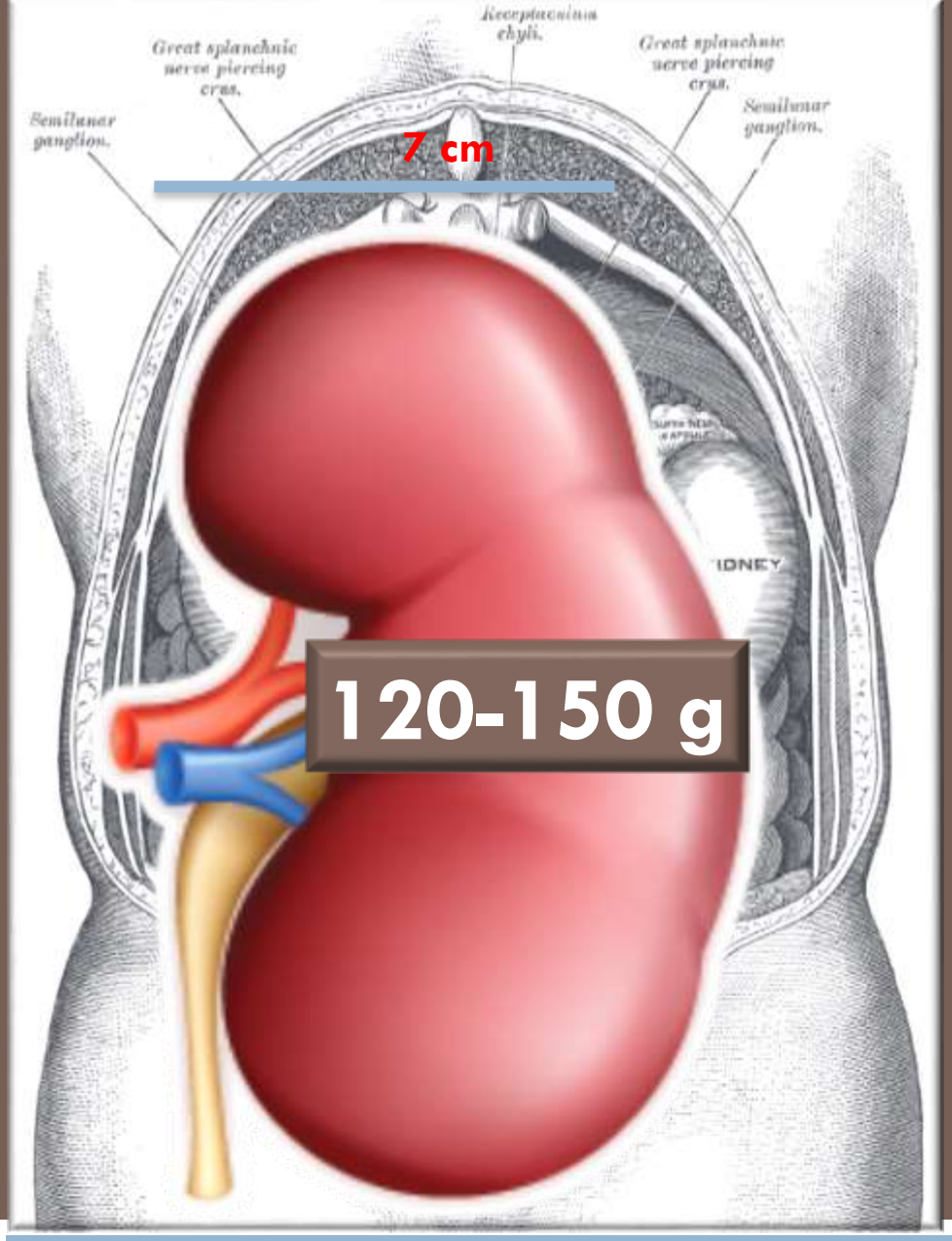
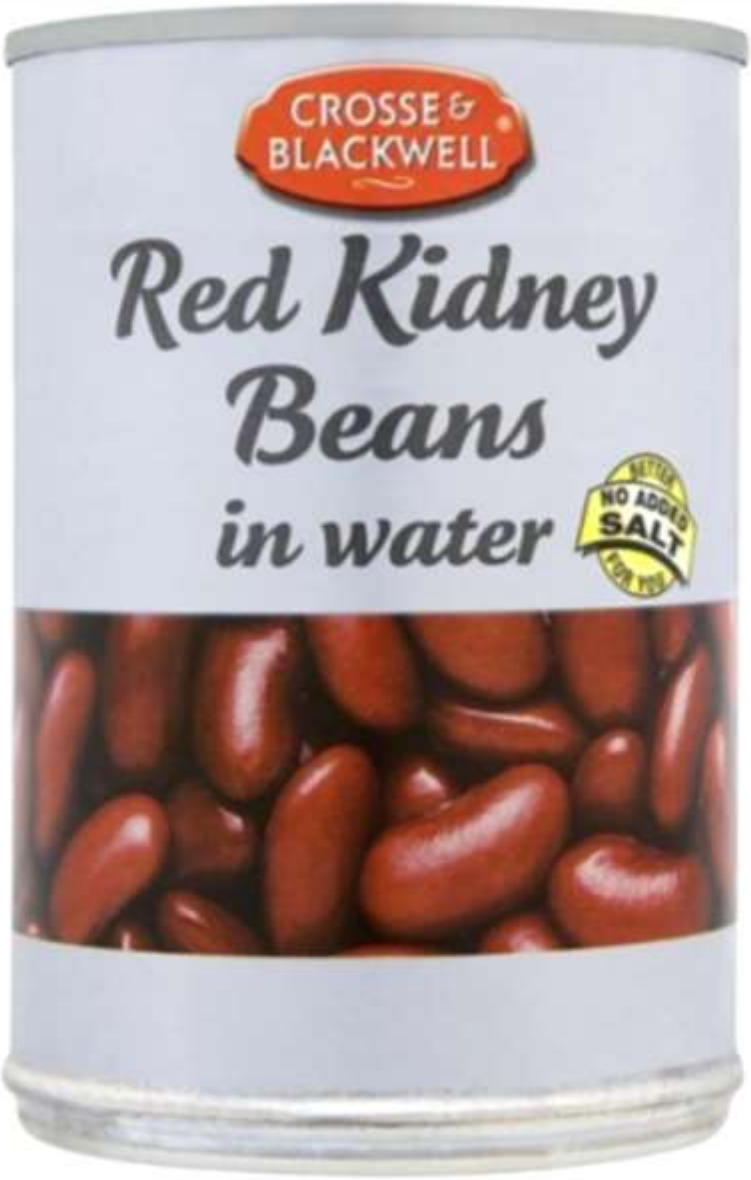
ANATOMIA E FISIOLOGIA RENALE

Carmelo Libetta

Capitolo 1°


Great splanchnic nerve piercing crus.
Great splanchnic nerve piercing crus.
Semilunar ganglion.
Semilunar ganglion.
7 cm
3-4 cm
120-150 g
11-12 cm

1a) ANATOMIA



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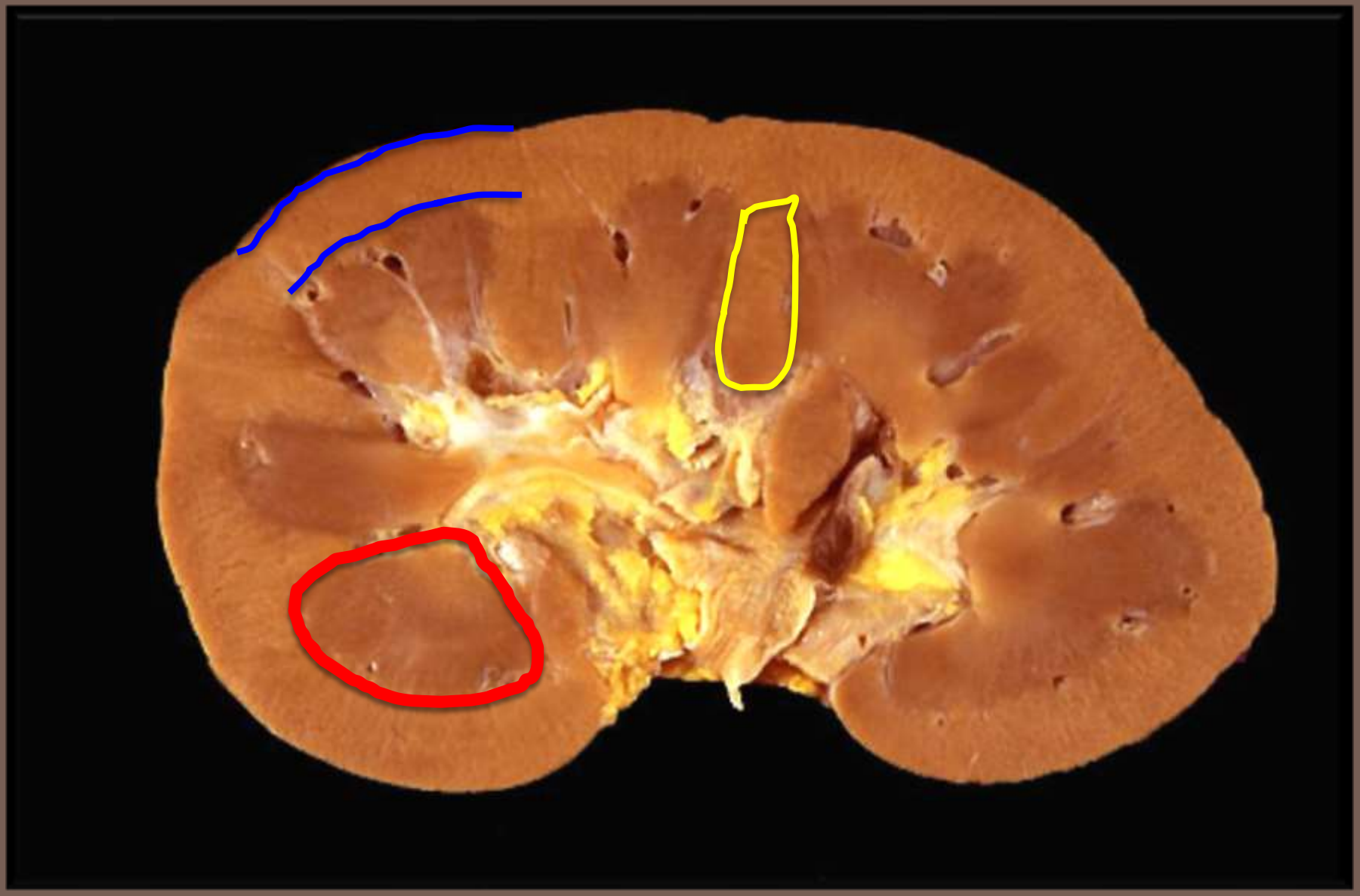
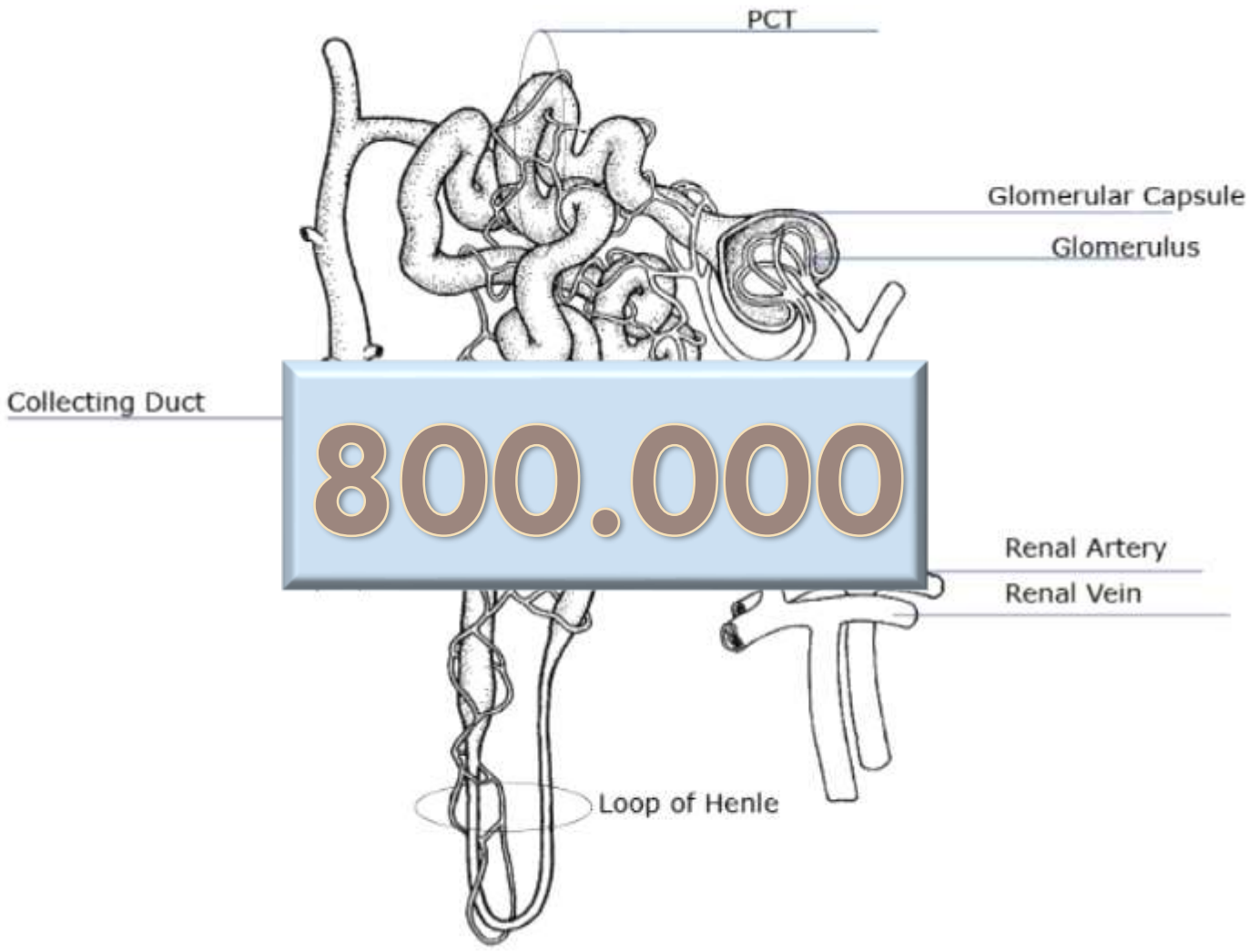
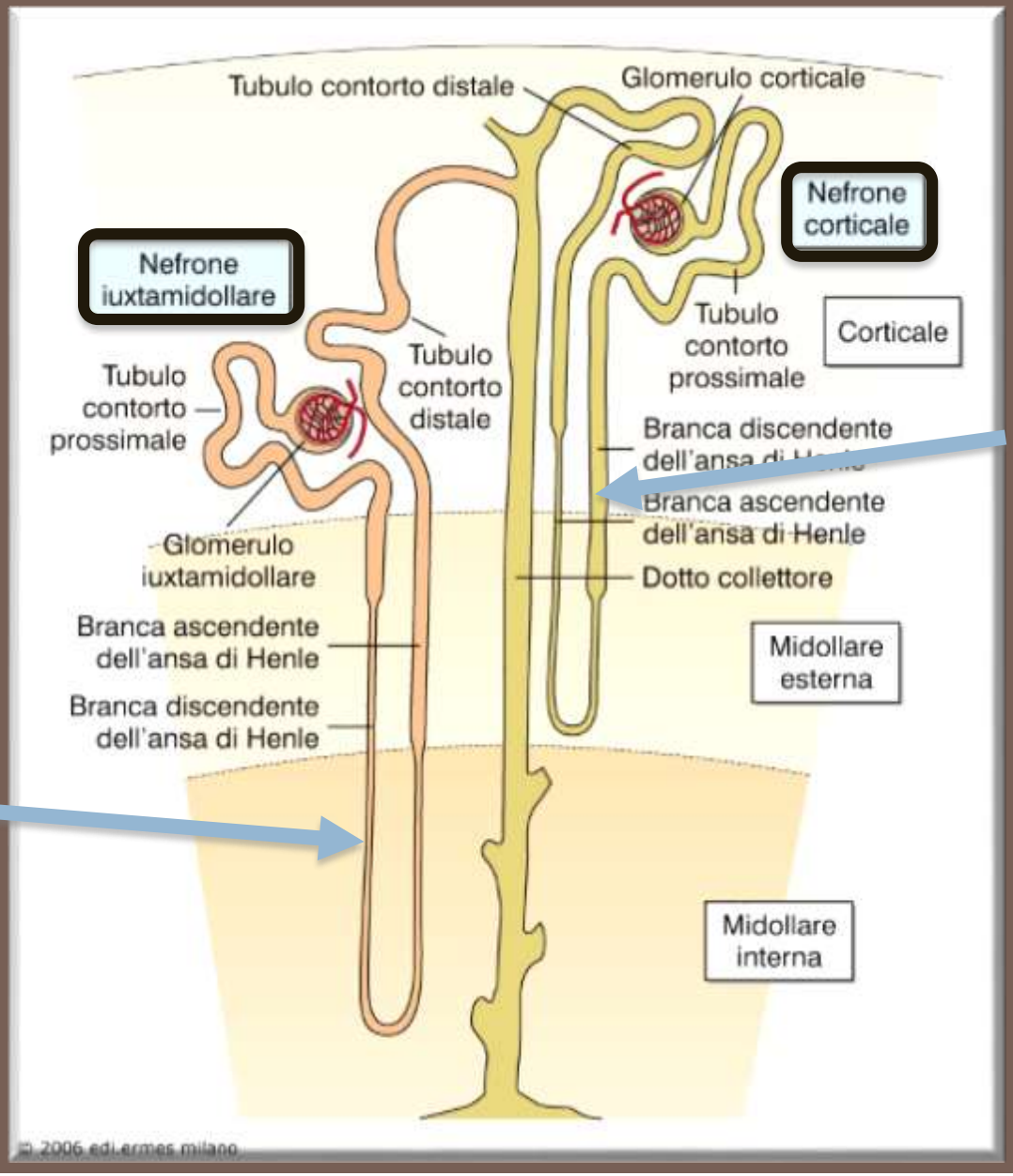
RED KIDNEY




PCT
Glomerular Capsule
Glomerulus
Collecting Duct
800.000
Renal Artery
Renal Vein
Loop of Henle



80%

20%

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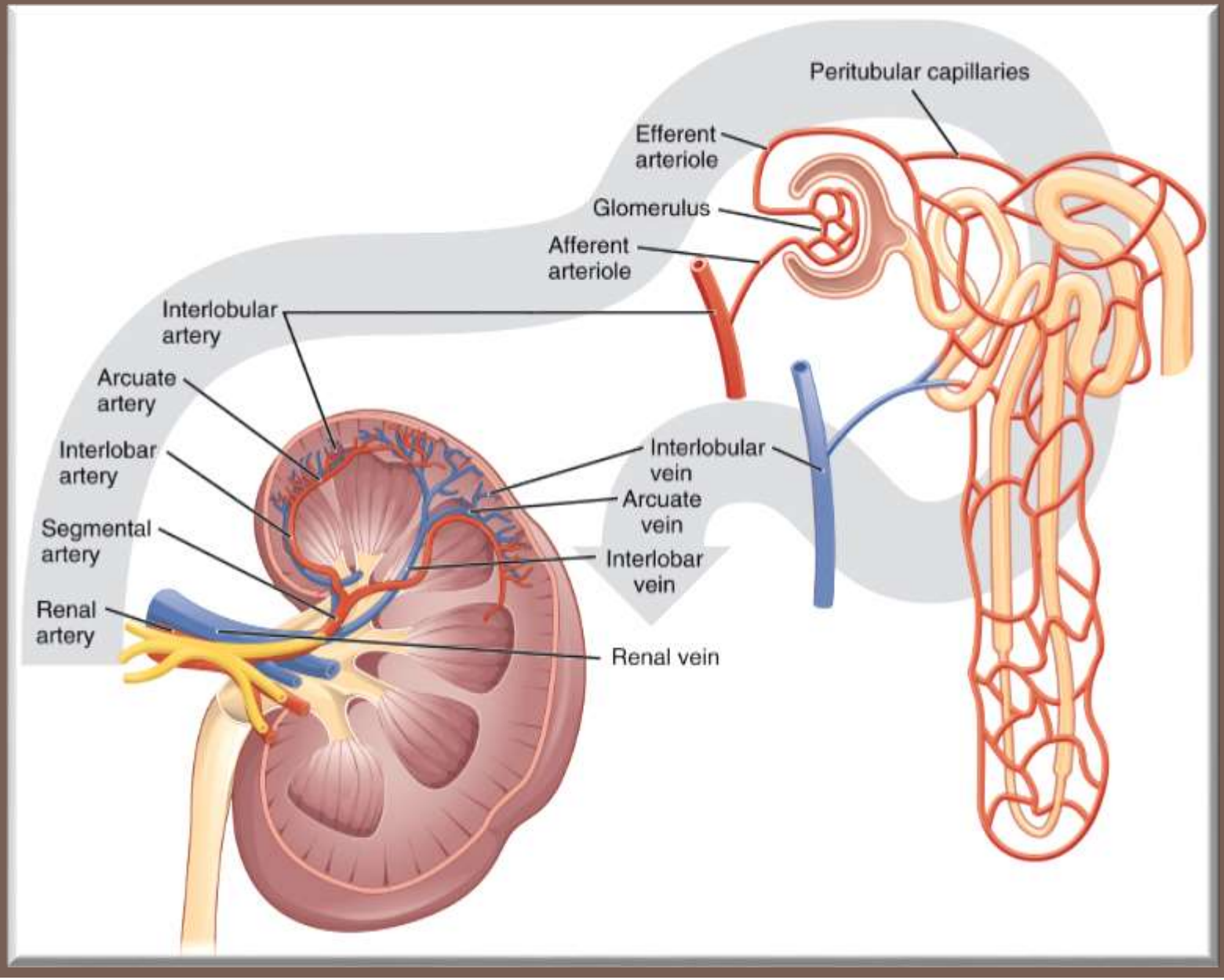
NEFRONE



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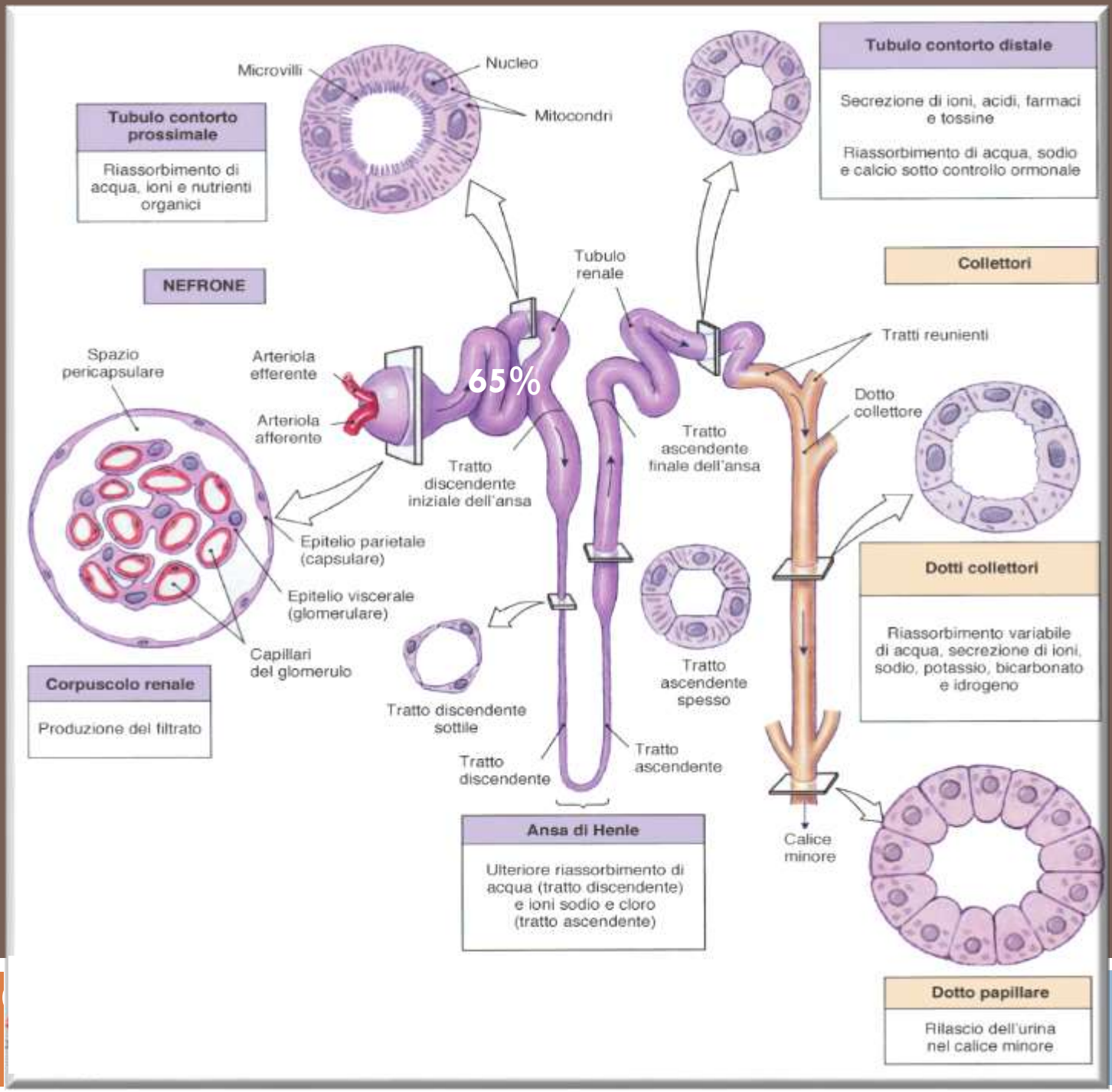
Vascolarizzazione



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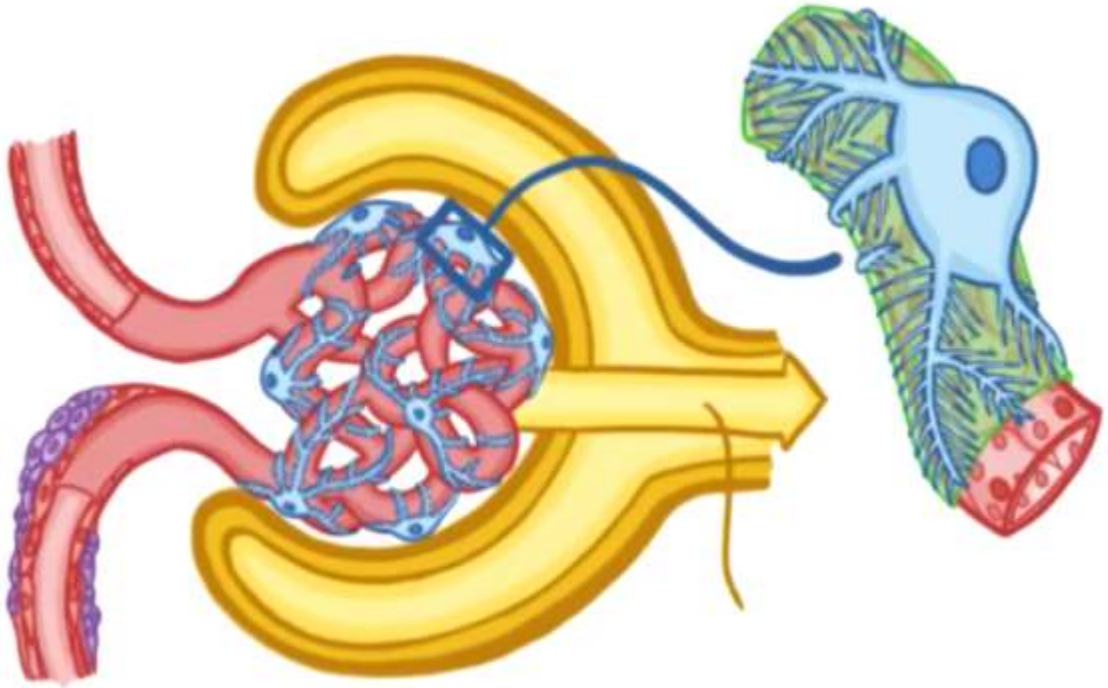
Anatomia: Glomerulo

GLOMERULAR FILTRATION BARRIER - 3 LAYERS



1. ENDOTHELIUM
   - FENESTRATIONS
   - ✓ Solutes & proteins
   - ✗ Red blood cells
   - ↳ PLASMA
2. BASEMENT MEMBRANE
   - TINY PORES
   - ✗ Plasma proteins (Negative charge)
3. EPITHELIUM
   - PODOCYTES
   - FILTRATION SLITS
   - ✗ Plasma proteins

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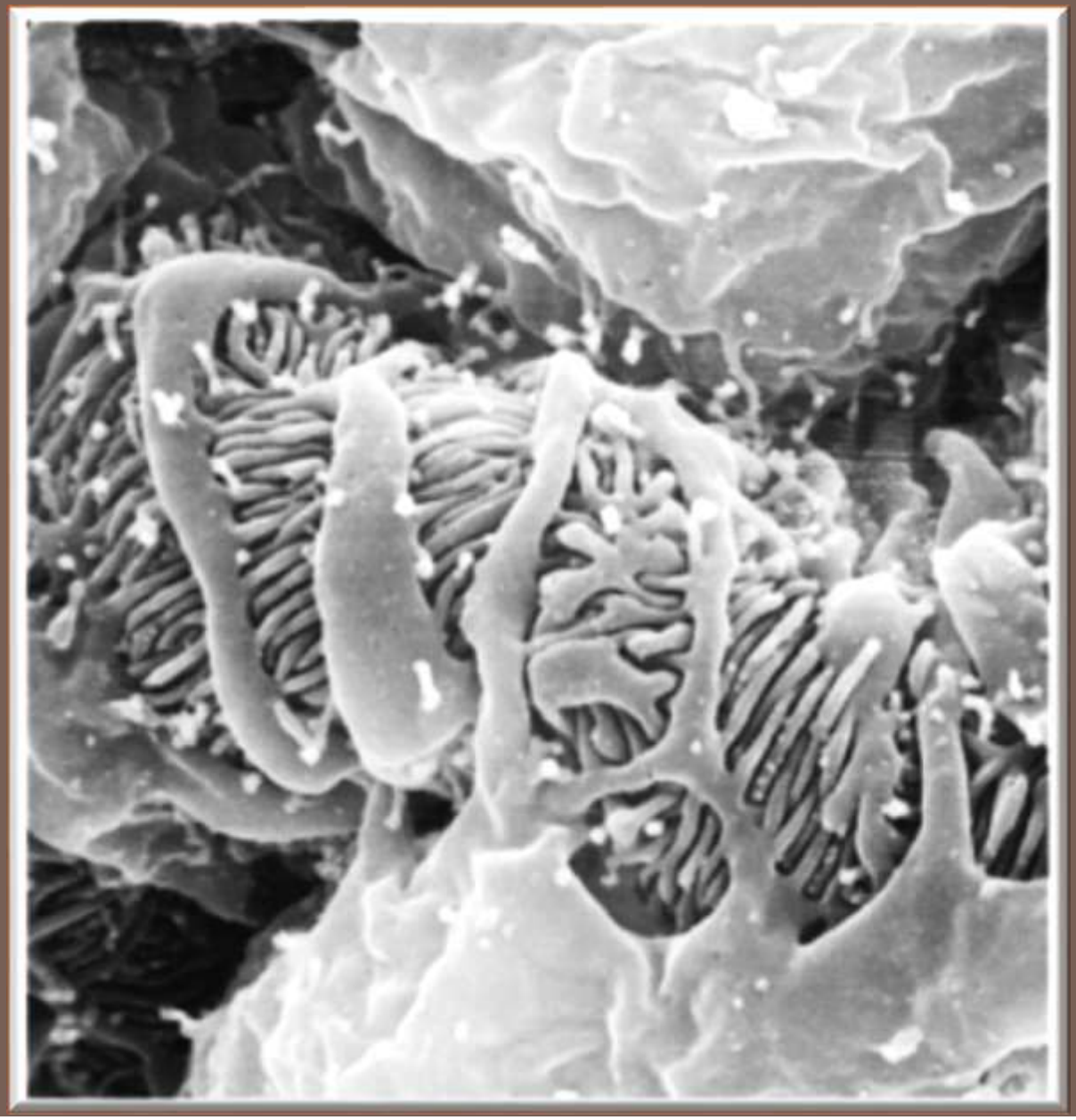
Barriera di filtrazione



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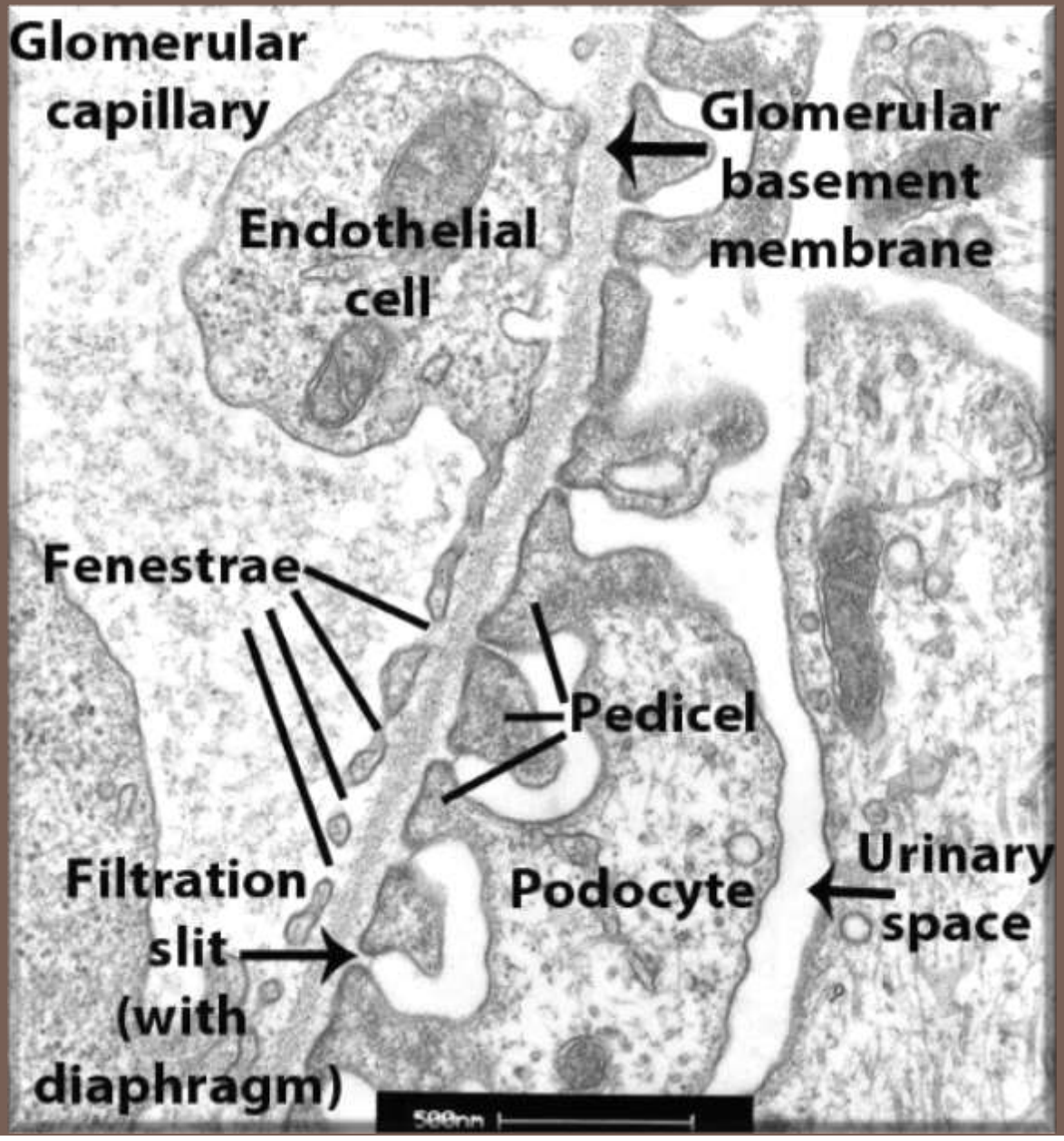
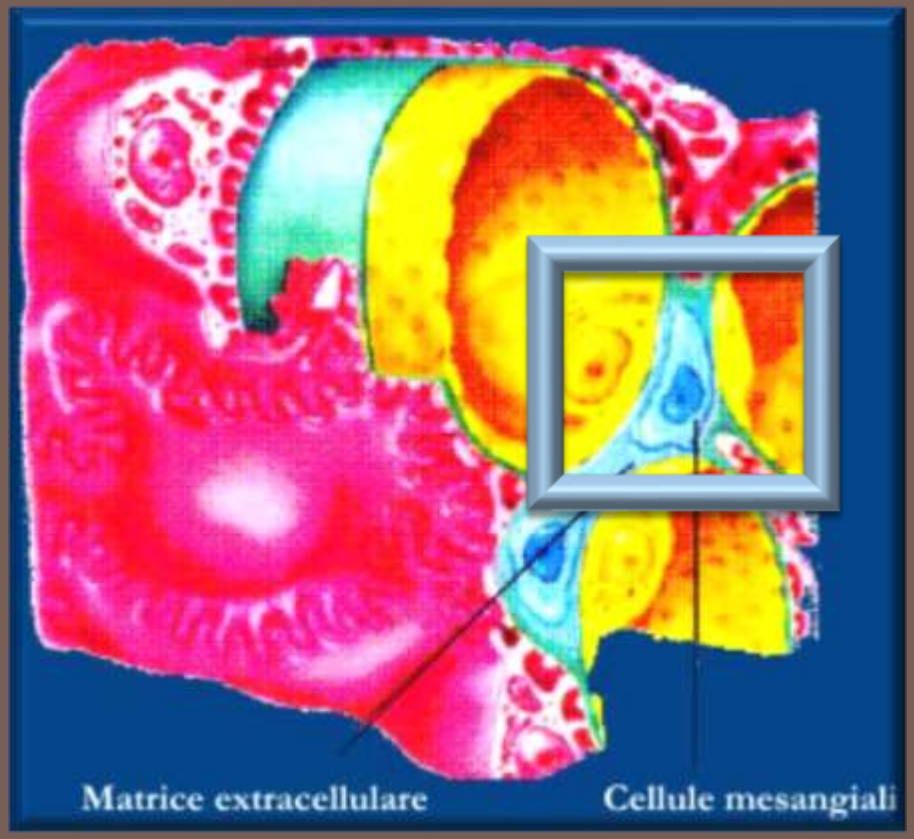
Microscopia Elettronica Glomerulo

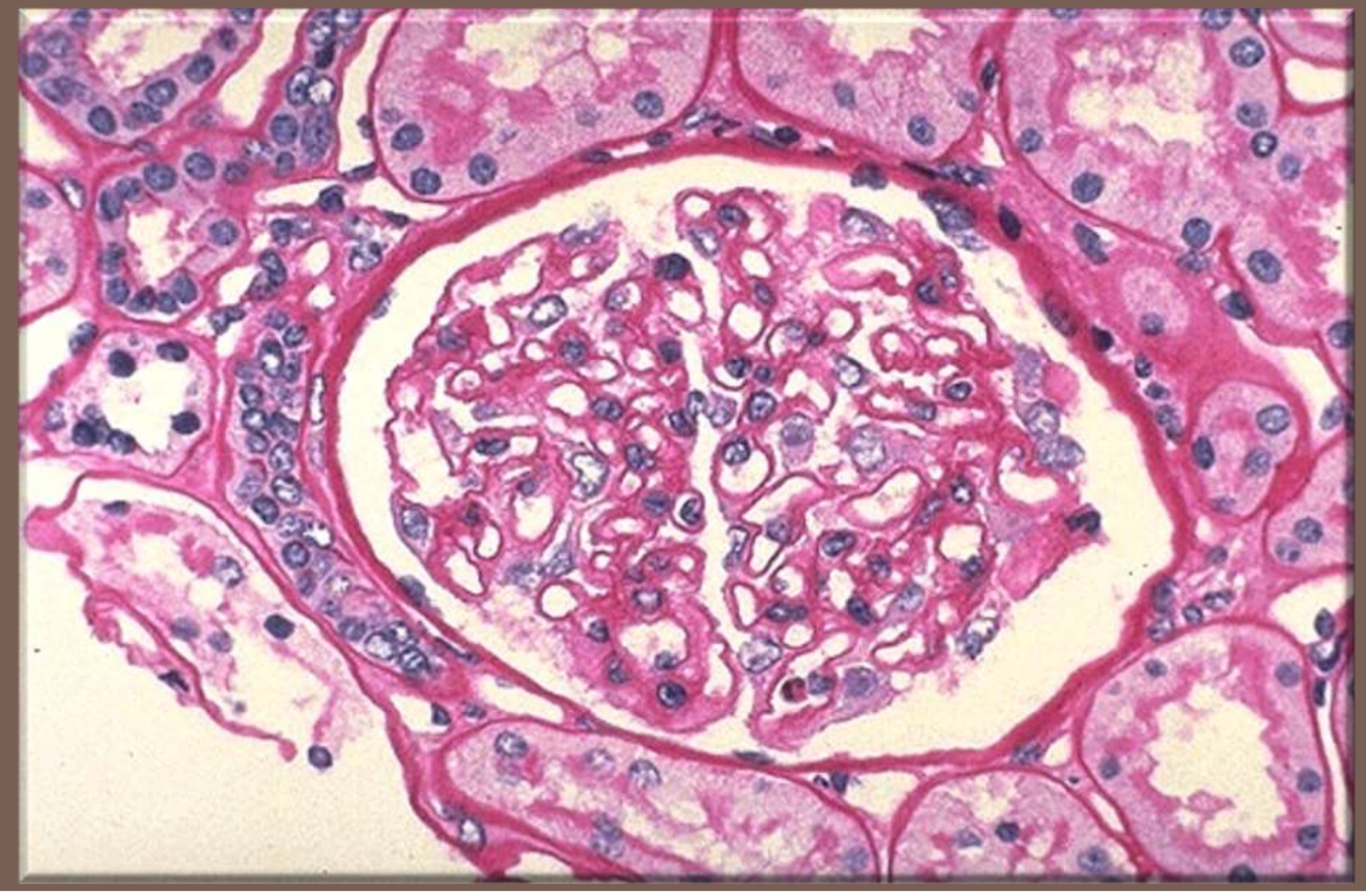


Microscopia Elettronica Glomerulo

1) Sostegno capillari glomerulari
2) Capacità contrattile
3) Recettori angiotensina II



Cellule Mesangiali



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Istologia

FISIOLOGIA RENALE

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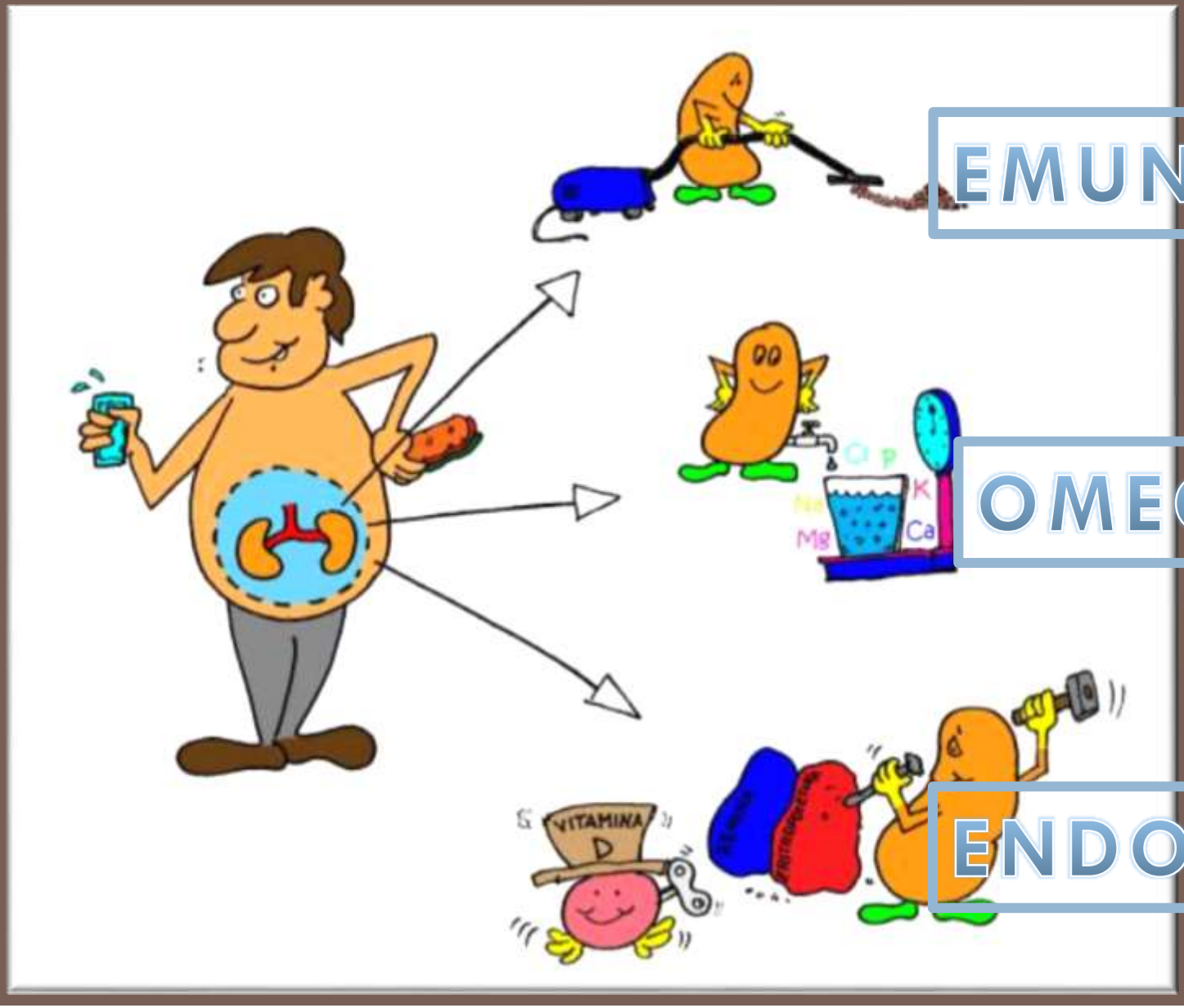
1b) FISIOLOGIA



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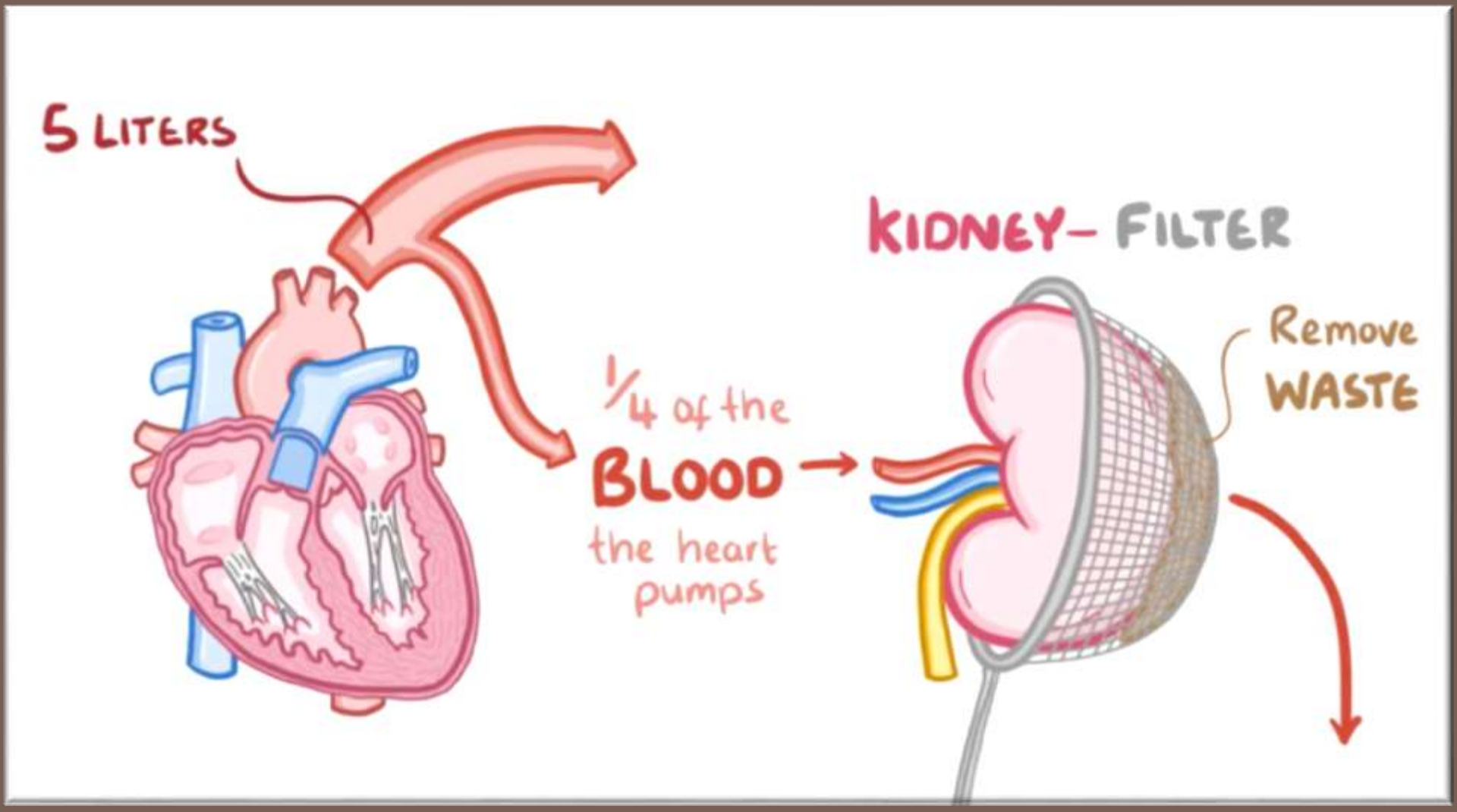
Funzioni dei Reni



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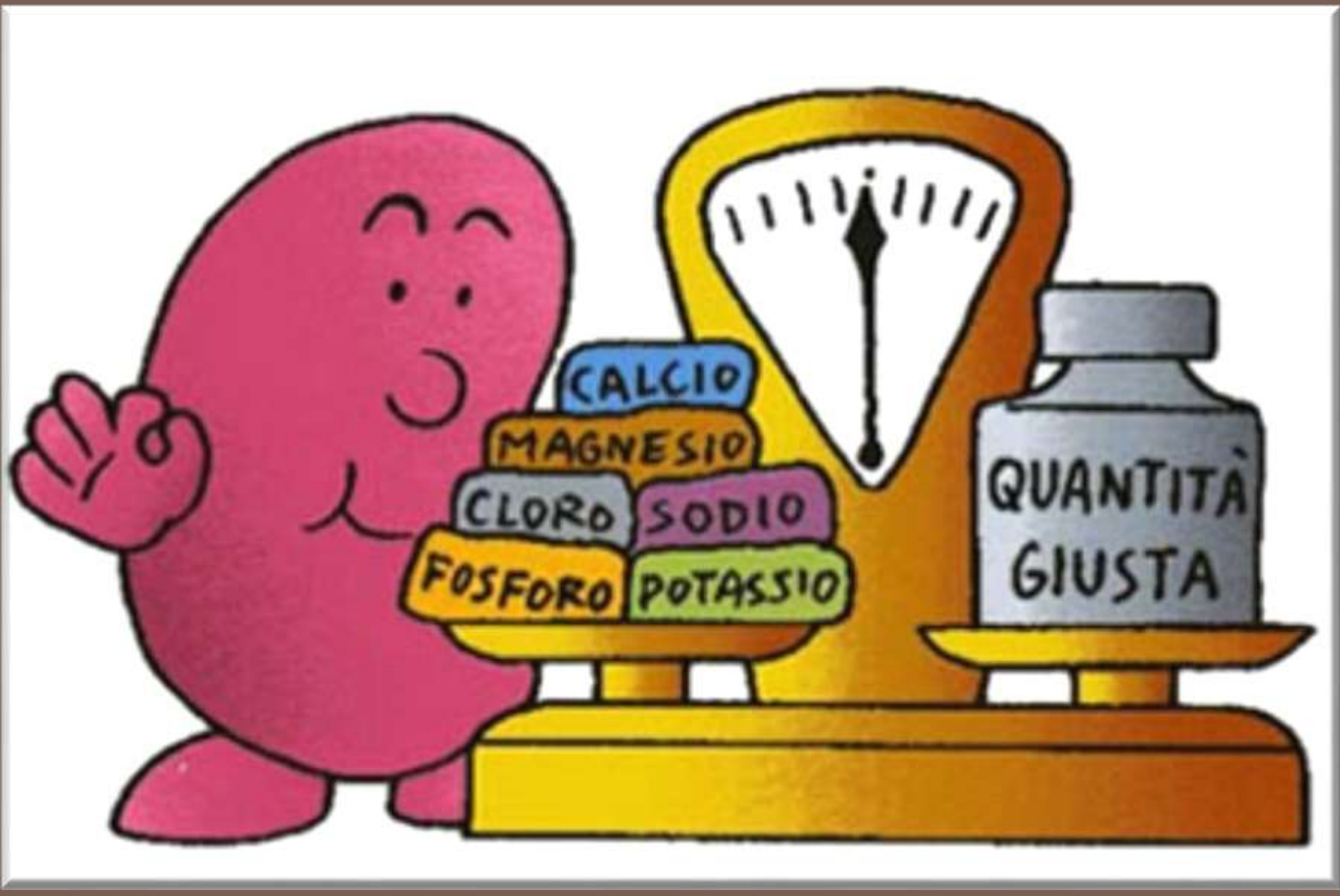
FUNZIONE EMUNTORIA



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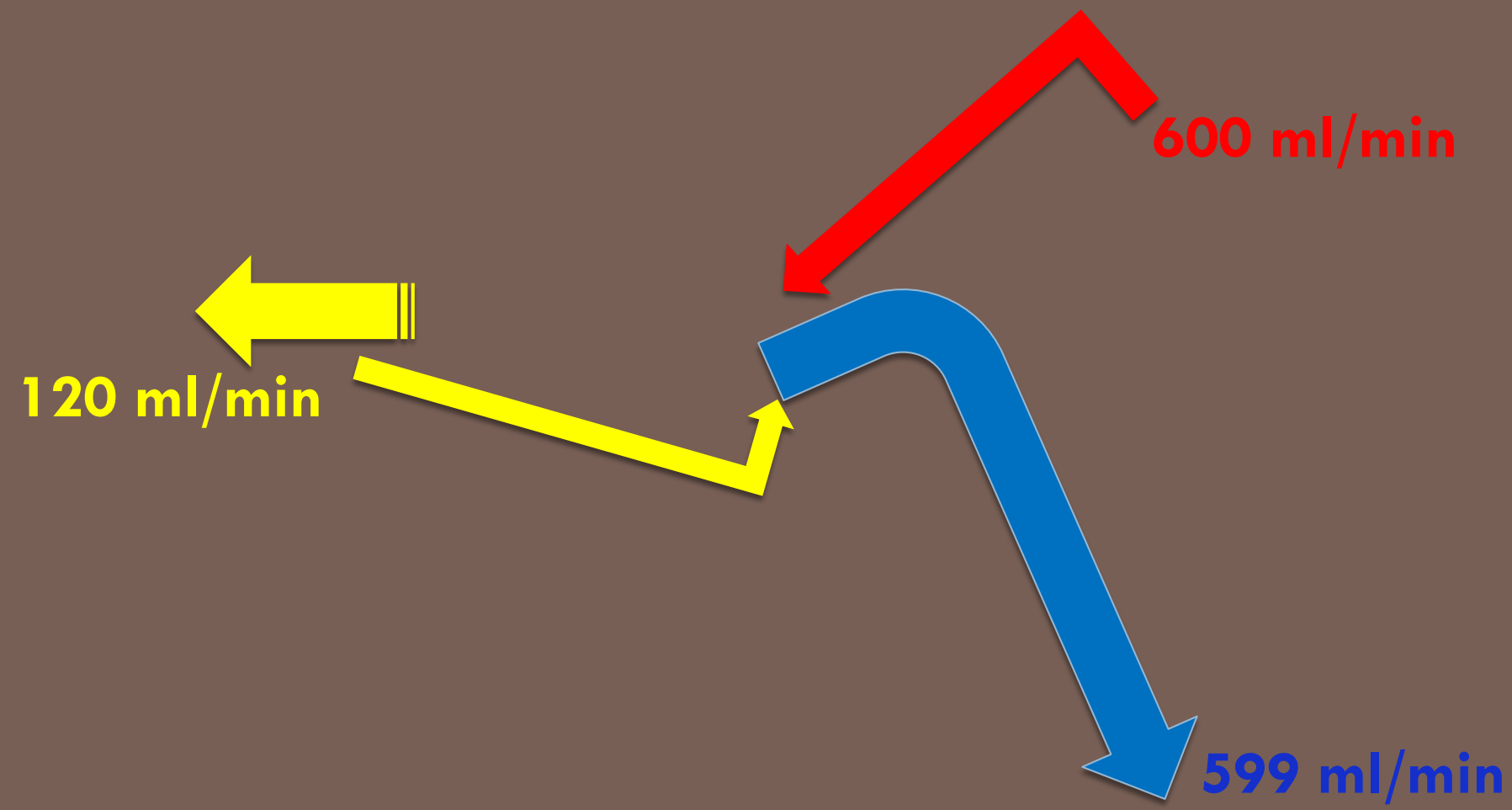
Omeostasi renale



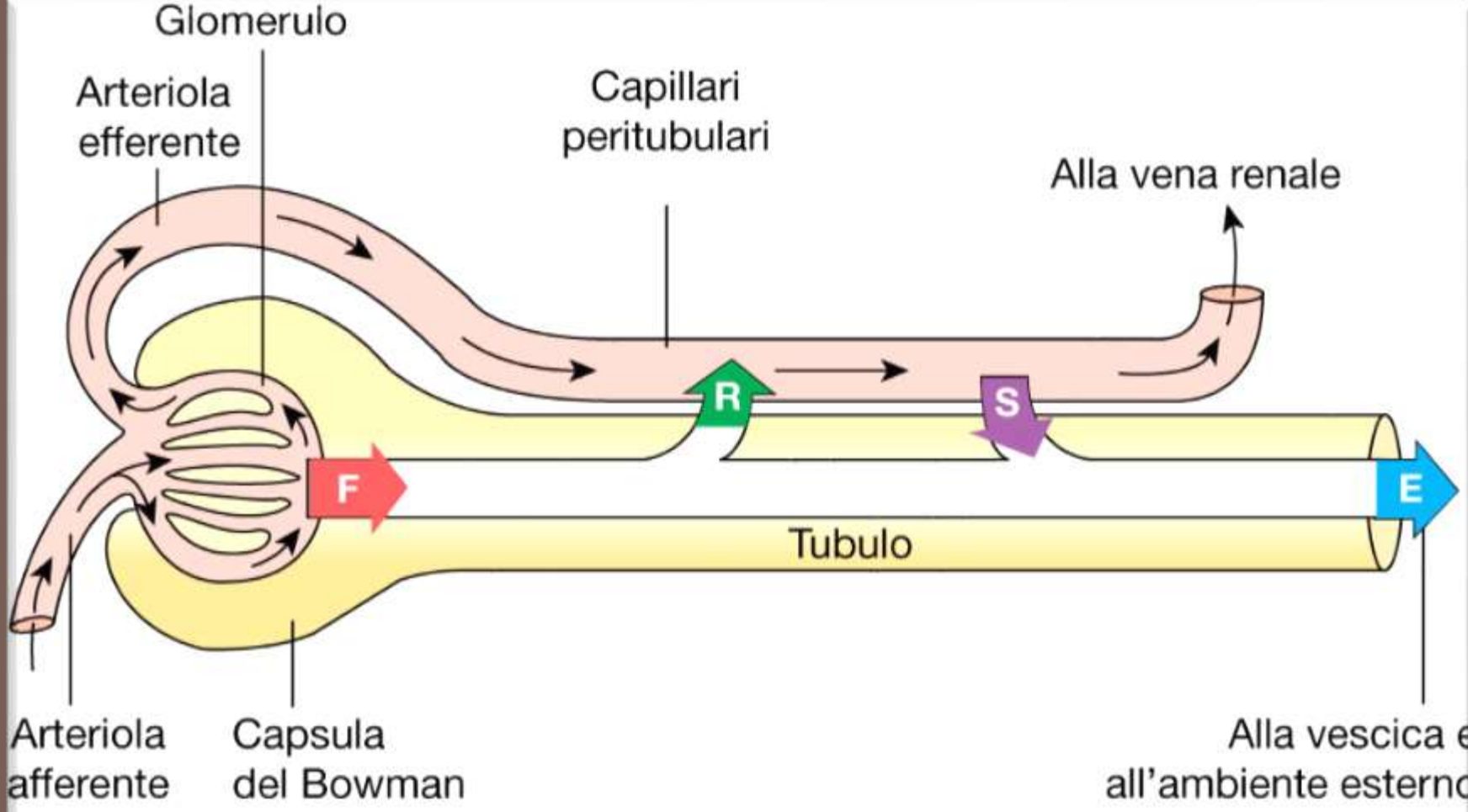
Come si formano le urine?

- FILTRAZIONE GLOMERULARE (120 ml/min)

- RIASSORBIMENTO DI ACQUA E SOLUTI

- SECRESIONE SELETTIVA DI ALCUNE SOSTANZE

Come si formano le urine?



Quantità filtrata	–	quantità riassorbita	+	quantità secreta	=	Quantità di soluto escreta
F		R		S		E

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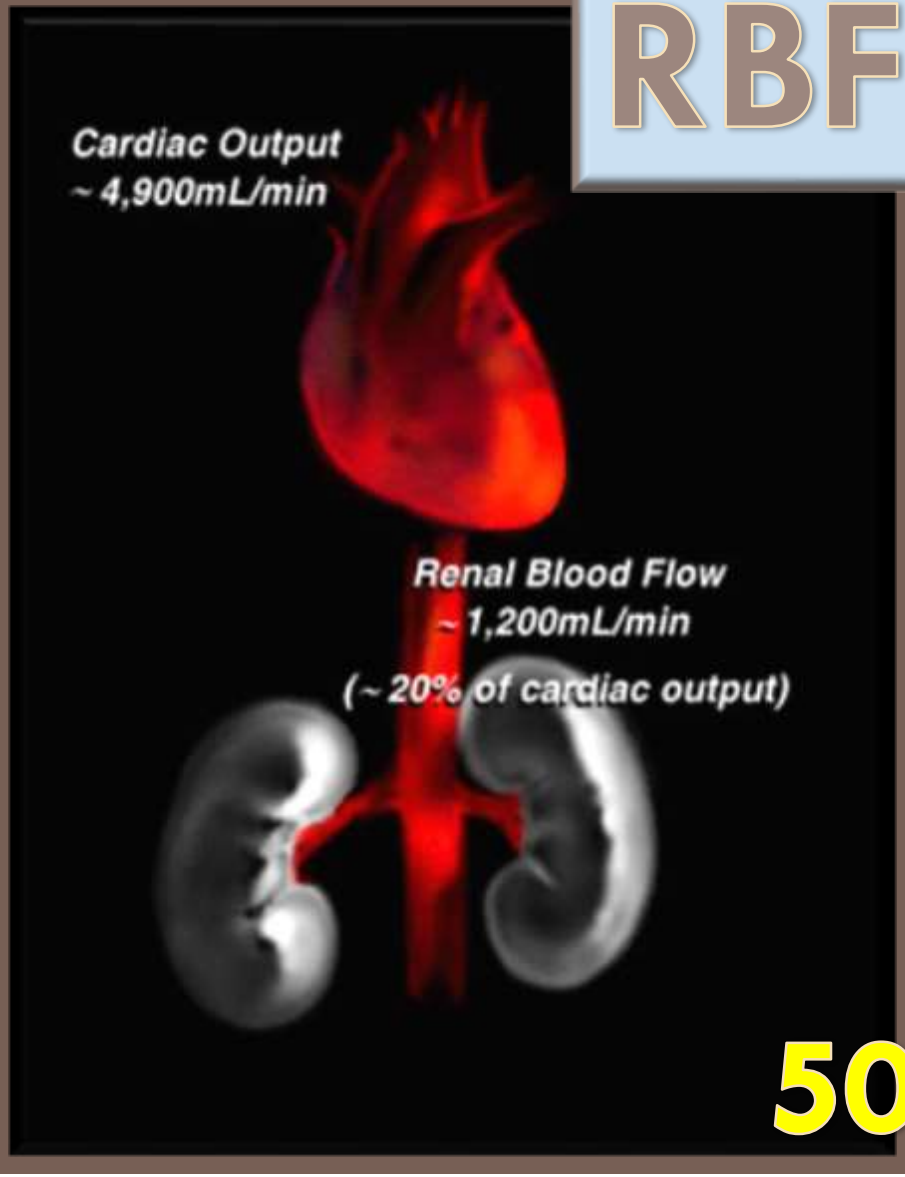
FUNZIONI DEL NEFRONE

RBF:1728 L/24h



50,5 milioni di litri

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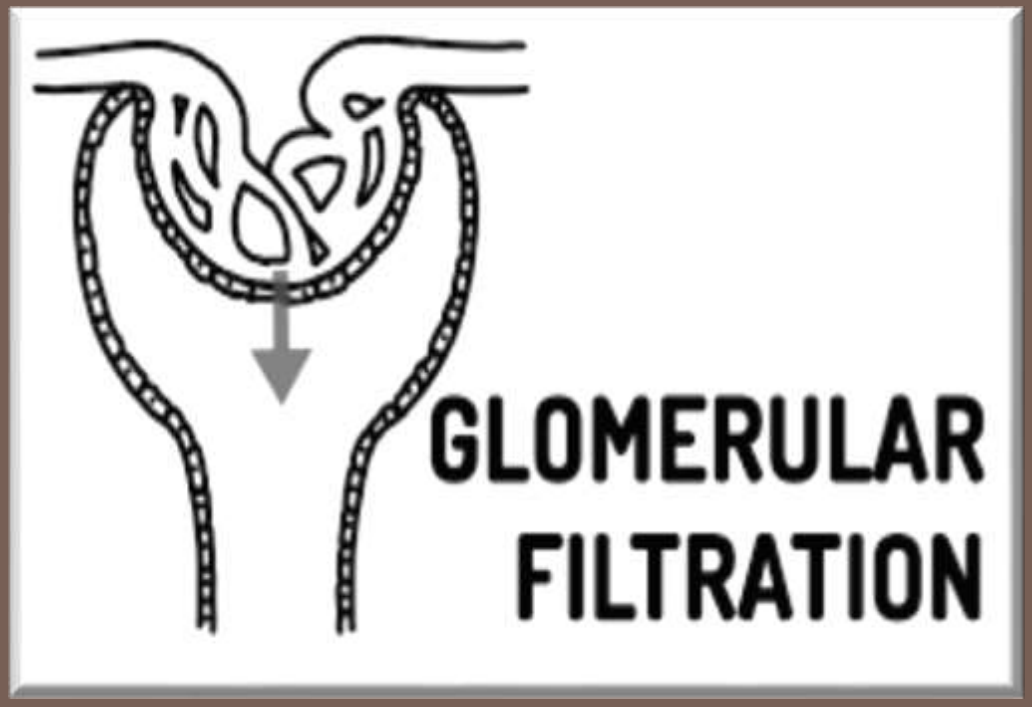
QUANTO SANGUE PASSA NEI RENI?

GFR:150 L/24h



5,5 milioni di litri

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QUANTO FILTRANO I RENI?

Diuresi: 1 L/24h

30.000 litri

QUANTA PIPI' HANNO PRODOTTO I SUOI RENI?

Acqua

- Quantità filtrata: 150 L/24h

- quantità escreta: 1,5 L/24h

- Riassorbimento: 99 %

Sodio

- Quantità filtrata: 630 g/24h

- Quantità escreta: 3,2 g/24h

- Riassorbimento: 99,5 %

Glucosio

- Quantità filtrata: 180 g/24h
- Quantità escreta: 0 g/24h
- Riassorbimento: 100 %

Urea

- Quantità filtrata: 56 g/24h
- Quantità escreta: 28 g/24h
- Riassorbimento: 50 %

Albumina

- AI RENI ARRIVANO: 37 Kg/24h
- QUANTITÀ FILTRATA: 1,3 g/24h
- QUANTITA' ESCRETA: 15 MG/24h
- Riassorbimento: 99 %

PERCHE' IL NEFRONE

LAVORA TANTO ?

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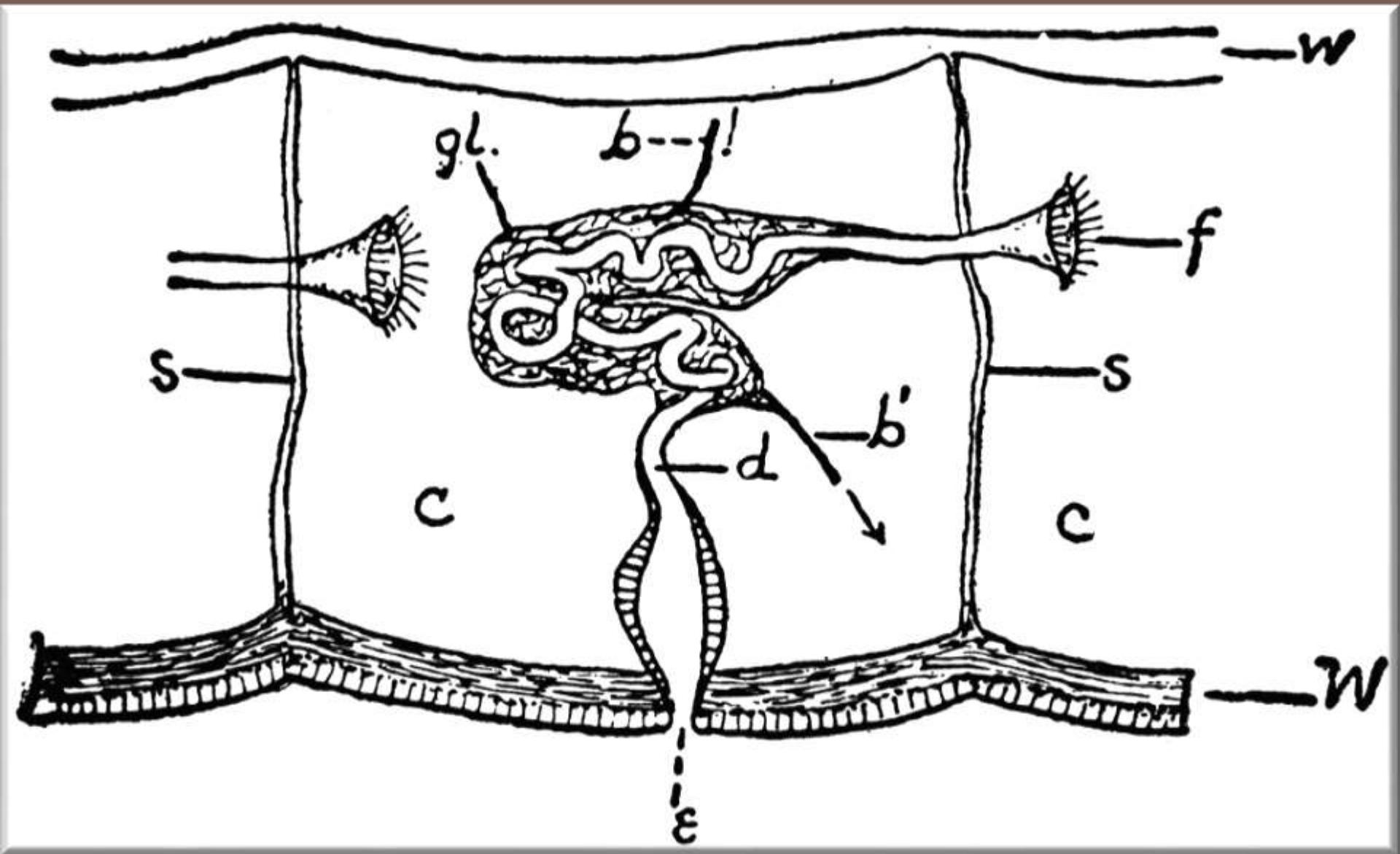
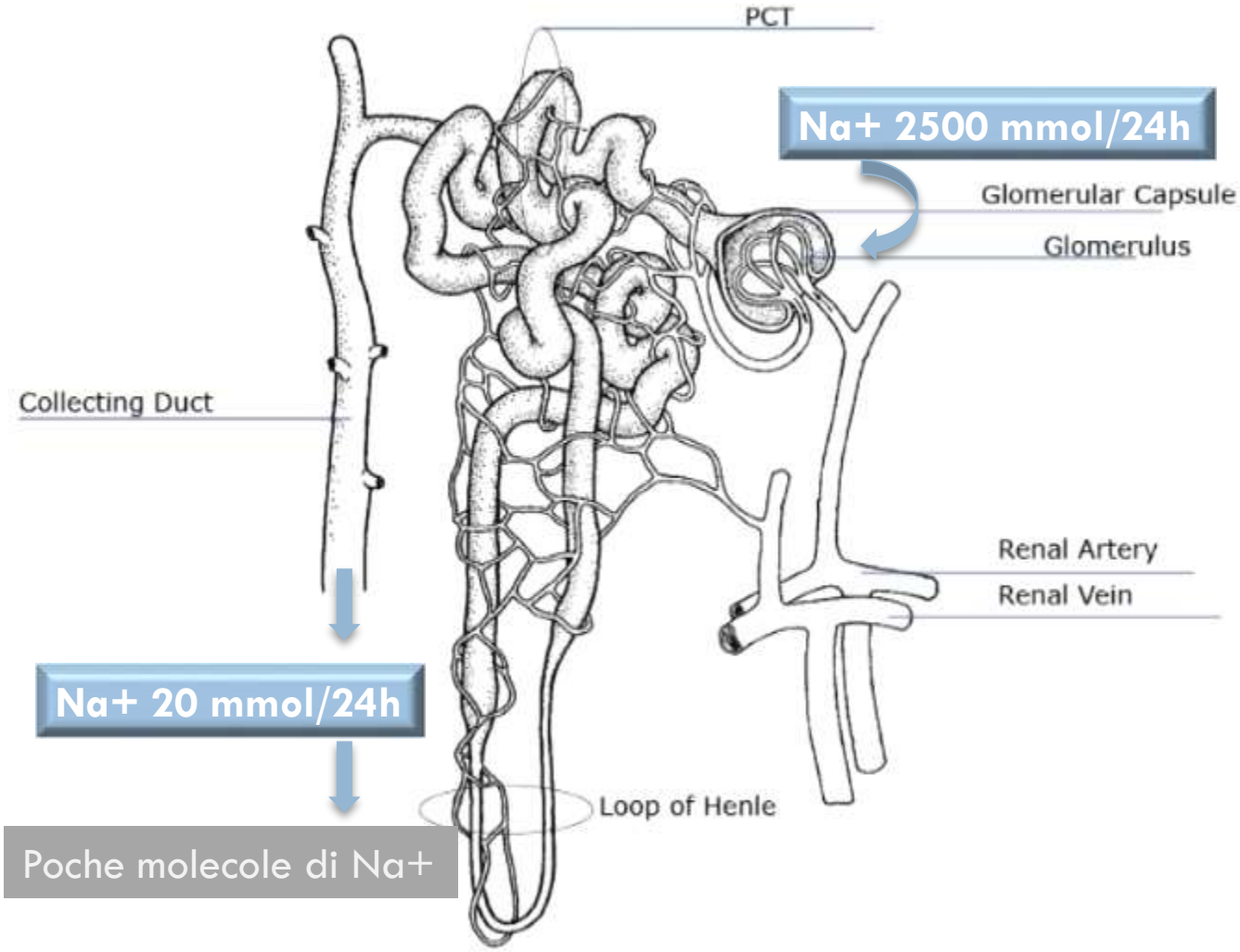

w
gl.
b--f!
f
s
s
b'
d
c
c
W
ε



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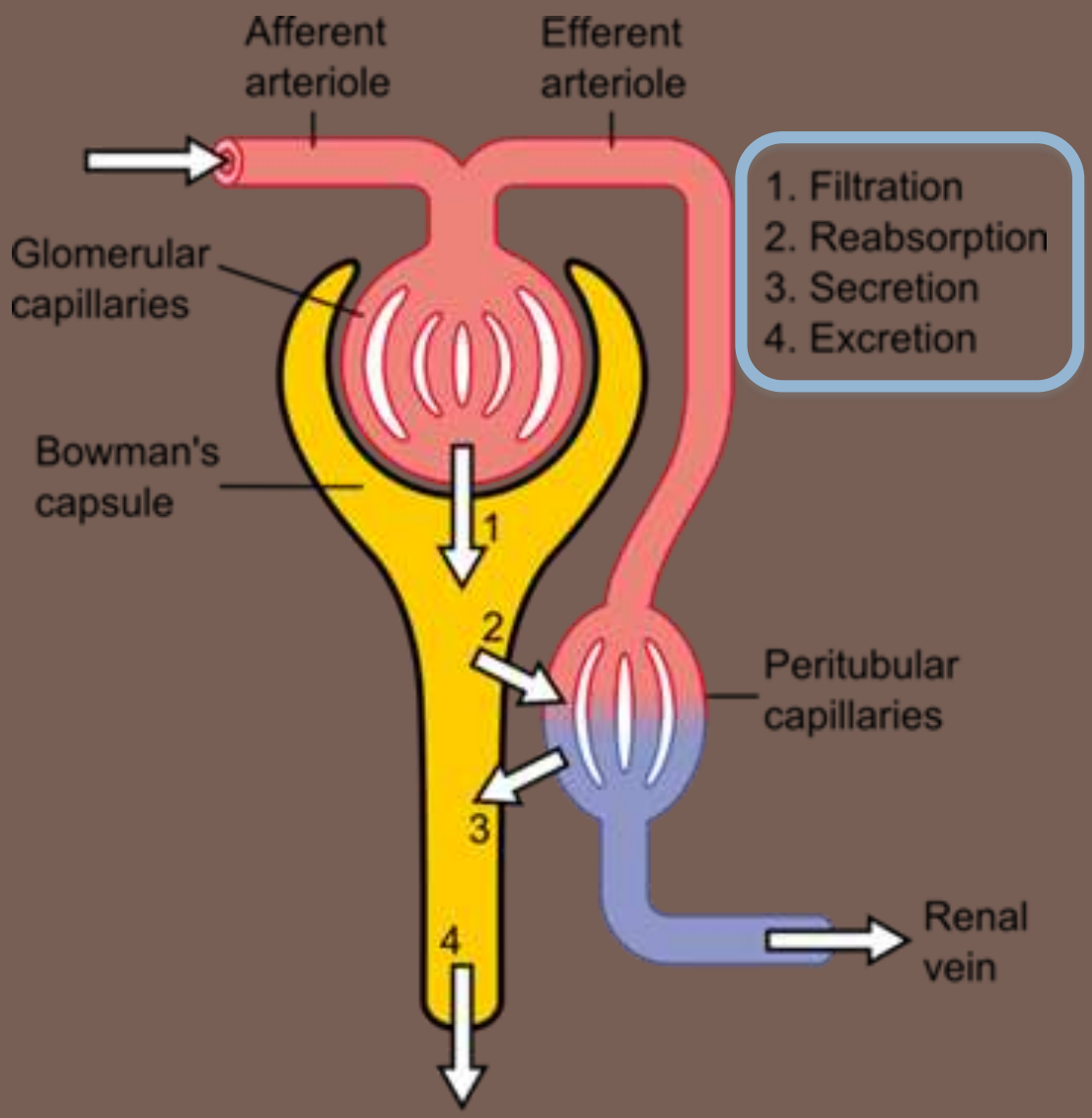
SUPERLAVORO NEFRONE



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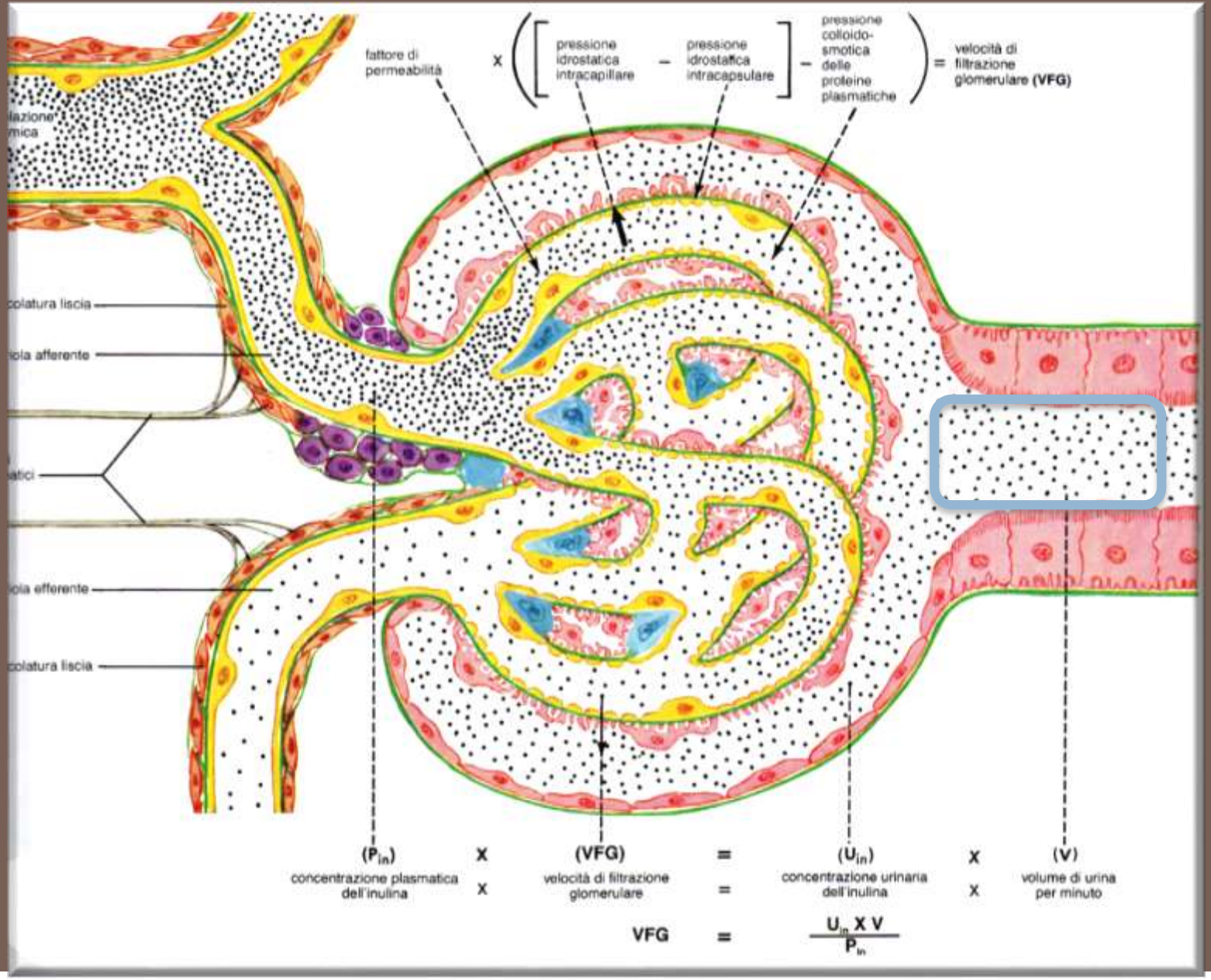
FUNZIONE NEFRONICA



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LA FILTRAZIONE GLOMERULARE

Legge di Starling

$$PF = Kf(Pc - Pi) - \sigma(\pi c - \pi i)$$

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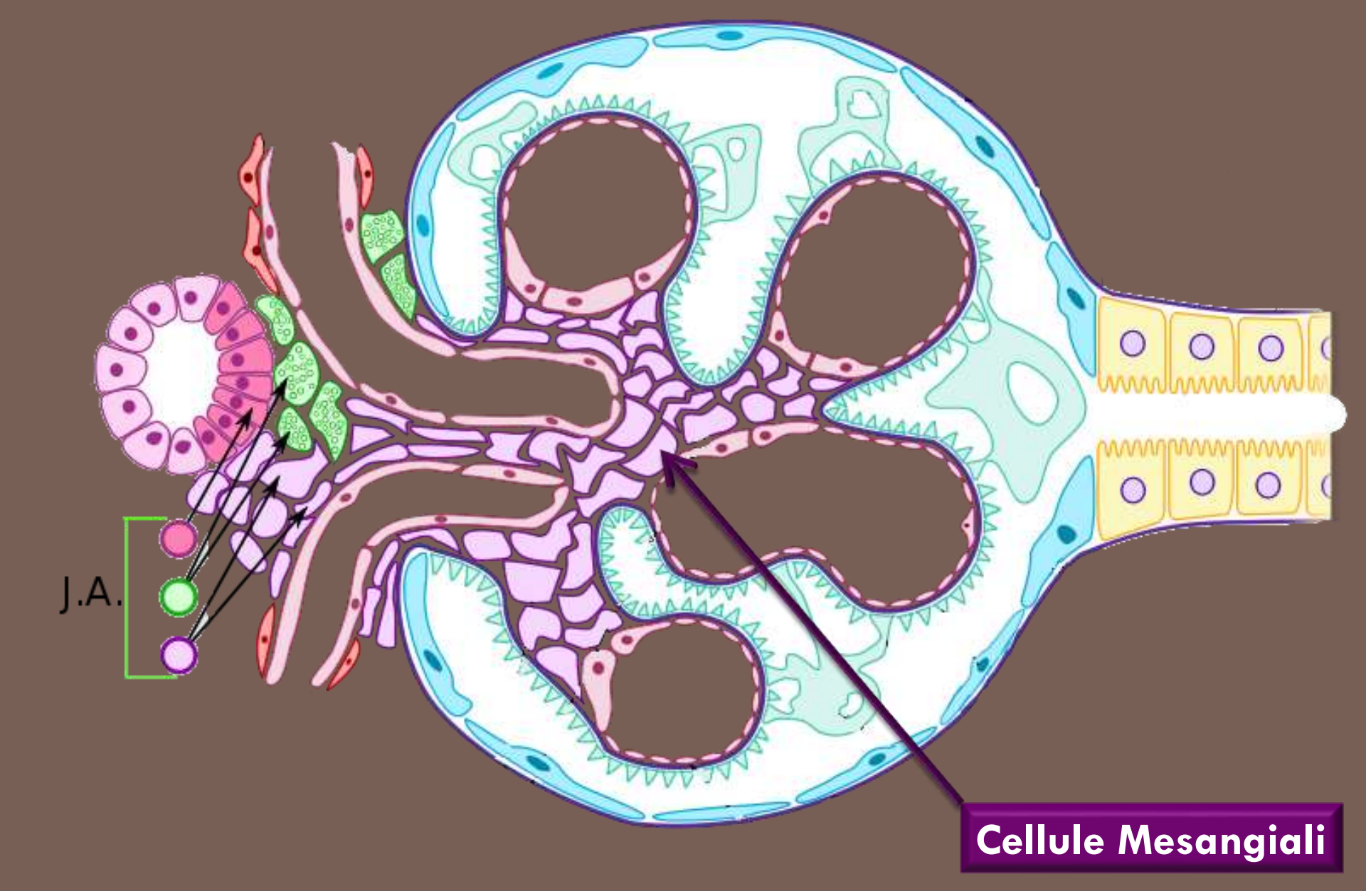
Ernest Starling

K_f dipende da due componenti:

1. L'area della superficie dei capillari glomerulari disponibili per la filtrazione.

2. Permeabilità della Barriera di Filtrazione.



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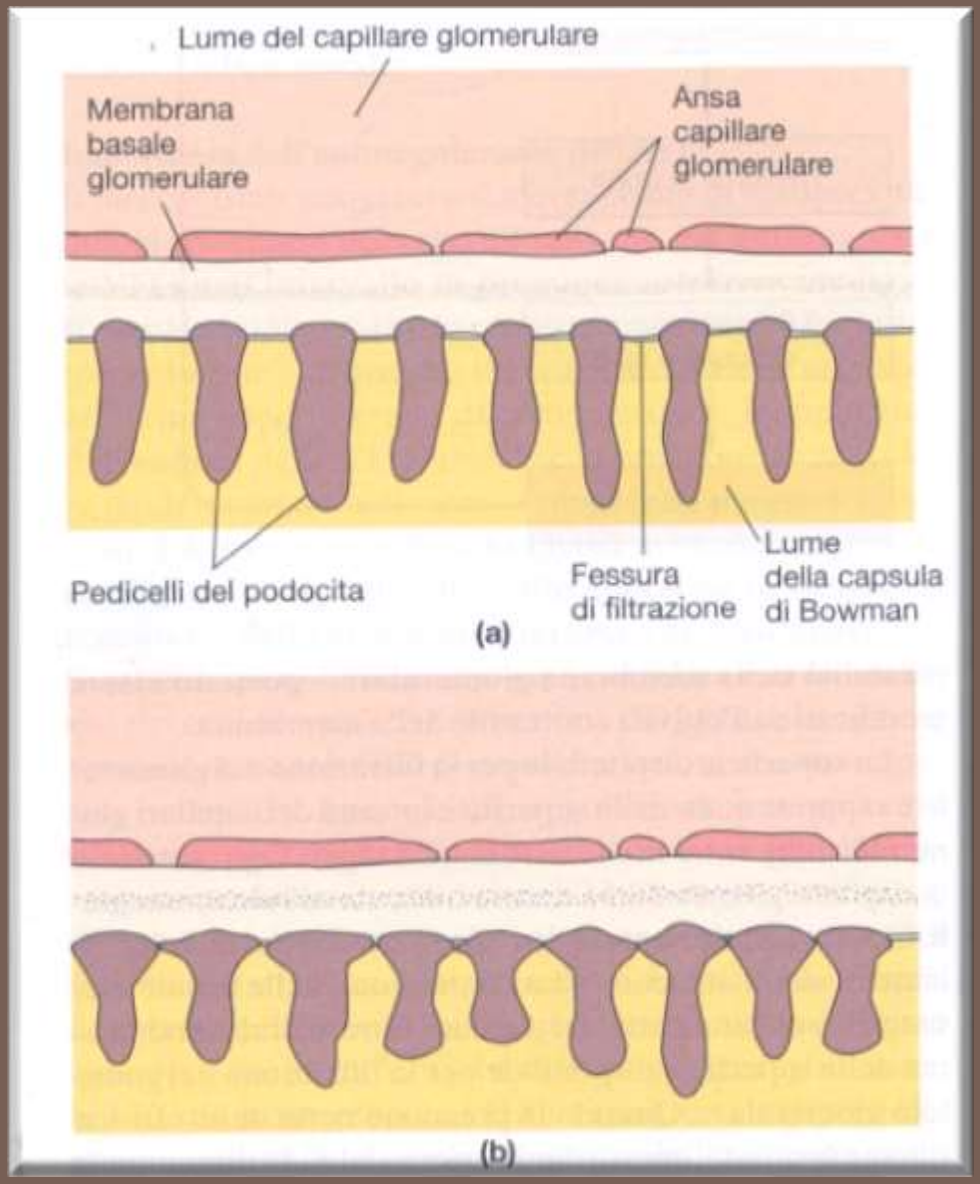
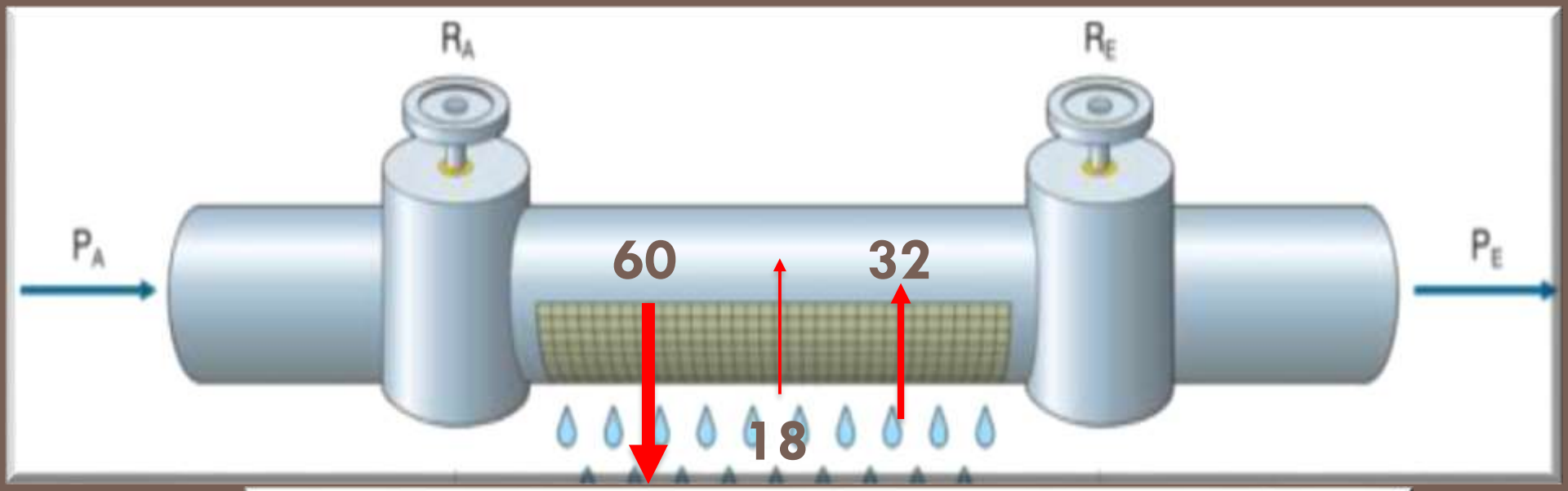
SUPERFICIE DI FILTRAZIONE


Lume del capillare glomerulare
Membrana basale glomerulare
Ansa capillare glomerulare
Pedicelli del podocita
Fessura di filtrazione
Lume della capsula di Bowman
(a)
(b)

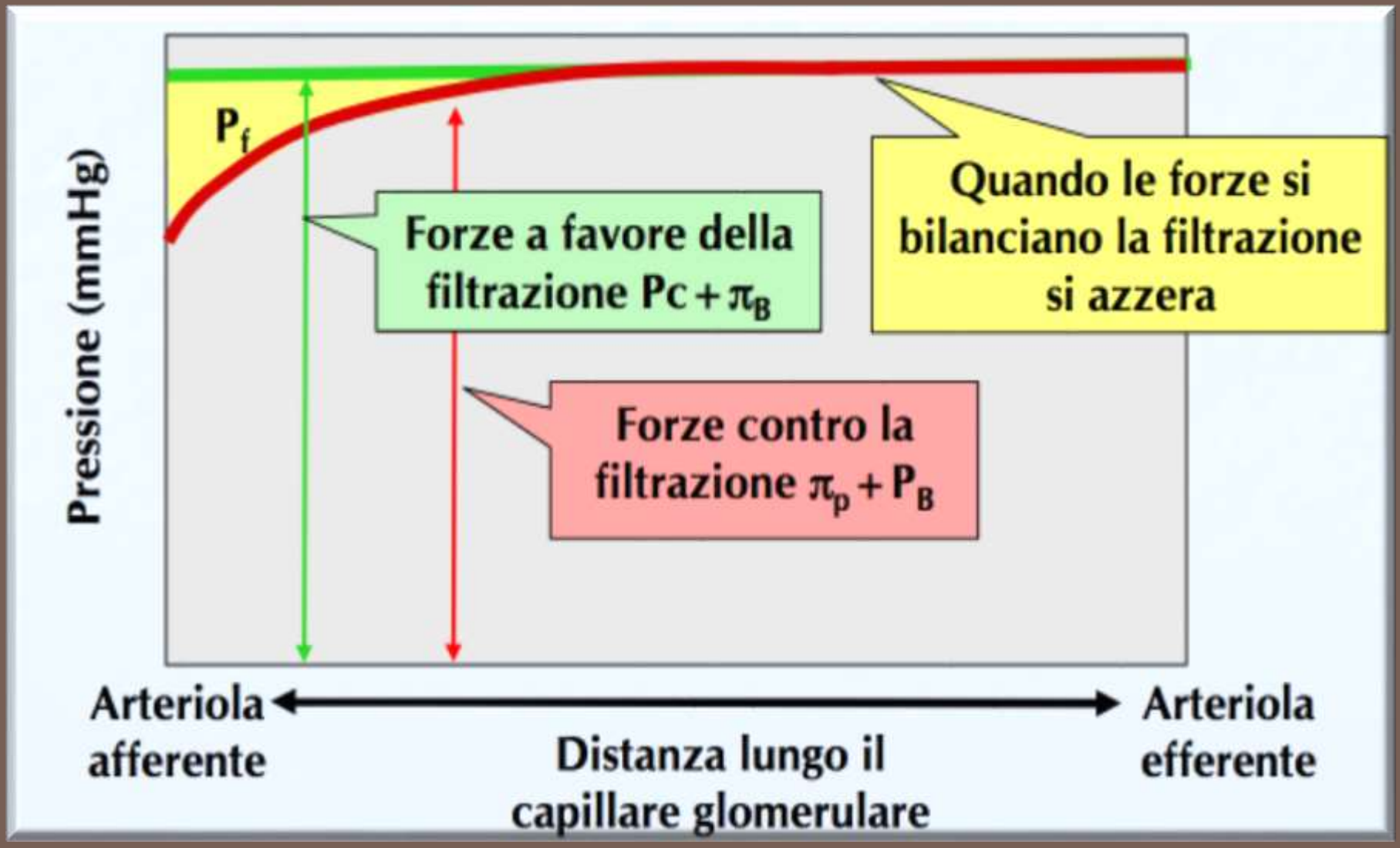
PERMEABITA’



Legge di Starling

PF=(60-18)-(32-0)=10

PF=10 mmHg

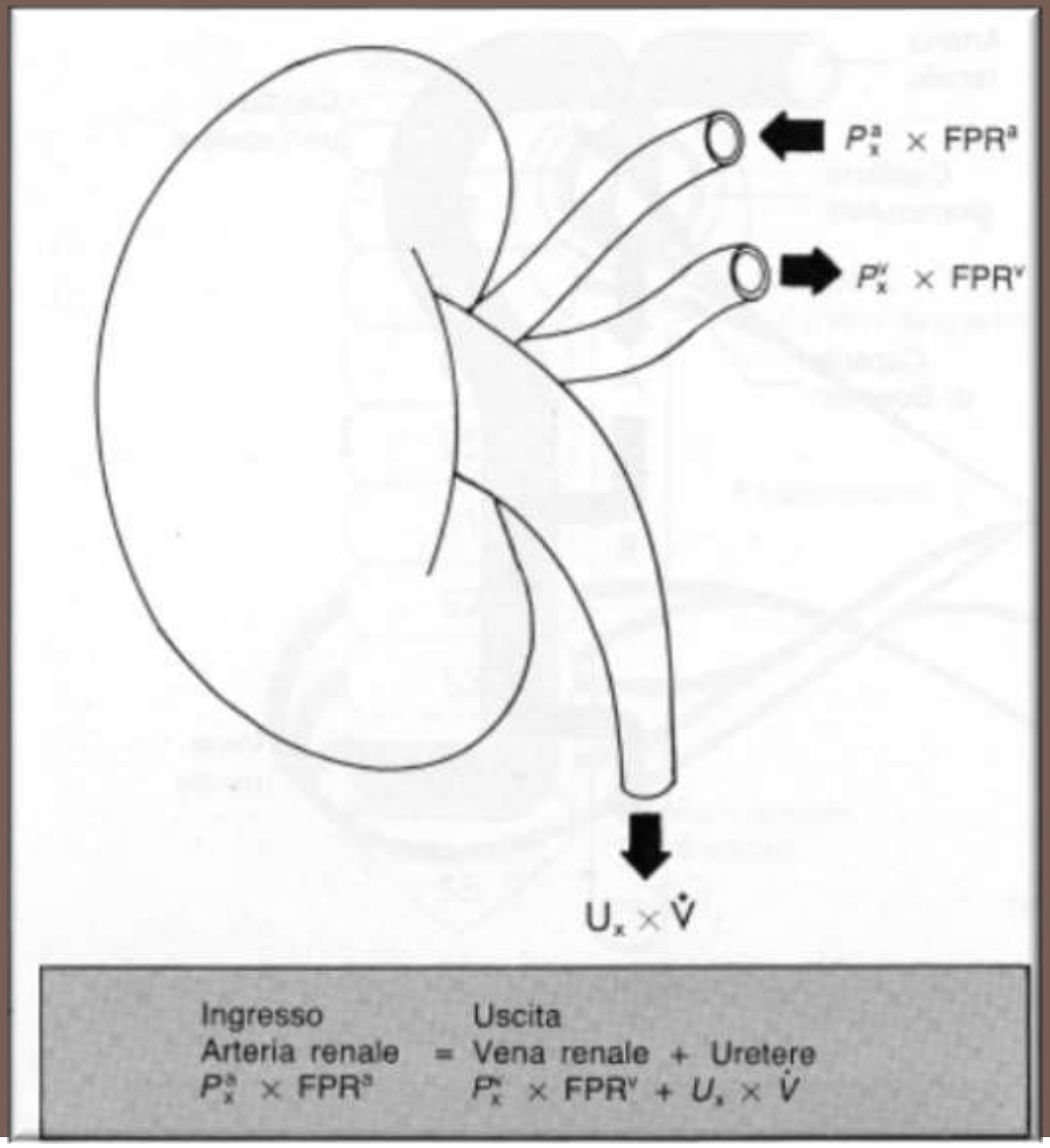


Modificazione delle forze di Starling

Come facciamo a sapere quanto filtrano i reni ?

Clearance renale

Principio di conservazione della massa



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Clearance renale

Il volume di plasma depurato da una sostanza nell'unità di tempo

$$Cl.\ (a)\ ml/min = \frac{Ua \times V}{Pa}$$

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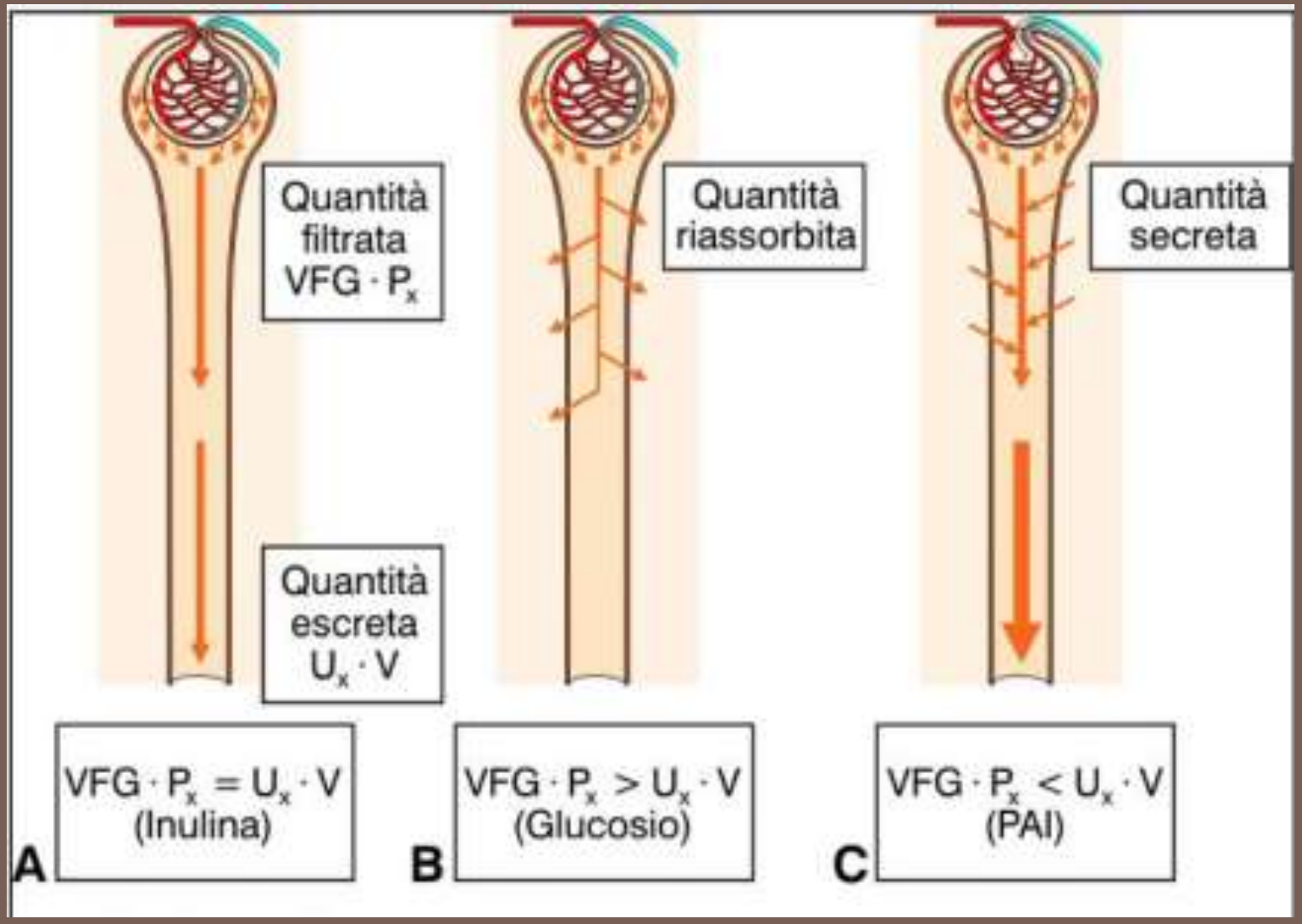
Clearance renale



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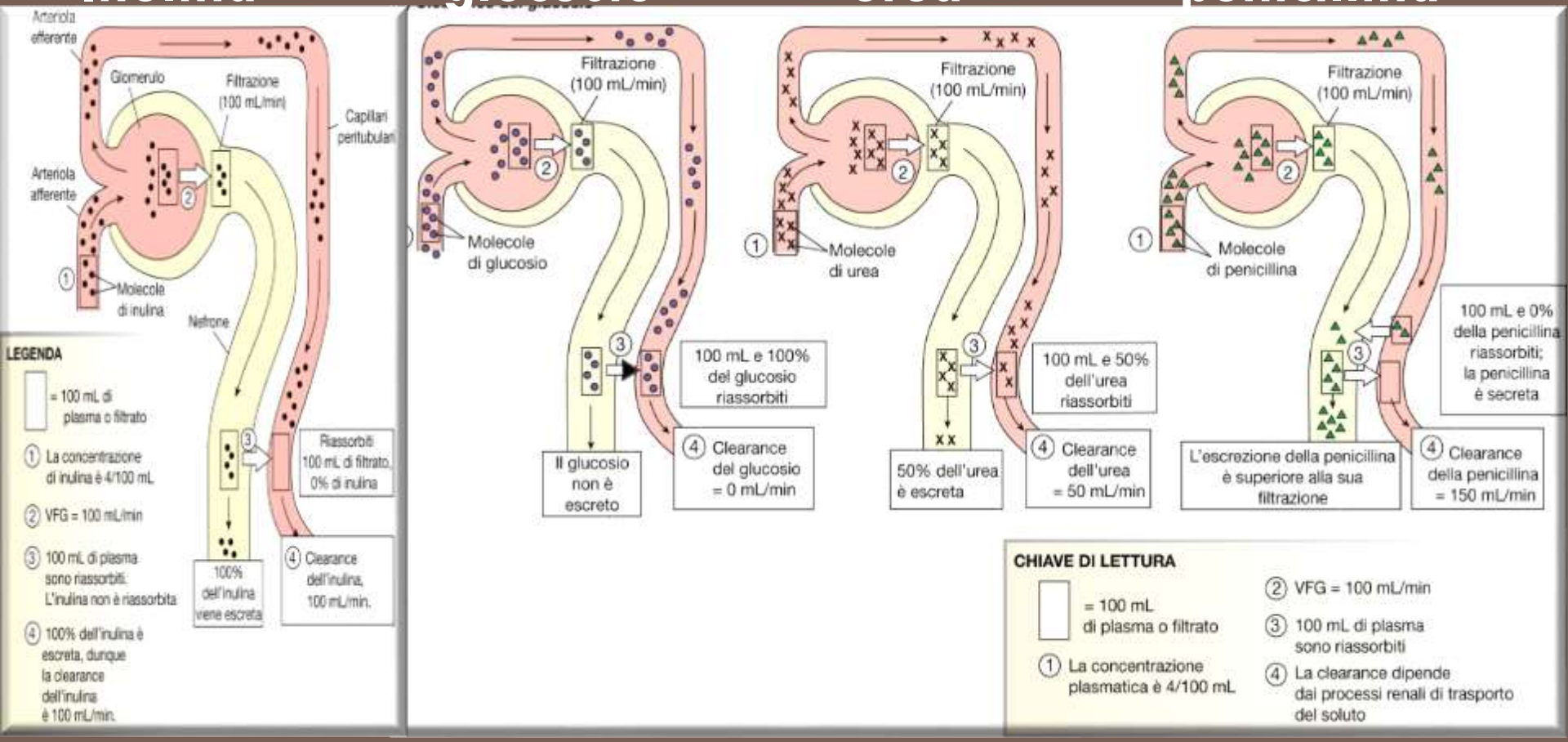
Clearance Inulina



- **A - Filtrate ma non riassorbite (inulina)**
- **B - Filtrate e completamente riassorbite (aminoacidi e glucosio)**
- **C - Filtrate e parzialmente riassorbite (Urea, Na^+, Cl^-, bicarbonato)**
- **D - Filtrate e completamente secrete (acido paraamminoippurico)**
- **E - Filtrate e parzialmente secrete (creatinina)**
- **F - Filtrate, parzialmente riassorbite e parzialmente secrete (penicillina)**

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Clearance renale

1) Liberamente filtrata
2) Non riassorbita
3) Non secreta
4) Non tossica

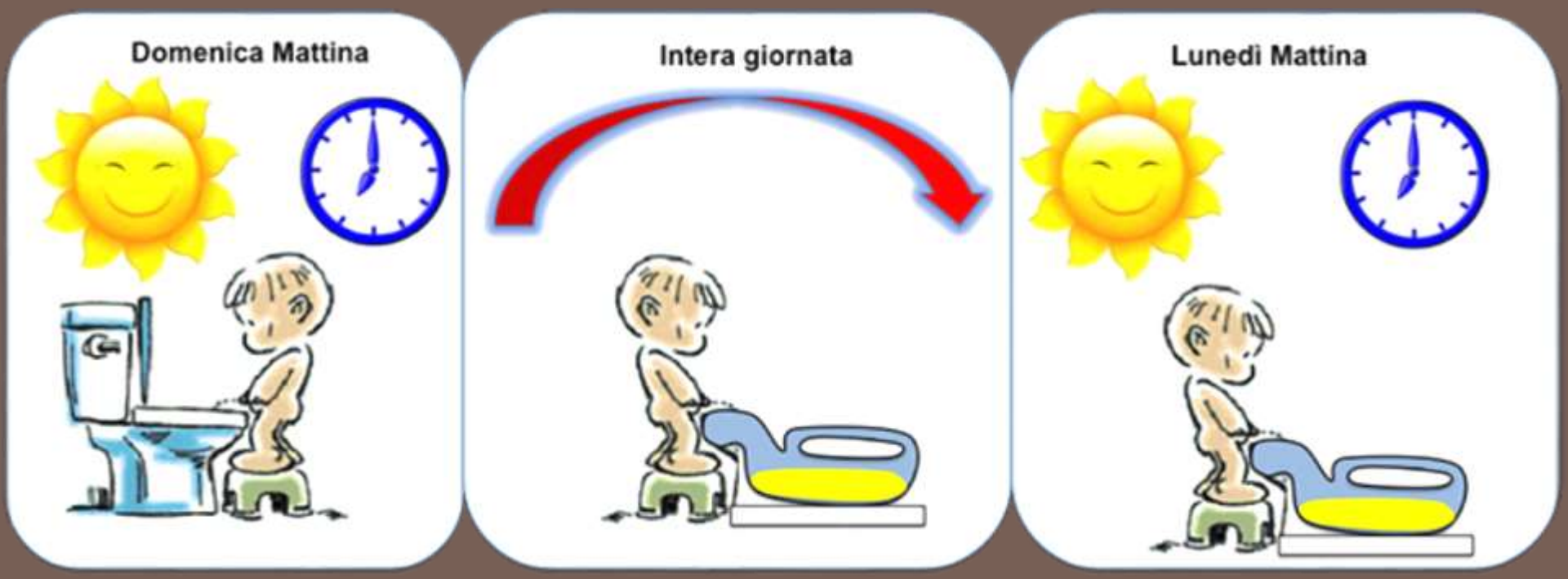
Diuresi=1000 ml

ml/min=1000:1440min/24h=0,69

Ucr = 150 mg/dl

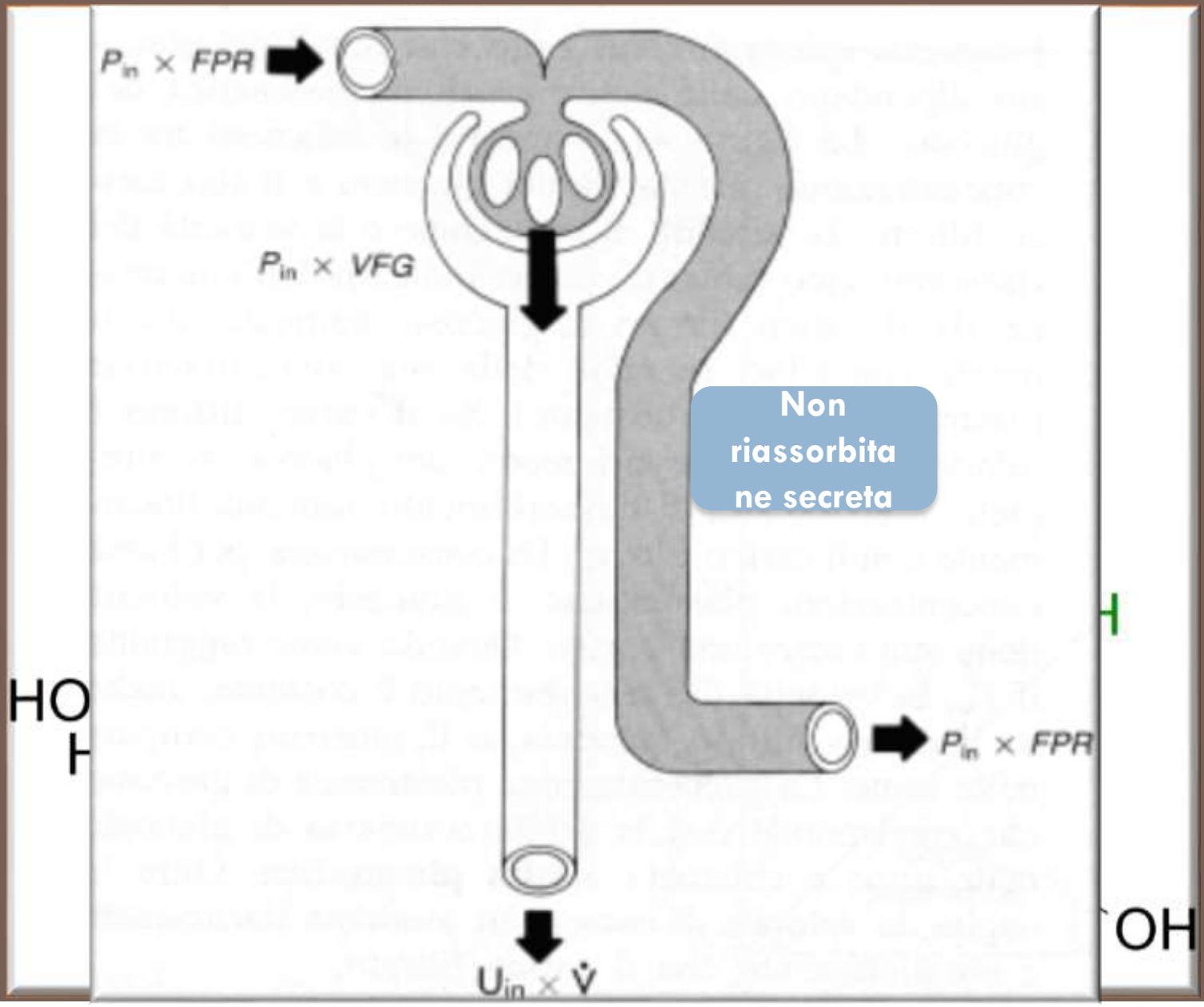
Pcr = 1 mg/dl

$$FG = \frac{150 \times 0{,}69}{1} = 104{,}16$$



E' secreta a livello tubulare

FG sovrastimato (10-20%)



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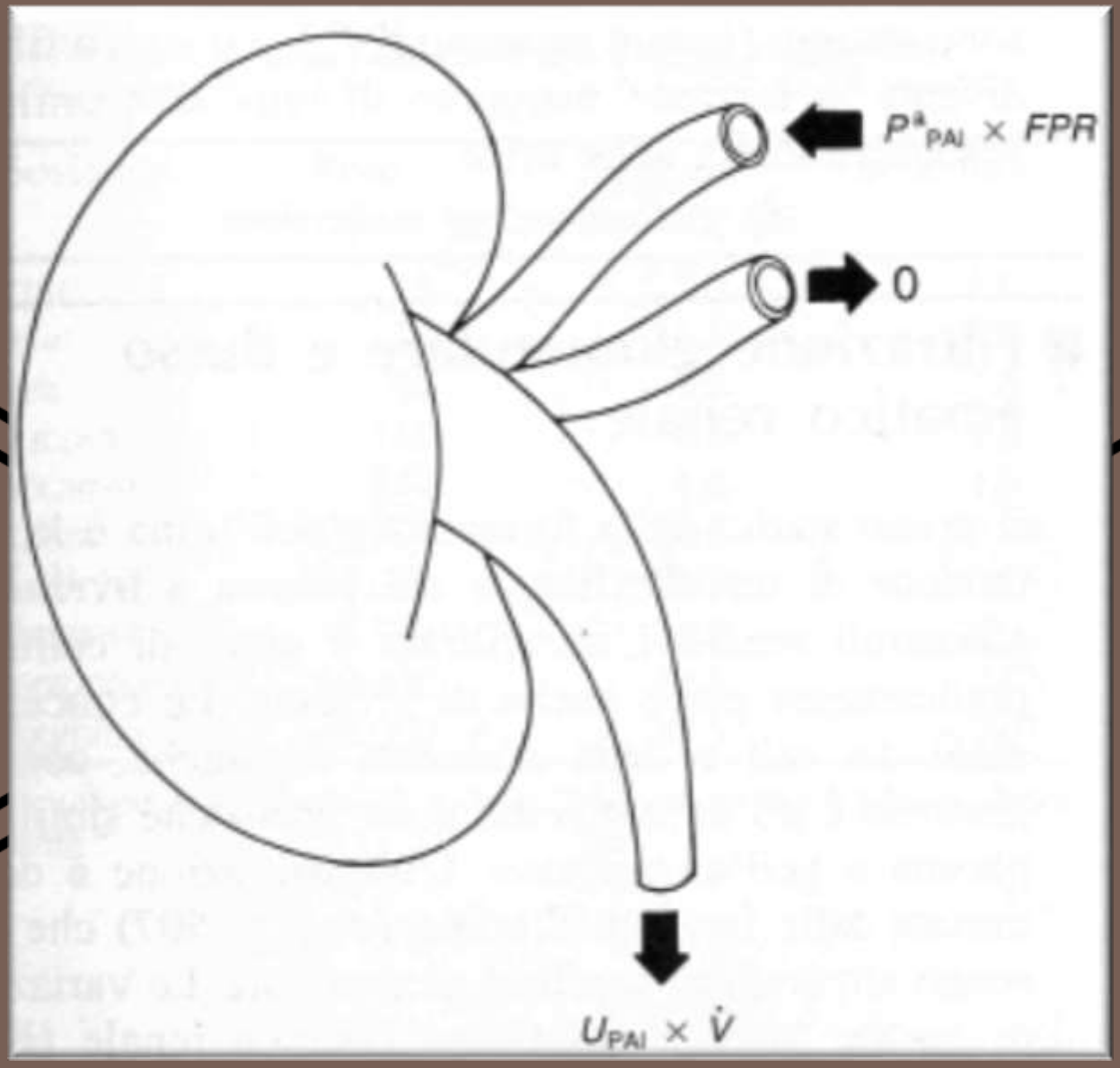
Clearance Inulina



OH

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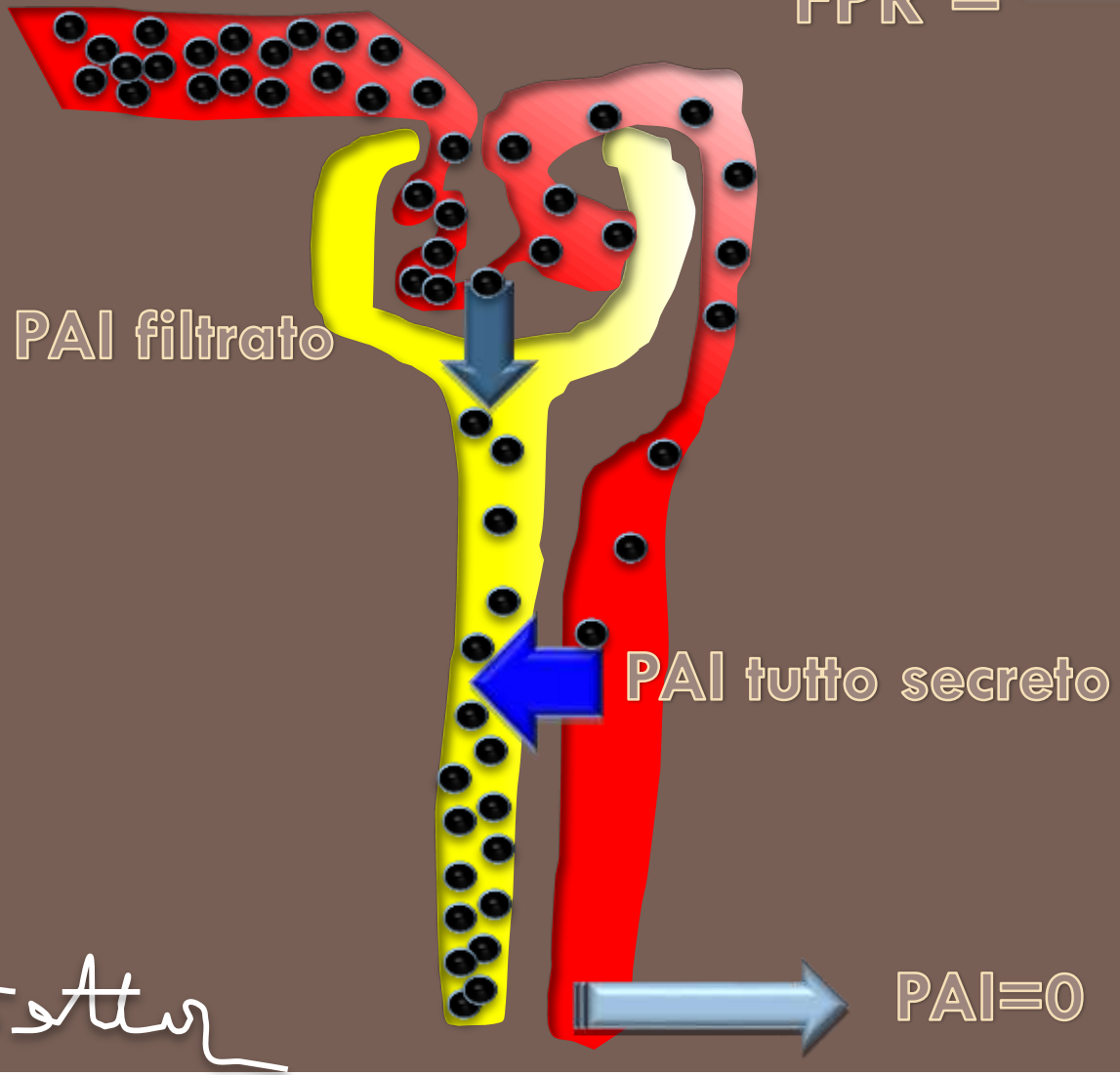
Libetta

Acido Para-Aminoippurico

$$FPR = \frac{U \times V}{P(a) - P(v)}$$



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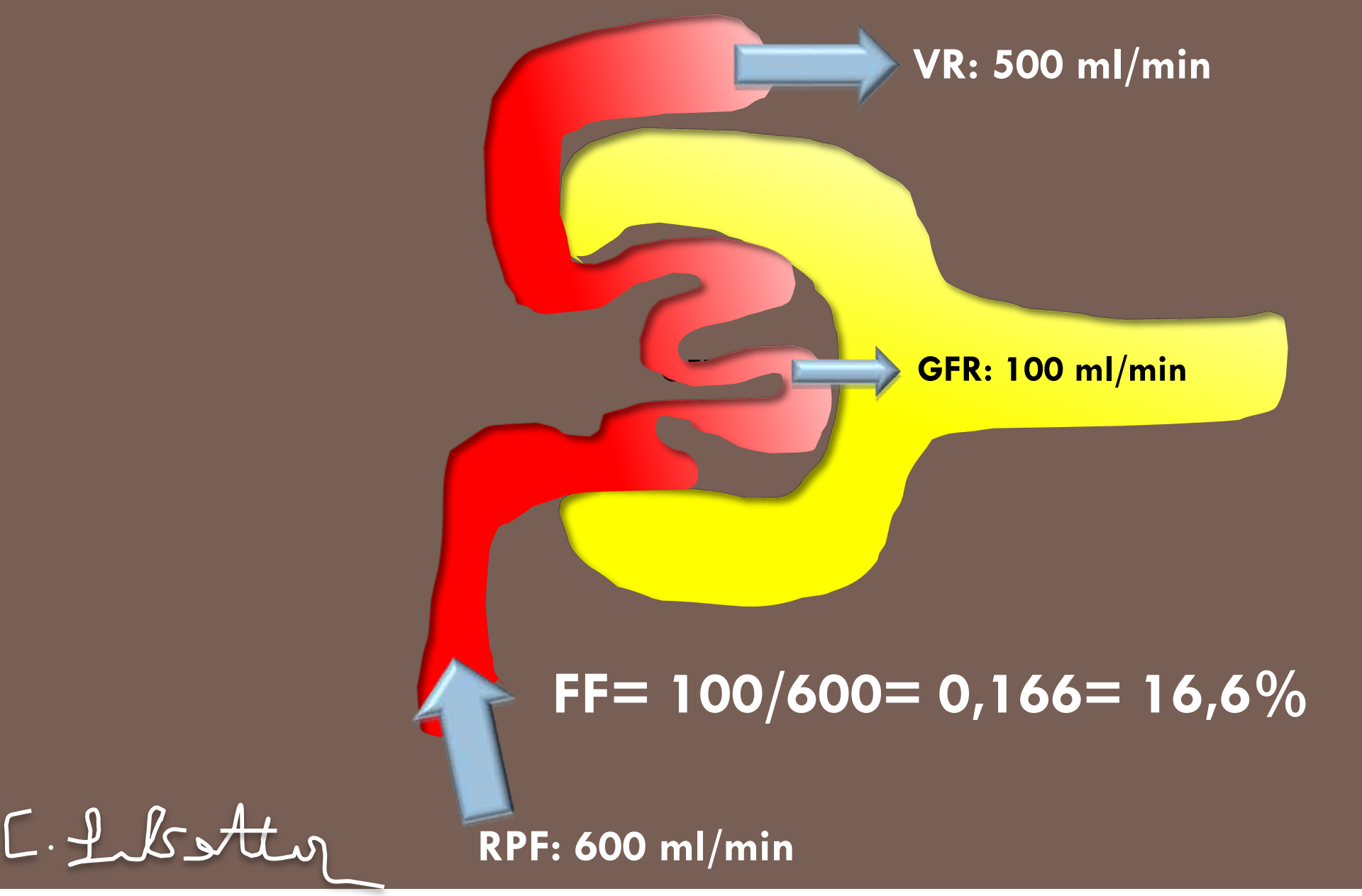
Clearance PAI



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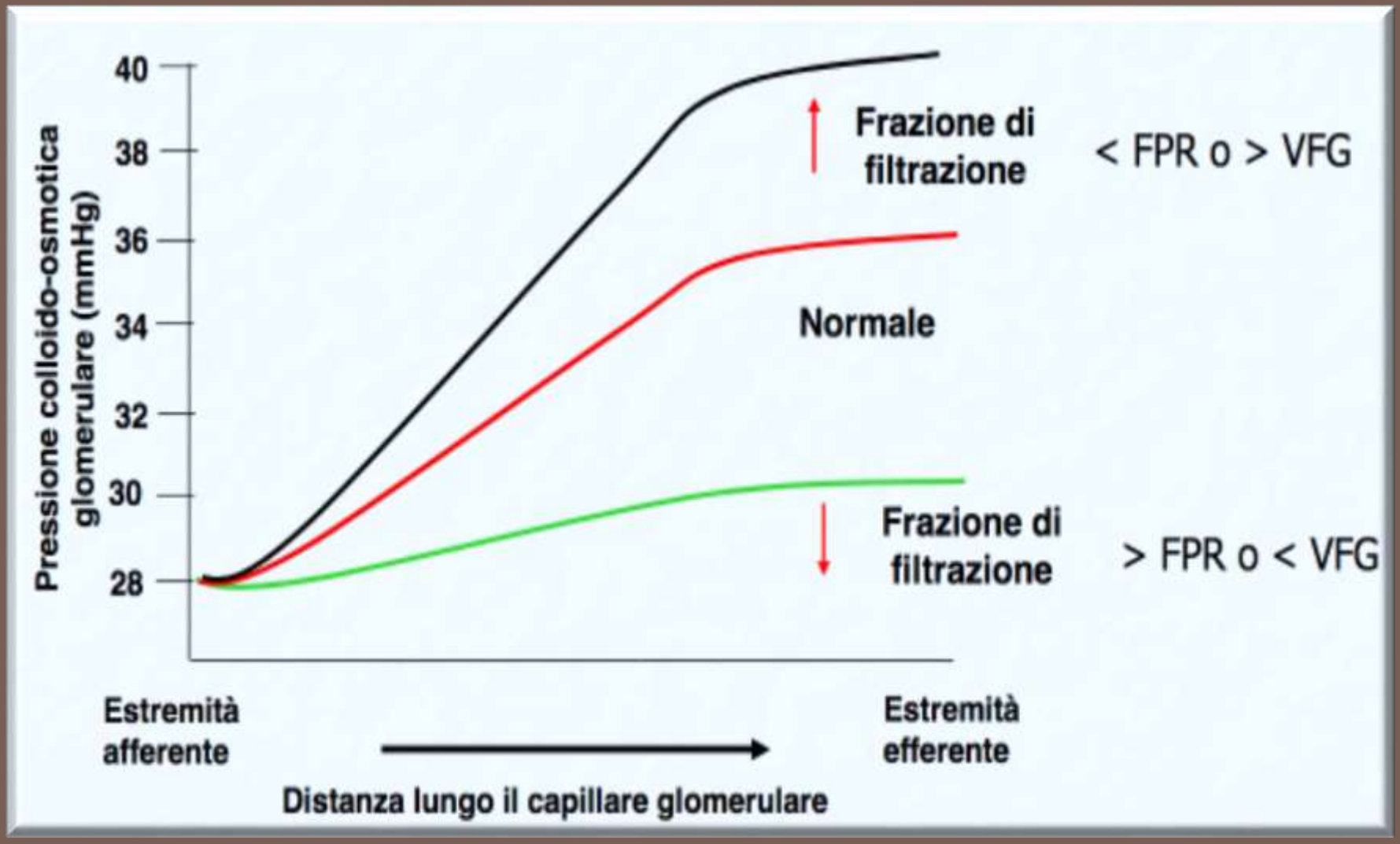
Frazione di filtrazione



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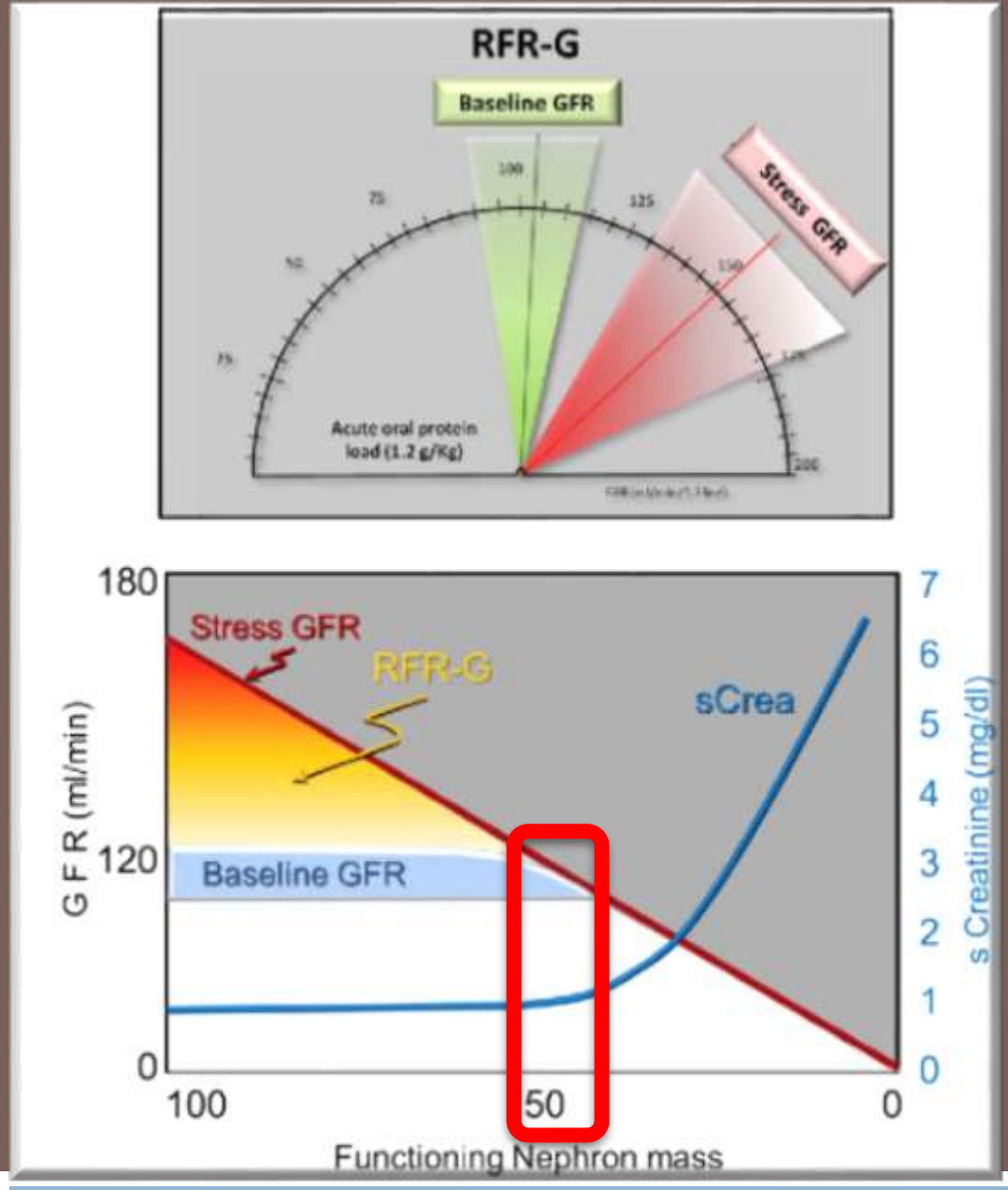
Frazione di Filtrazione



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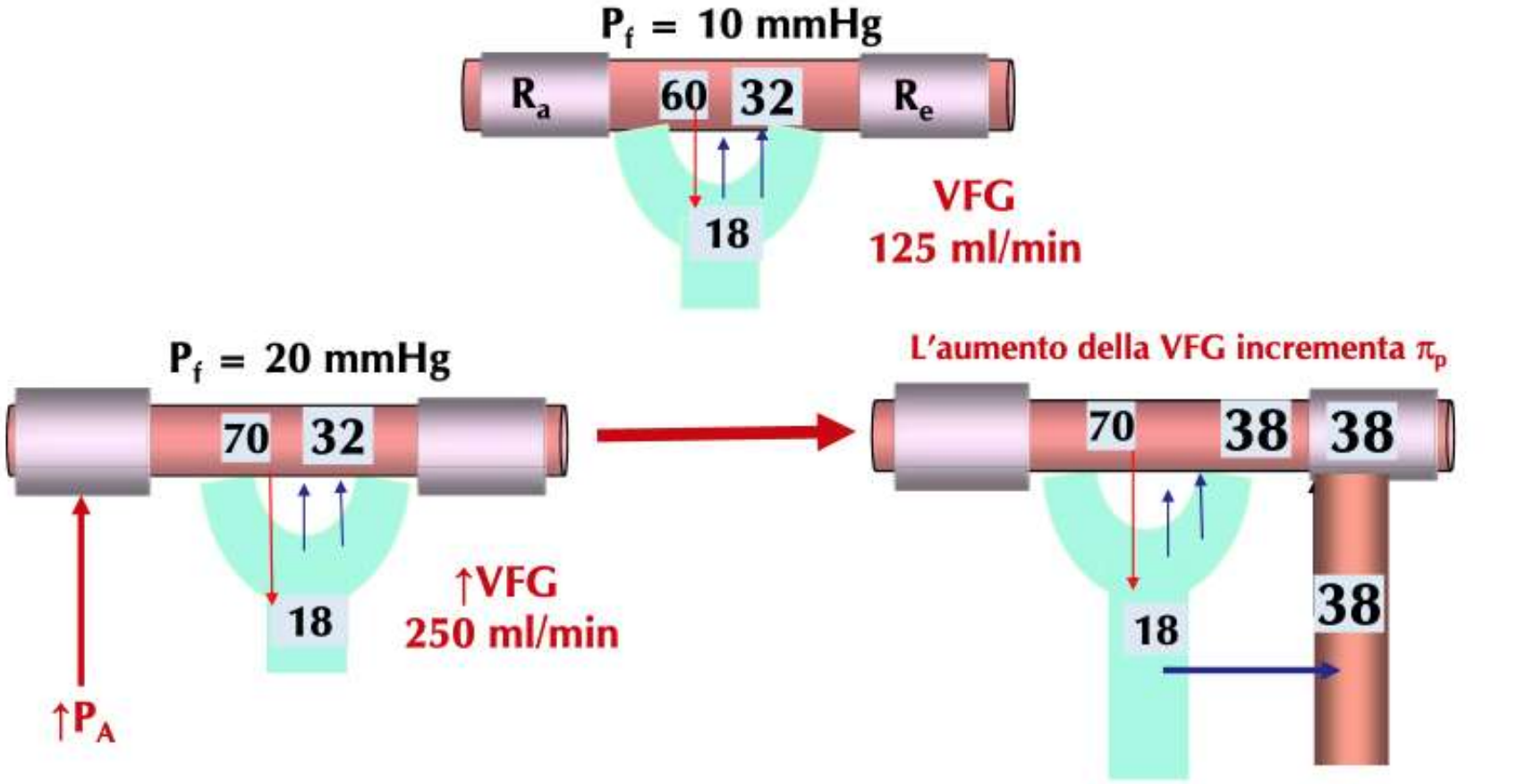
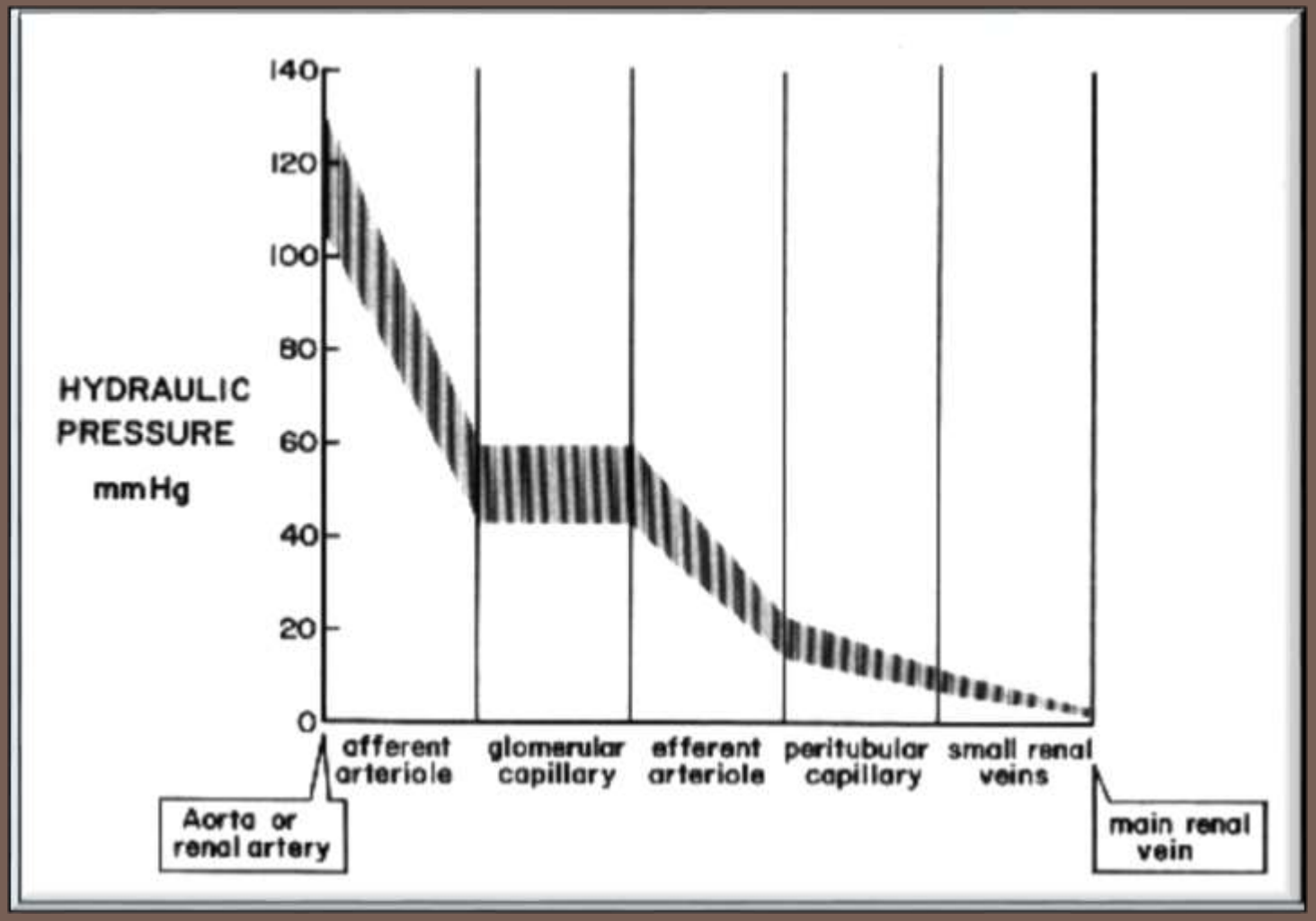
Riserva renale funzionale

Bilancio glomerulo-tubulare (effetto della P colloido-osmotica)



In seguito ad aumenti della VFG il flusso tubulare a valle è riportato alla norma, per aumento del riassorbimento, evitando variazioni ampie del flusso nei tubuli distali quando varia la P_A



PROFILO PRESSORIO VASI RENALI

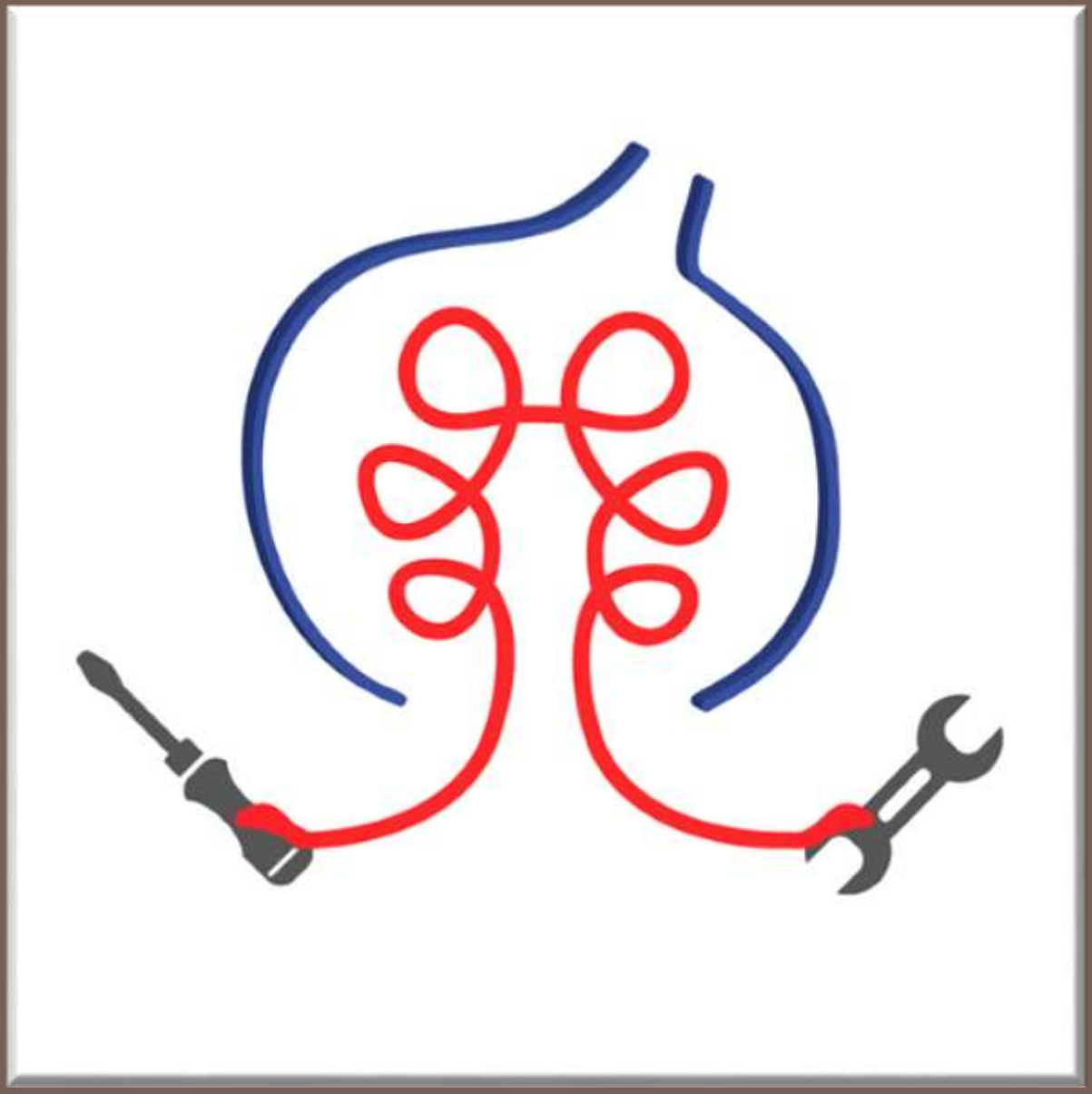
FG dipende [illegible]nente dalla P. A.?

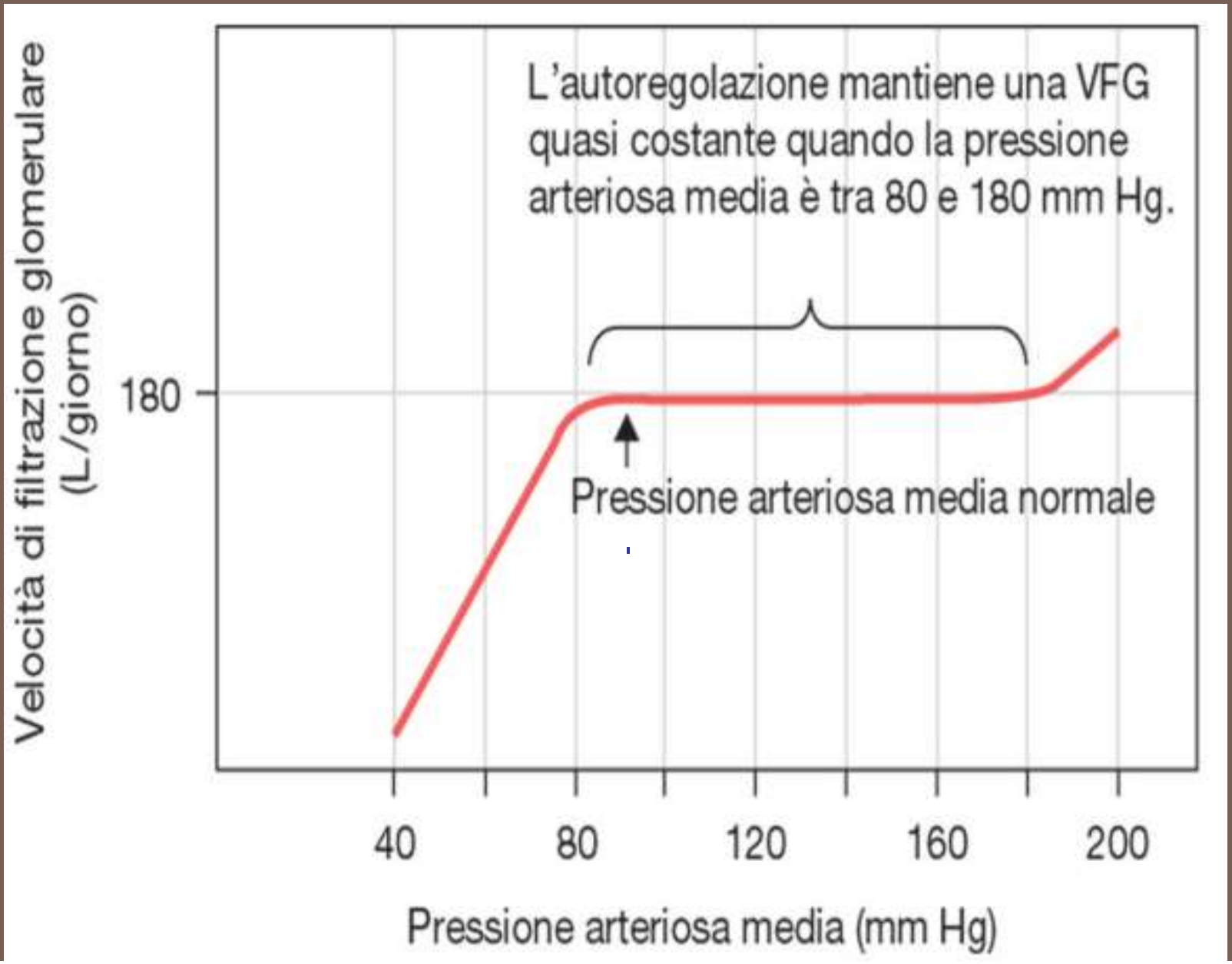
A) Pressione arteriosa sistemica

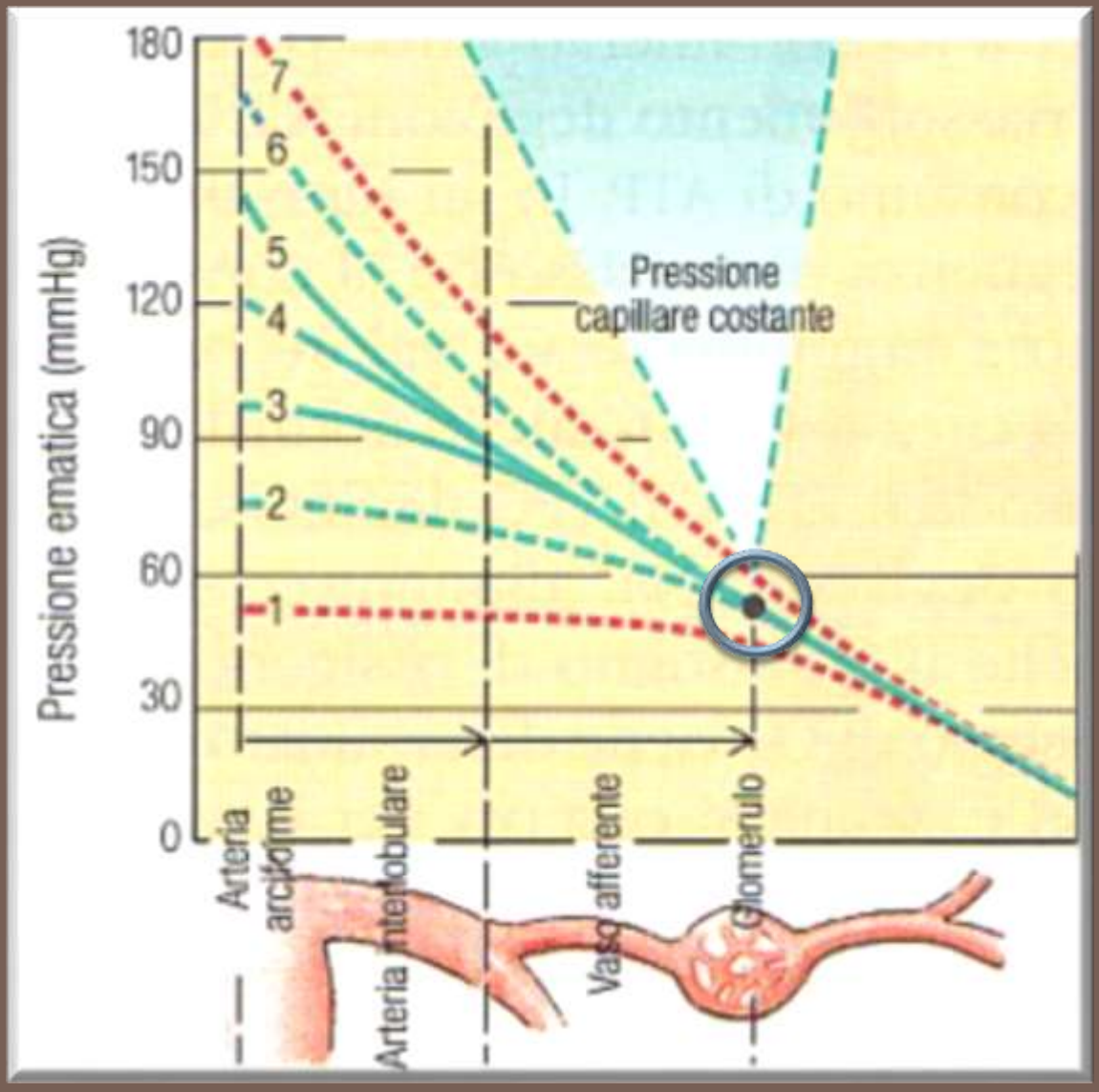
B) Tono delle arteriole afferente ed efferente

C) Pressione oncotica del plasma

E) Permeabilità e superficie della barriera di filtrazione




L'autoregolazione mantiene una VFG quasi costante quando la pressione arteriosa media è tra 80 e 180 mm Hg.
Velocità di filtrazione glomerulare (L/giorno)
180
Pressione arteriosa media normale
40
80
120
160
200
Pressione arteriosa media (mm Hg)



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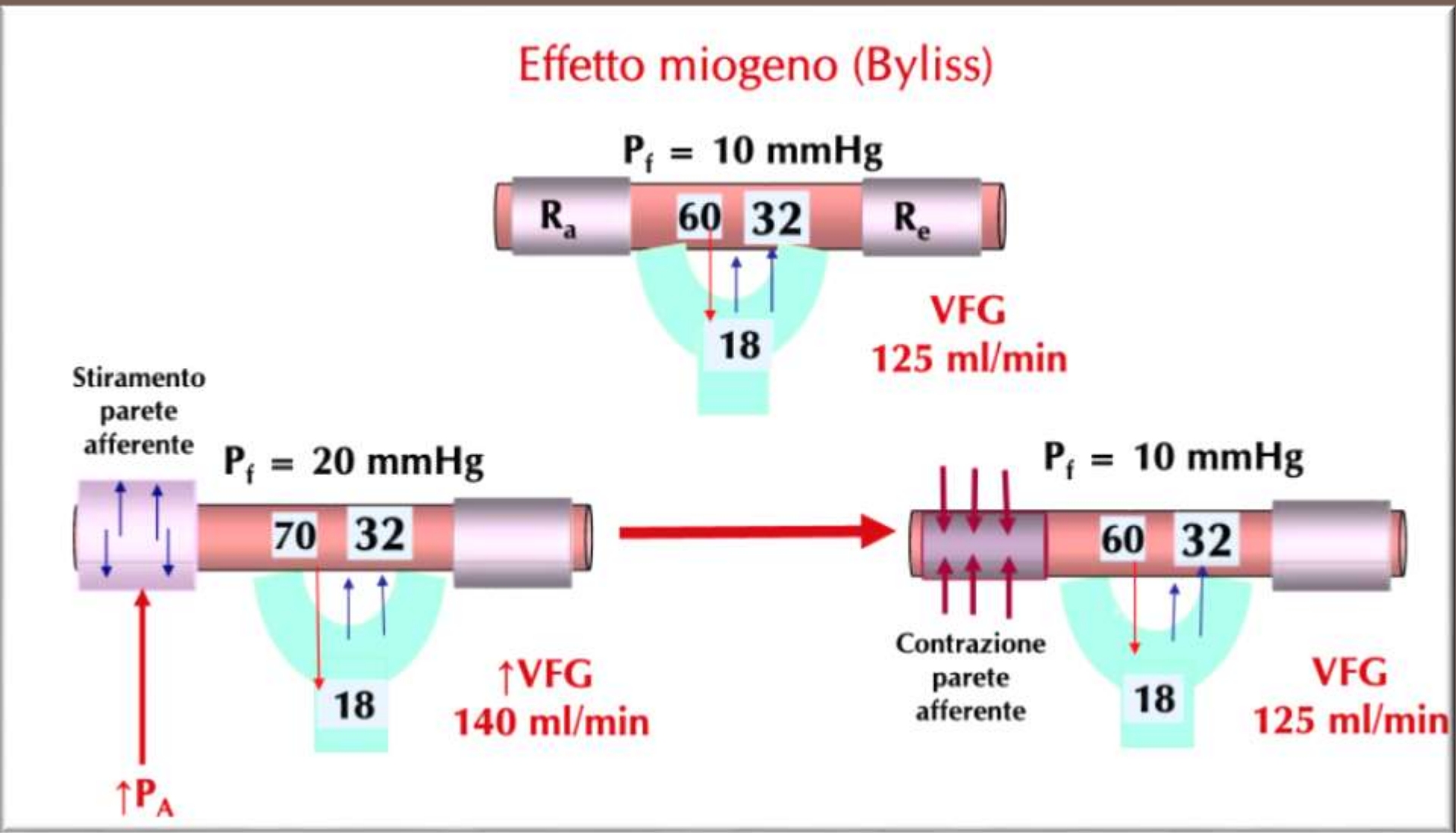
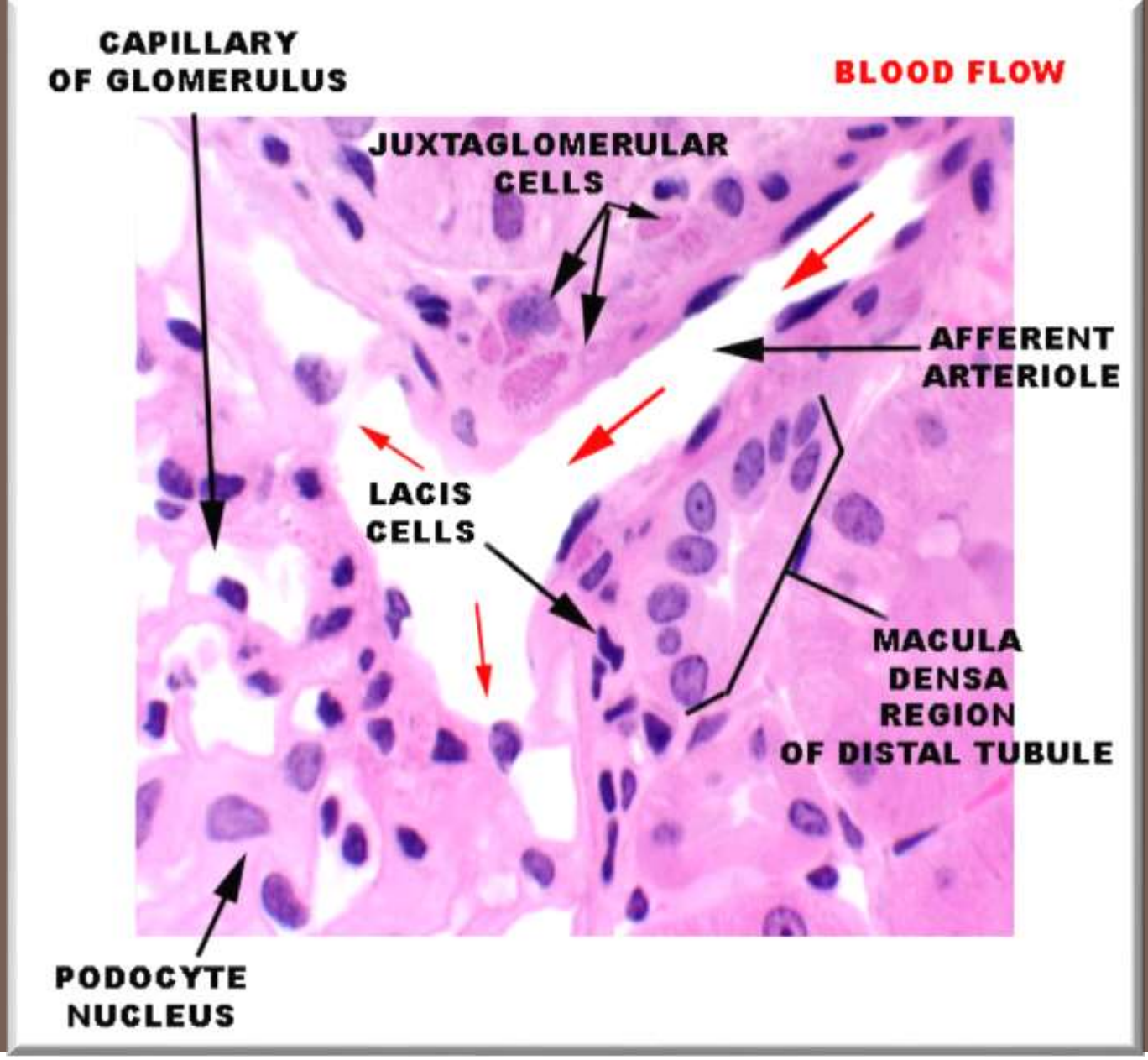
Autoregolazione renale

A) Risposta miogena vascolare

B) *Feedback* tubulo-glomerulare



Meccanismo Miogeno



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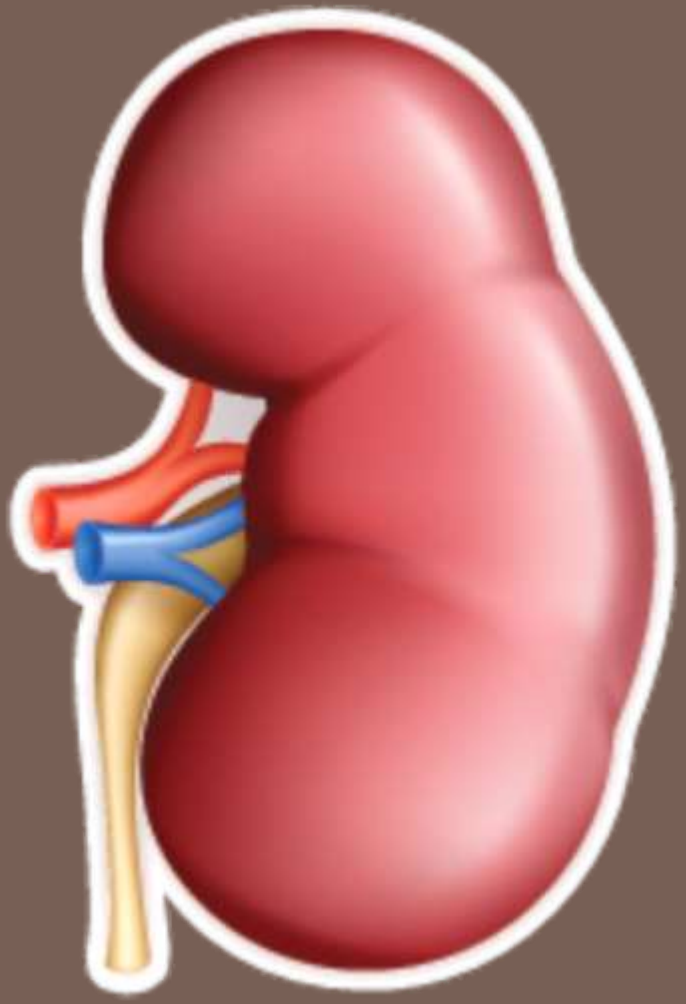
Apparato iuxtaglomerulare

Aumentata Perfusione



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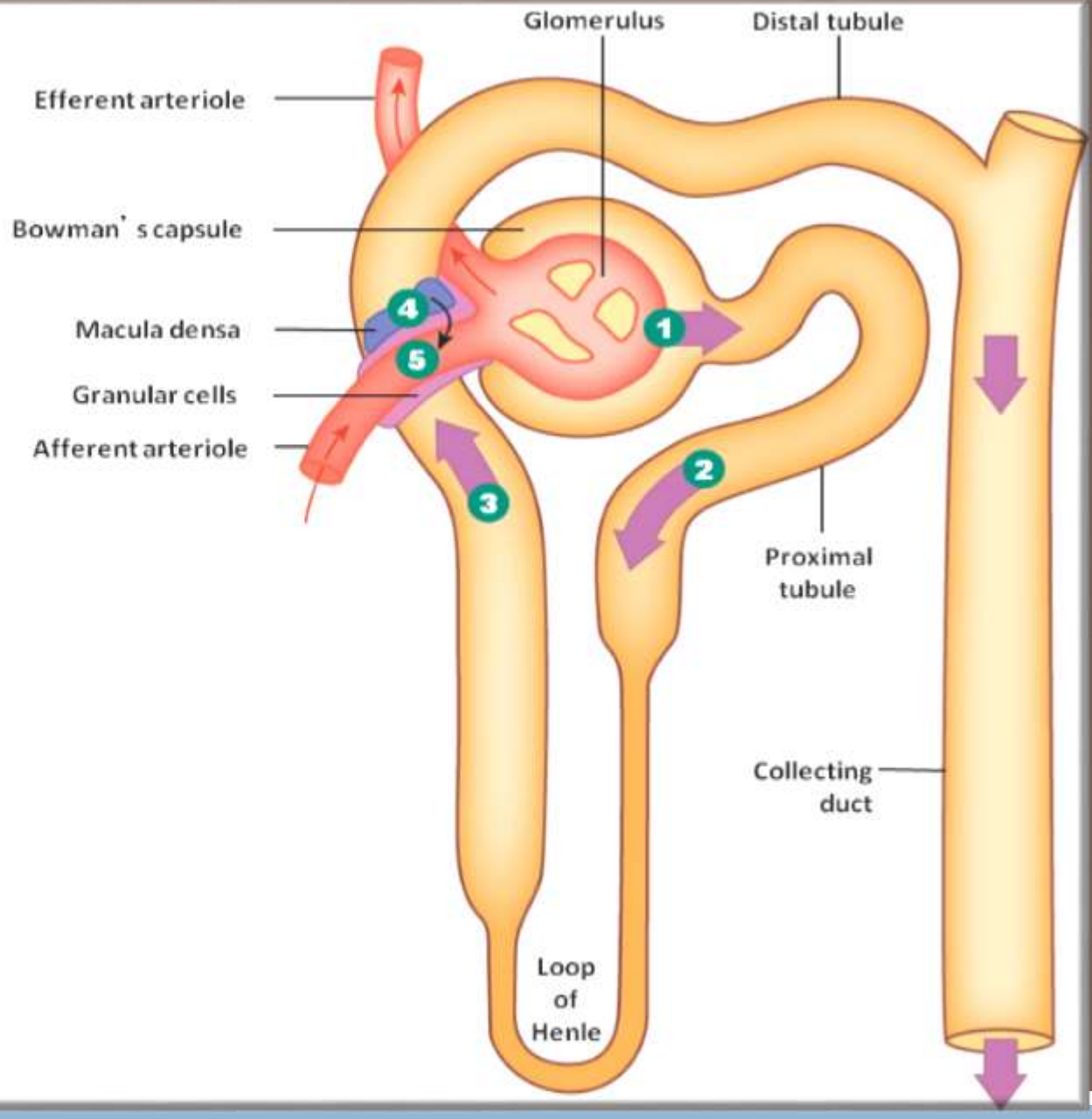
Feedback Tubulo-glomerulare

1. GFR increases.
2. Flow through tubule increases.
3. Flow past macula densa increases.
4. Paracrine from macula densa to afferent arteriole
5. Afferent arteriole constricts.

Resistance in afferent arteriole increases.

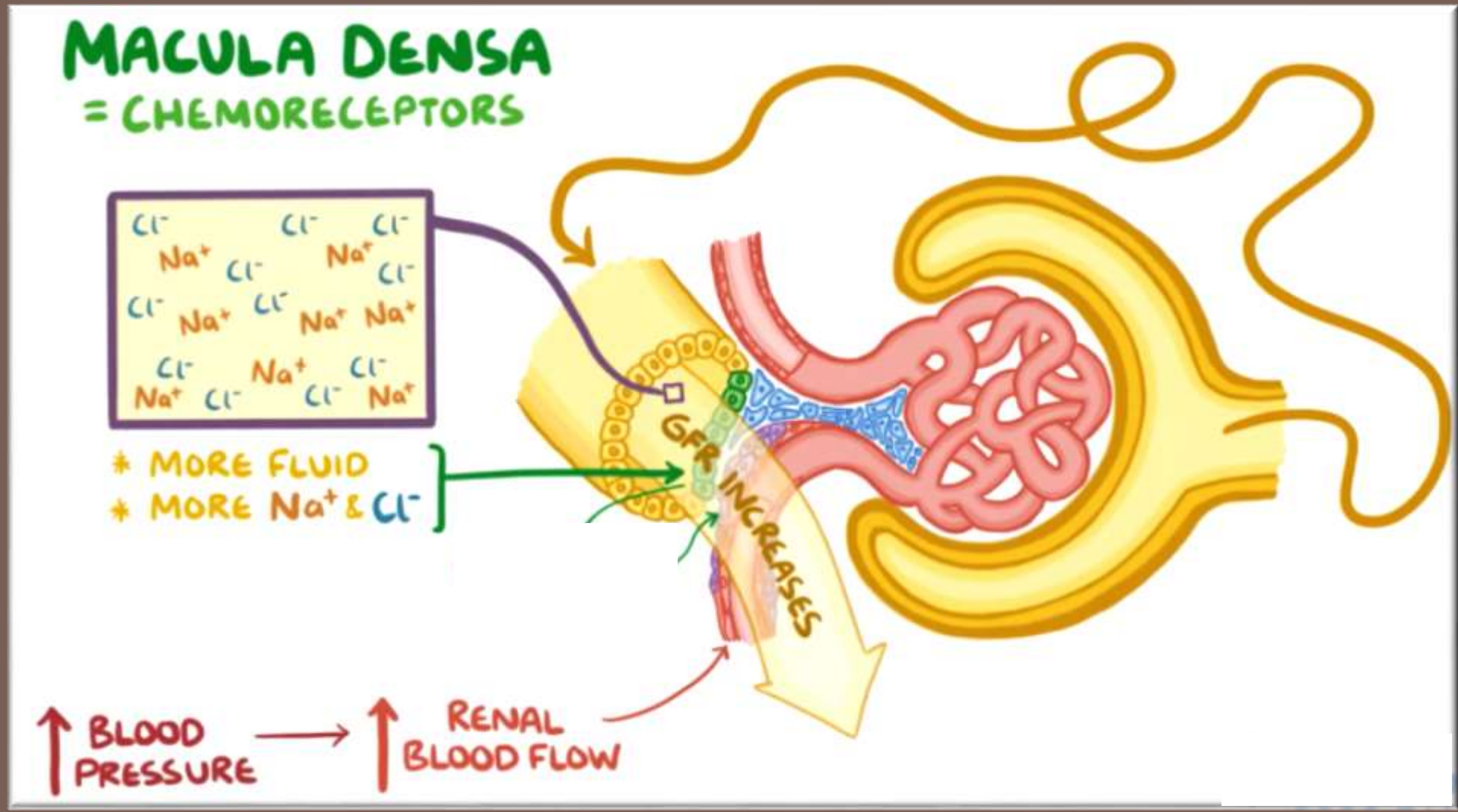
Hydrostatic pressure in glomerulus decreases.

GFR decreases.



Carmel Libetta

Feedback Tubulo-glomerulare



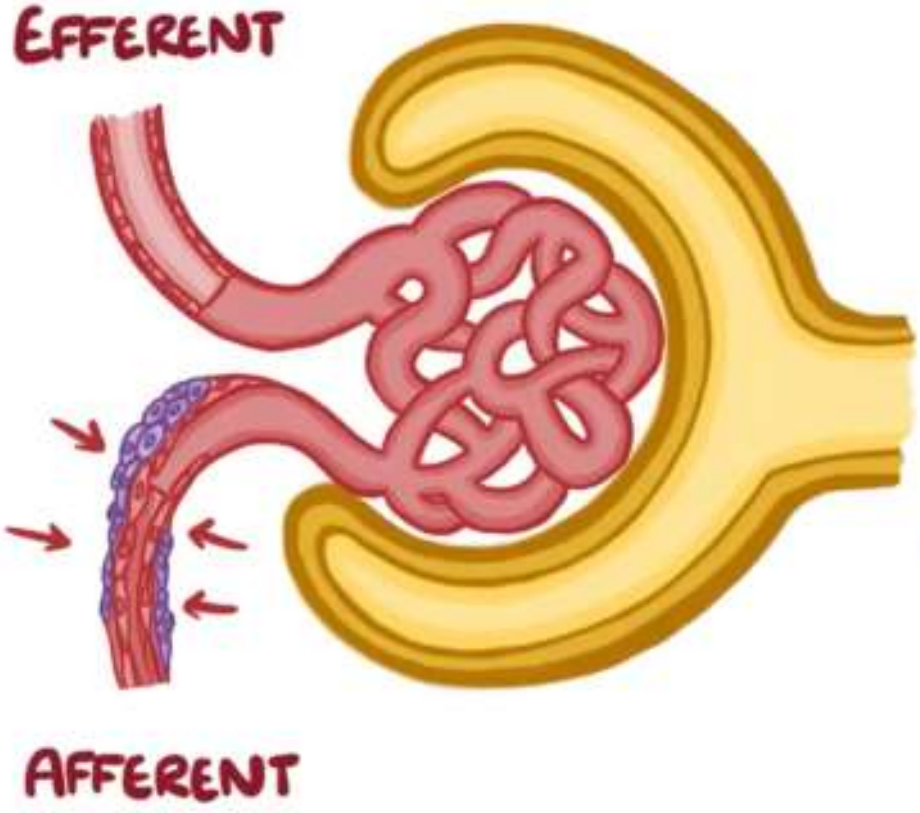
Carmel Libetta

Feedback Tubulo-glomerulare

- Potent renal vasoconstrictor (A1R)
- Peripheral vasodilator (Sistemic, A2R)
  - Infusion of methylxanthines (adenosine receptor blockers) inhibits the decrease in GFR

Adenosina

CAPILLARY HYDROSTATIC PRESSURE



VASOCONSTRICTION of AFFERENT ARTERIOLE

↓

↓ RENAL BLOOD FLOW

↓

↓ CAPILLARY HYDROSTATIC PRESSURE

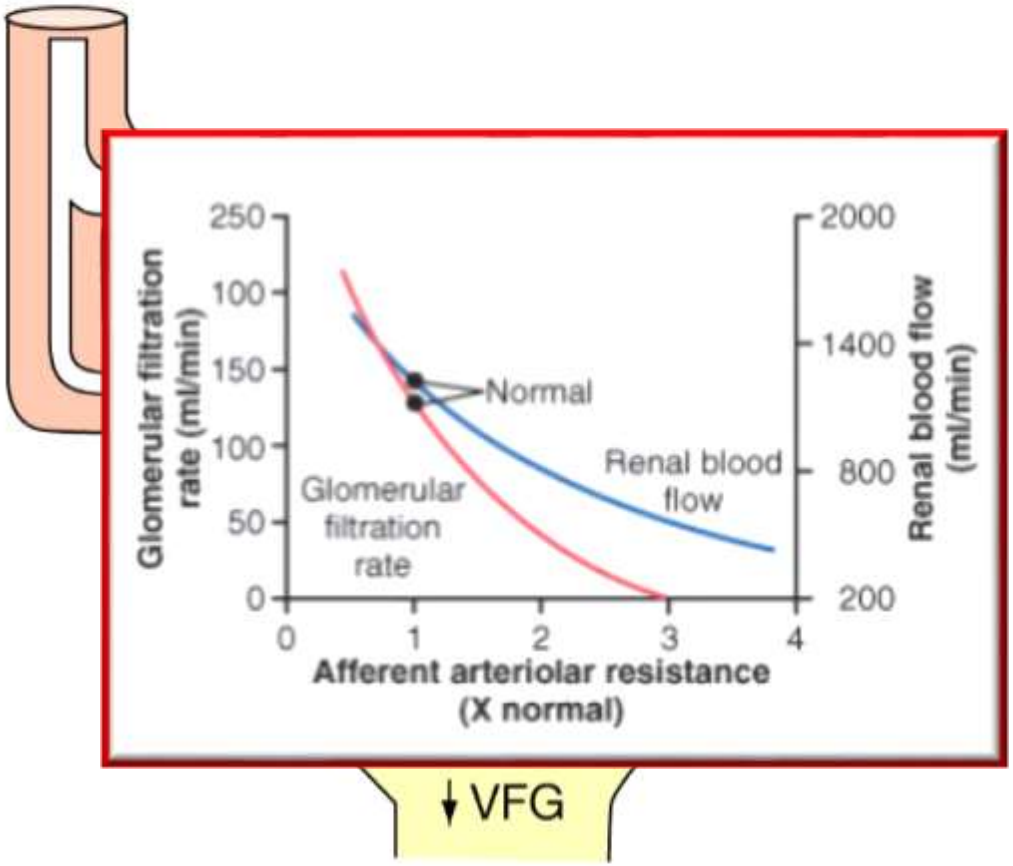
↓

↓ GFR

Carmelo Libetta

Feedback Tubulo-glomerulare

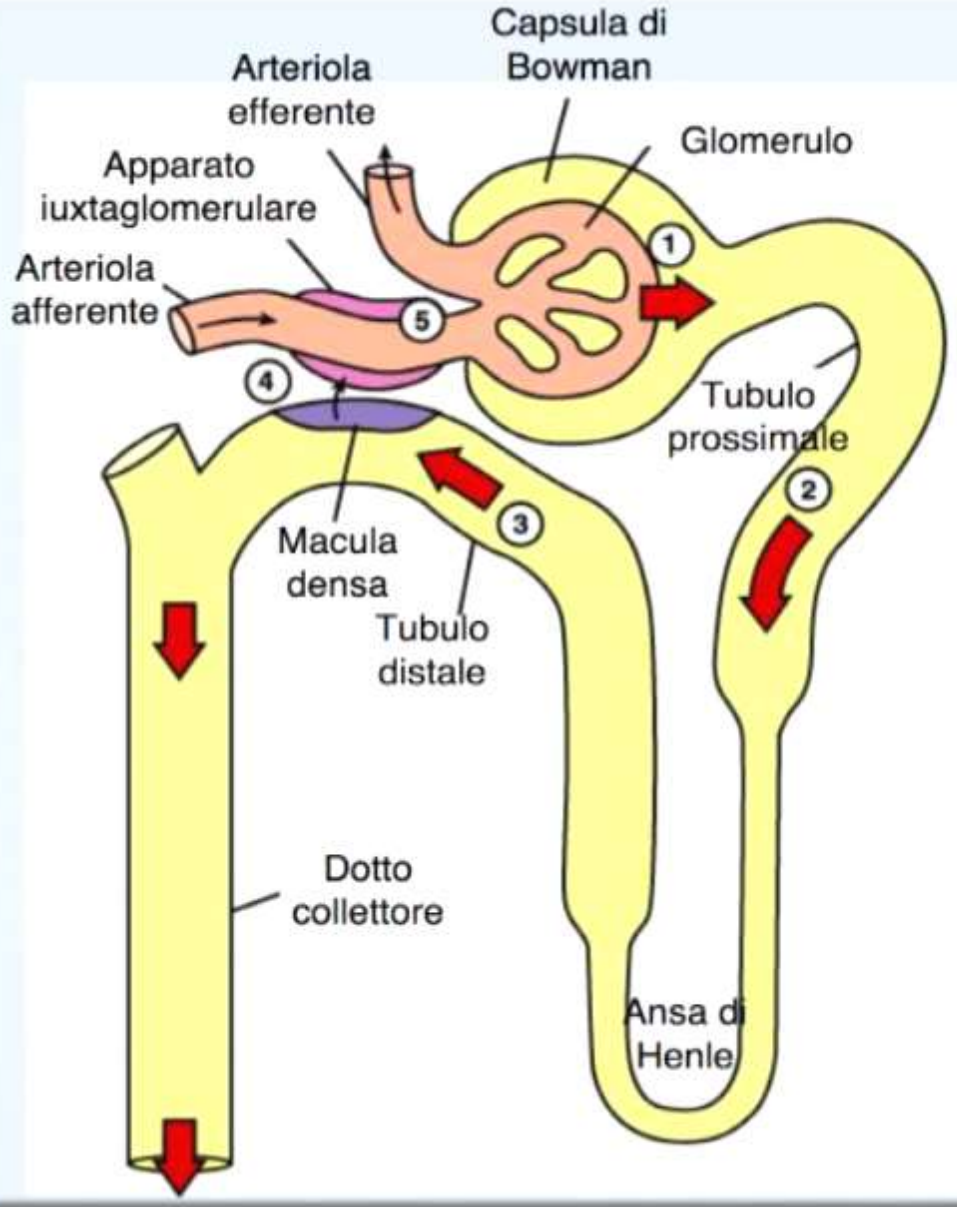
La vasocostrizione dell'arteriola afferente aumenta la resistenza e riduce il flusso ematico glomerulare la pressione ematica capillare (P_l) e la VFG.



Ridotta Perfusione

Carmel Libetta

Feedback Tubulo-glomerulare



1. <Pa <VFG
2. < Flusso nel tubulo
3. > Riassorbimento NaCl
4. < Concentrazione NaCl alla macula densa
5. Liberazione di sostanze paracrine dalla macula densa e vasodilatazione arteriole afferenti (PG)

Rilascio di Renina dall' apparato iuxta-glomerulare, formazione di Angiotensina II e vasocostrizione arteriole efferenti,

- >Pressione capillari glomerulari
- > VFG

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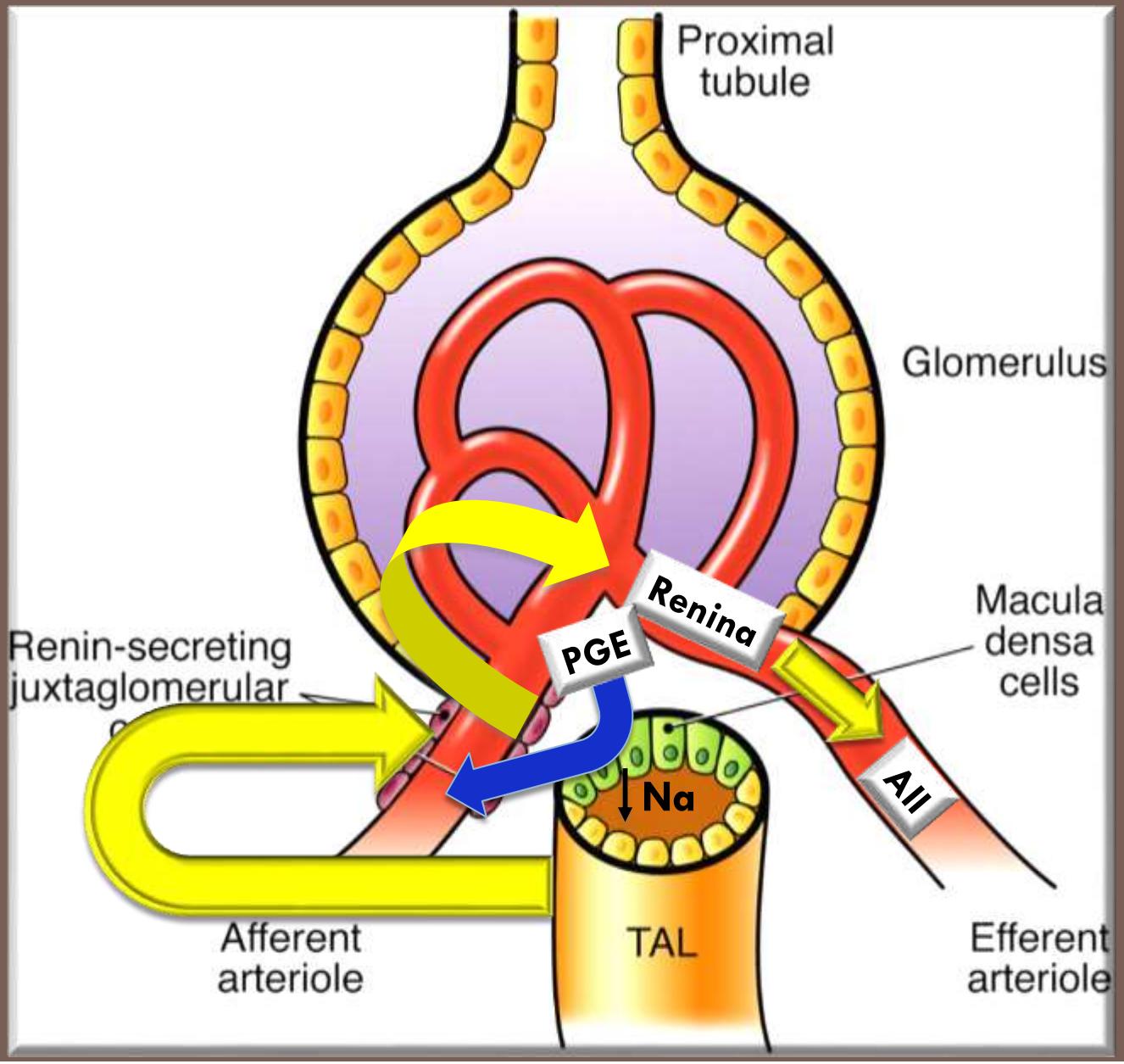
Ridotta perfusione renale



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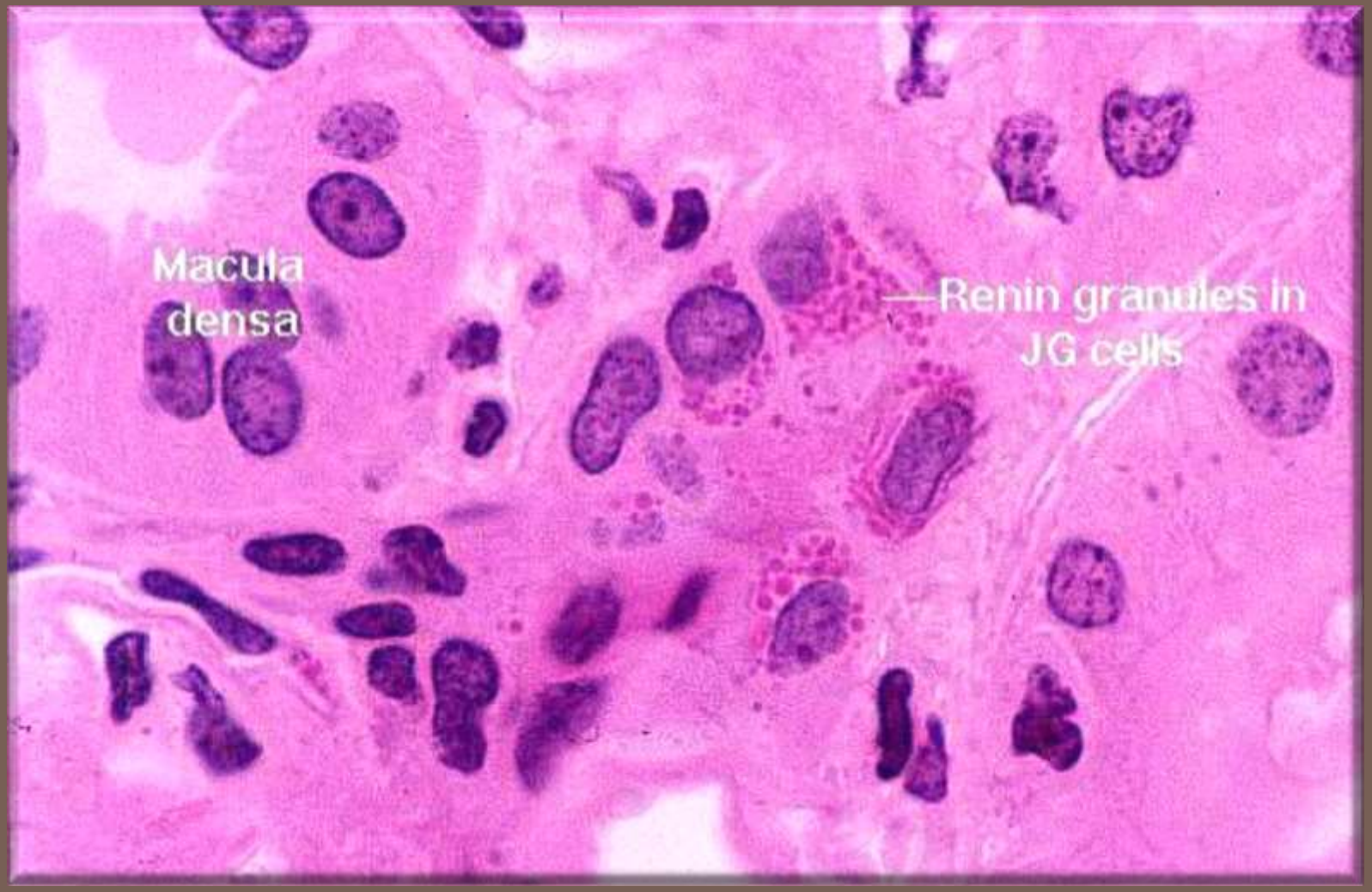
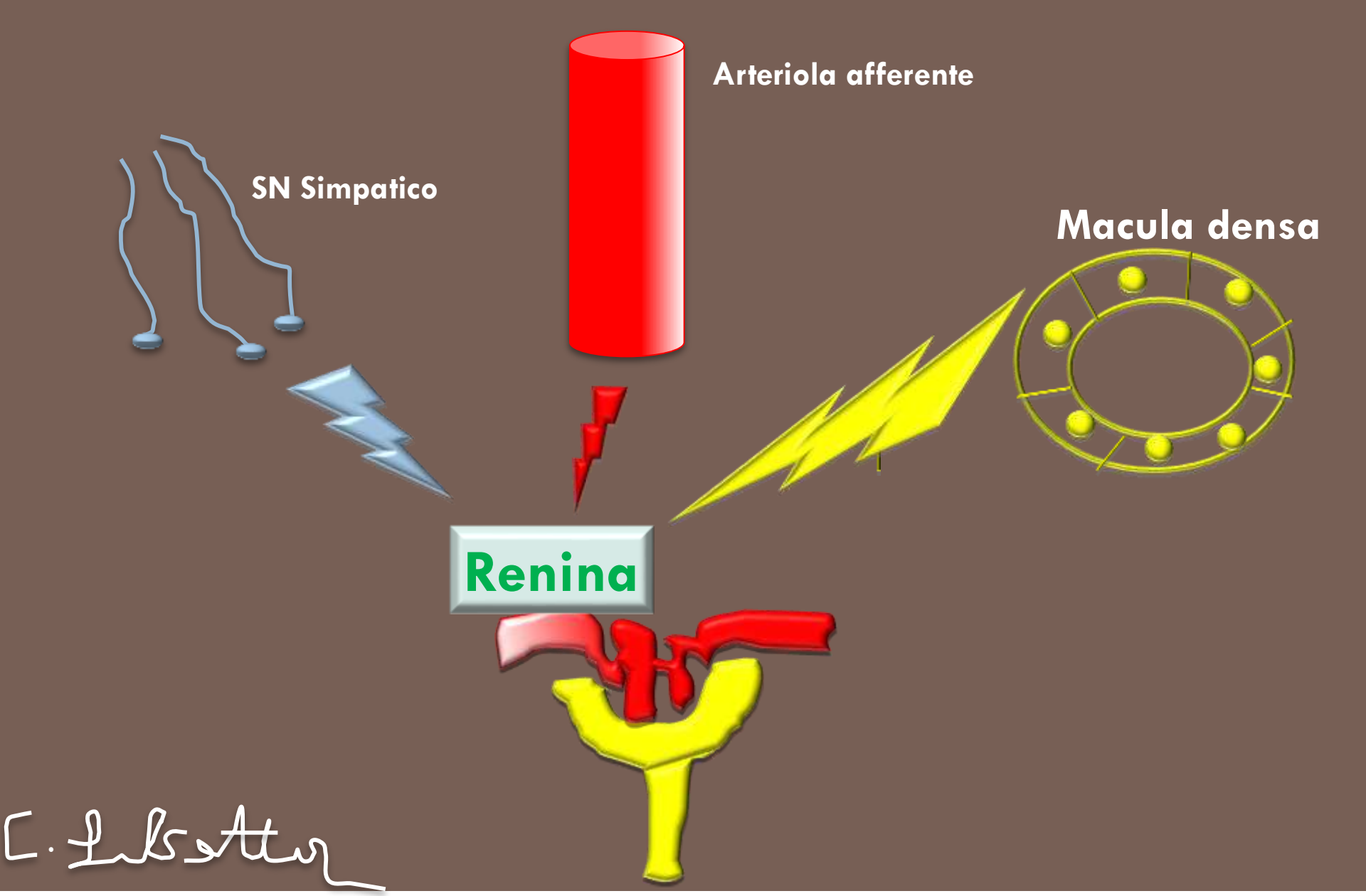
Ridotta perfusione renale

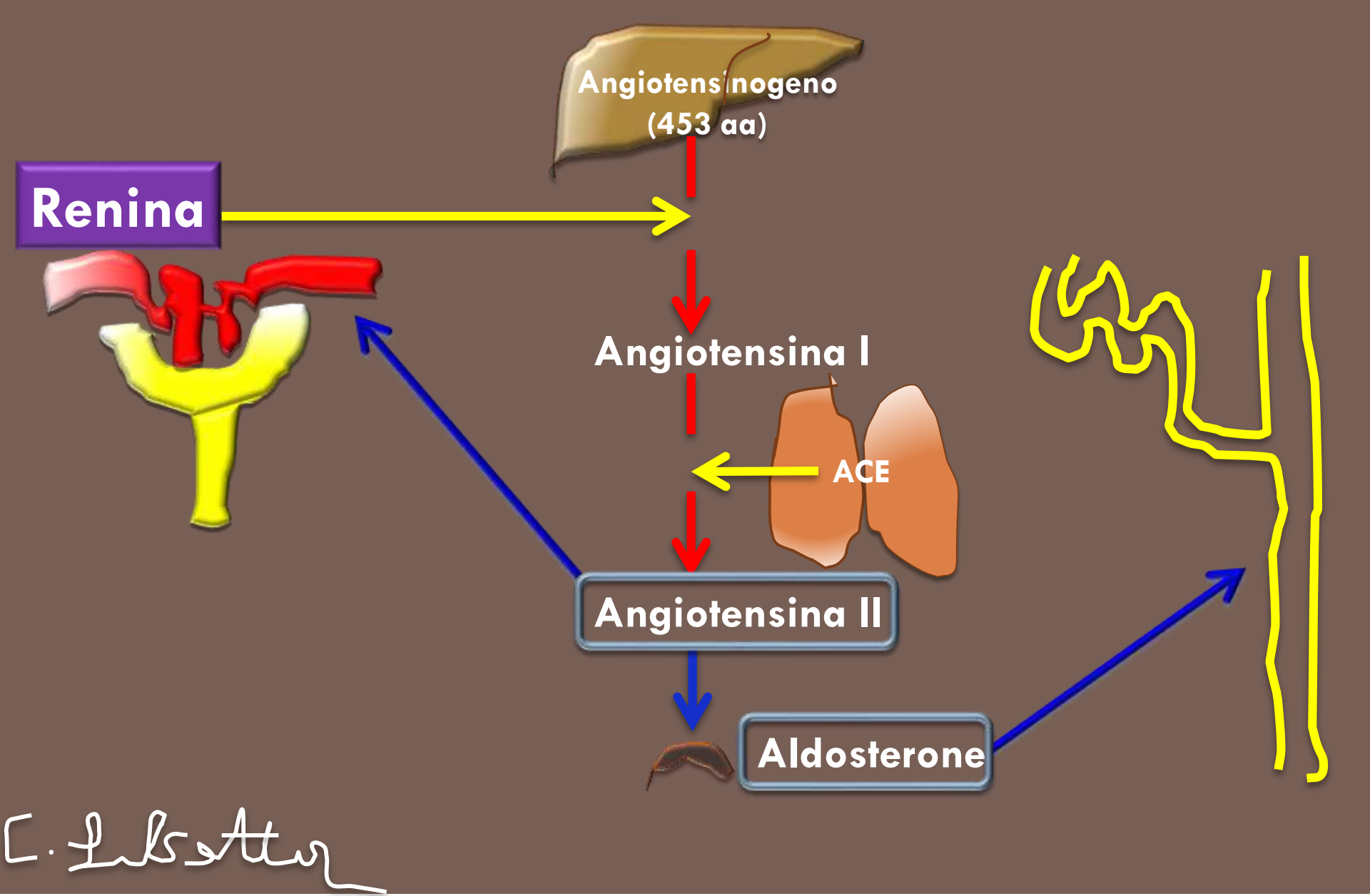


SRAA



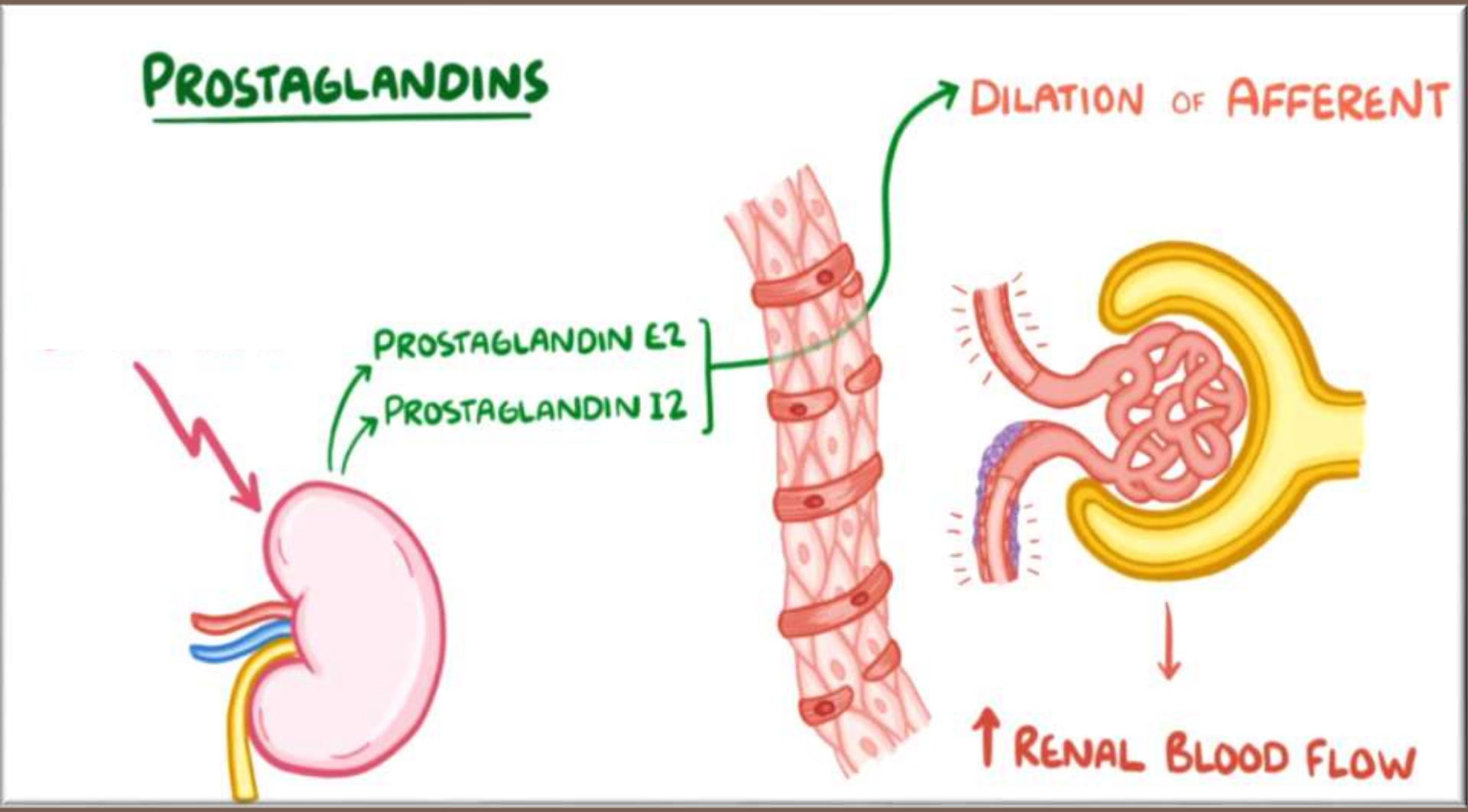
Carmelo Libetta

SRAA

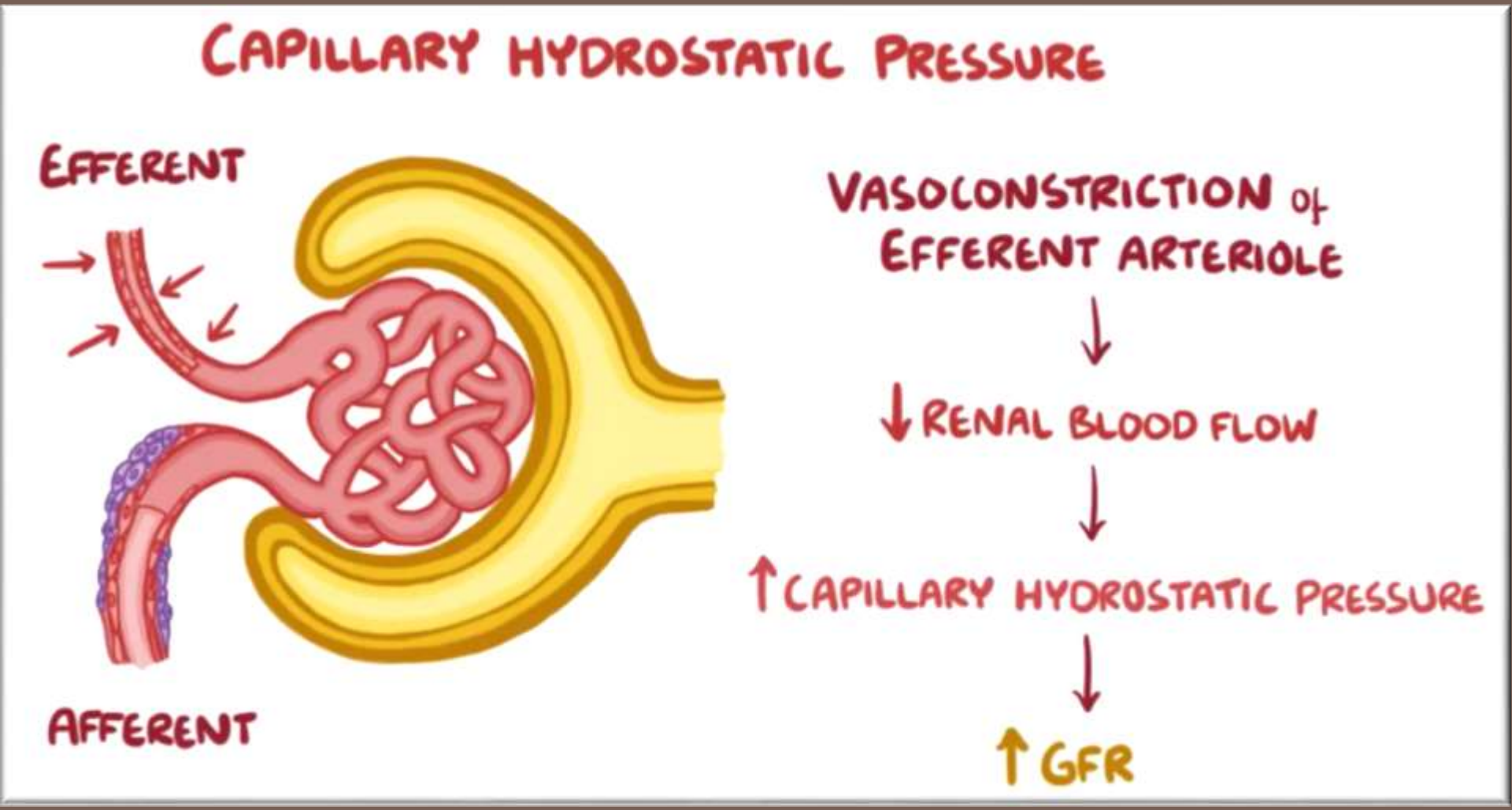


Carmelo Libetta

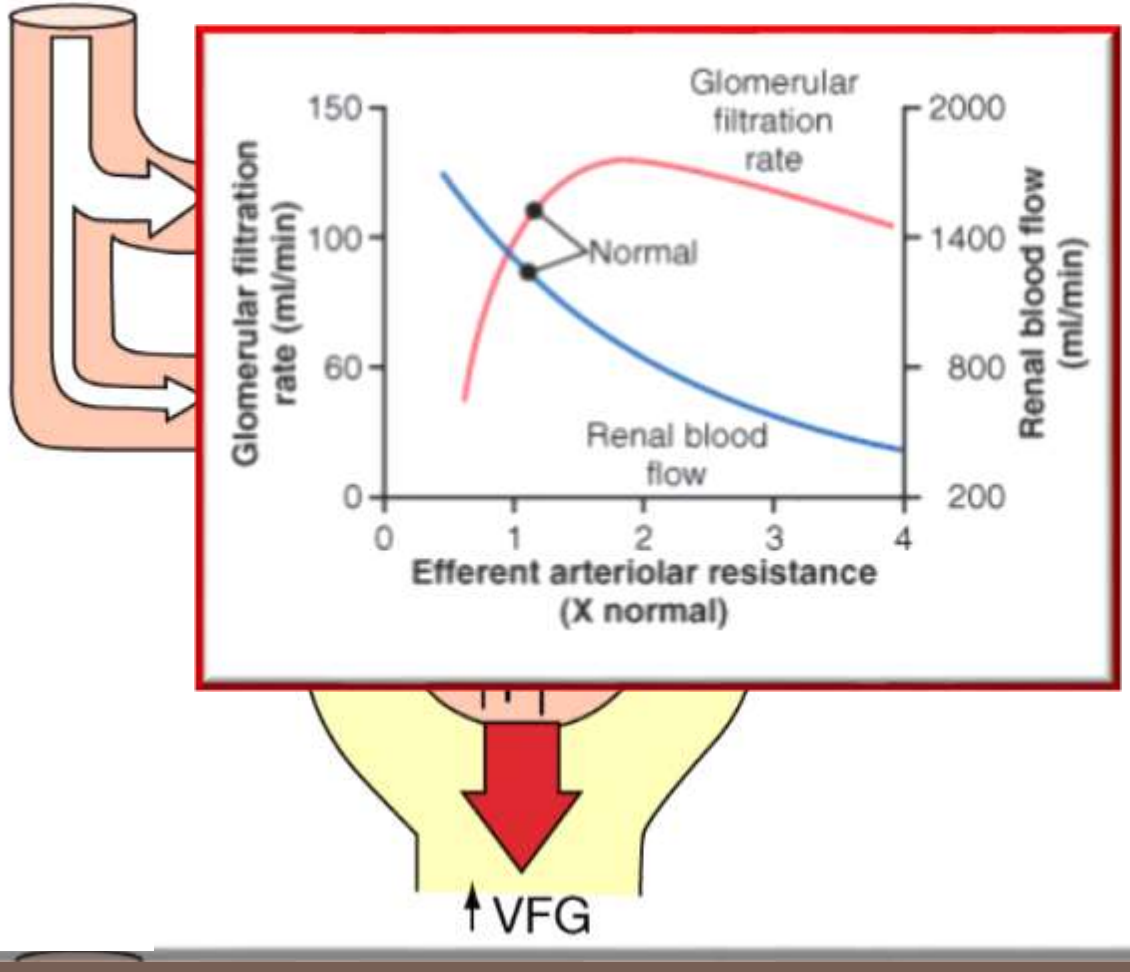
SRAA



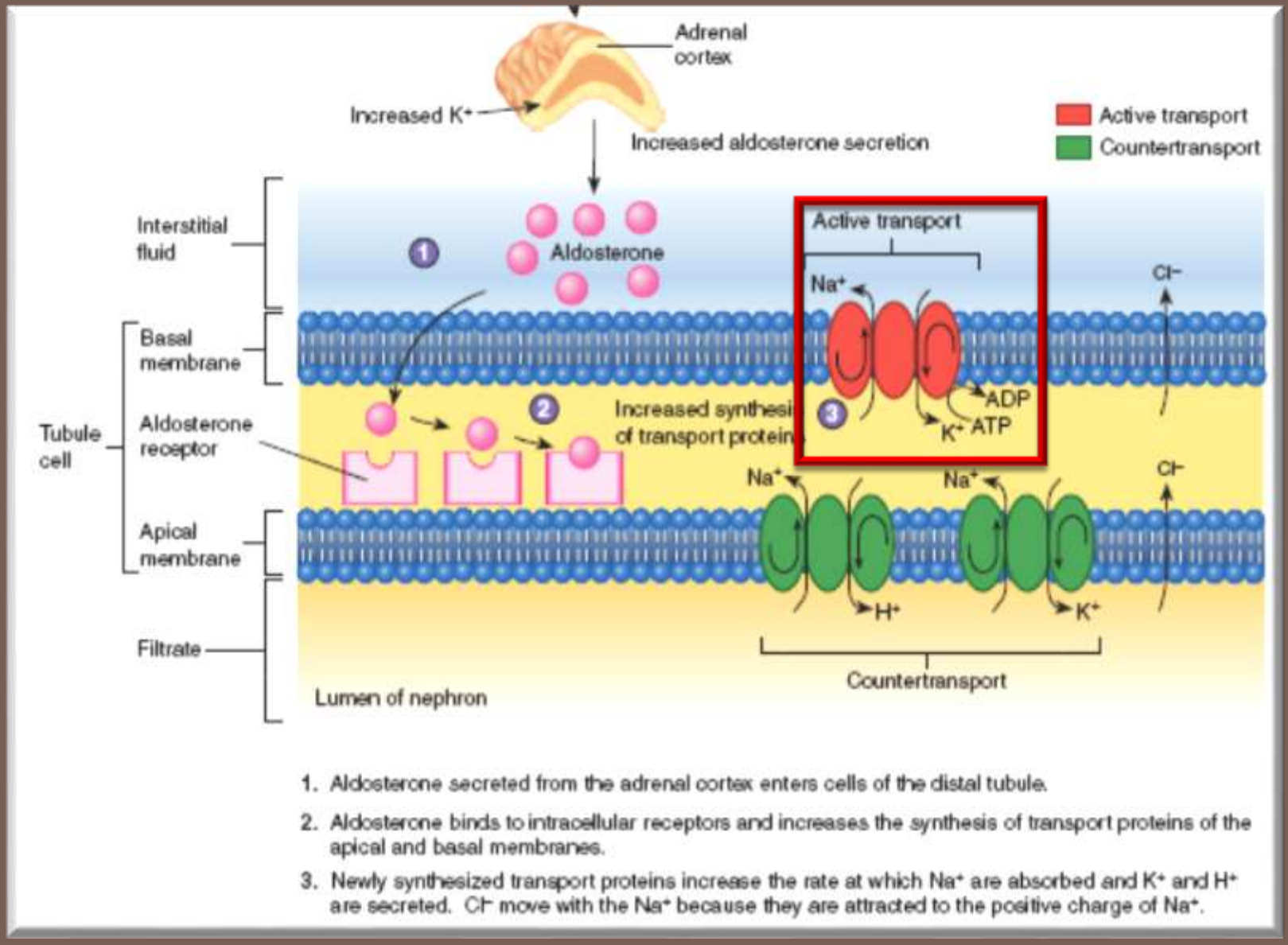
AUTOREGOLAZIONE


CAPILLARY HYDROSTATIC PRESSURE
EFFERENT
AFFERENT
VASOCONSTRICTION of EFFERENT ARTERIOLE
↓ RENAL BLOOD FLOW
↑ CAPILLARY HYDROSTATIC PRESSURE
↑ GFR

L'aumento della resistenza dell'arteriola efferente riduce il flusso ematic glomerulare aumenta la P_I e la VFG.



Vasocostrizione Arteriola Efferente



1. Aldosterone secreted from the adrenal cortex enters cells of the distal tubule.
2. Aldosterone binds to intracellular receptors and increases the synthesis of transport proteins of the apical and basal membranes.
3. Newly synthesized transport proteins increase the rate at which Na^+ are absorbed and K^+ and H^+ are secreted. Cl^- move with the Na^+ because they are attracted to the positive charge of Na^+.

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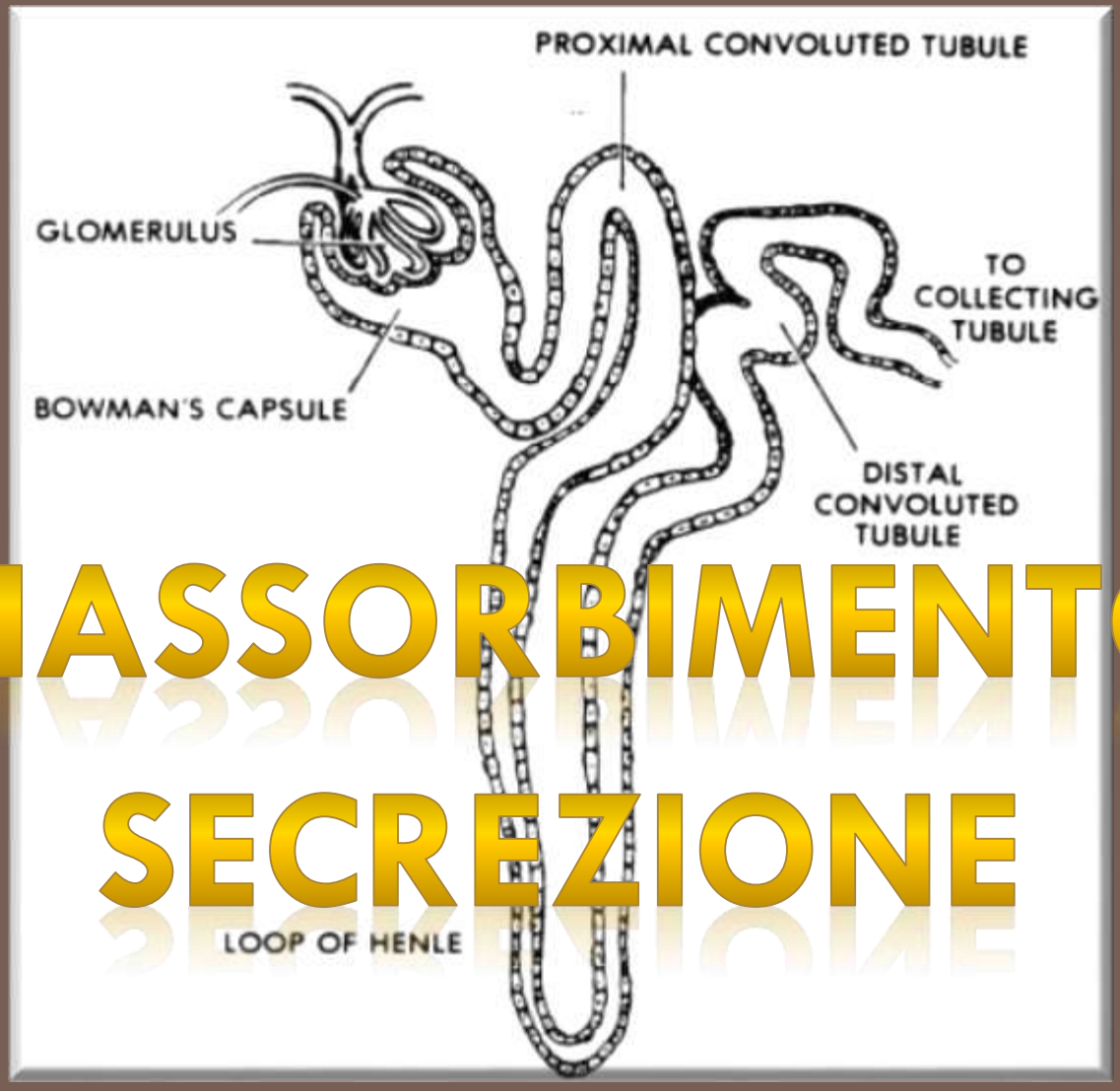
Aldosterone



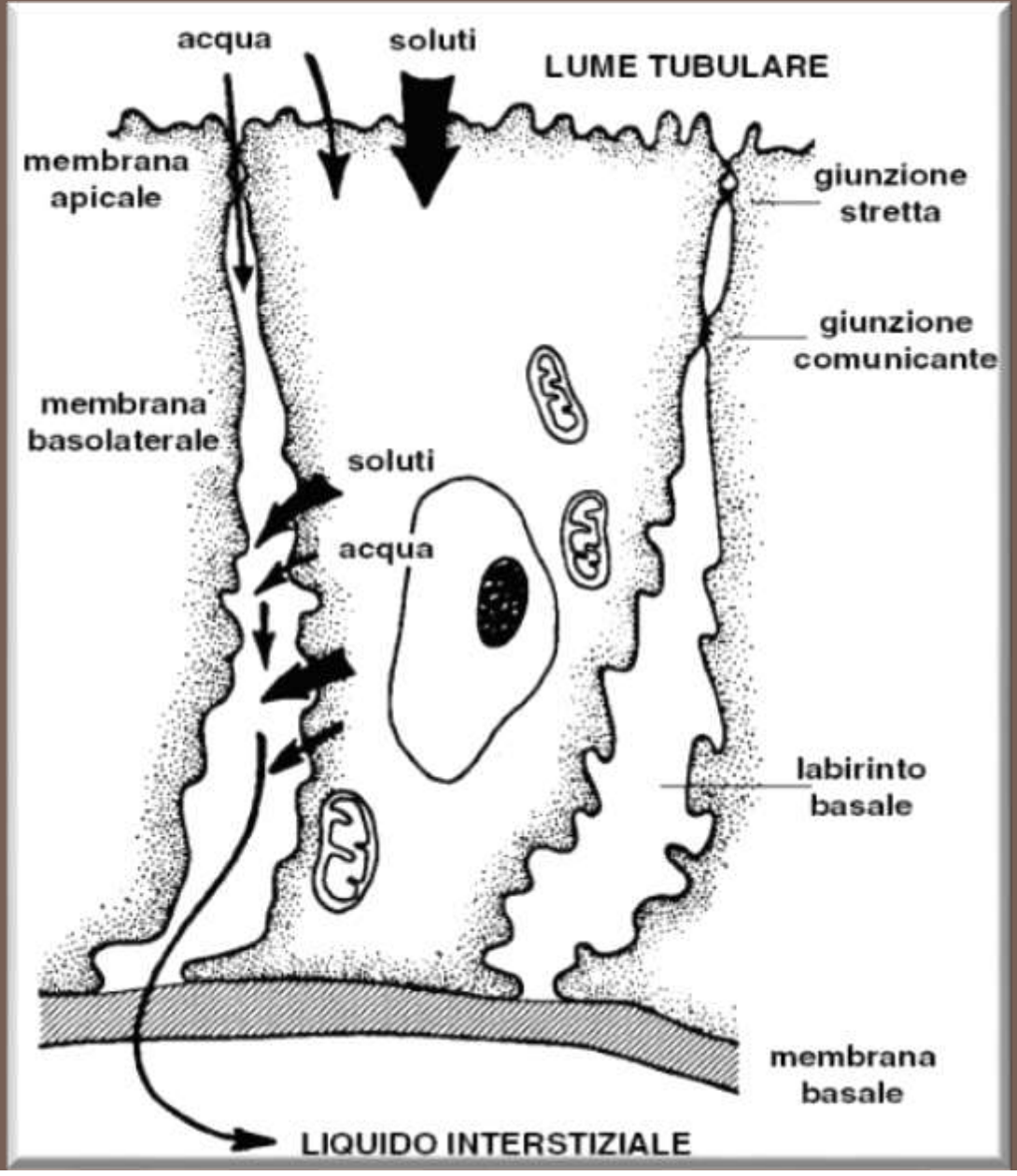
RIASSORBIMENTO

SECREZIONE

Carmel
Libetta

Funzioni Tubulari

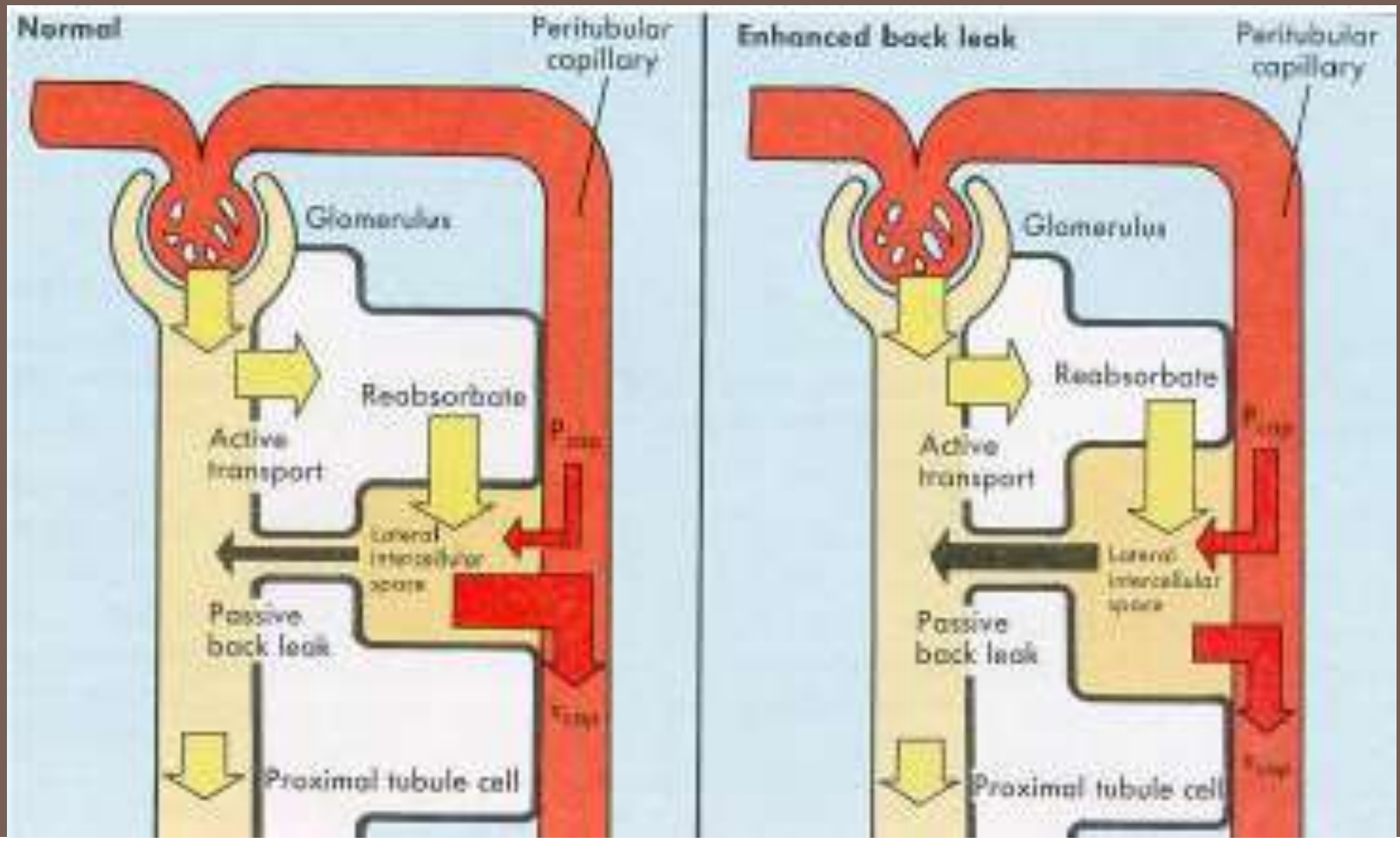
99% preurina è riassorbita



Carmelo Libetta

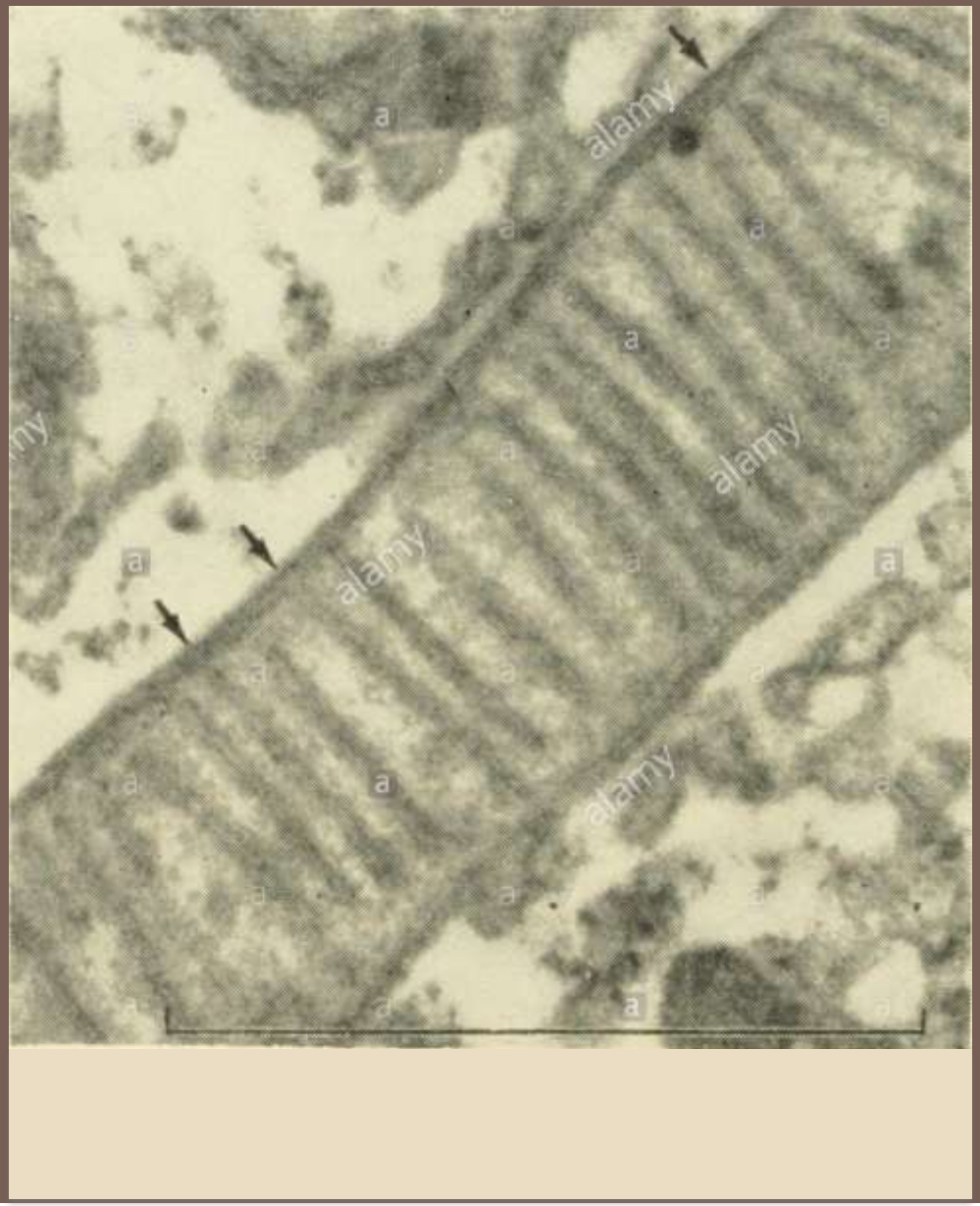
RIASSORBIMENTO

IPERTENSIONE= Aumento del filtrato,
Riduzione riassorbimento,
aumento delivery

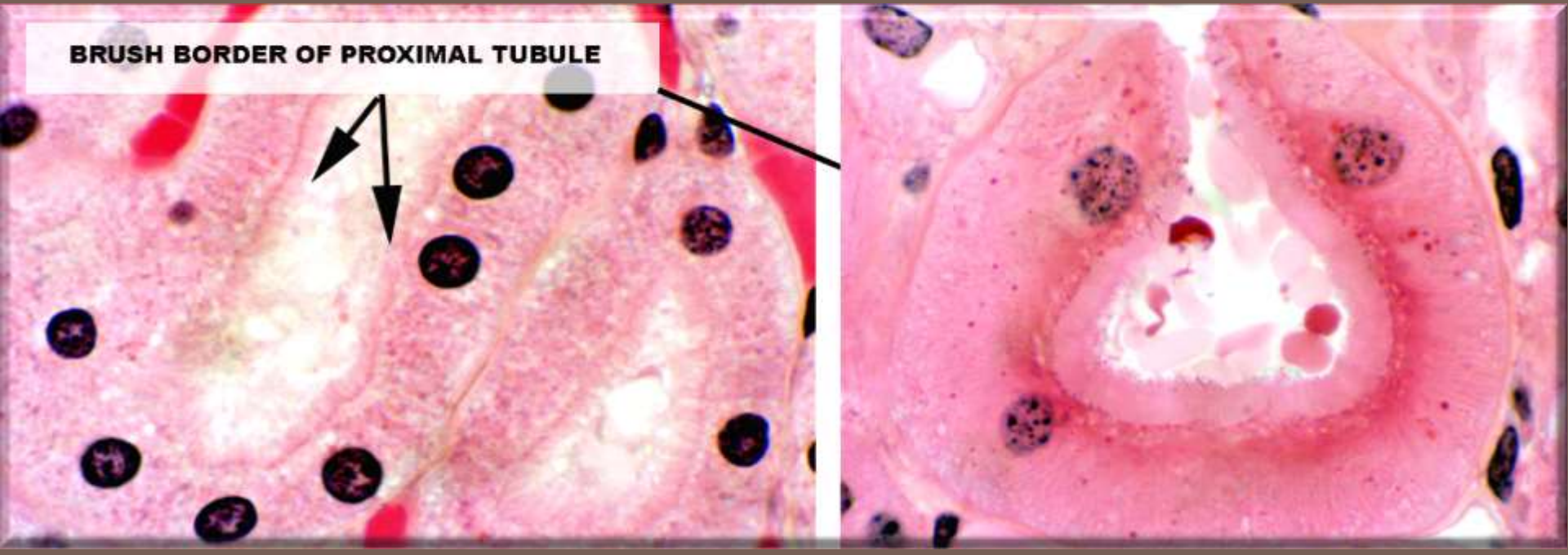


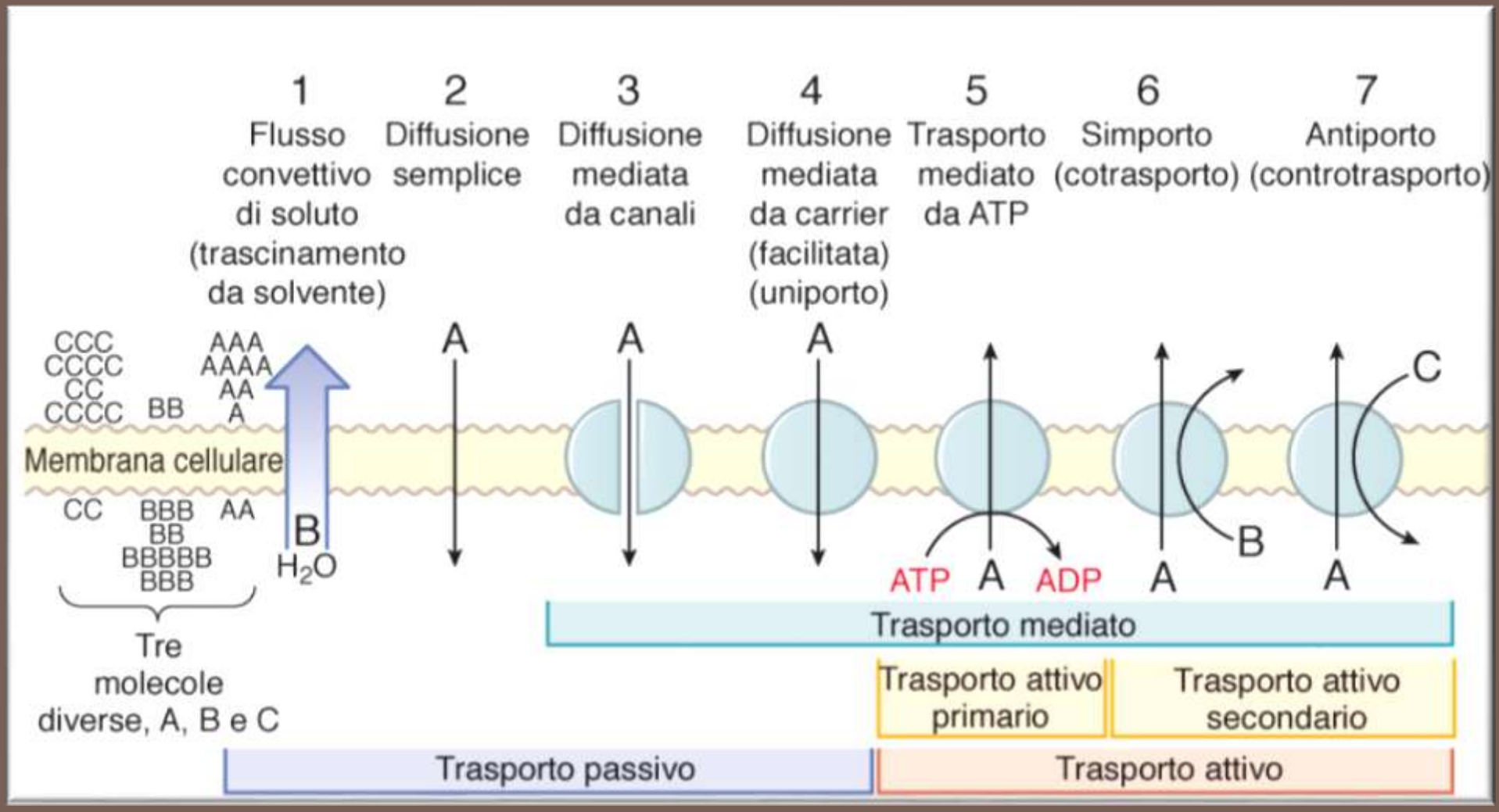
RIASSORBIMENTO

Mitocondri



65%





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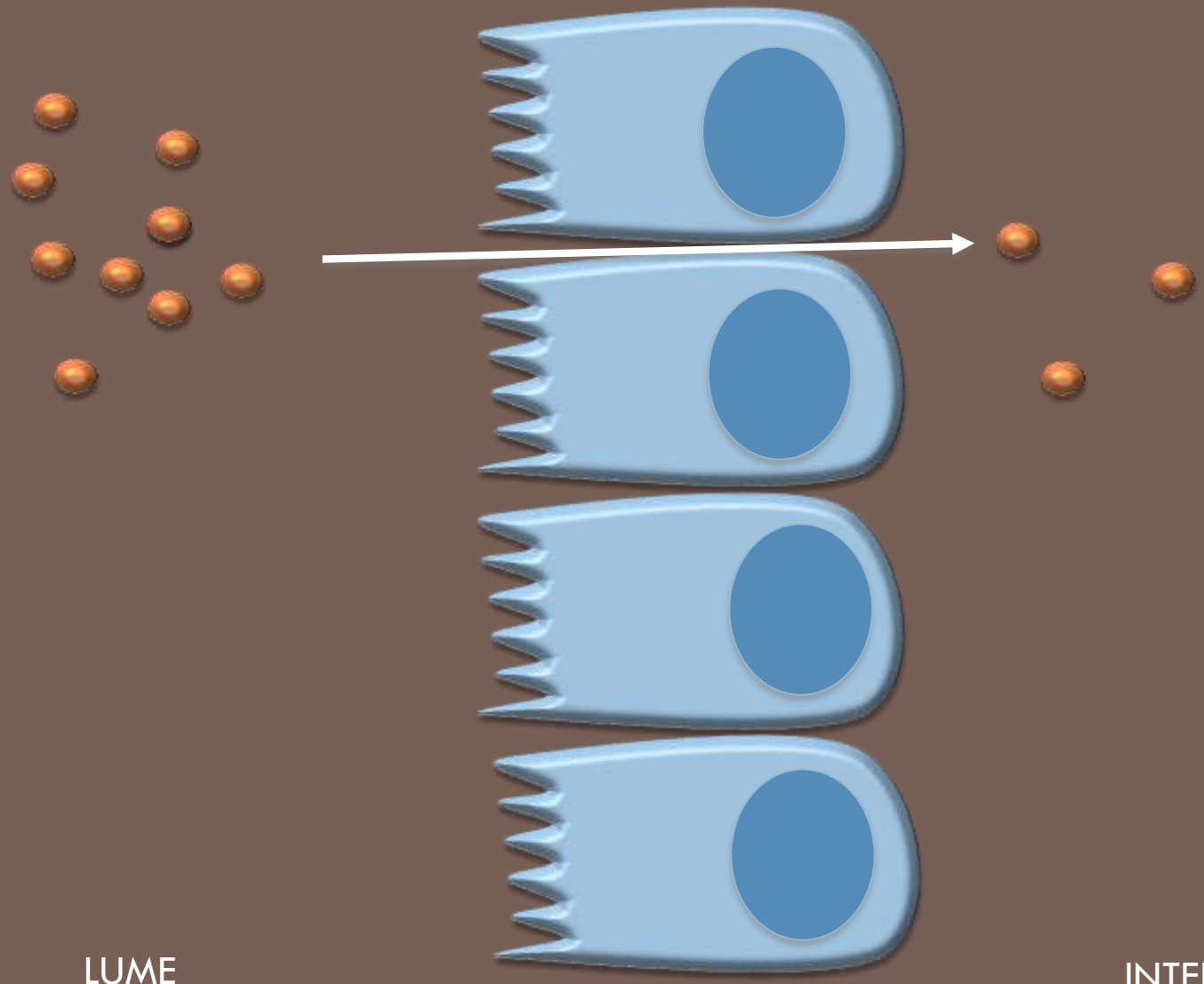
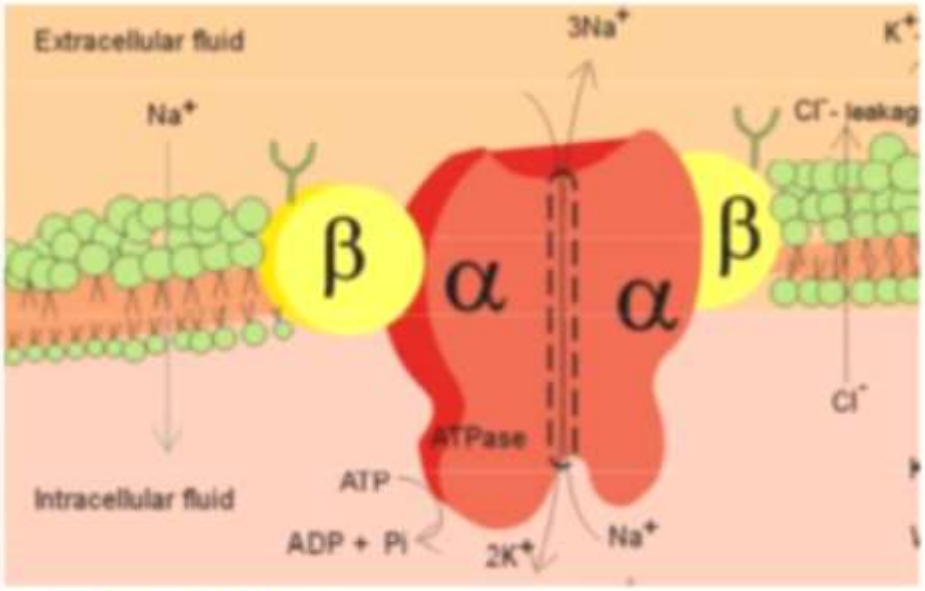
Trasporto Tubulare



Carmel
Libetta

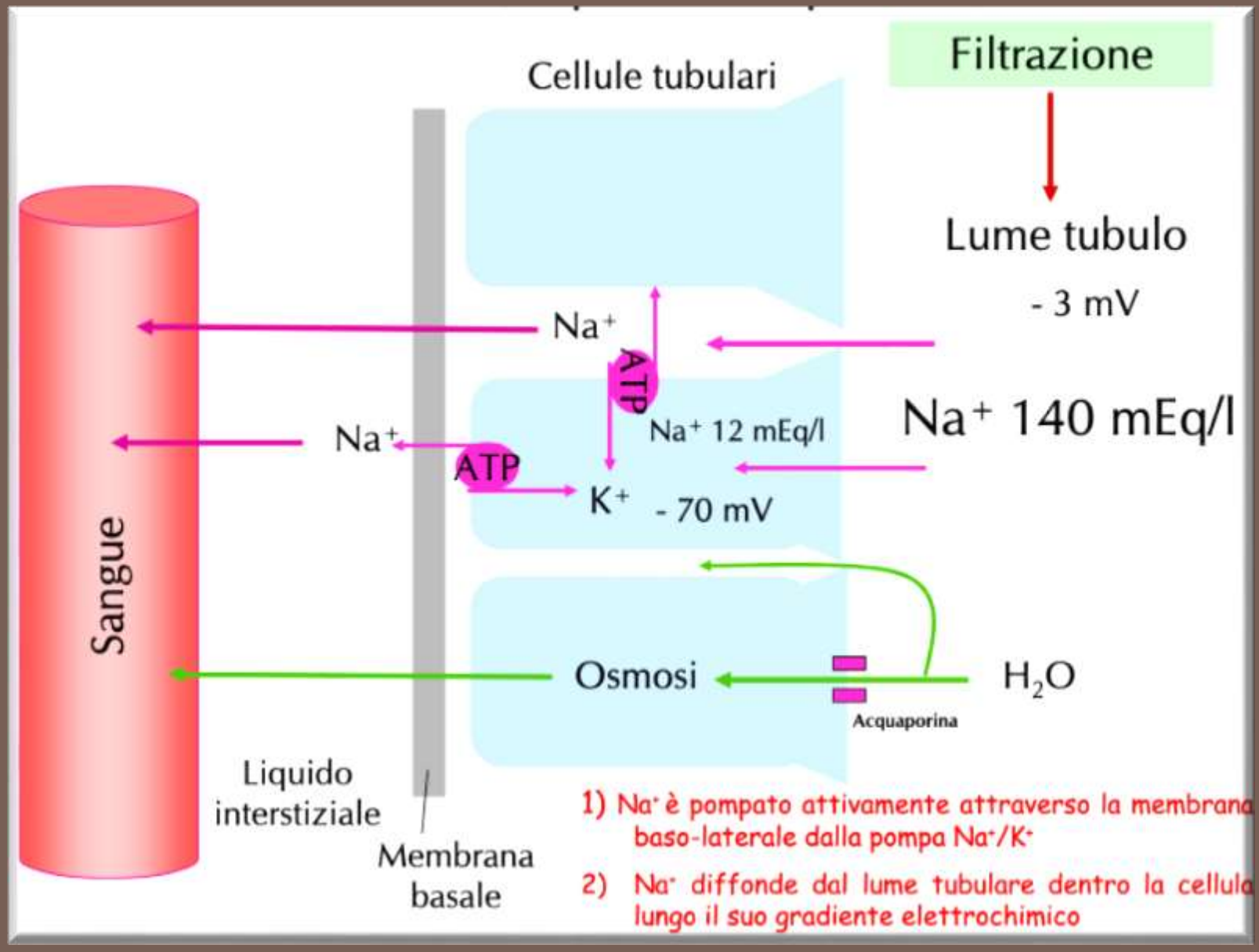
Riassorbimento Tubulare Passivo

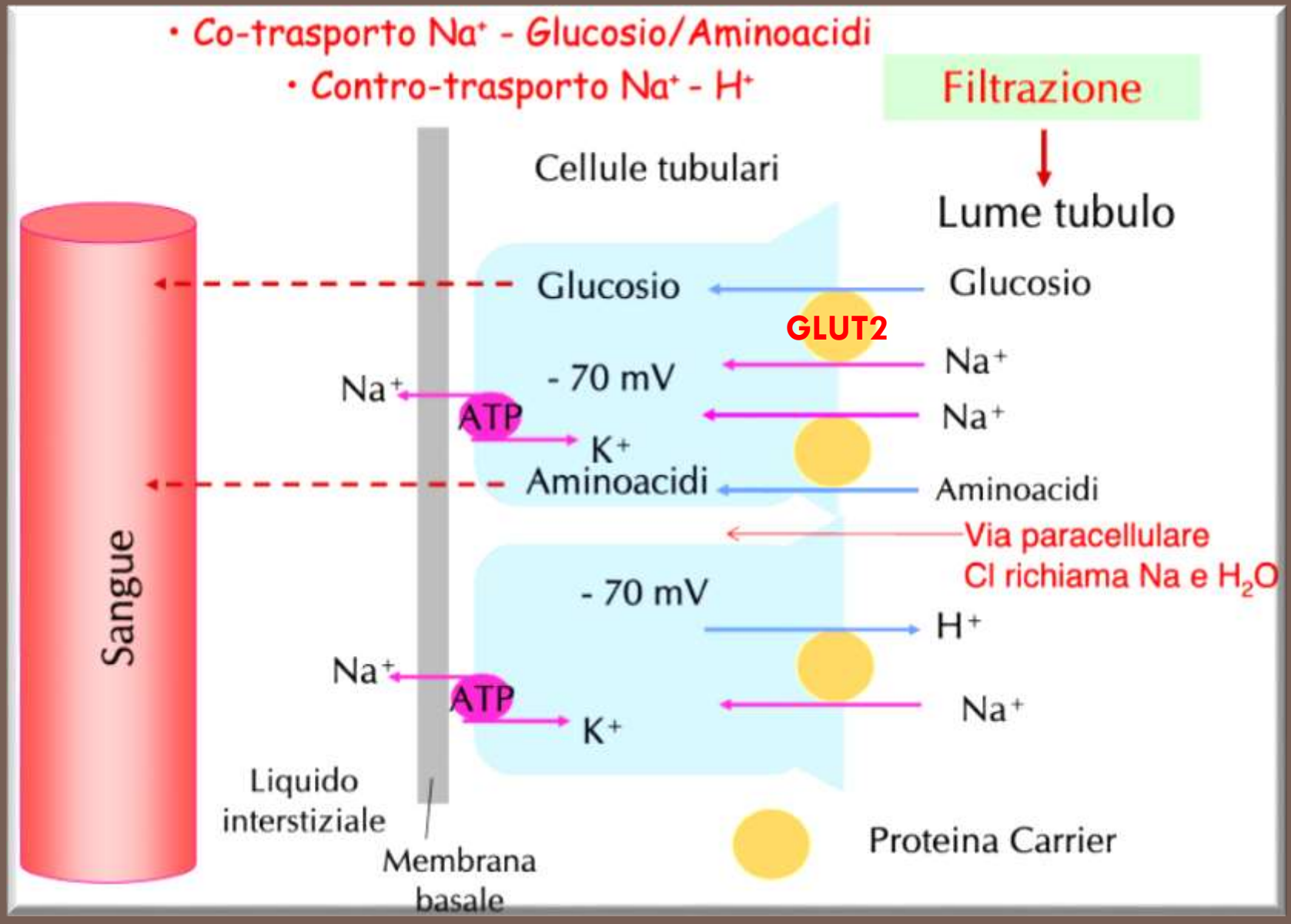


La pompa Na^+/K^+ATPasi consiste di 4 subunità principali (2 α e 2 β)

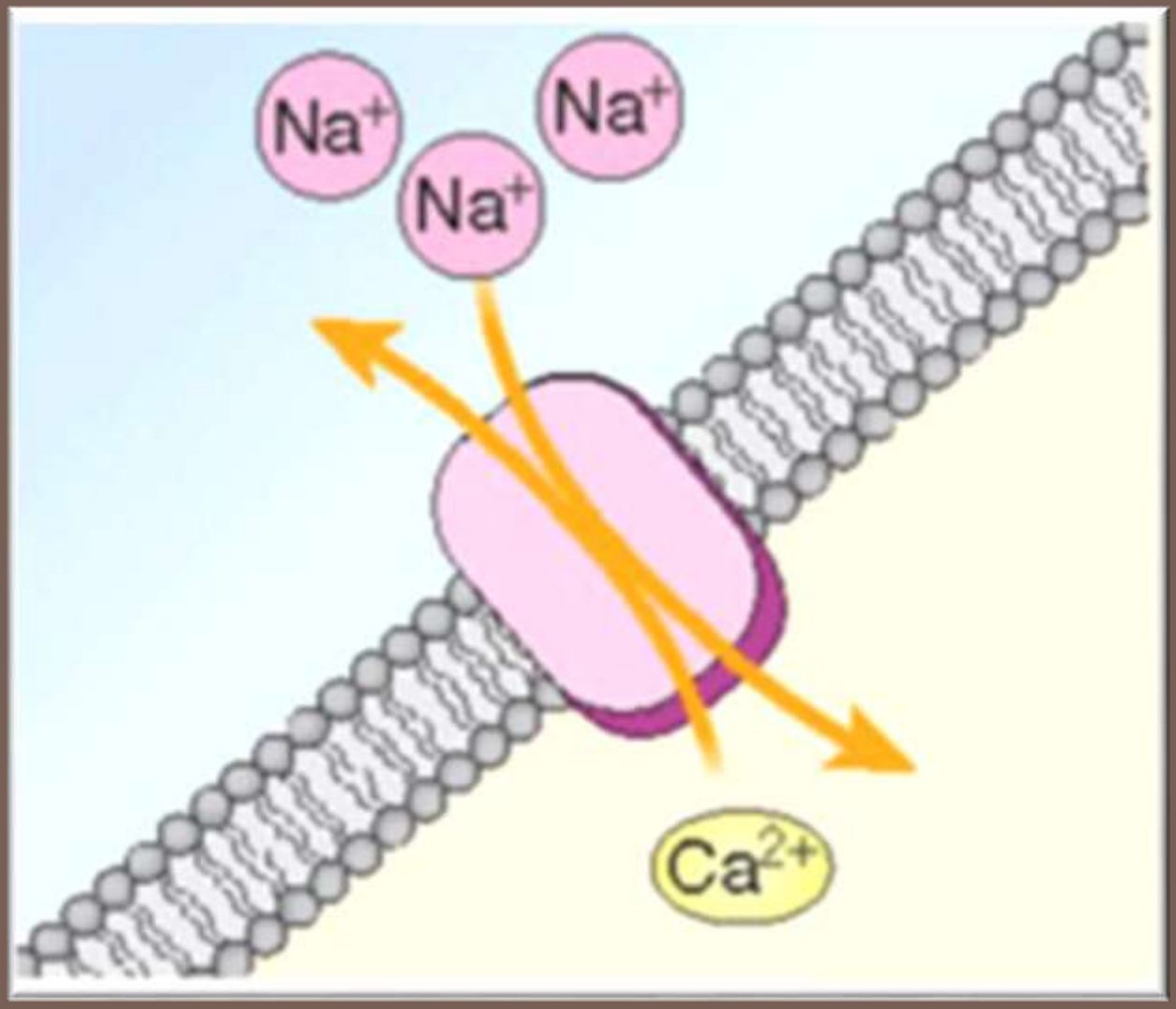
subunità α = 1000 aa; 110 KDa, 10 segmenti transmembrana. contiene i siti di legame per Na^+ e ATP e un sito di fosforilazione nel dominio citoplasmatico; nel dominio extracellulare ha i siti di legame per il K^+ e la ouabaina

subunità β = 300 aa; ~45 KDa, 1 segmento transmembrana, senza attività enzimatica e di trasporto. La sua associazione con la α-subunità è necessaria per l'attività della pompa in quanto stabilizza la subunità α all'interno della membrana

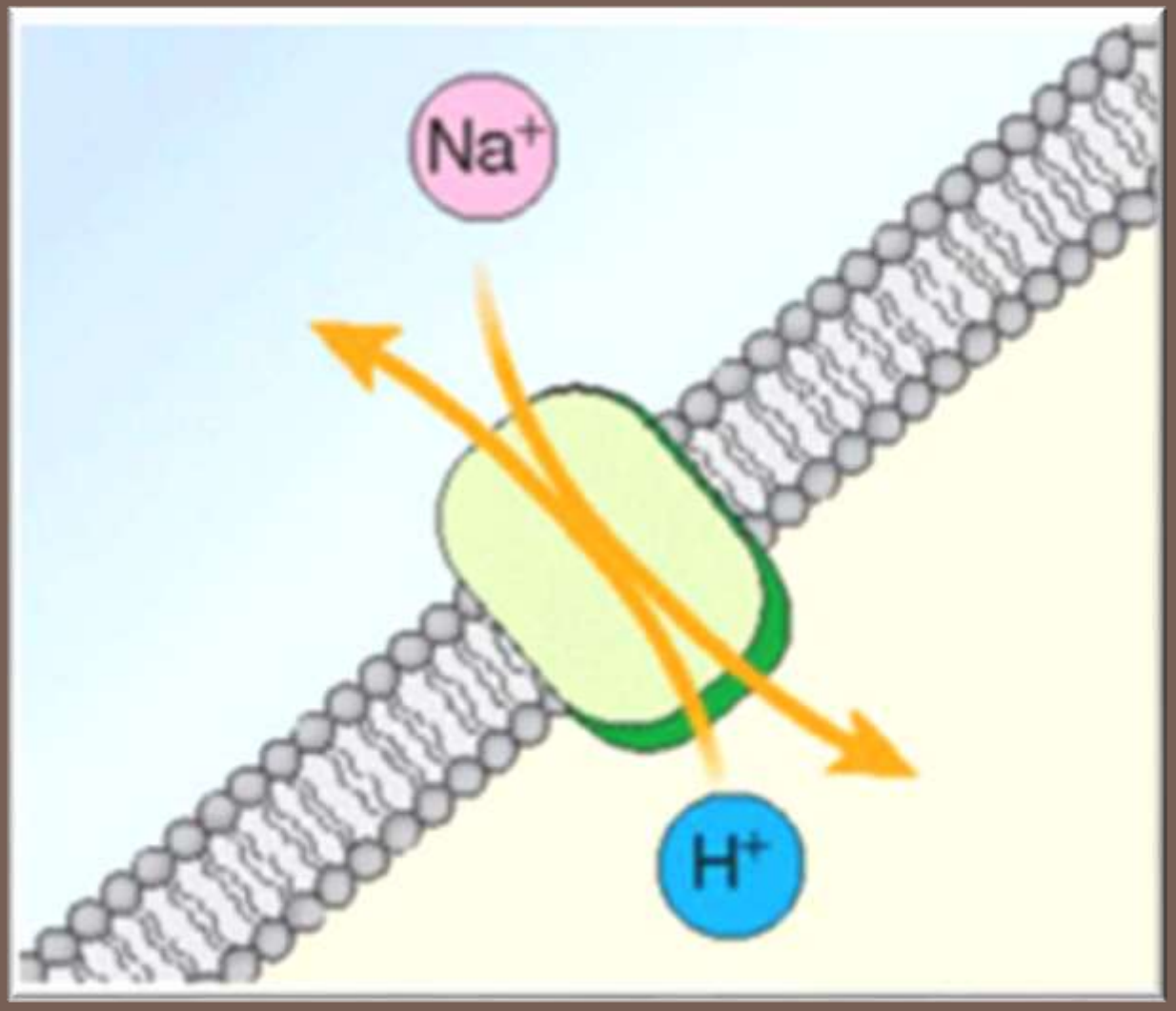

Filtrazione
Cellule tubulari
Lume tubulo
- 3 mV
Na+
ATP
Na+ 12 mEq/l
Na+ 140 mEq/l
Na+
ATP
K+
- 70 mV
Sangue
Osmosi
H2O
Acquaporina
Liquido interstiziale
Membrana basale
1) Na+ è pompato attivamente attraverso la membrana baso-laterale dalla pompa Na+/K+
2) Na+ diffonde dal lume tubulare dentro la cellula lungo il suo gradiente elettrochimico


• Co-trasporto Na⁺ - Glucosio/Aminoacidi
• Contro-trasporto Na⁺ - H⁺
Filtrazione
Cellule tubulari
Lume tubulo
Glucosio
Glucosio
GLUT2
Na⁺
- 70 mV
Na⁺
ATP
K⁺
Na⁺
Aminoacidi
Aminoacidi
Via paracellulare
Cl richiama Na e H2O
- 70 mV
H⁺
Na⁺
ATP
K⁺
Na⁺
Sangue
Liquido interstiziale
Membrana basale
Proteina Carrier

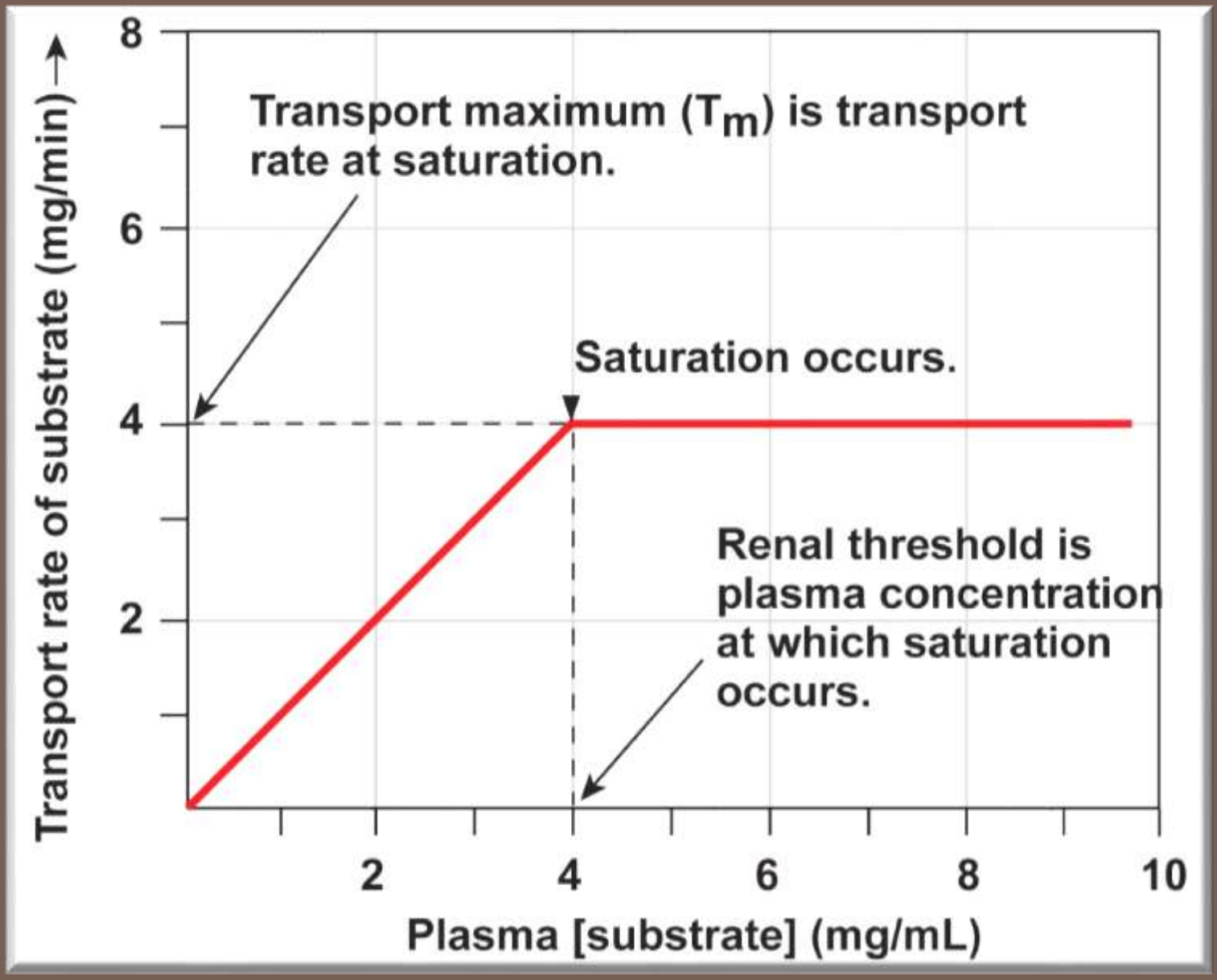
ANTIPORTO



ANTIPORTO

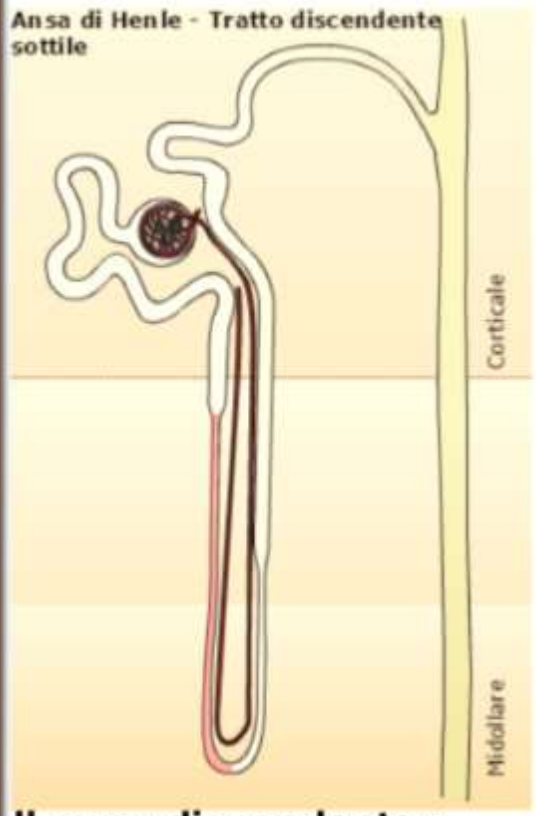


TRASPORTATORI PER SIMPORTO	TRASPORTATORI PER ANTIPORTO
Trasportatori sodio-dipendenti	
Na^+-glucosio (SGLT)	Na^+/H^+
Na^+/aminoacidi (diversi tipi)	Na^+/Ca^{2+}
Na^+-K^+-2 Cl^- (NKCC)	


Transport maximum (T_m) is transport rate at saturation.
Saturation occurs.
Renal threshold is plasma concentration at which saturation occurs.
Transport rate of substrate (mg/min)
Plasma [substrate] (mg/mL)
8
6
4
2
2
4
6
8
10

Tm tubulare

2 Ansa di Henle



TSD - Tratto sottile discendente (II tratto)

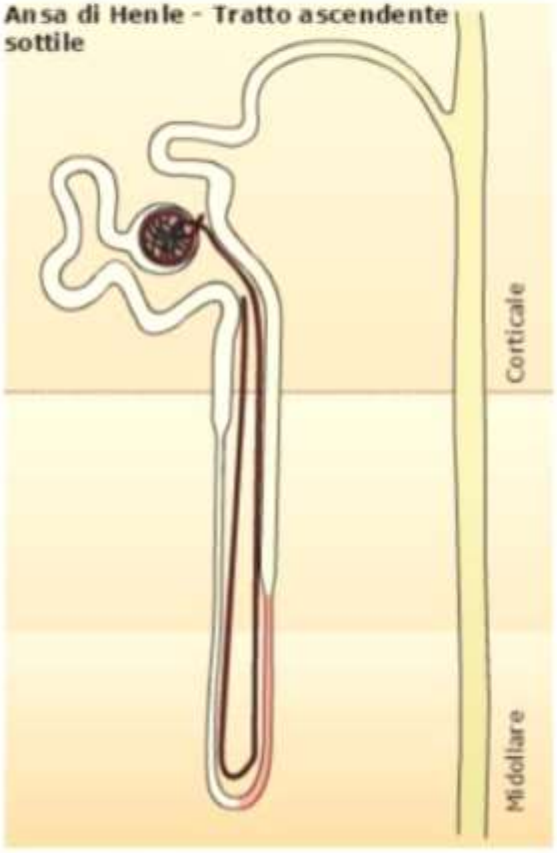
- Riassorbimento di H20 (25% di quella filtrata) per via transcellulare attraverso AQP1
- No riassorbimento di Na+

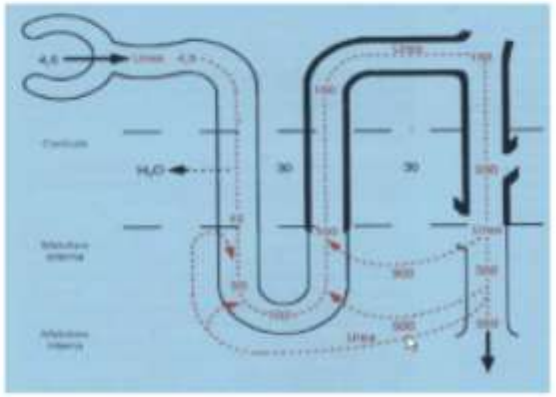
Il ramo discendente :

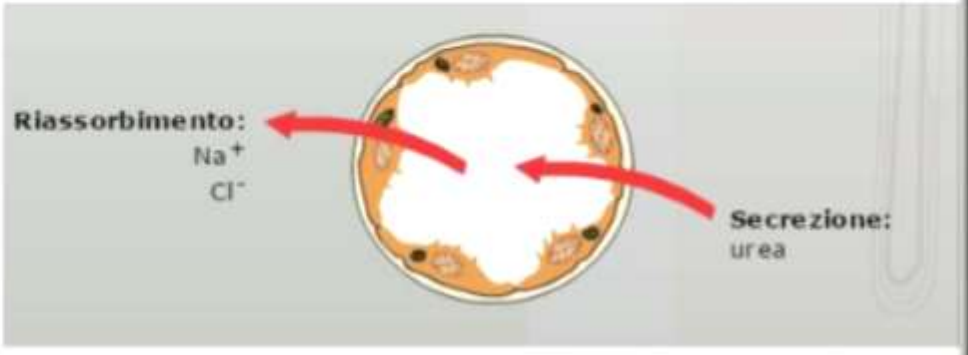
- è altamente permeabile all'acqua
- non riassorbe il Na^+ : è l'unico segmento dell'intero tubulo a non farlo

TAs è il tratto sottile ascendente (III tratto)

anch'esso impermeabile all'H2O come il TAS (tratto ascendente)
Riassorbimento urea
Piccolo riassorbimento passivo di NaCl





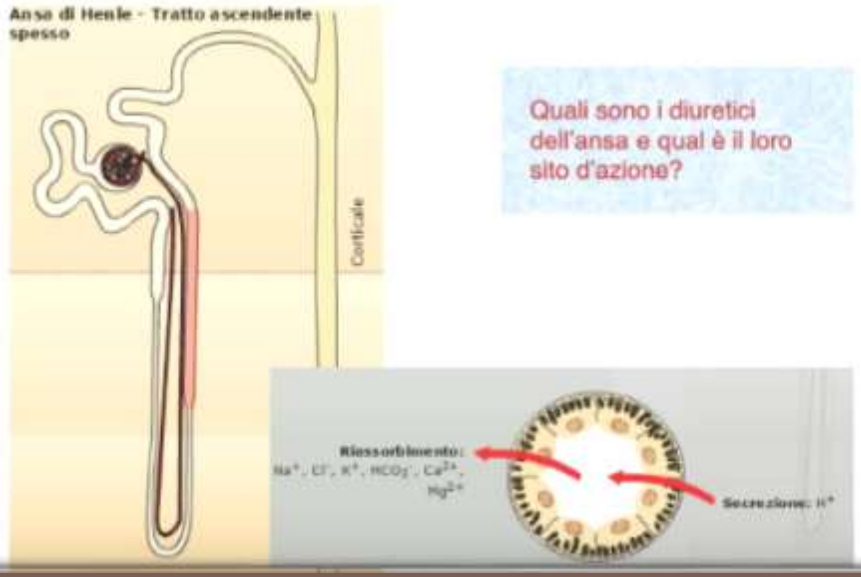


TAS o Tratto ascendente (IV tratto) o segmento diluente

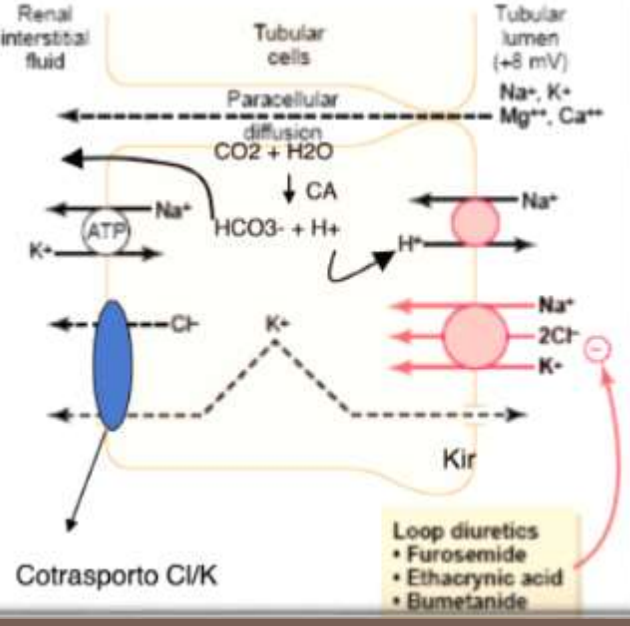
1) IMPERMEABILE all'H2O. La presenza di giunzioni occludenti rende poco impermeabile anche agli ioni e all'urea (via paracellulare)

2) Riassorbimento di Na+ e Cl- mediato da un simporto elettroneutro Na+/2Cl-/K+ che è inibito dai "*diuretici dell'ansa*" (furosemide e bumetanide). **Na+ segue passivamente il Cl-**

a) -K+ riciclato tramite un canale inibito dall'ATP (KIR/ROMK) e regolato dal pH intra e dal Ca2+ . Il ritorno K+ determina lume + (+8 mV) favorisce riass Ca2+ e Mg2+



Quali sono i diuretici dell'ansa e qual è il loro sito d'azione?



TAS (Spesso)

Tubulo contorto distale (TCD)

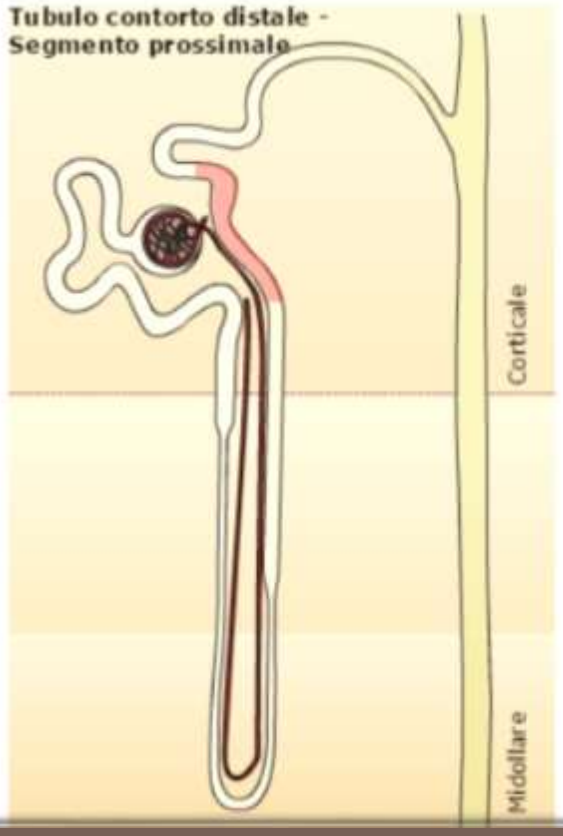
Parte prossimale del TCD (segmento diluente)

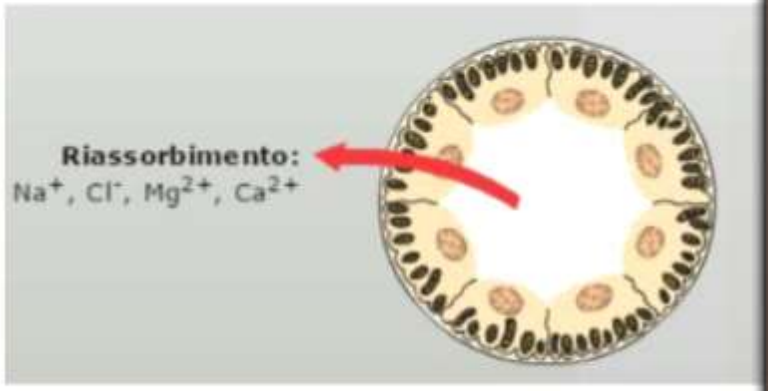
E' localizzato interamente nella corticale, parte del complesso juxtaglomerulare

Riassorbimento attivo di Na+ (aldosterone dipendente) e passivo di Cl-

Riassorbimento di Ca2+ e Mg2+

Impermeabile all'H2O

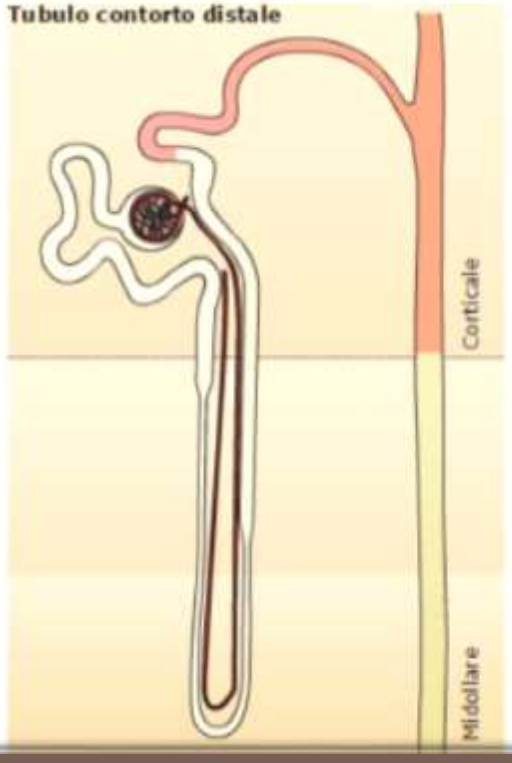


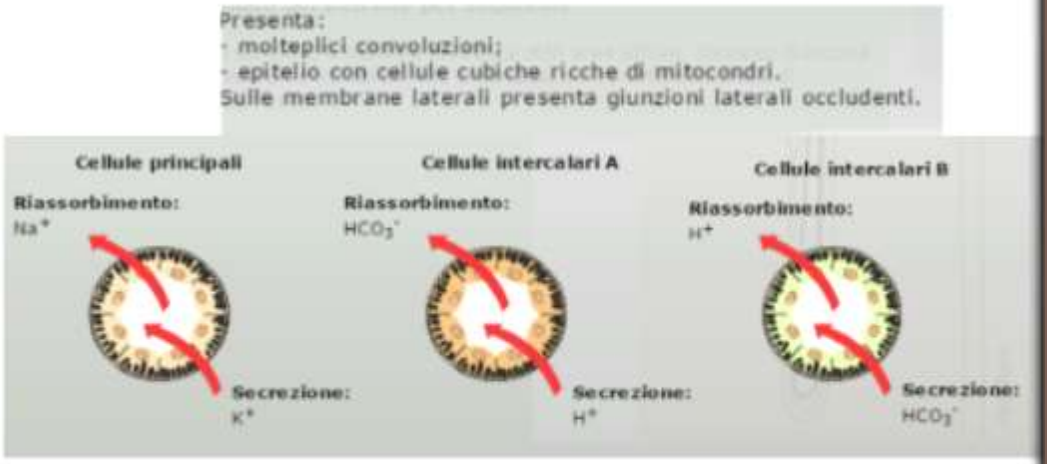


Parte distale del TDS **e DOTTO COLLETTORE CORTICALE**

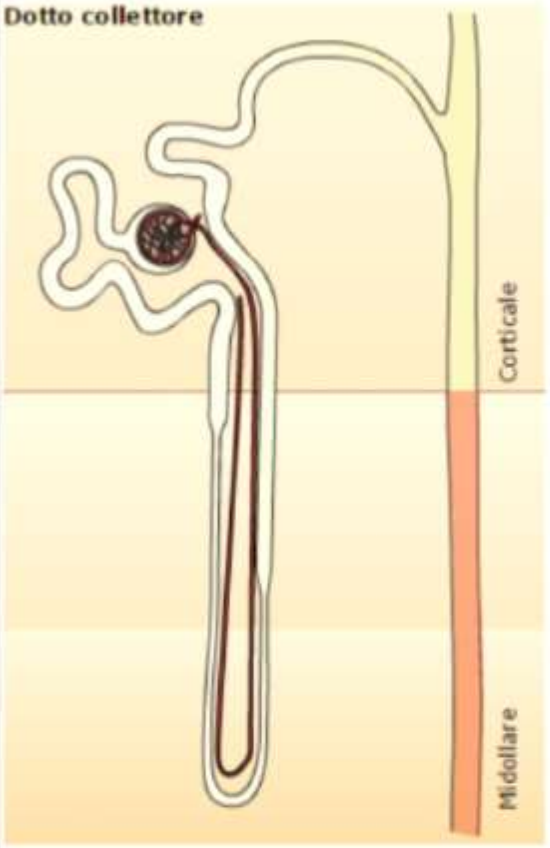
Troviamo le cellule principali e le cellule intercalate

- Impermeabile all'urea
- Permeabilità H2O regolata da ADH
- Permeabilità Na regolata da aldosterone

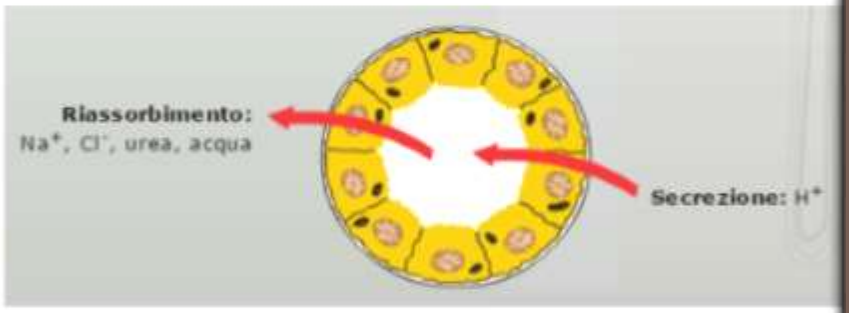




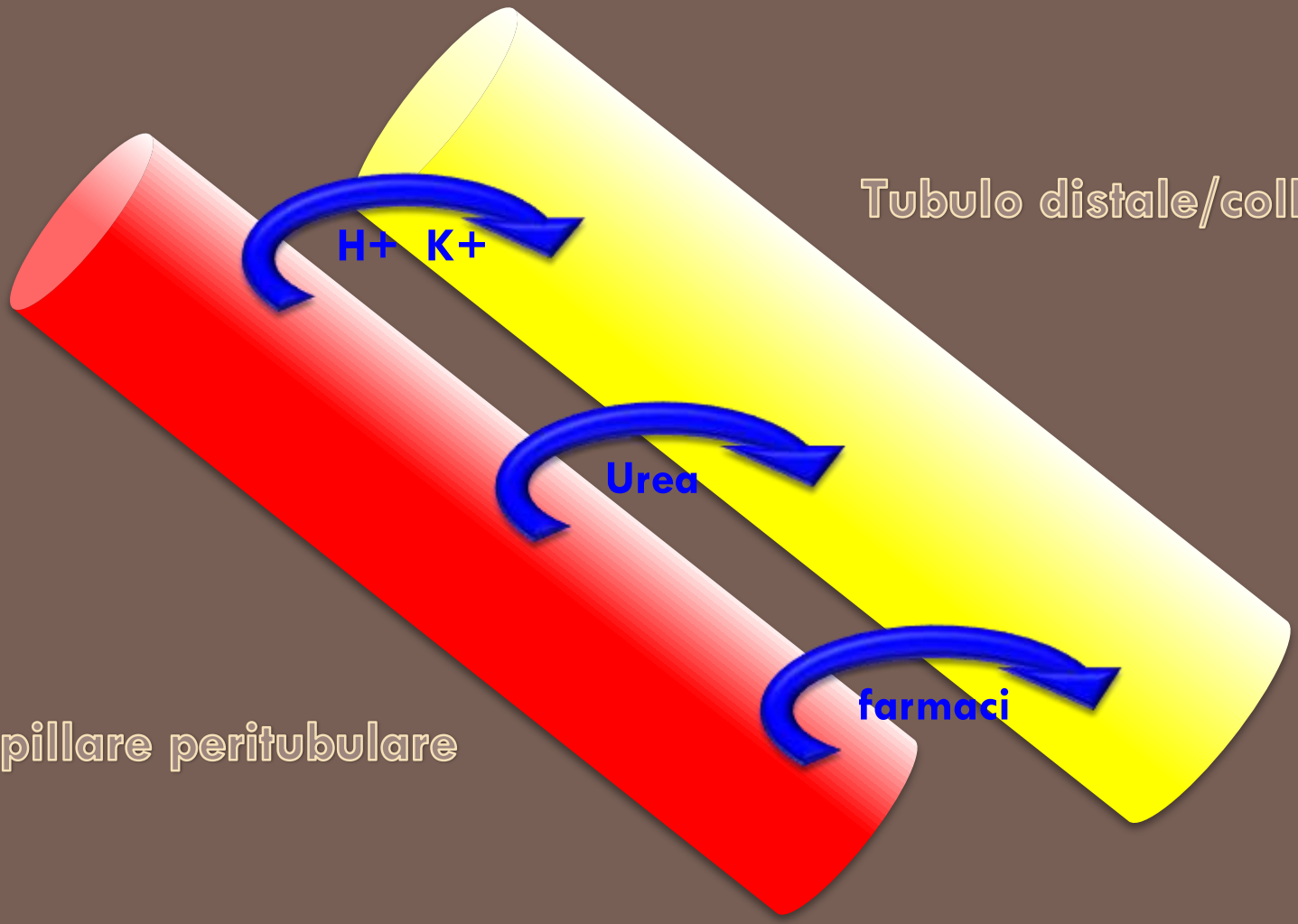
DOTTO COLLETTORE porzione MIDOLLARE



Regola il riassorbimento dell'acqua secondo gradiente osmotico
Regola la secrezione di idrogenioni



Permeabilità H_2O (ADH dipendente)
Permeabilità urea
Secrezione di H+ controgradiente

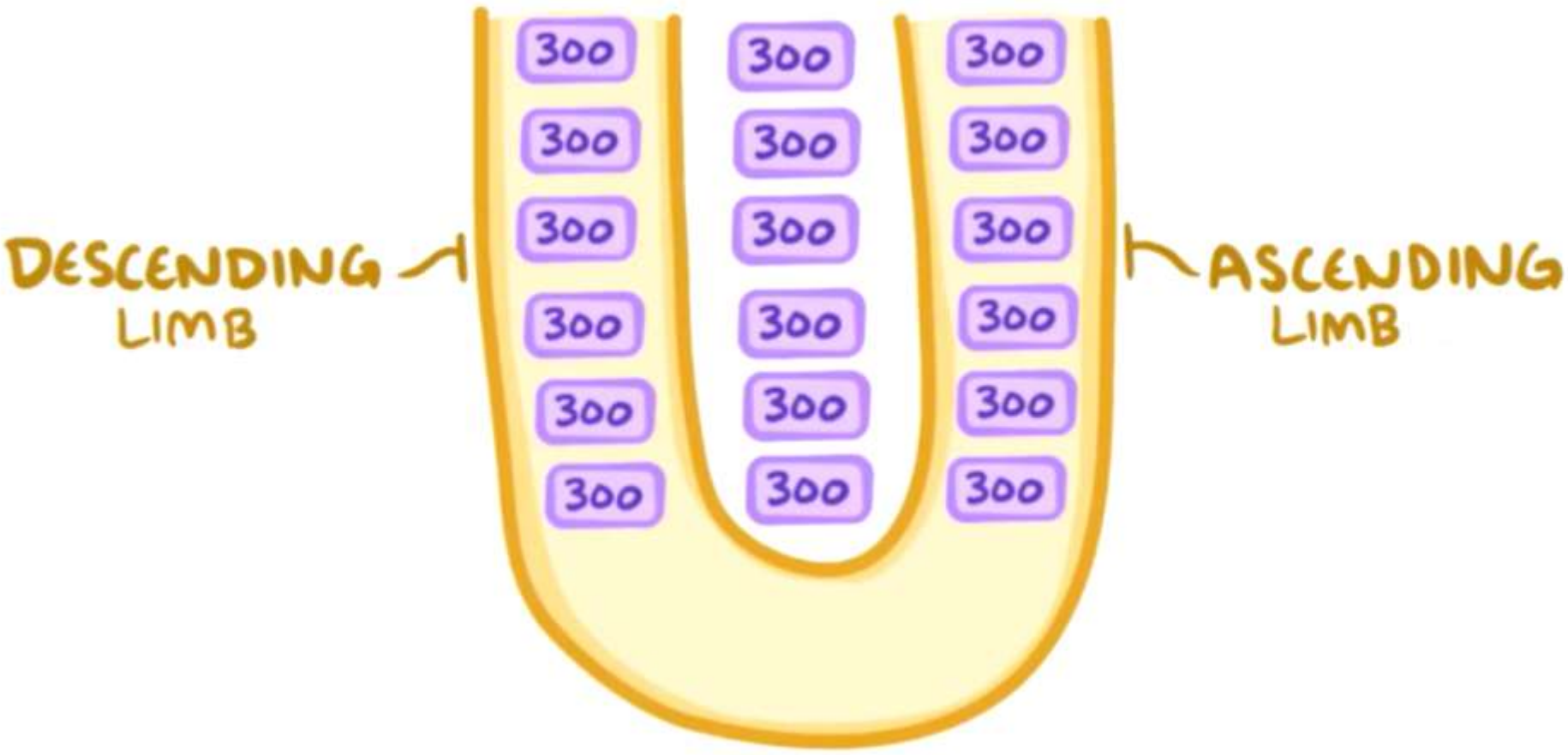


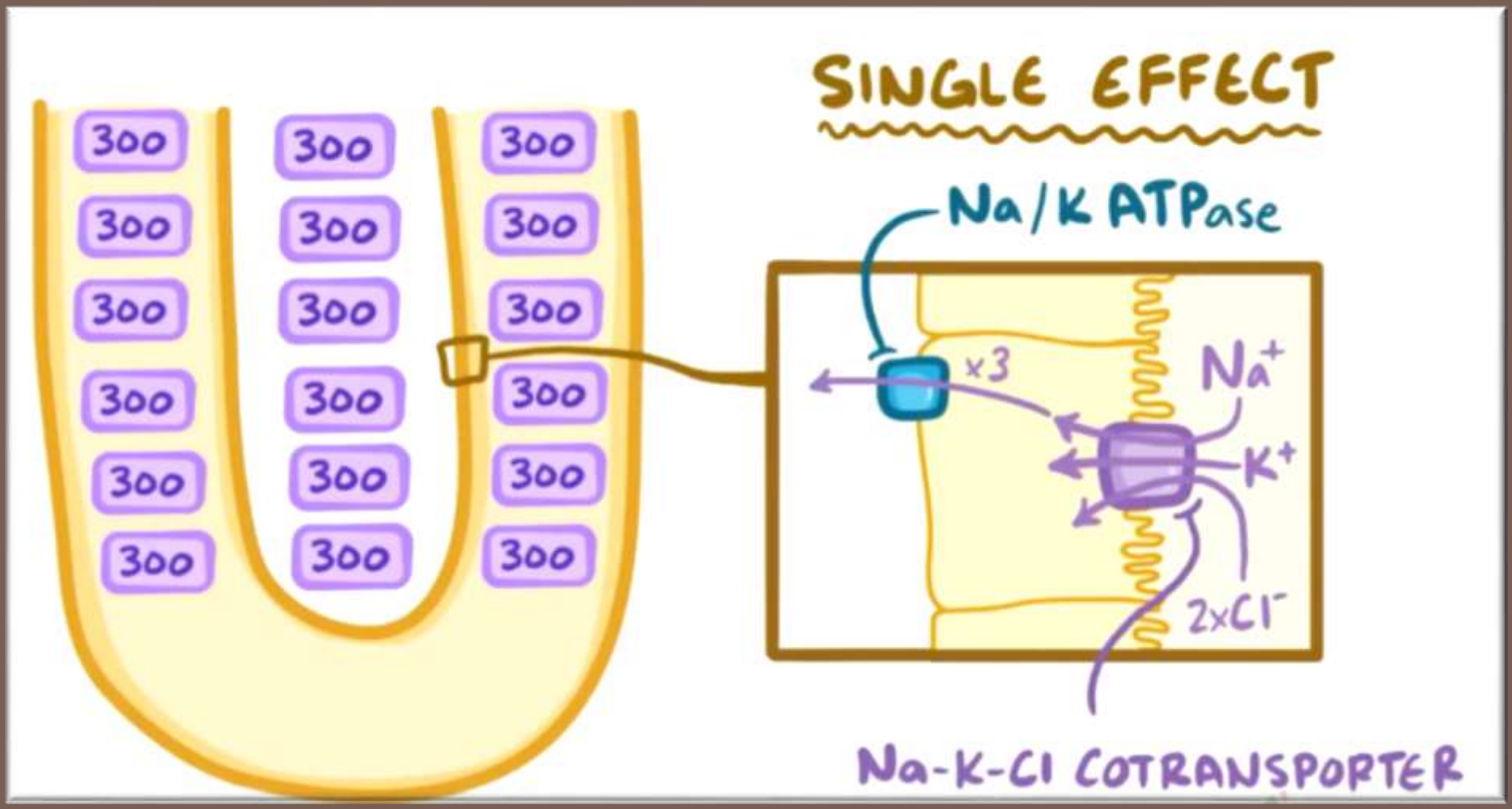
Carmela Libetta

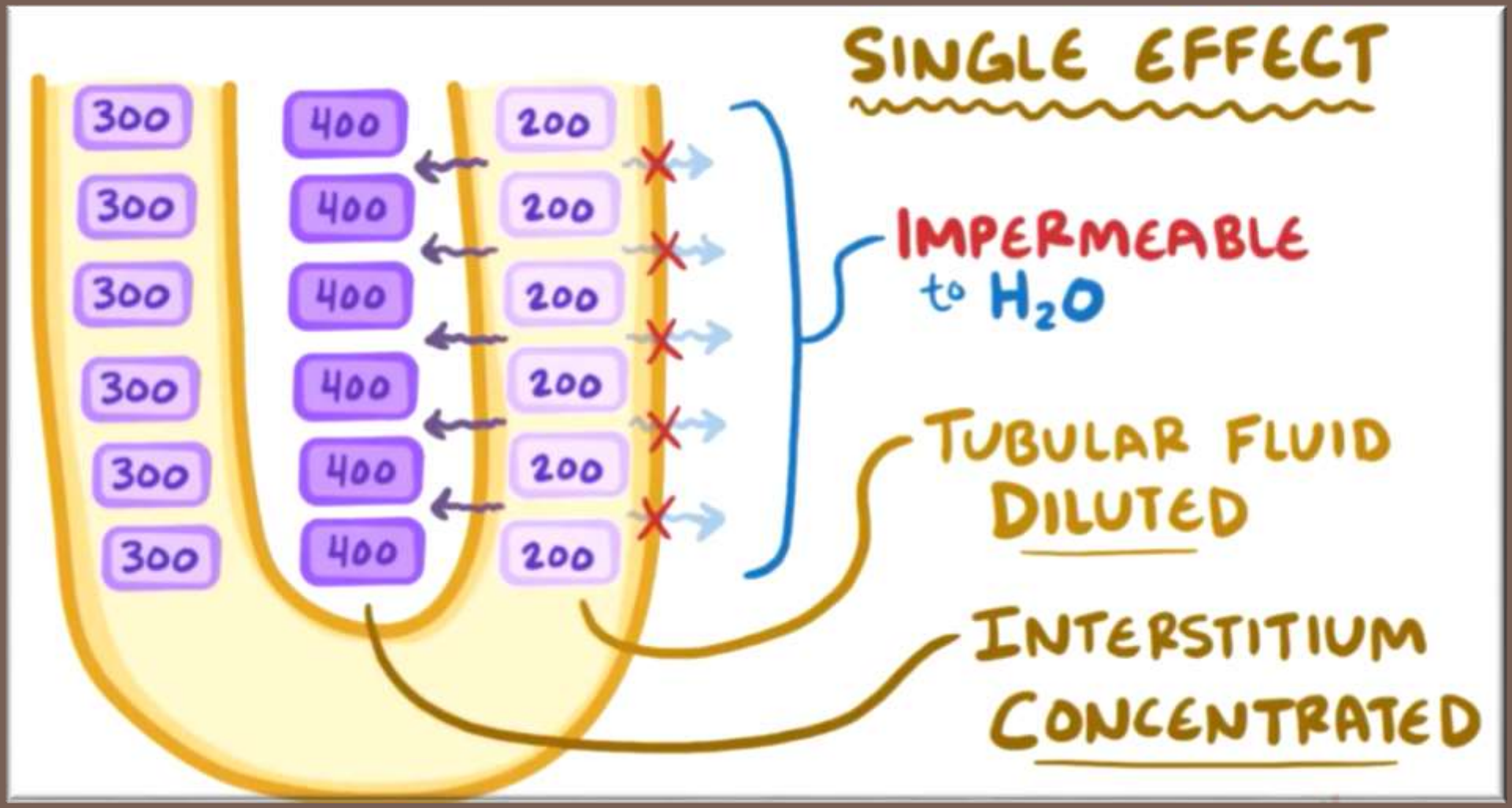
Secrezione tubulare

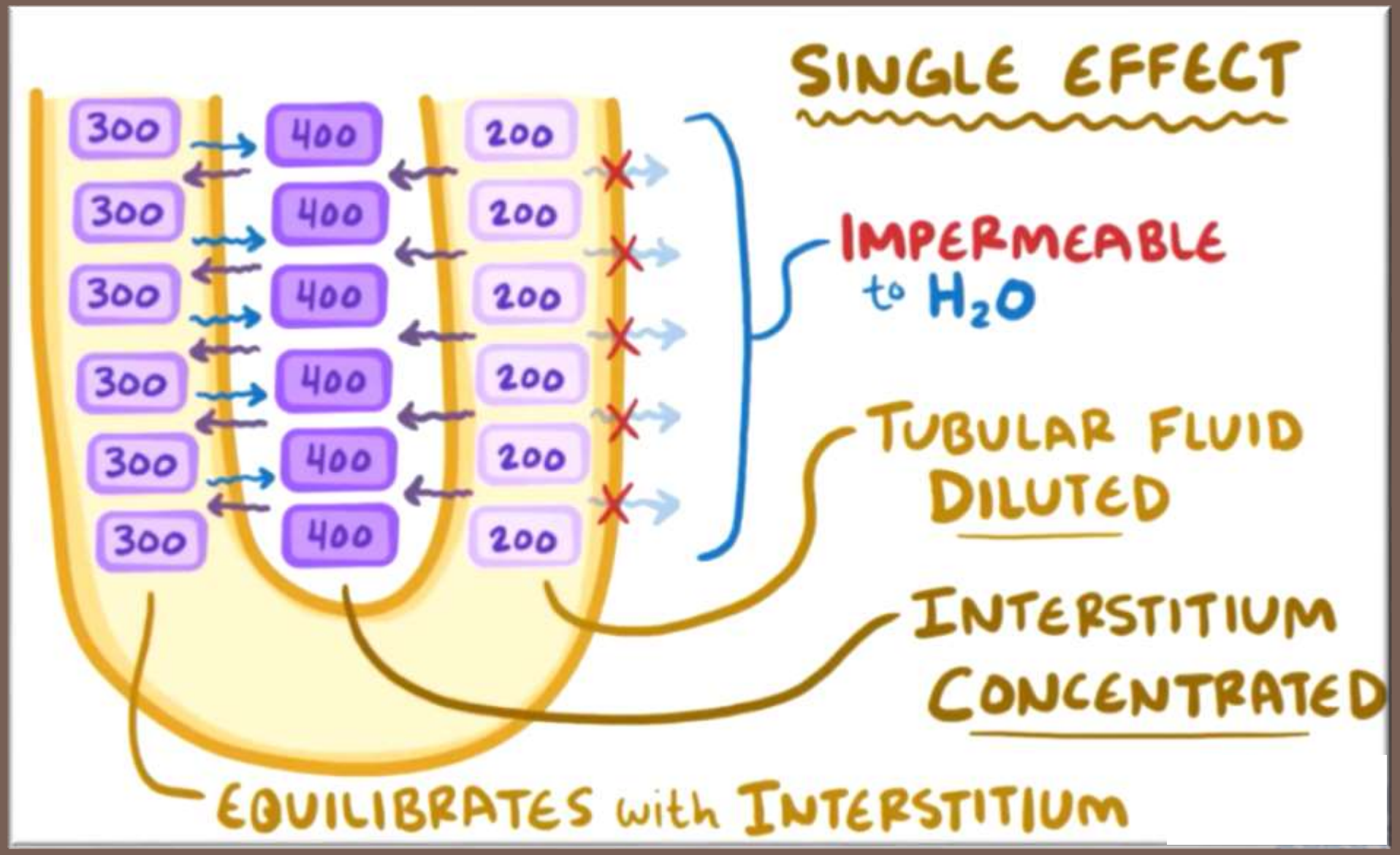
Urine Color Chart

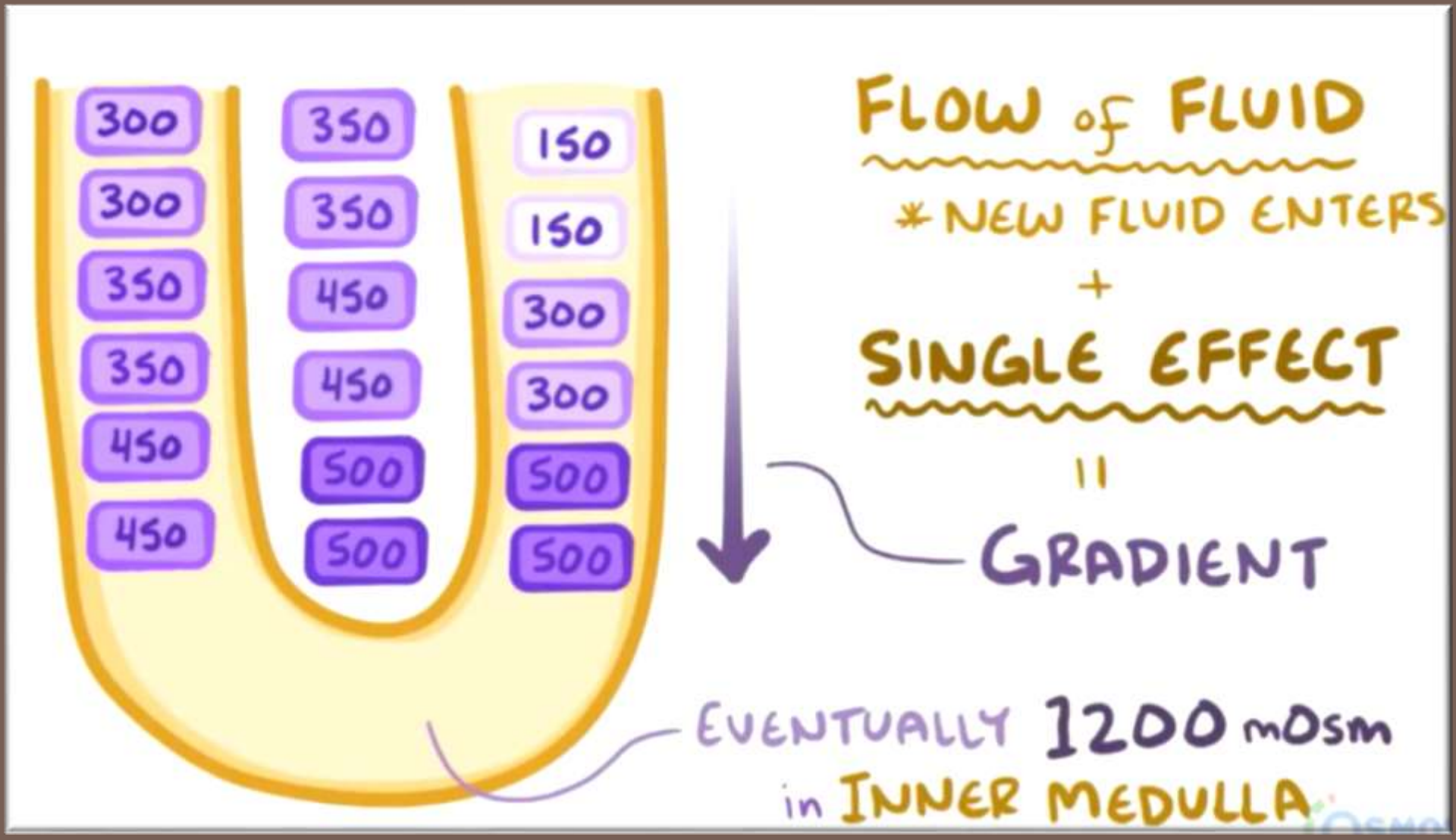
Urine Color	Possible Meaning
Clear	Good hydration, overhydration or mild dehydration
Pale Yellow	Good hydration or mild dehydration
Bright Yellow	Mild or moderate dehydration or taking vitamin supplements
Orange, Amber	Moderate or severe dehydration
Tea-Colored	Severe dehydration

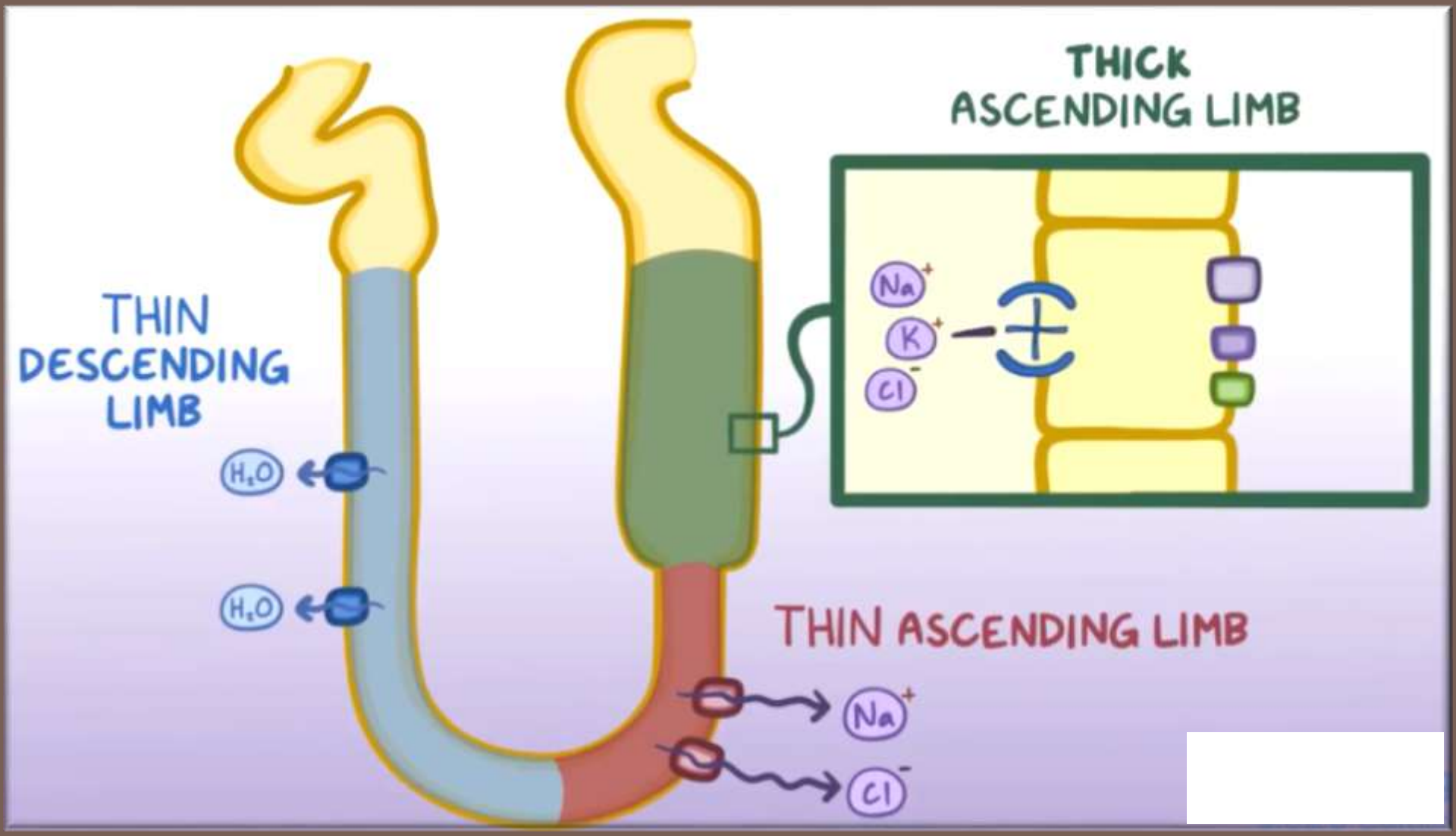

DESCENDING LIMB
ASCENDING LIMB
300
300
300
300
300
300
300
300
300
300
300
300
300
300
300
300
300
300


SINGLE EFFECT
300
Na/K ATPase
x3
Na+
K+
2xCl-
Na-K-Cl COTRANSPORTER


SINGLE EFFECT
300
300
300
300
300
300
400
400
400
400
400
400
200
200
200
200
200
200
IMPERMEABLE
to H_2O
TUBULAR FLUID
DILUTED
INTERSTITIUM
CONCENTRATED


SINGLE EFFECT
300
400
200
IMPERMEABLE to H_2O
TUBULAR FLUID DILUTED
INTERSTITIUM CONCENTRATED
EQUILIBRATES with INTERSTITIUM

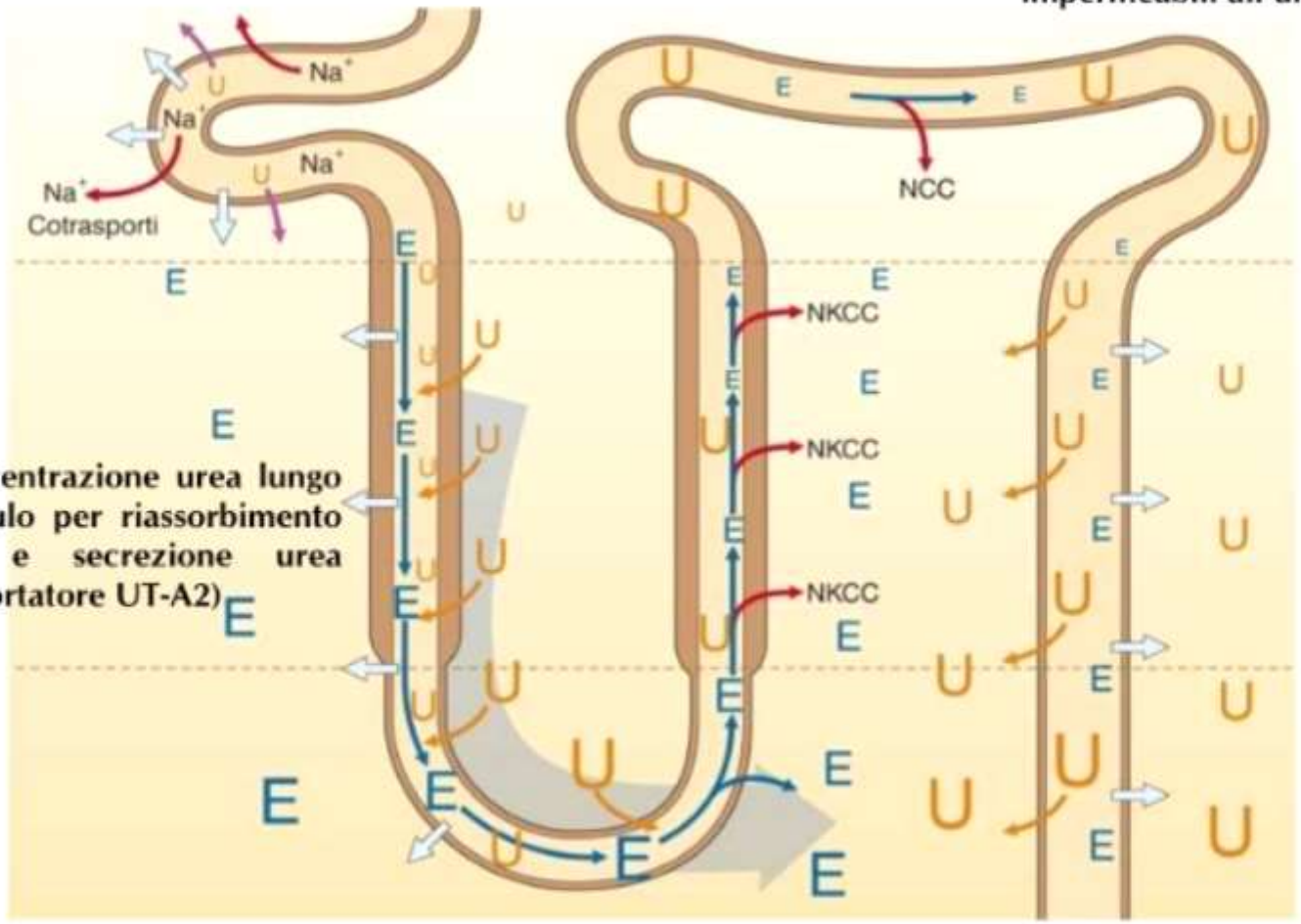

300
300
350
350
450
450
350
350
450
450
500
500
150
150
300
300
500
500
FLOW of FLUID
* NEW FLUID ENTERS
+
SINGLE EFFECT
=
GRADIENT
EVENTUALLY 1200 mOsm
in INNER MEDULLA



Carmelo
Libetta

Generazione del gradiente midollare

2) ↑↑concentrazione urea nel tubulo distale e collettore impermeabili all'urea

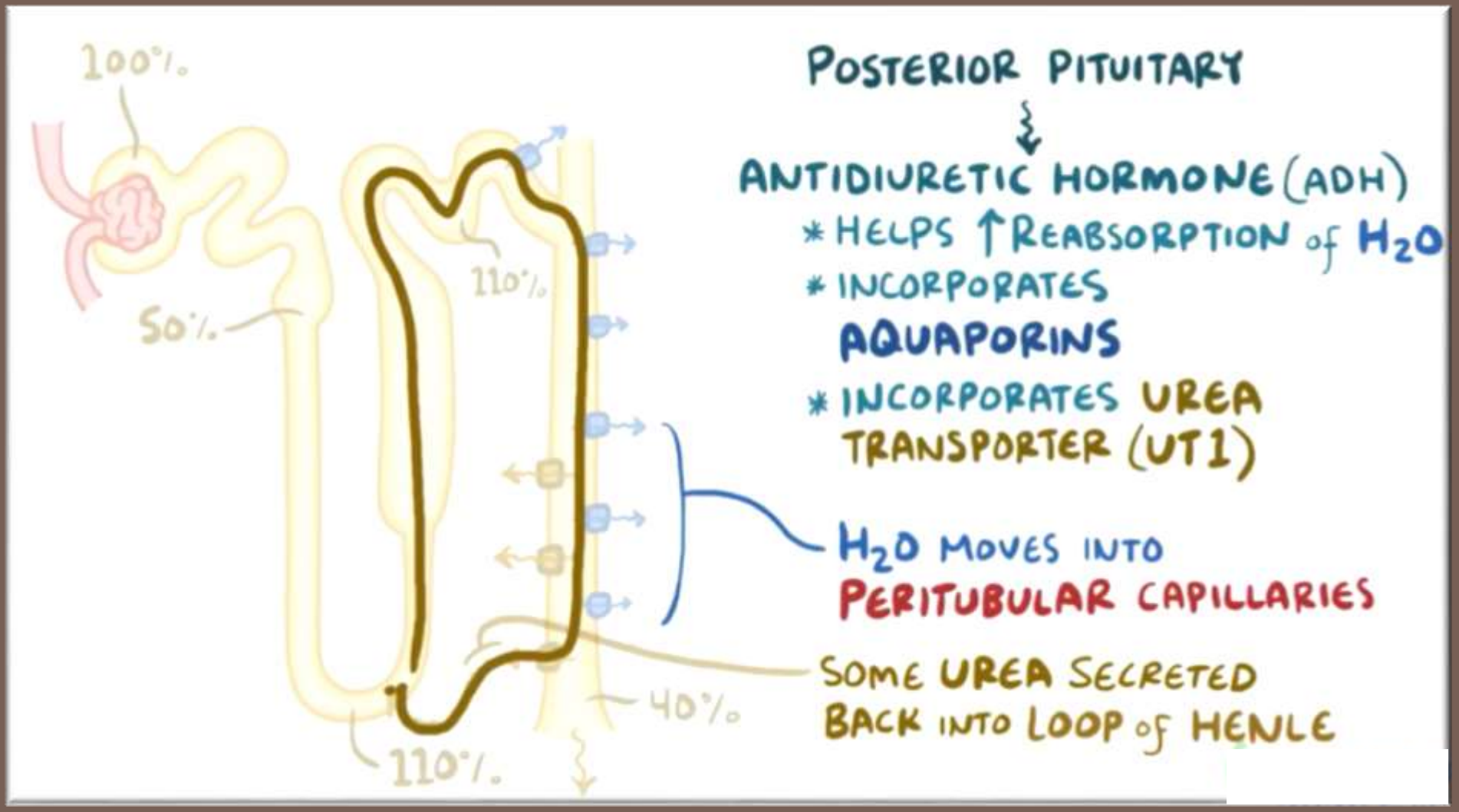


1) ↑concentrazione urea lungo il tubulo per riassorbimento H_2O e secrezione urea (trasportatore UT-A2)

U=Urea

3) urea diffonde passivamente nell'interstizio a livello del dotto collettore della midollare interna (permeabilità controllata da ADH) e

Urea/Meccanismo controcorrente



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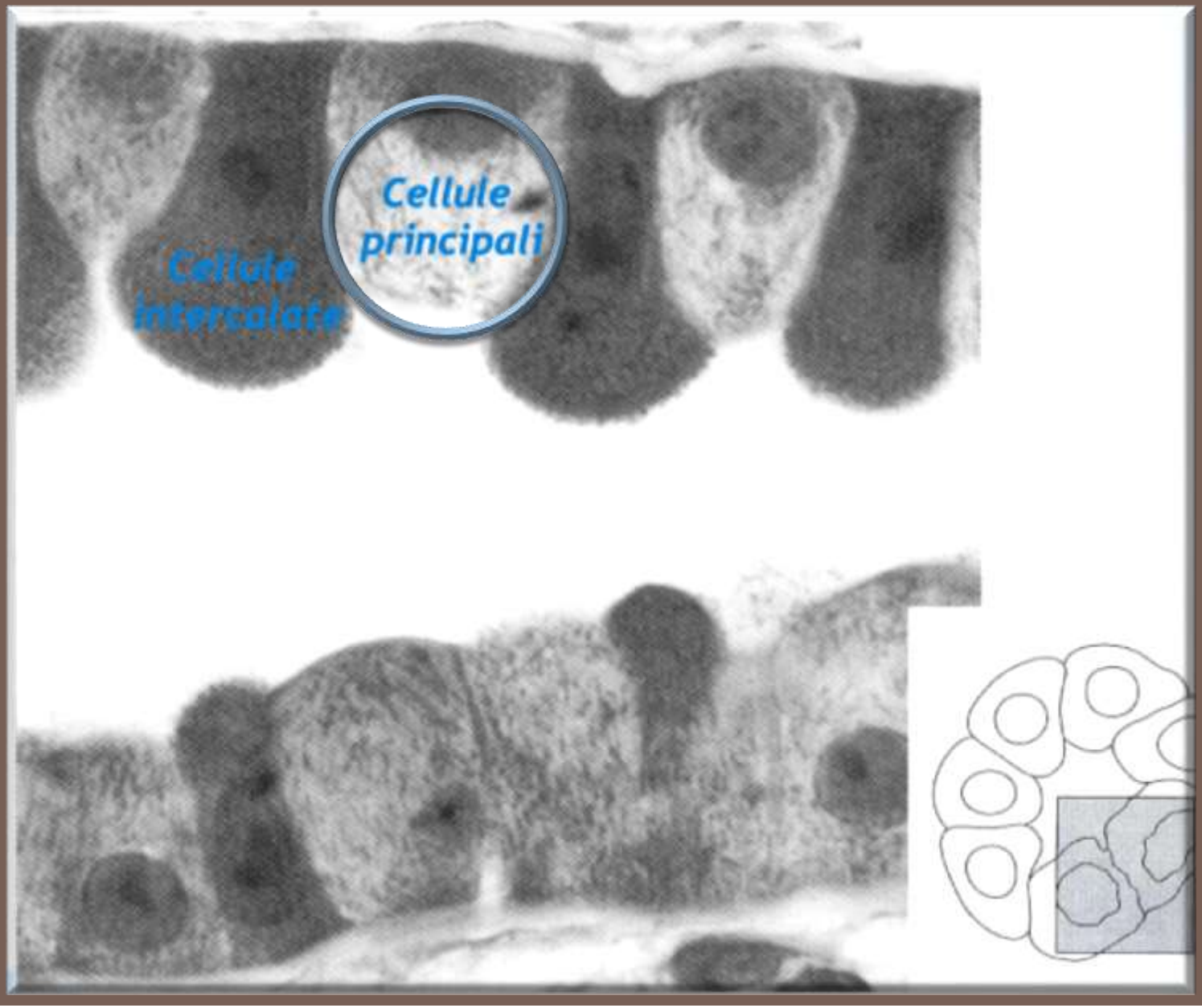
RICICLO DELL'UREA

TUBULO COLLETTORE



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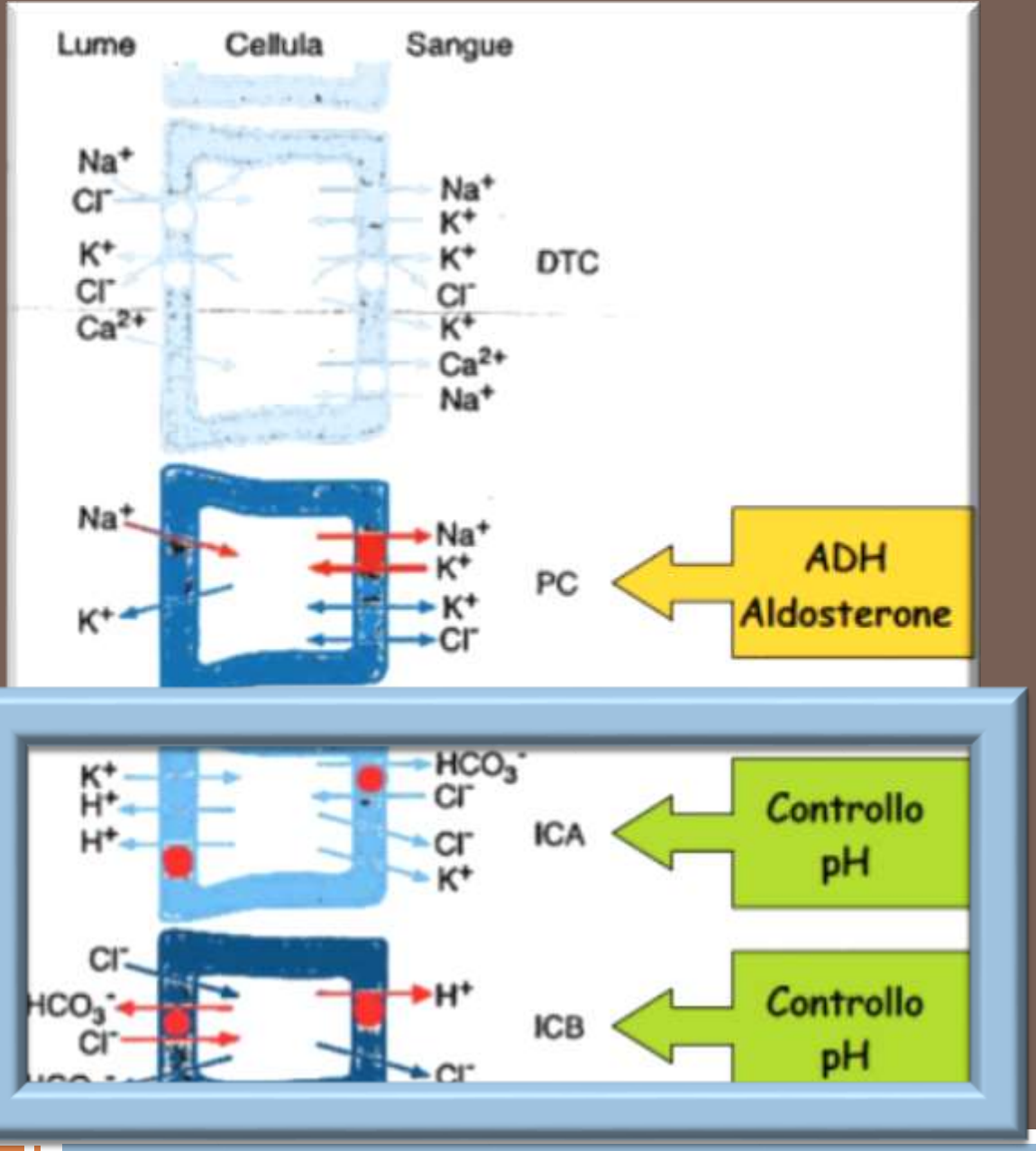
Concentrazione/diluizione



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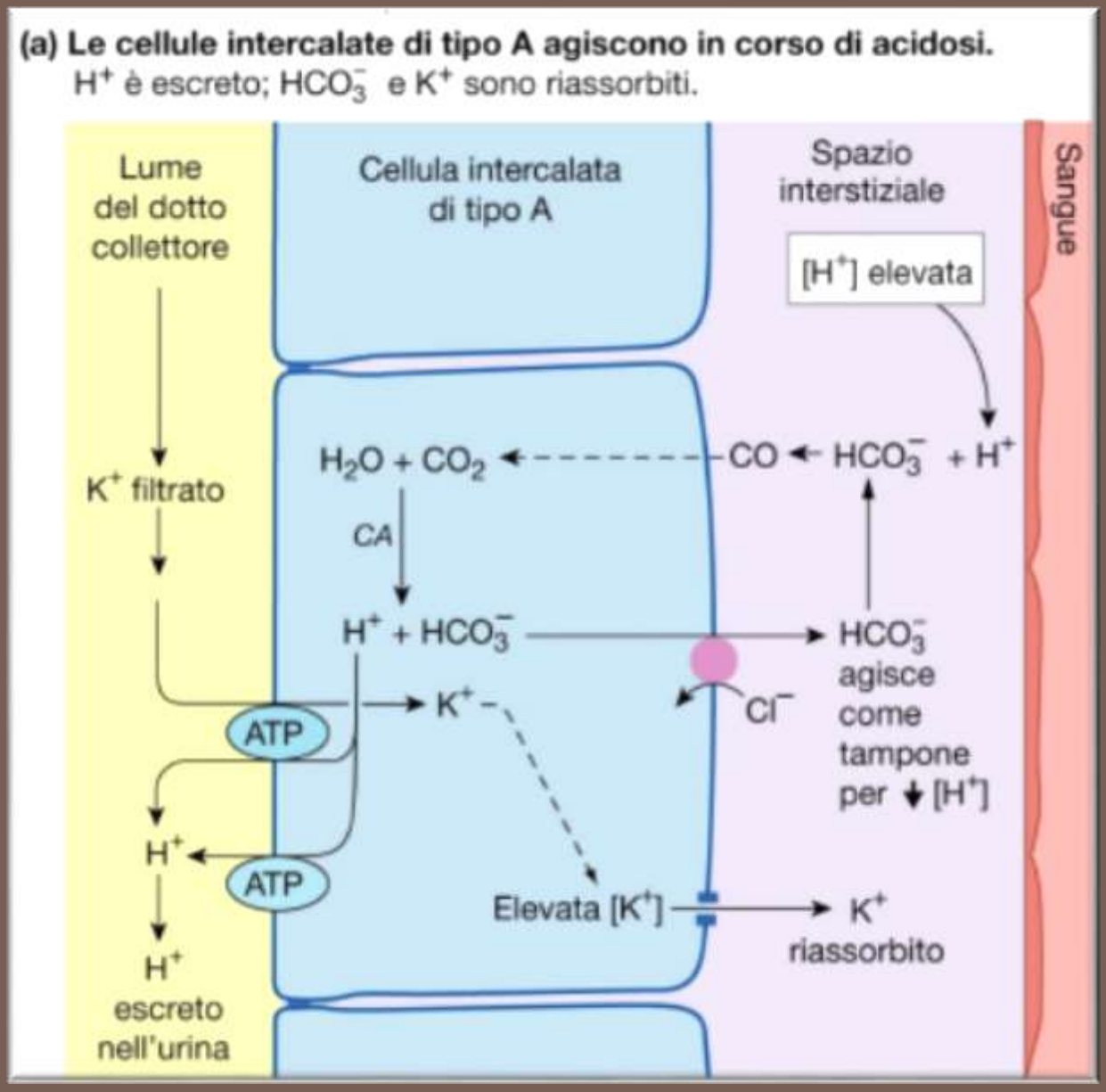
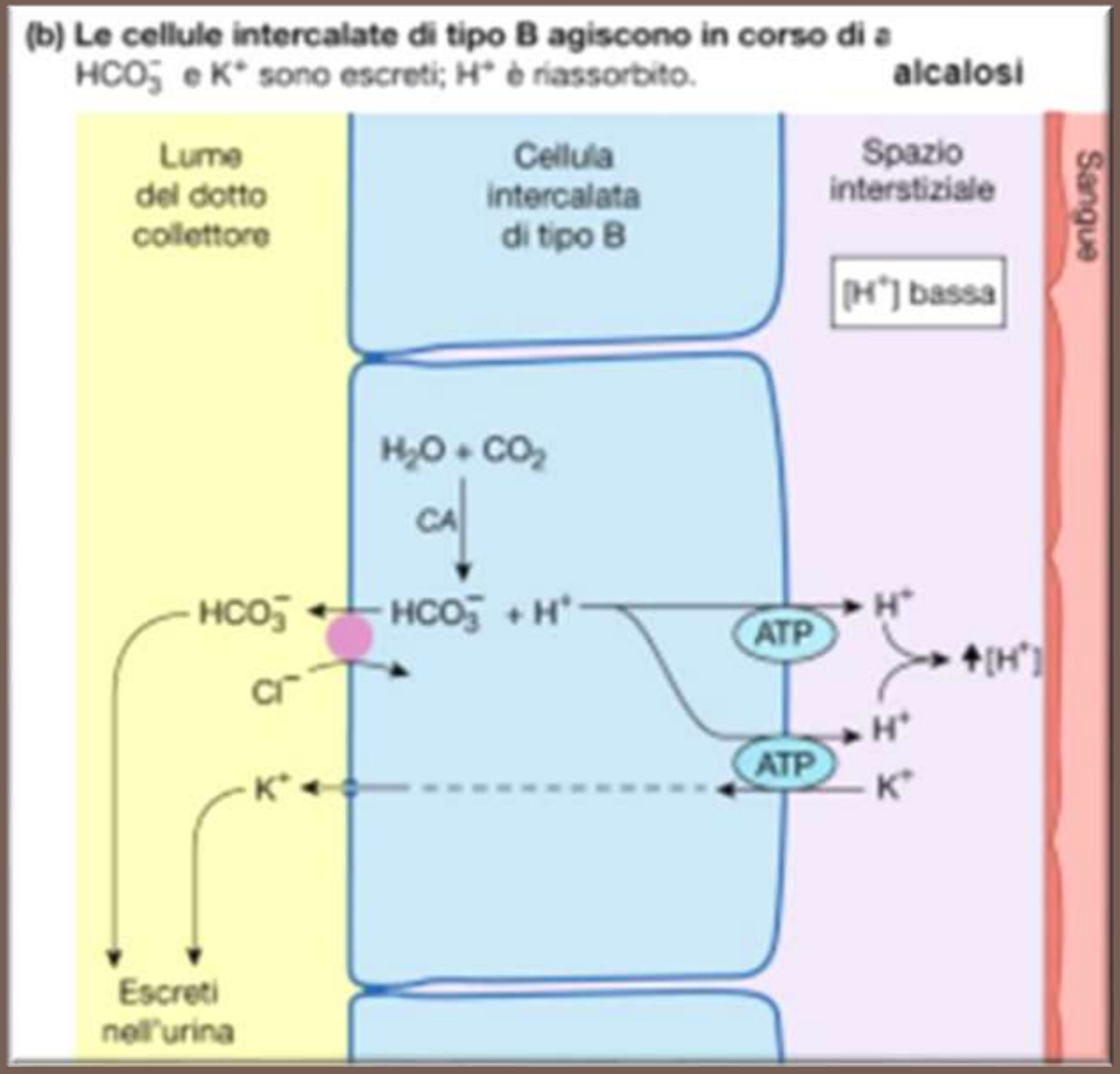
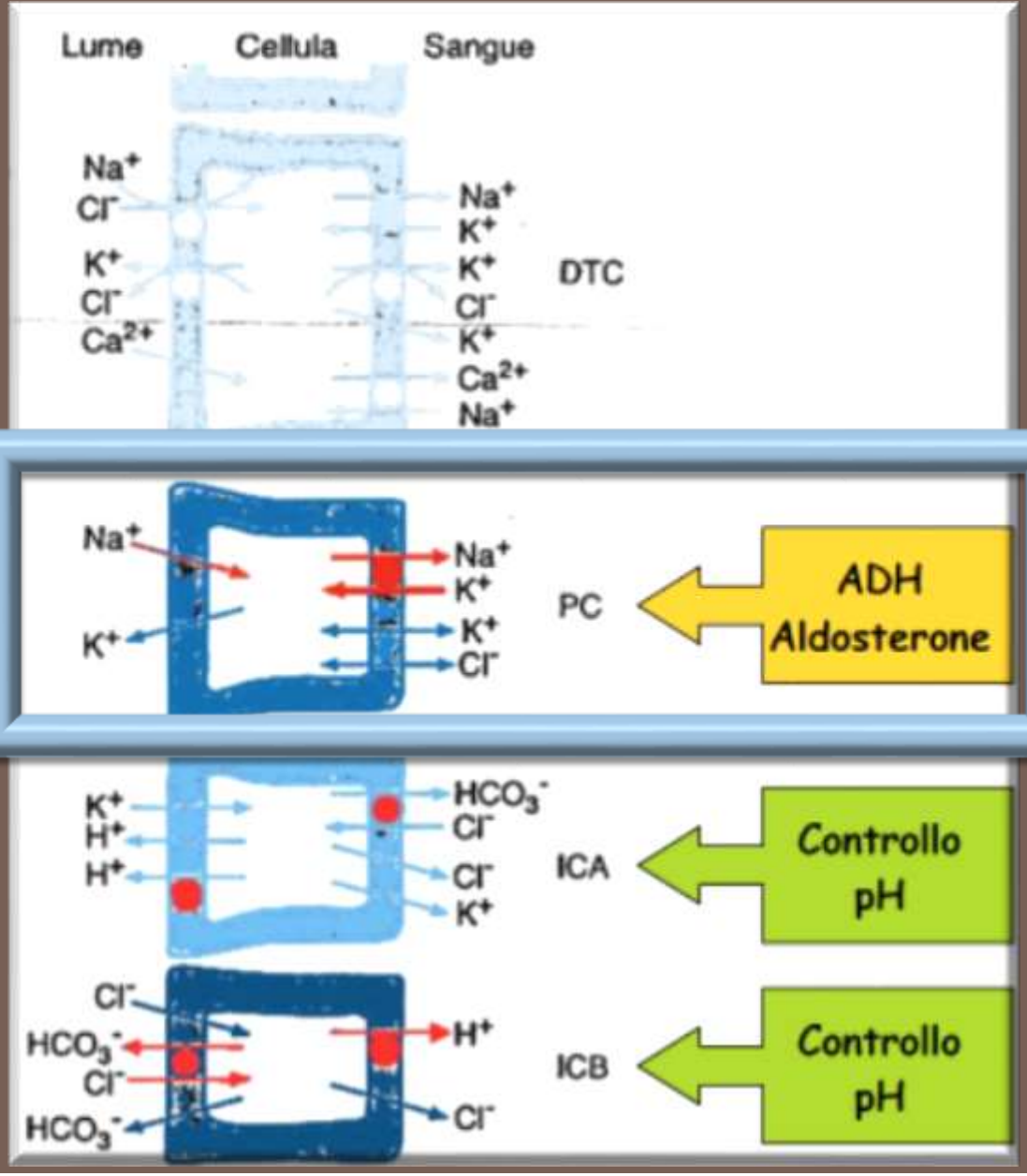
Tubulo collettore

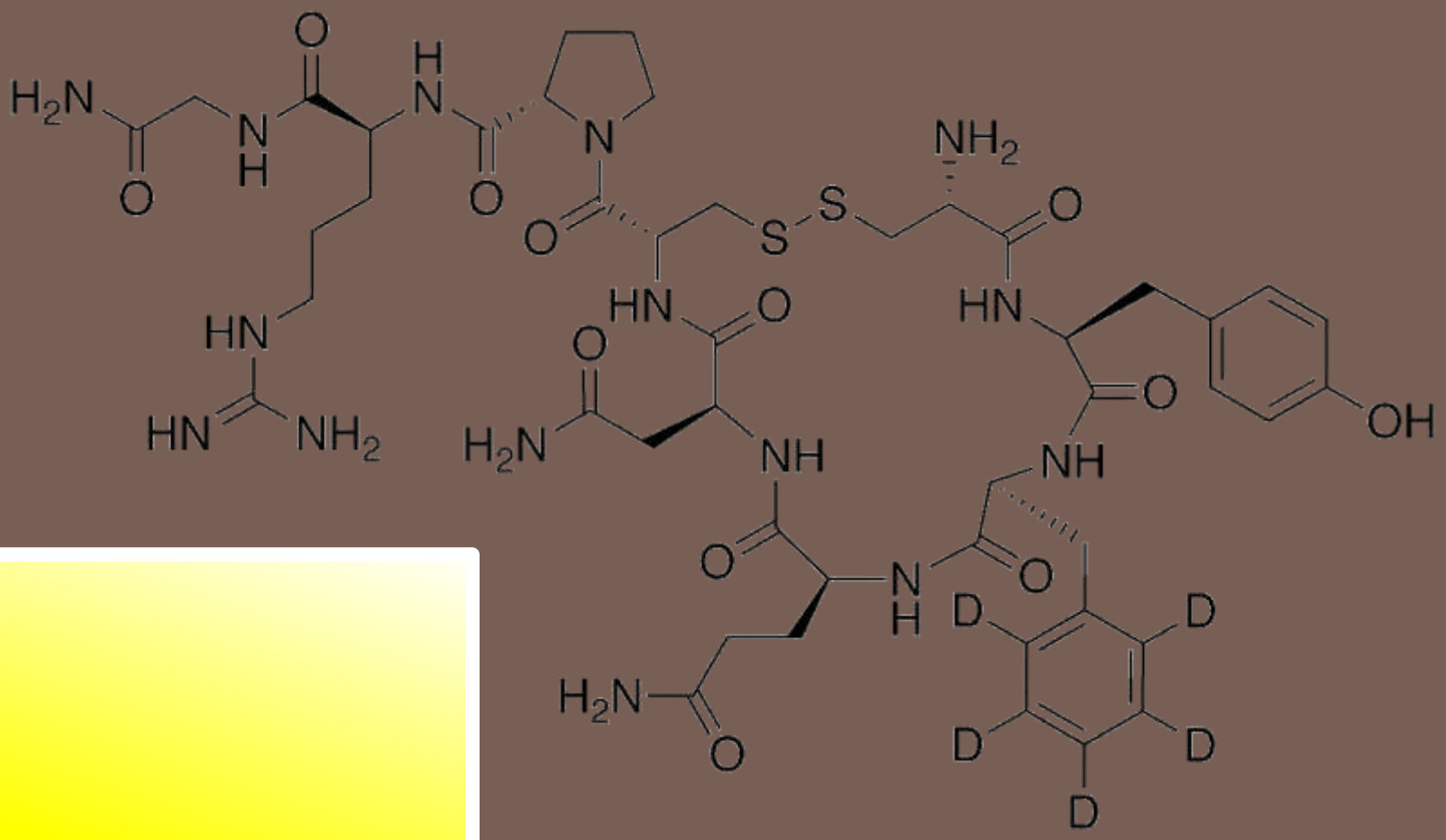

(a) Le cellule intercalate di tipo A agiscono in corso di acidosi.
H+ è escreto; HCO3− e K+ sono riassorbiti.
Lume del dotto collettore
Cellula intercalata di tipo A
Spazio interstiziale
Sangue
[H+] elevata
K+ filtrato
H2O + CO2
CO
HCO3− + H+
CA
H+ + HCO3−
HCO3− agisce come tampone per ↓ [H+]
K+
Cl−
ATP
H+
ATP
Elevata [K+]
K+ riassorbito
H+ escreto nell'urina


(b) Le cellule intercalate di tipo B agiscono in corso di a
HCO_3^- e K^+ sono escreti; H^+ è riassorbito.
alcalosi
Lume del dotto collettore
Cellula intercalata di tipo B
Spazio interstiziale
Sangue
[H+] bassa
$H_2O + CO_2$
CA
HCO_3^-
$HCO_3^- + H^+$
Cl^-
K^+
ATP
ATP
H^+
H^+
K^+
↑[H+]
Escreti nell'urina



Carmelo Libetta

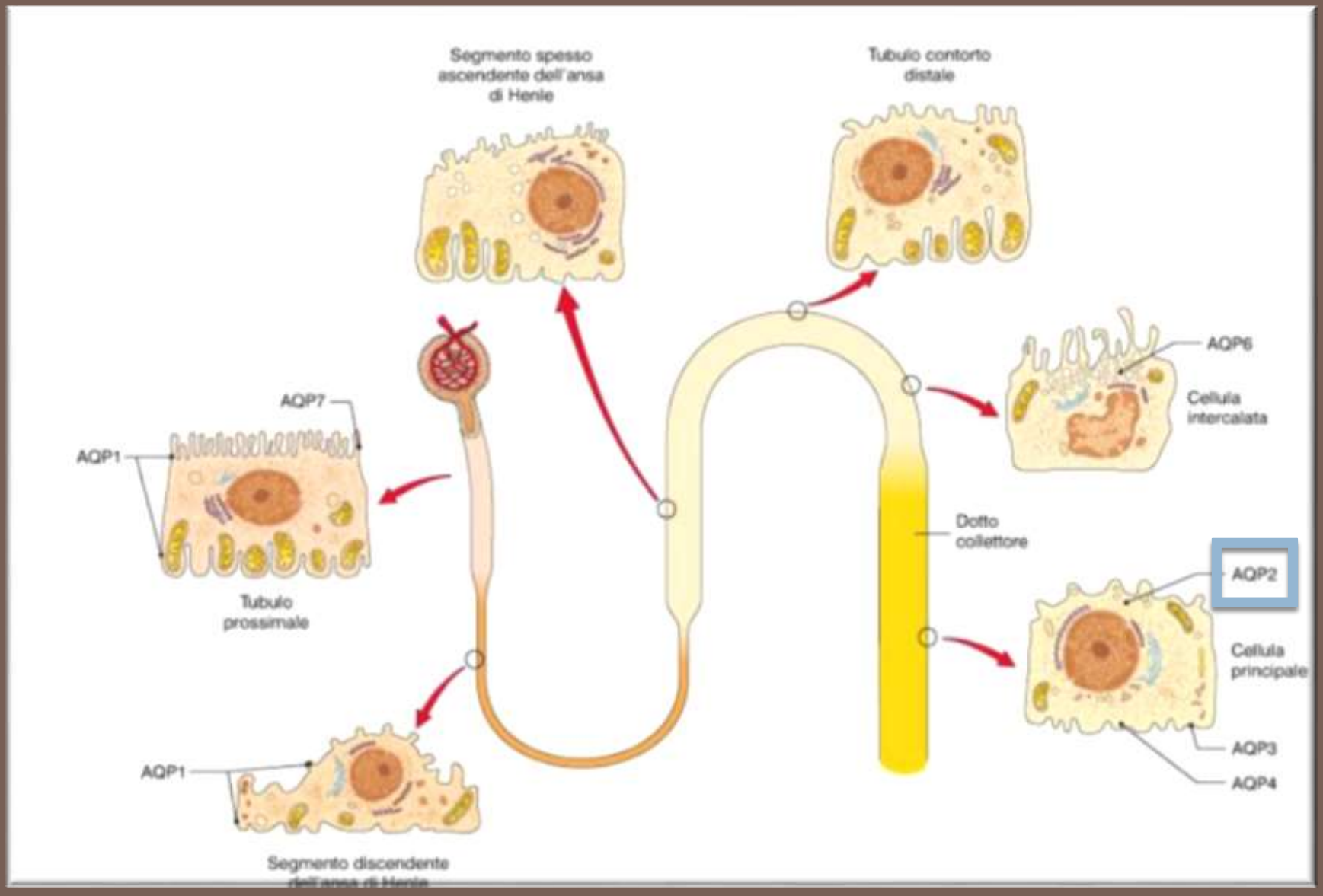
Tubulo collettore



ADH

Carmelo Libetta

Concentrazione/diluizione



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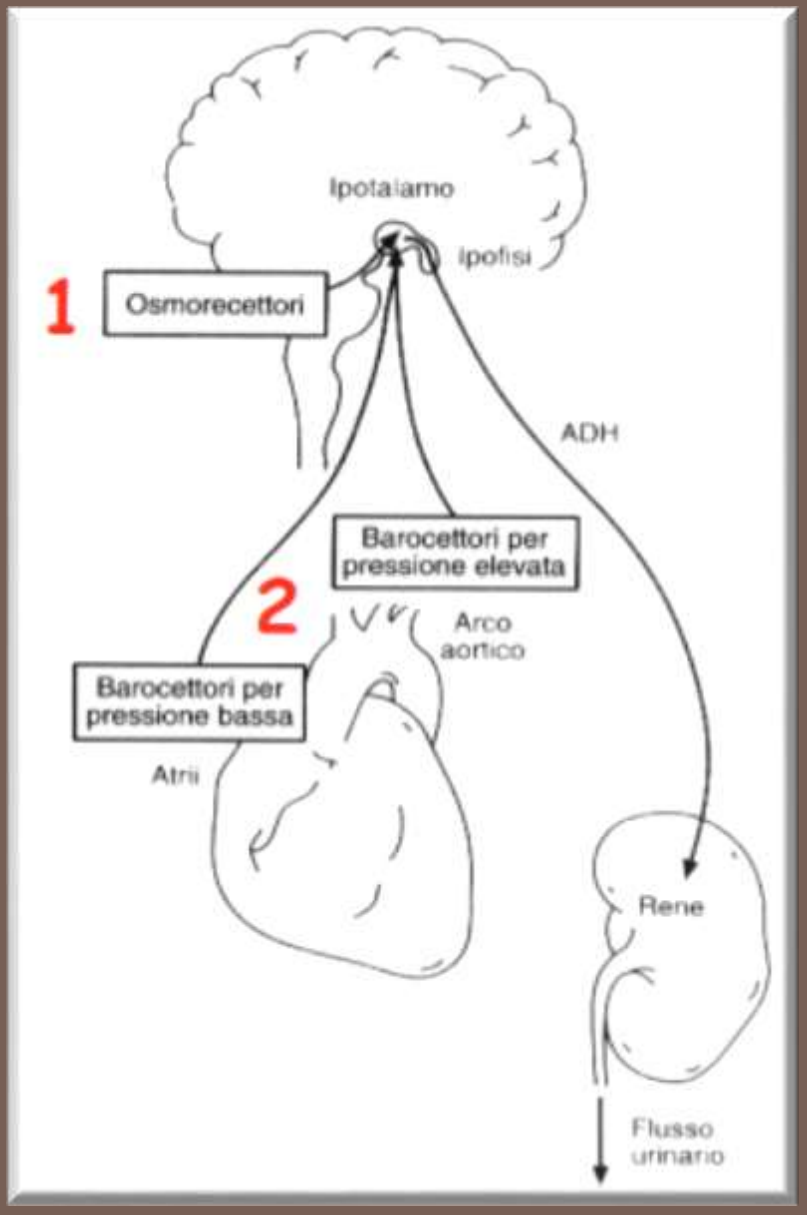
Acquaporine



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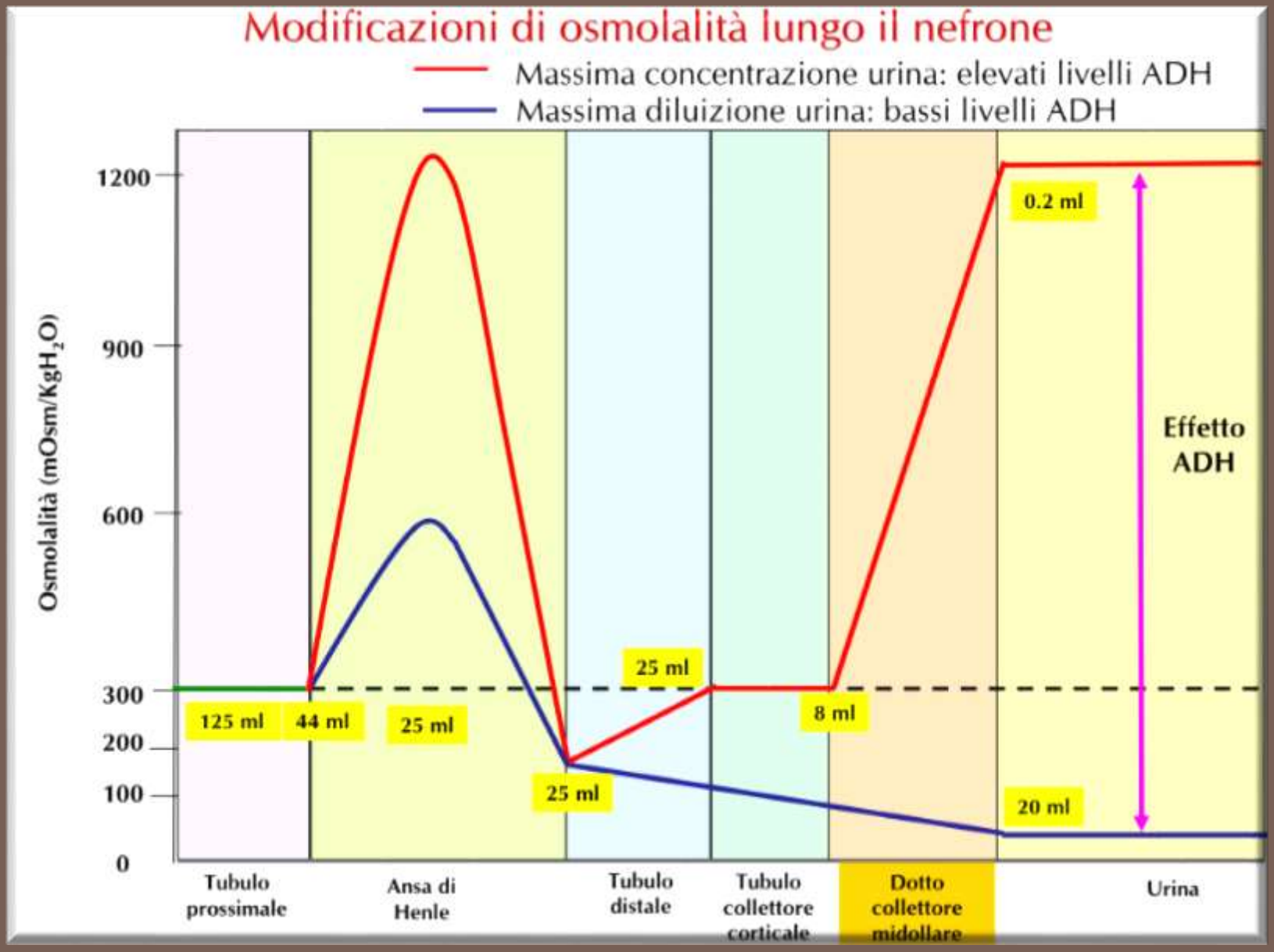
Controllo ADH



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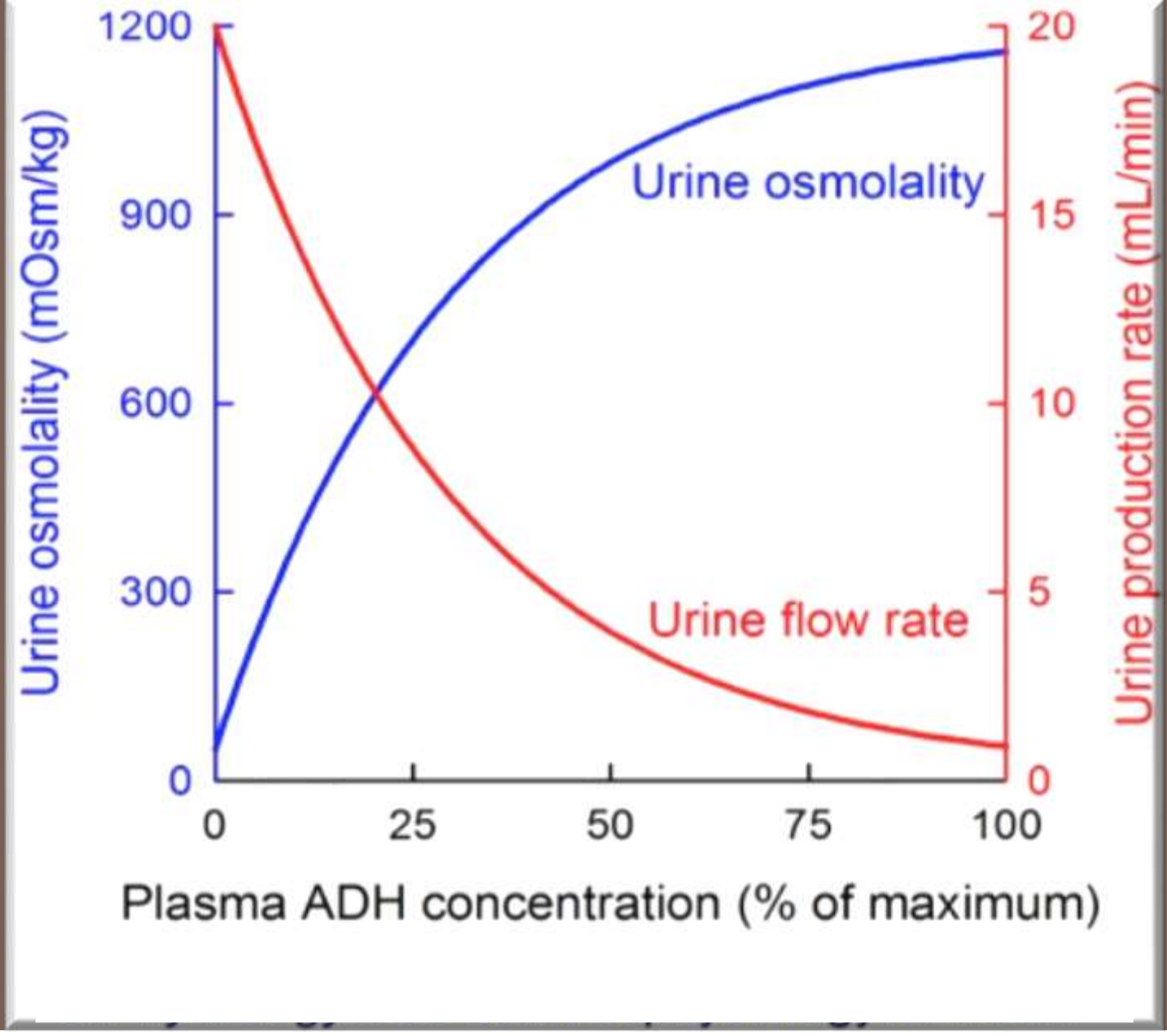
Riassorbimento dell'acqua


1200
900
600
300
0
Urine osmolality (mOsm/kg)
20
15
10
5
0
Urine production rate (mL/min)
Urine osmolality
Urine flow rate
0
25
50
75
100
Plasma ADH concentration (% of maximum)

ADH

Co cità
dei
cor

CLEARANCE
ACQUA LIBERA

C Osm = volume di plasma che nell'unità di tempo è depurato completamente dei soluti osmoticamente attivi, presenti nel plasma.

$$C_{Osm} = \frac{UOsm \times V}{POsm}$$

$$C\,H_2O = V - C\,Osm$$

1) $C\ H_2O = C\ Osm$ U. isotoniche

2) $C\ H_2O > C\ Osm$ U. ipotoniche

3) $C\ H_2O < C\ Osm$ U. ipertoniche

H_2O legata osmoticamente ai soluti

1) URINE ISOTONICHE

1) Uosm = Posm

Normali livelli di ADH

C Osm=V

C H_2O = 0

H_2O legata osmoticamente ai soluti

+

Acqua libera

2) URINE IPOTONICHE

2) Urine diluite

Uosm < Posm

Bassi livelli di ADH

$$CH_2O = V - COsm$$

Cl H2O=Positiva

3)URINE IPERTONICHE

3) Urine concentrate

Uosm > Posm

Alti livelli di ADH

V< Cosm

C H_2O = V - Cosm

Cl H2O= Negativa

Cl H_2O

- **Eritropoietina:** fibroblasti peritubulari
- **Vitamina D:** idrossilasi cellule tubulo prossimale
- **Renina:** cellule granulari iuxtaglomerulari
- **Prostaglandine:** midollare

THE END