النادي الطبي

GENITOURINARY SYSTEM

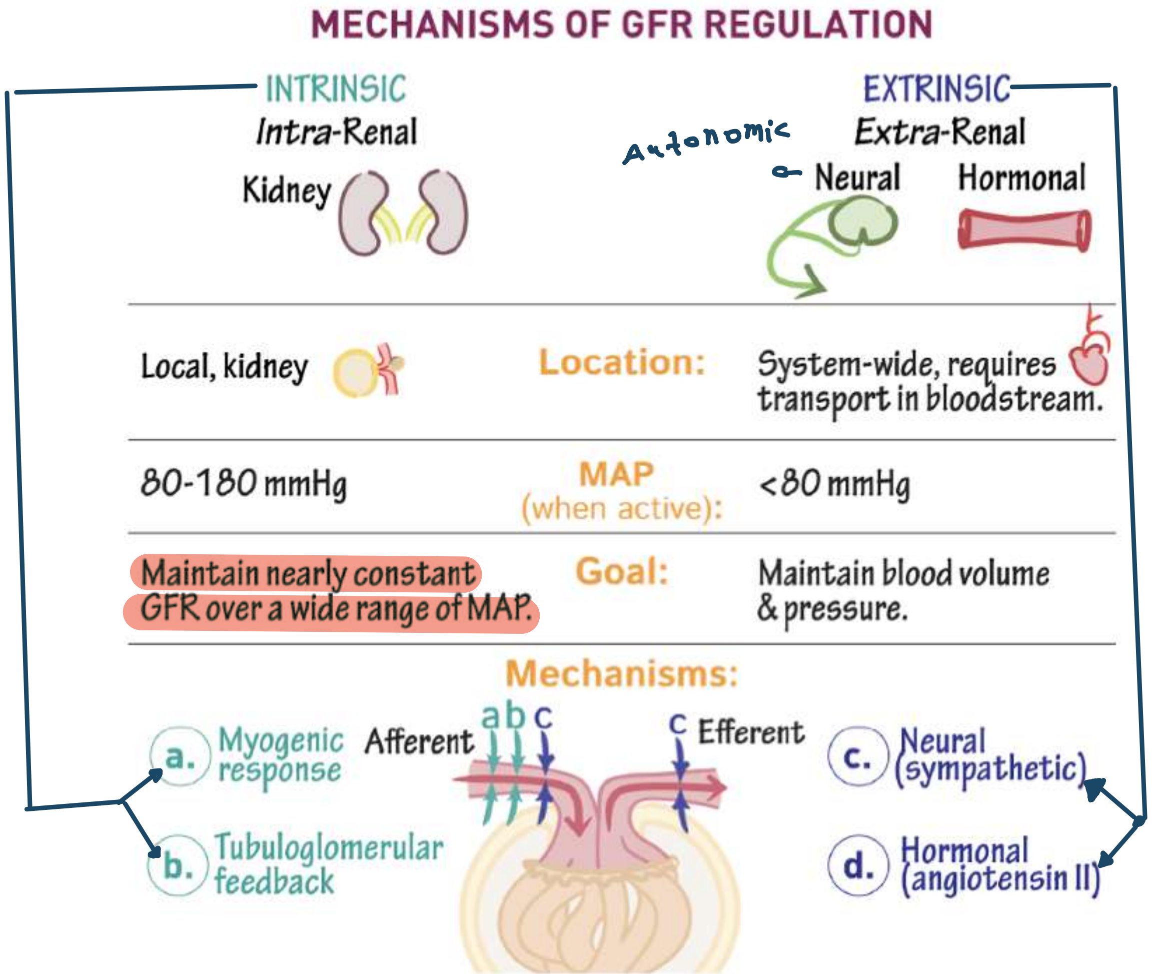
SUBJECT : Physiology

LEC NO. : 2

DONE BY : Hashem Ata

وقل رب زدني علماً

Control of GFR and RBF



الكلية عندها القدرة على التأقلم مع ضغط الجسم

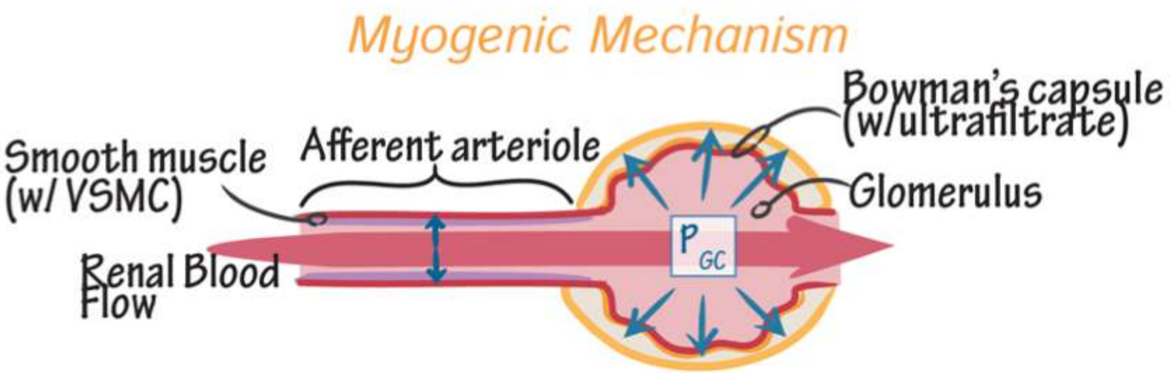
Autoregulation

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

① Myogenic response



1. ↑RBF = ↑Hydrostatic pressure against the walls of the afferent arteriole.
2. Stretch receptors in VSMC initiate VASOCONSTRICTION.

↑flow of Ca from ECF into cells

لما يزيد ضغط الدم على جدار الاوعية الدموية بحس فيه
ال streretch receptor وبحفز ادخال ال ca لداخل
الخلايا وبالتالي حدوث vasoconstriction فيقل ال
Renal blood flow ويقل ال GFR

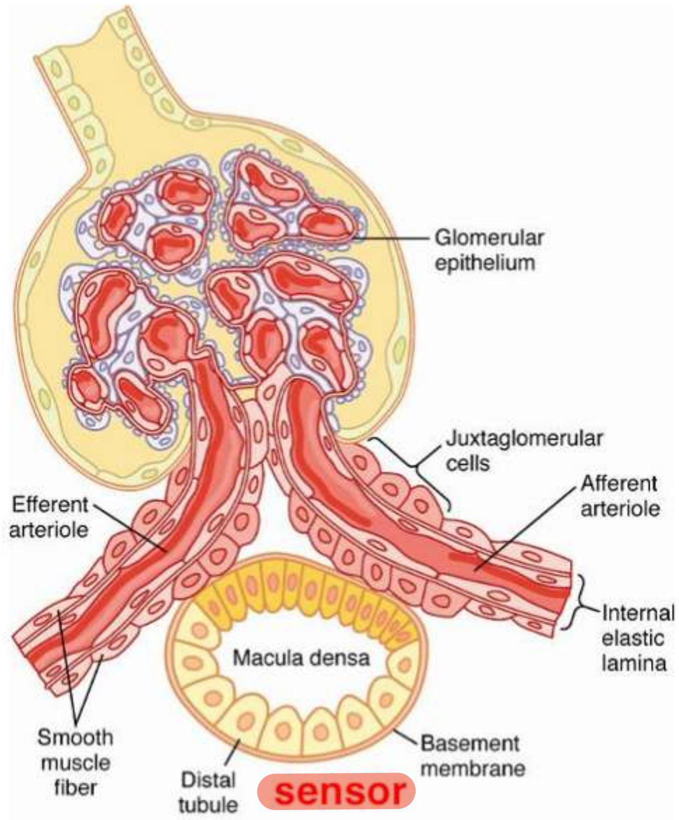
في عنا اشي اسمه juxtaglomerular apparatus وهو عبارة عن sensor موجود في Dct و glmerular affernt arteriole وهو حساس لتركيز ال Na

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**

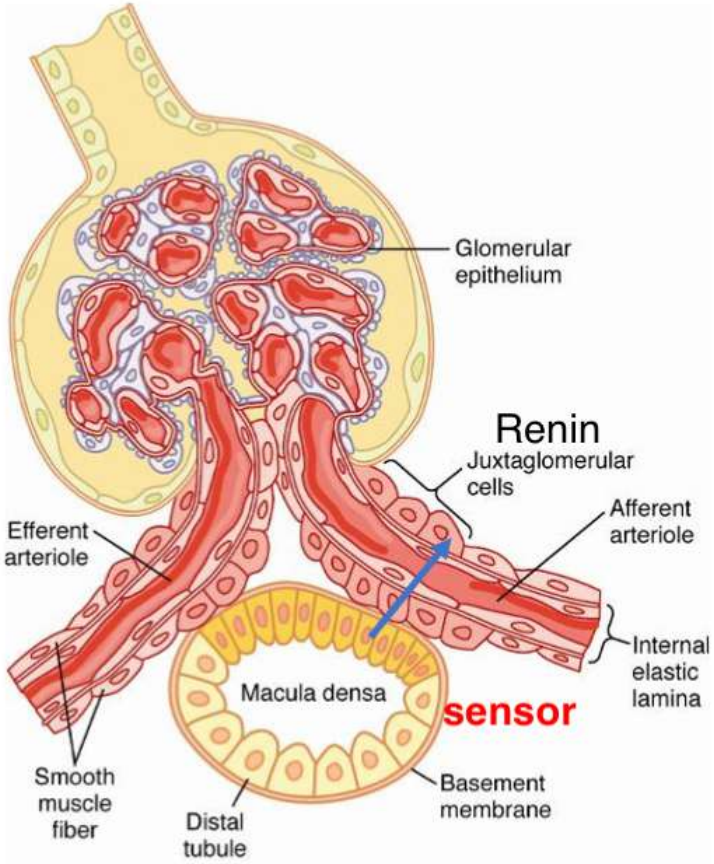
ال macula densa بتعطي الاوامر بس ال juxta هي يلي بتنفذ

- 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



انزل للسلايد يلي تحت

Juxtaglomerular apparatus



Tubuloglomerular feedback

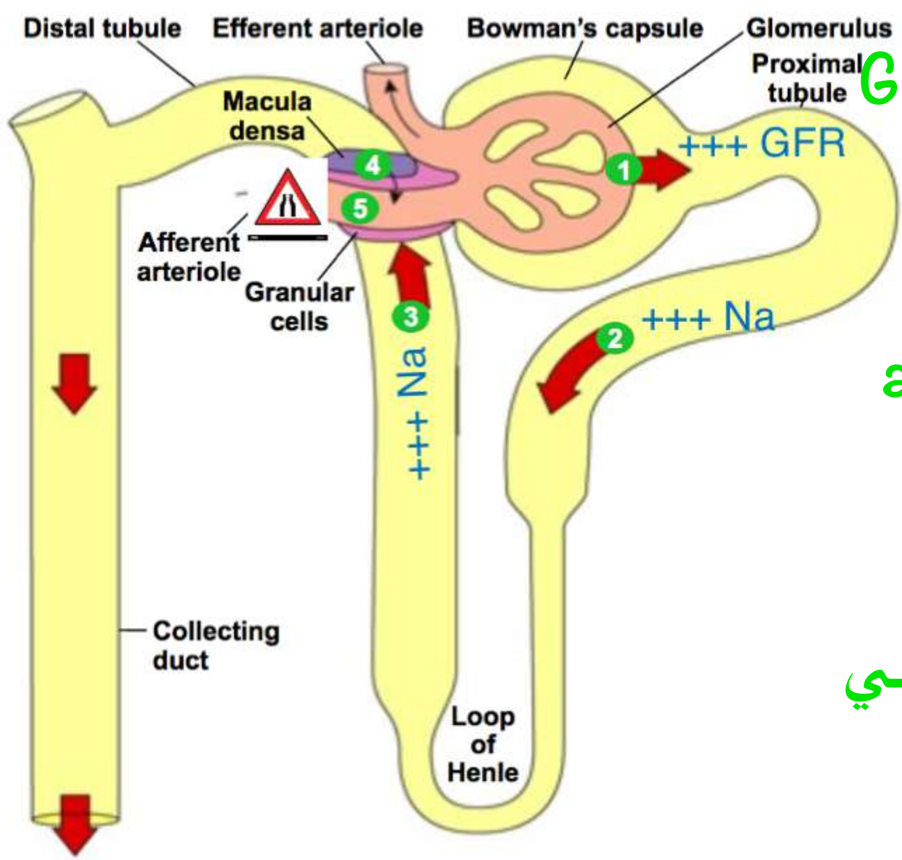
High Na→
↑ adenosib→ VC of A } ↓↓ GFR

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

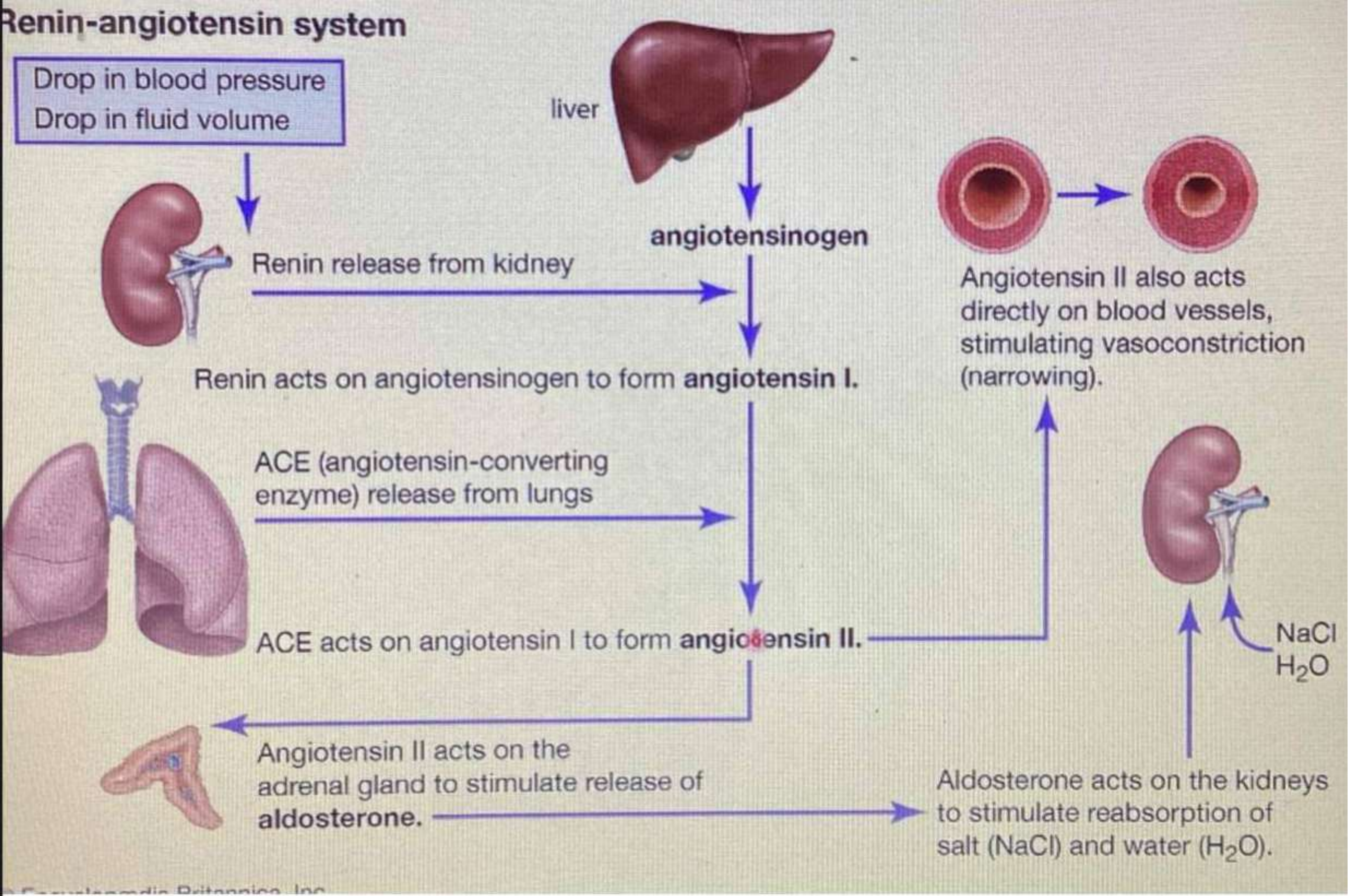
الية عمل هذا النظام هو انه بداية بيوصل الRBf وبتحدث عملية ال filtration ومن ضمن المواد يلي بتخرج هو الصوديوم Na وبيكمل لحد ما يوصل ال distal tubule وغاد بيكون موجود ال sensore يلي حكينا عنه من شوي وبيحس تركيز الصوديوم وهون عنا احتمالين :

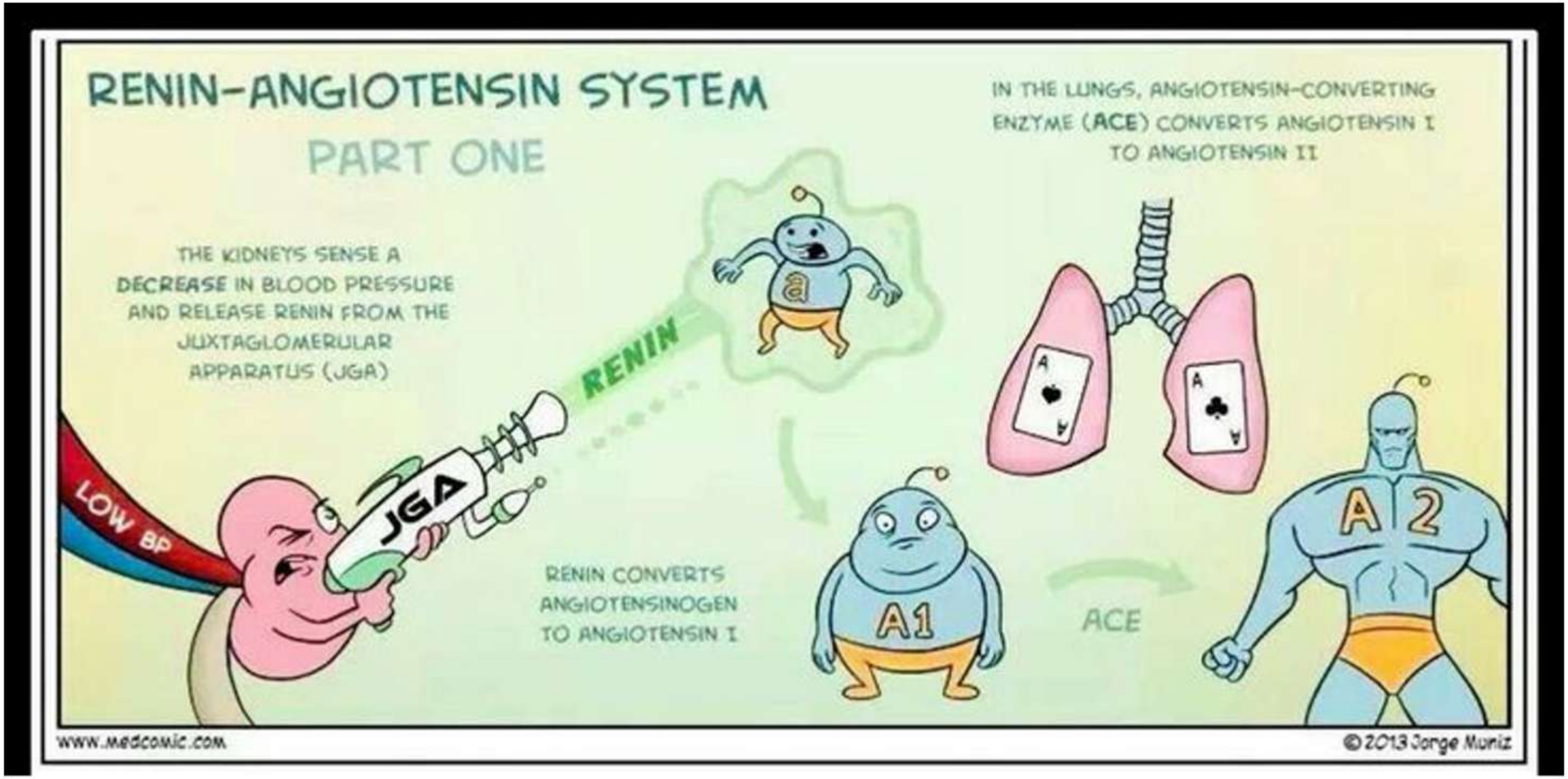
Tubuloglomerular feedback

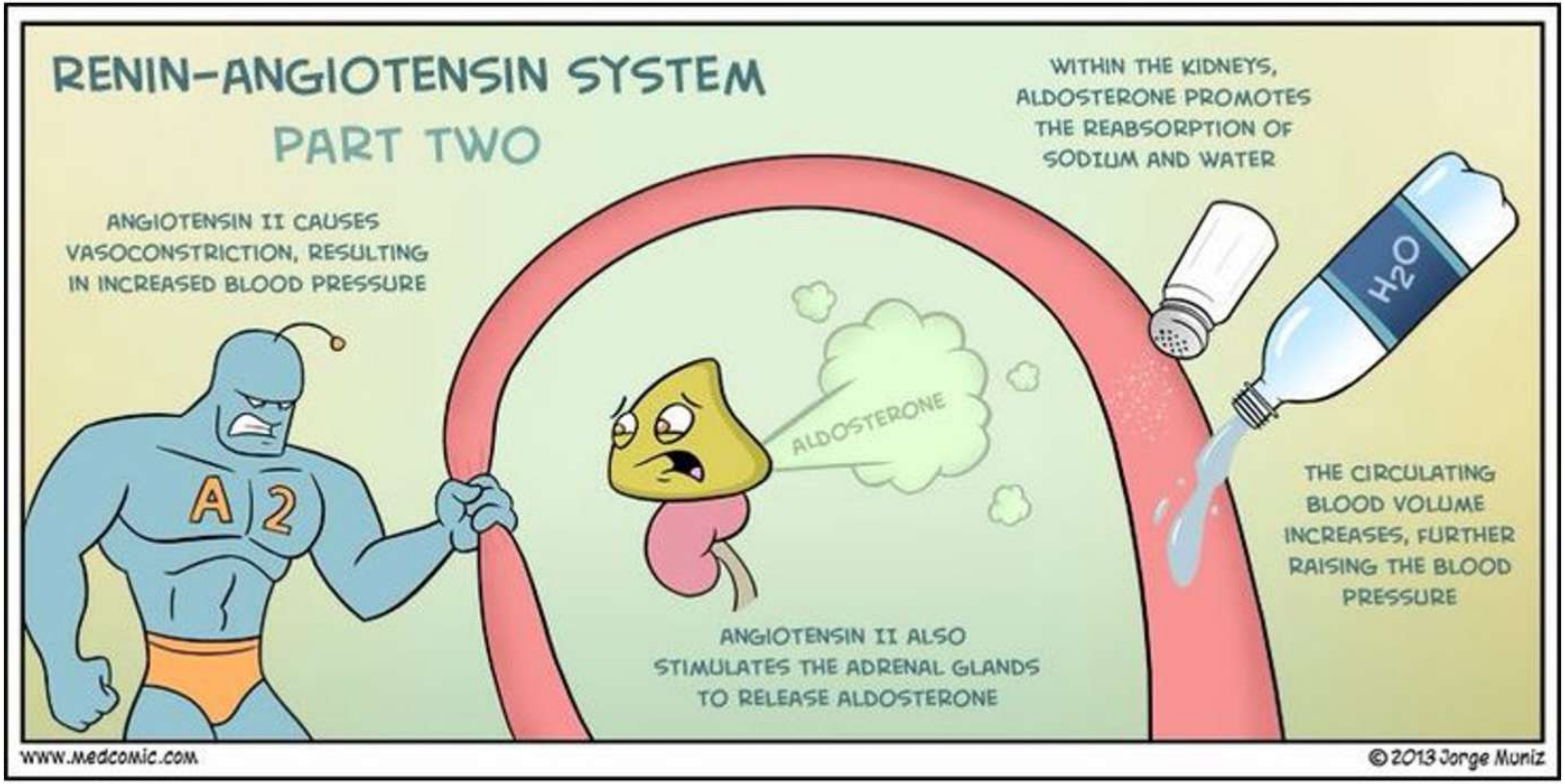
الأول لو كان تركيز ال Na عالي فبالتالي اكيد ال GFR كان عالي واحنا بحاجة نقلله بقوم هذا ال sensor بتحفيز افراز ال adenosine يلي راح يروح يقوم بعمل vasoconstriction في ال Afferent arteriole وبالتالي يقل ال GFR



والثاني لو كان تركيز ال Na منخفض بالتالي اكيد ال GFR قليل فبيتم افراز ال No و prostaglandin يلي بقومو بعمل vasodilation للEfferent arteriole وبنفس الوقت يتم افراز ال renin من ال juxtaglomerular يلي بقوم بعمل Vc لل efferent arteriole


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).


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
www.medcomic.com
©2013 Jorge Muniz


RENIN-ANGIOTENSIN SYSTEM
PART TWO
ANGIOTENSIN II CAUSES VASOCONSTRICTION, RESULTING IN INCREASED BLOOD PRESSURE
A2
ALDOSTERONE
ANGIOTENSIN II ALSO STIMULATES THE ADRENAL GLANDS TO RELEASE ALDOSTERONE
WITHIN THE KIDNEYS, ALDOSTERONE PROMOTES THE REABSORPTION OF SODIUM AND WATER
H2O
THE CIRCULATING BLOOD VOLUME INCREASES, FURTHER RAISING THE BLOOD PRESSURE
www.medcomic.com
© 2013 Jorge Muniz

Other Hormonal regulation of GFR

أكيد بياخذ وقت

Adrenaline, noradrenaline → **afferent** vasoconstriction → ↓ GFR

* renin- Angeotinsin → Efferent

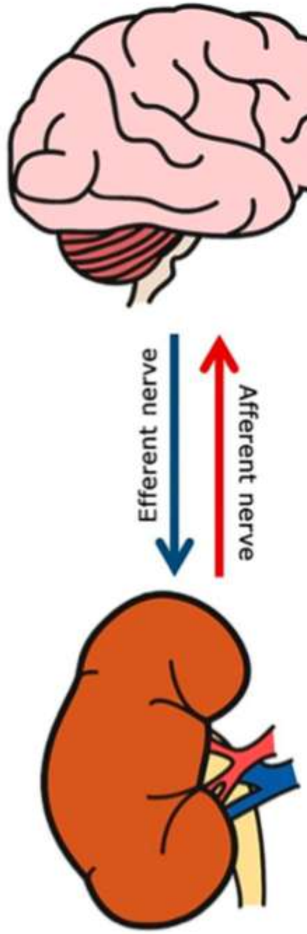
Prostaglandins and bradykinin → **afferent** vasodilator → ↑ GFR

في حالات sever

← تخفض الدم الواصل للكلى
في حالات الخطر و تزيد من
ضخ الدم للأعضاء الحيوية

Nervous regulation of GFR and RBF

Strong sympathetic stimulation→ vasoconstriction (Afferent) →↓GFR
Moderate sympathetic stimulation→ little effect
Sympathetic have **little** influence on RBF (↓RBF). → بالوضع الطبيعي
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.

clerance من ال المهم

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

Clearance measures how fast this substance is removed from bloodstream and excrete in urine

High clerance = quick removal. Low clearance = slow removal

Clearance Technique

* ما في حسابات بالامتحان

$$C_s \times P_s = U_s \times V$$

$$C_s = \frac{U_s \times V}{P_s} = \frac{\text{urine excretion rate}}{\text{Plasma conc.}}$$

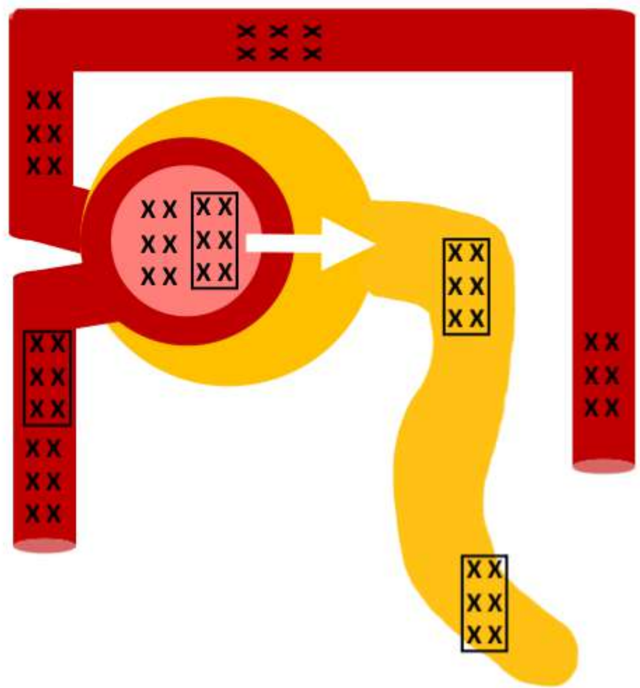
Where :
- C_s = clearance of substance S
- P_s = plasma conc. of substance S
- U_s = urine conc. of substance S
- V = urine flow rate

Use of clearance to measure GFR

For a substance that is freely filtered, but not reabsorbed or secreted (inulin, [125] I-iothalamate, creatinine), renal clearance is **equal to GFR**

مهم

مادة يعطيها للمريض
لحتى نحسب ال 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

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

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

$$Cx = \text{renal plasma flow}$$

Use of PAH clearance to estimate renal plasma flow

Total clearance تقريبًا حفظ مهم

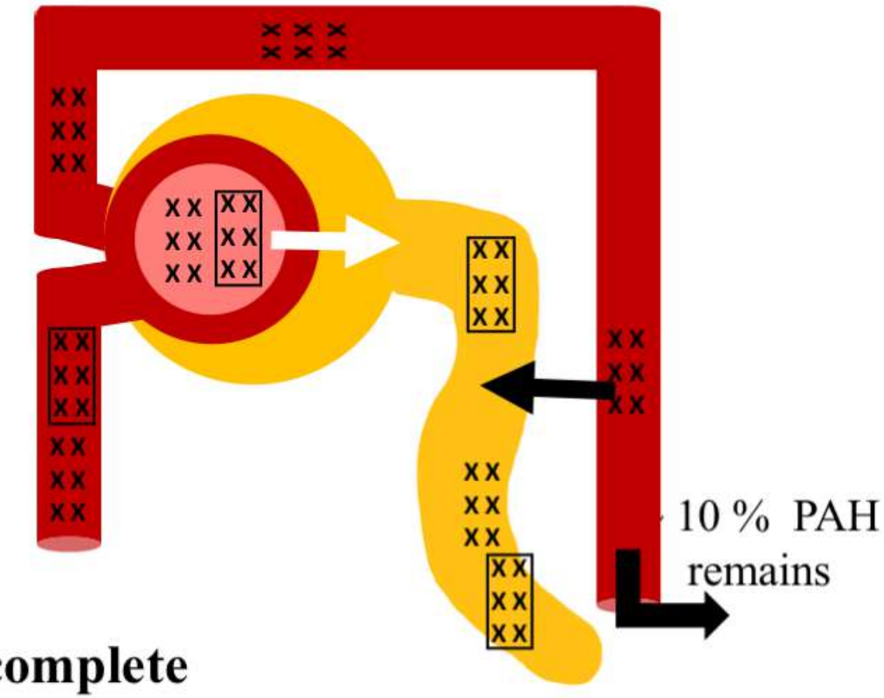
Paraminohippuric acid (PAH) is 90% filtered and secreted and is almost completely cleared from the renal plasma

amount entered $\cong$ amount excreted

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

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

$$RPF = \text{Clearance PAH}$$



To calculate actual RPF , one must correct for incomplete extraction of PAH

بعد ايجاد ال clearance to PAH لازم نقسم الناتج على 0.9 لحتى يطلع معي ال actual RBF

مهم

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.

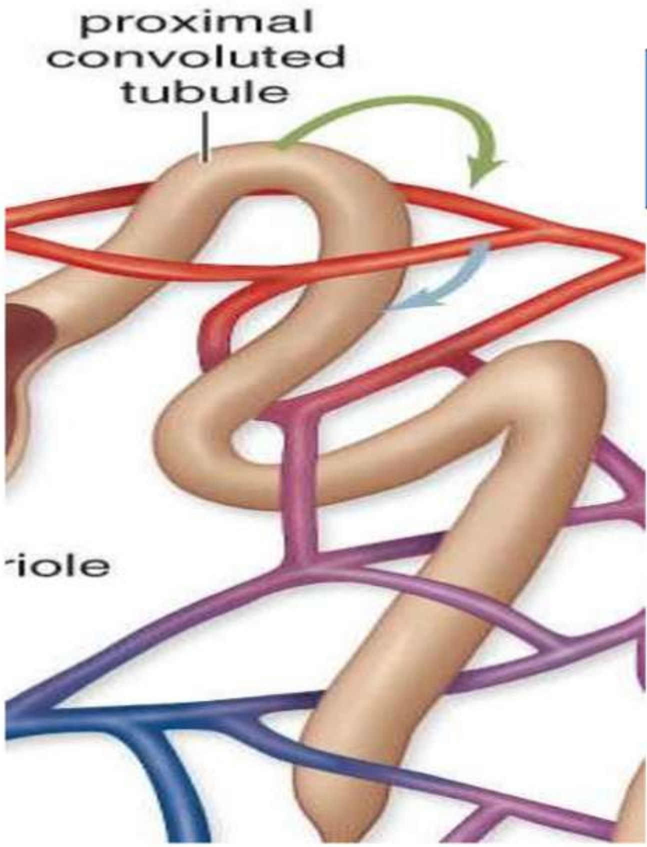
- If the rate of **excretion** of the substance (Us x V) < the **filtered load** of the substance (GFR x Ps), then some of the substance must have been **reabsorbed** from the renal tubules.

لو اعطيت من مادة 10 حبات ونزل بال 6 urine حبات اذا صار reabsorbtion

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

لو اعطيت من مادة 10 حبات ولاقيت بال urine نزل 20 حبة اذاً صار عندي secretion

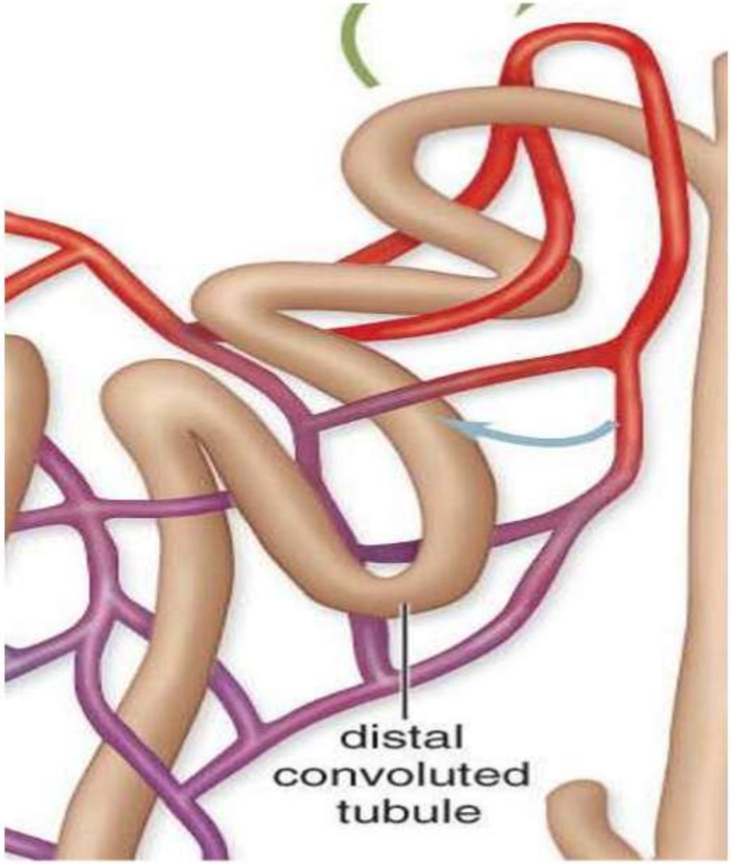
Tubular eabsorption



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

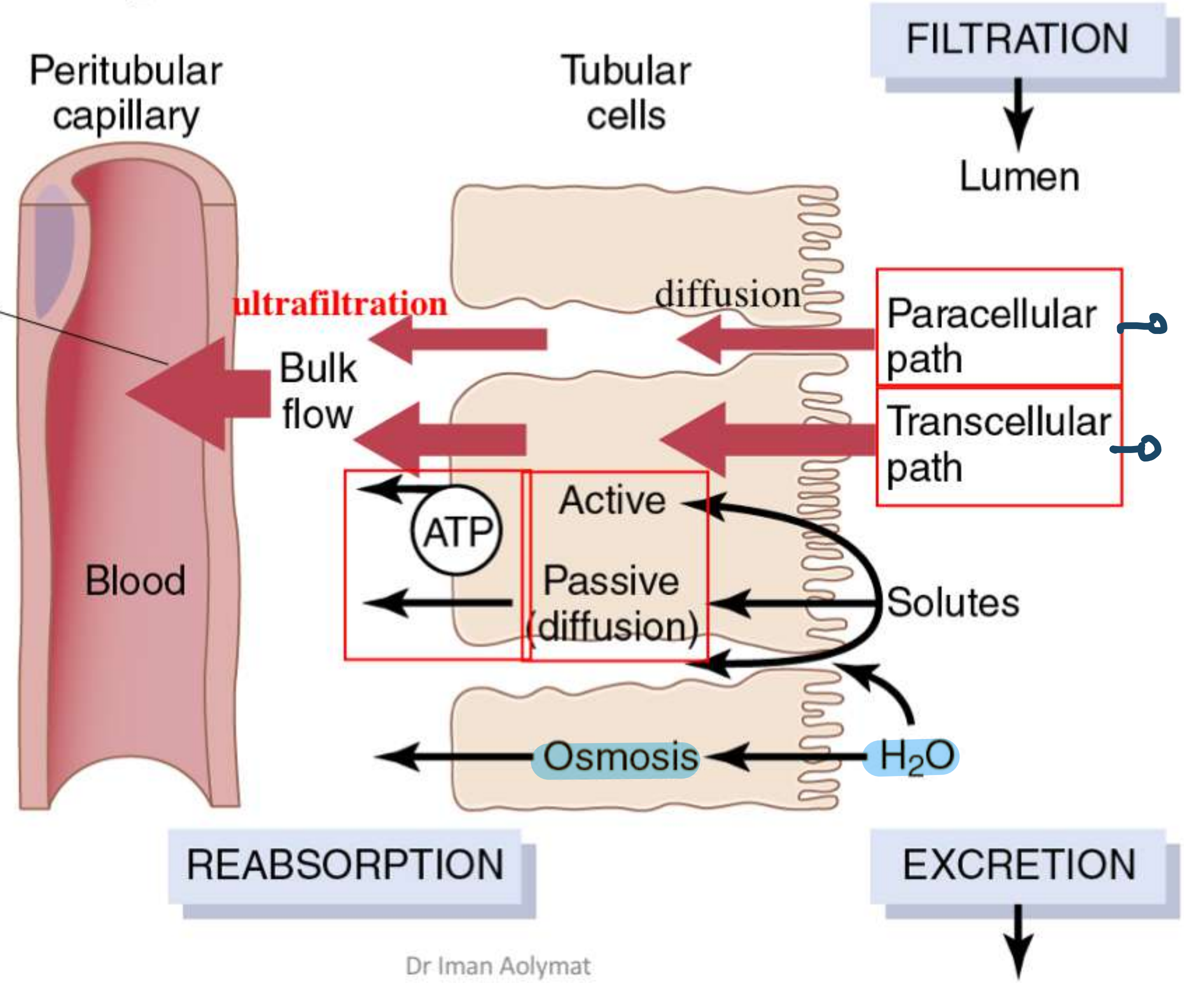


Movement of molecules from blood into tubule

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

Reabsorption of H_2O and solutes

Mediated by hydrostatic & colloid osmotic forces



Paracellular path — من بين الخلايا

Transcellular path — من الخلايا مباشرة

ACTIVE TRANSPORT

- Moved against electrochemical gradient
- ATP-dependent

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

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

*الارقام مش محفظ

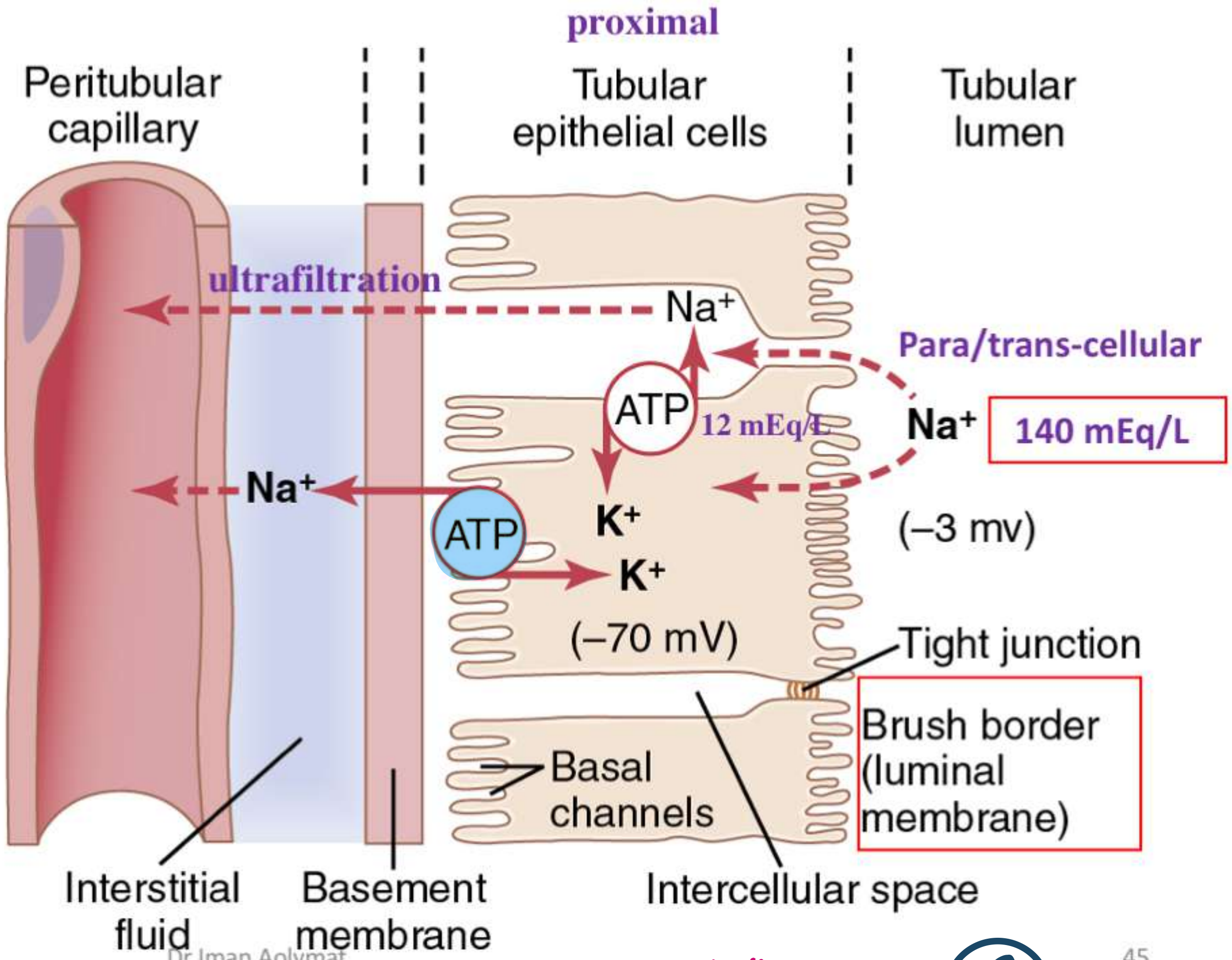
Primary active transport of Na^+

Passive diffusion of Na

1) Concentration gradient difference

2) -70 mV intracellular potential attracts positive Na

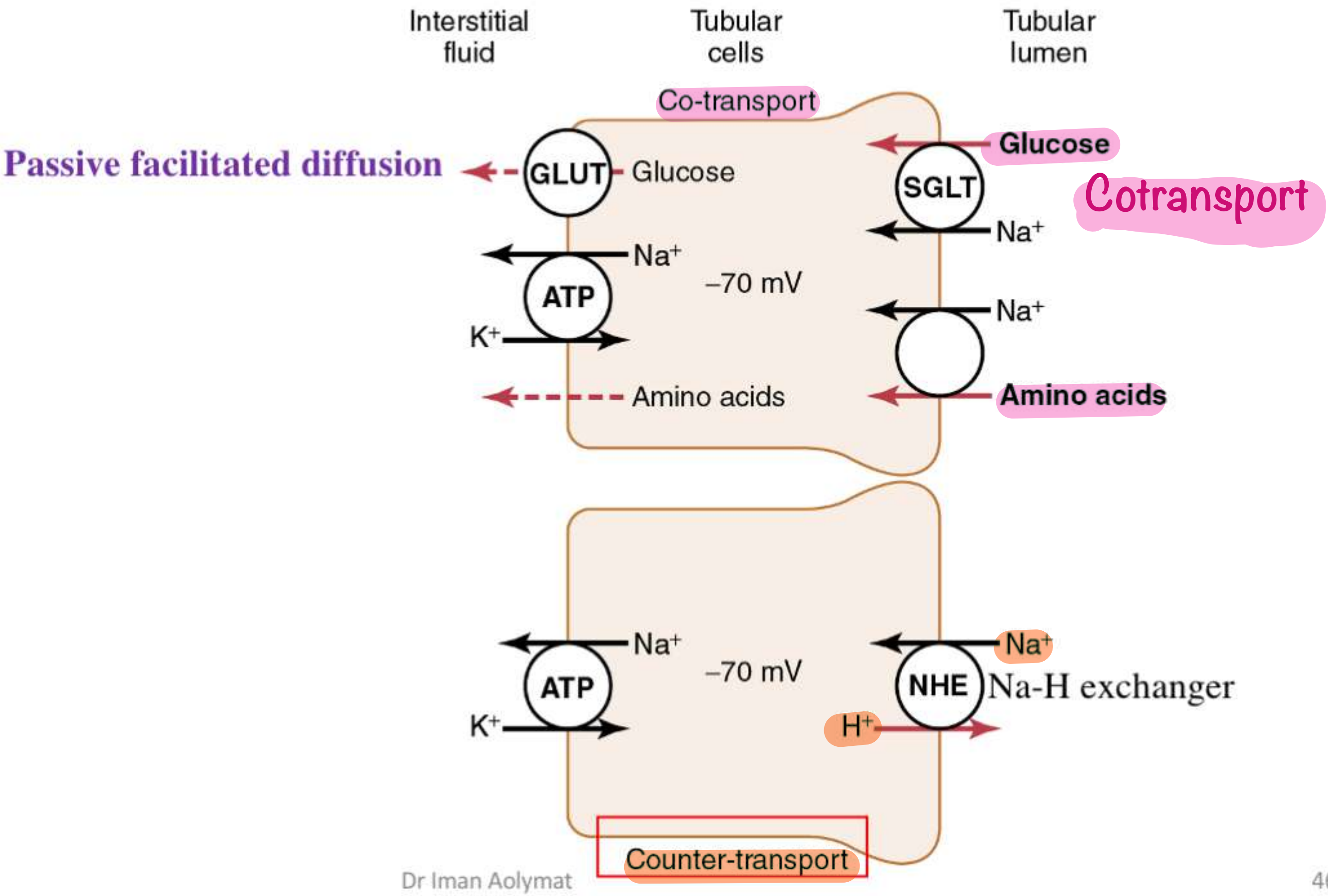
تركيز الصوديوم يقل داخل الخلية بسبب عمل ال Na/k pump يلي بتخرج صوديوم وتدخل بوتاسيوم) لان الماء يتبع ال Na وبالتالي يدخل ال كمية من الصوديوم من خلال passive diffusion لداخل الخلايا من ال lumen



مضخة ال Na/k تقوم باخراج ثلاث ايونات صوديوم موجبة وادخال ايوني بوتاسيم فتكون المحصلة اكتساب شحنة سالبة تجذب الصوديوم للدخول من ال lumen عن طريق ال pd

2

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*.

ال cl بدخل مع ال Na لانه بكون مرتبط فيه بسبب اختلاف الشحنة وبس يدخل جوا الخلية بلاقي كل الخلية اصلا سالبة الشحنة فبنطرد برا لانه سالب كمان

Reabsorption of Cl & urea

- Cl reabsorption
  - Passive diffusion (paracellular pathway) due to Na (+ve) and water reabsorption
  - Secondary active transport → Na-Cl cotransport

- Urea reabsorption
  - passive
  - Urea transporters