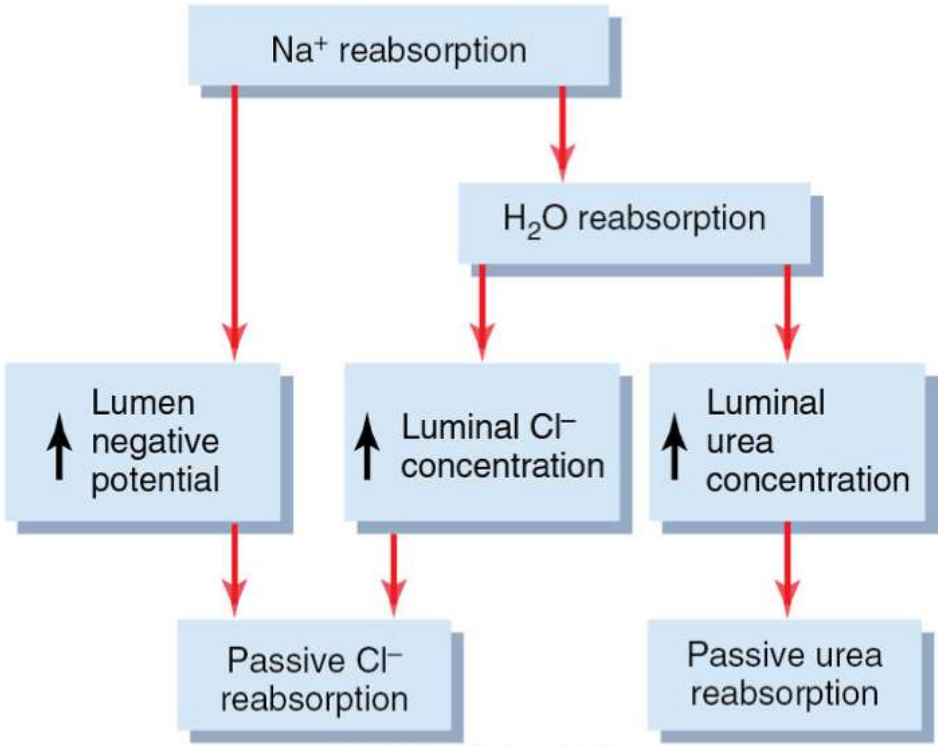
  - **Passive diffusion** (paracellular pathway) due to **Na (+ve)** and water reabsorption

  -Secondary active transport → Na-Cl cotransport

- <u>Urea reabsorption</u>

  -Passive

  -Urea transporters



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The End

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