



# VEC E SODIO

Carmelo  
Libetta

Capitolo 3°



**Regolazione bilancio idrico**

**Regolazione equilibrio elettrolitico**

**Regolazione equilibrio acido-base**



**Carmelo  
Libetta**

**Rene e Funzione Omeostatica**

# HOW MUCH WATER IS IN THE HUMAN BODY?



75%

60%

50%

WATER IS THE MAIN CONSTITUENT OF **CELLS, TISSUES & ORGANS**

Sources : • Mentes J. Oral hydration in older adults. AJN 2006; 106 (6):40-49.  
• Jéquier et al. Water as an essential nutrient: the physiological basis of hydration. EJCN 2010; 64: 115-23



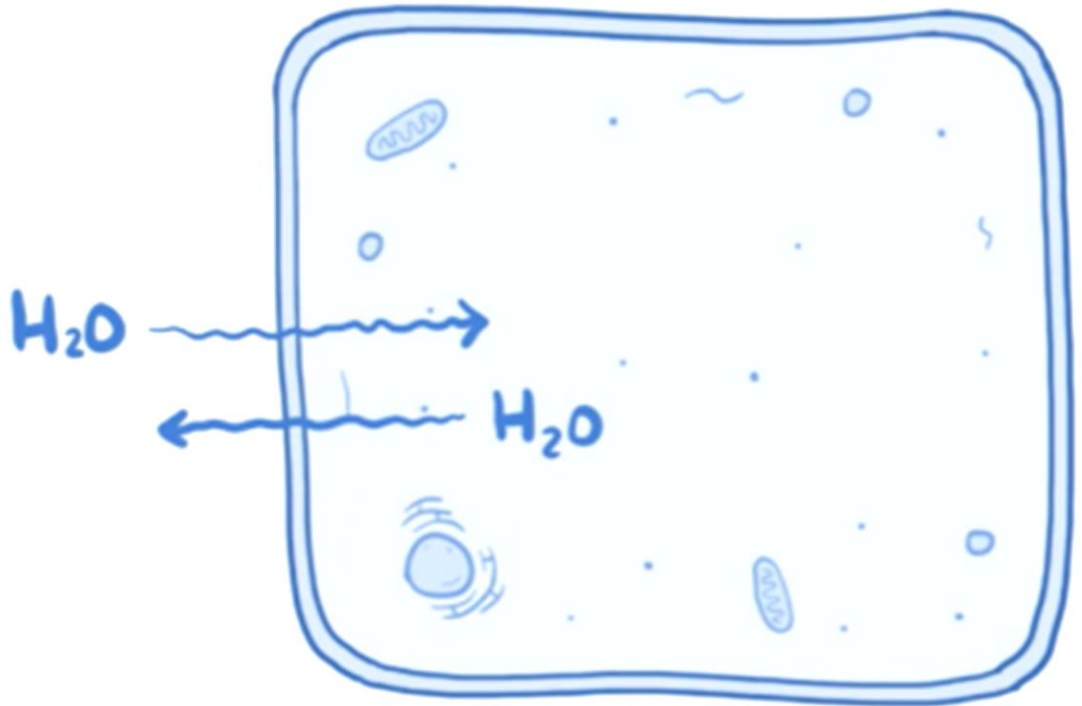
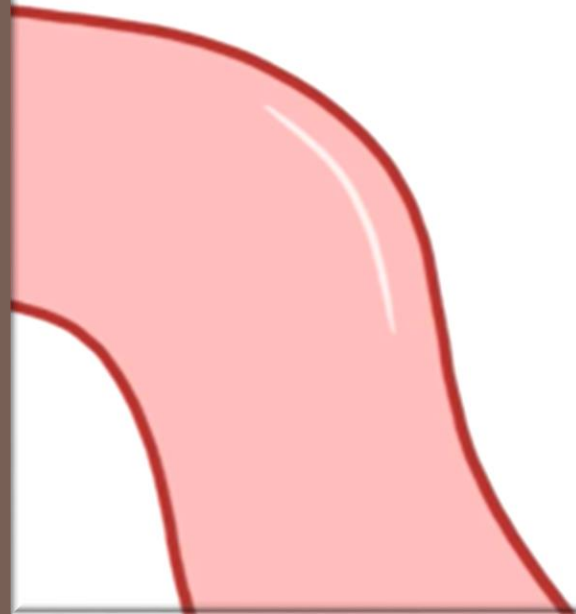
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Libetta

Acqua del corpo umano

EXTRACELLULAR  
OSMOLARITY

=

INTRACELLULAR  
OSMOLARITY



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Composizione fluidi corporei

**Tubo digerente**

**Cavità peritoneale**

**Cavità pleurica**

**Cavità pericardica**

**Cavità sinoviale**

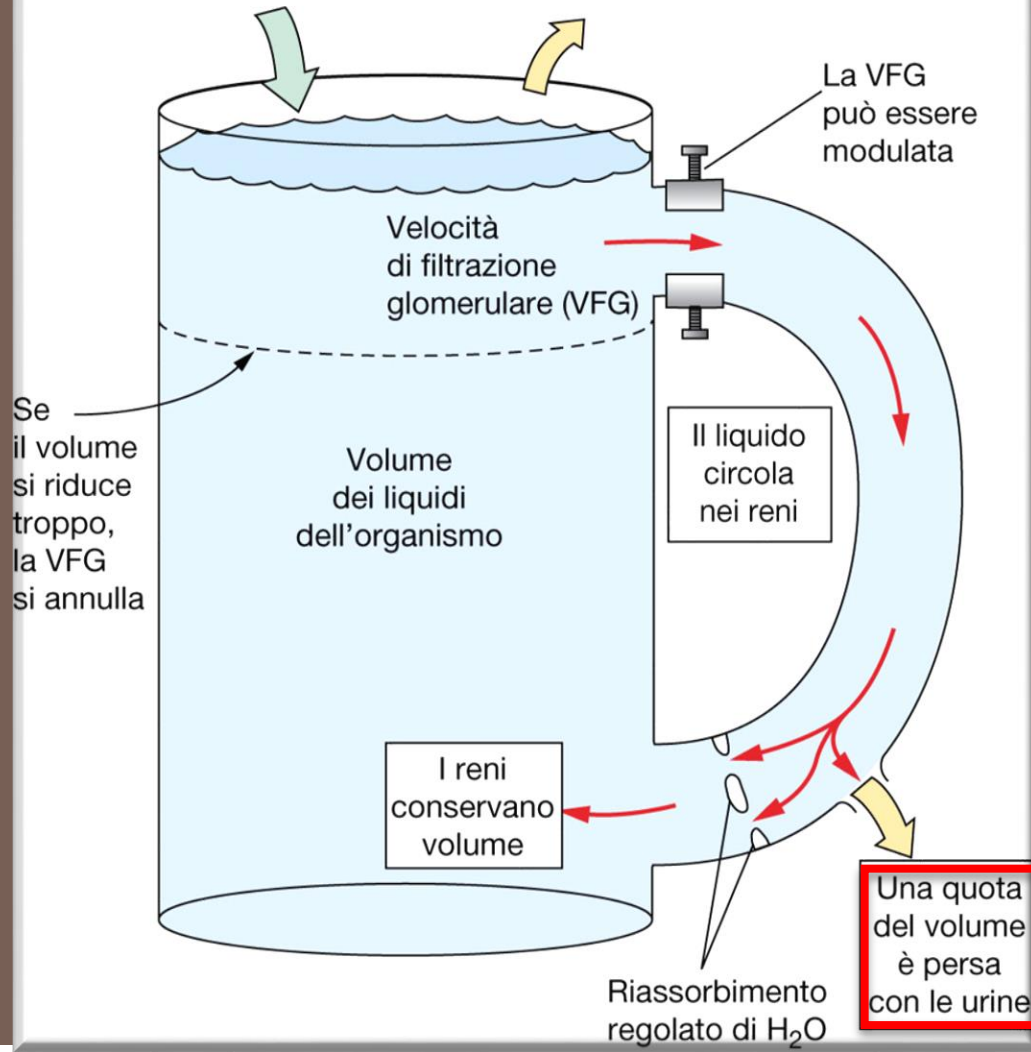
**Terzo spazio**



I reni possono solo conservare liquidi:  
non possono rigenerare il volume  
perduto.

Guadagno di volume

Perdita di volume



Se il volume si riduce troppo, la VFG si annulla

La VFG può essere modulata

Velocità di filtrazione glomerulare (VFG)

Il liquido circola nei reni

Volume dei liquidi dell'organismo

I reni conservano volume

Una quota del volume è persa con le urine

Riassorbimento regolato di H<sub>2</sub>O



Carmelo Libetta

# RENE E BILANCIO IDRICO

**VEC**

- **SODIO**
- **CLORO**
- **BICARBONATO**

**VIC**

- **POTASSIO**
- **MAGNESIO**



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**ELETTROLITI**



Sodiemia  
135-145 mEq/L

EXTRACELLULARE



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SODIO





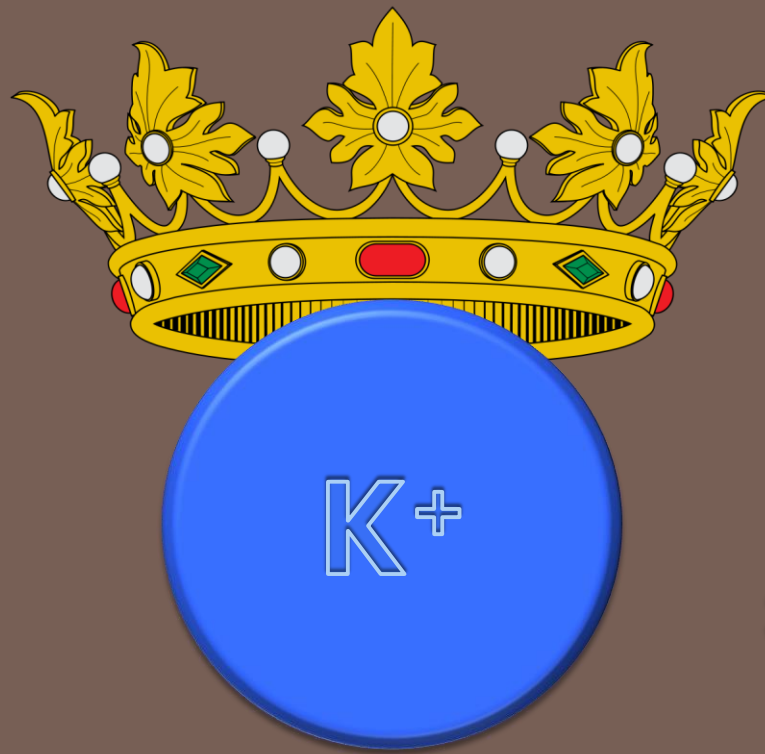
Cloremia  
95-110 mEq/L

# ANIONI PREVALENTI EXTRACELLULARE



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COLORO



Potassiemia  
3,5-5,1 mEq/L

**INTRACELLULARE**



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**POTASSIO**



Calcemia  
8,5-10 mg/dl

- **Coagulazione del sangue.**
- **Mantenimento del tono muscolare.**
- **Eccitabilità del sistema nervoso.**



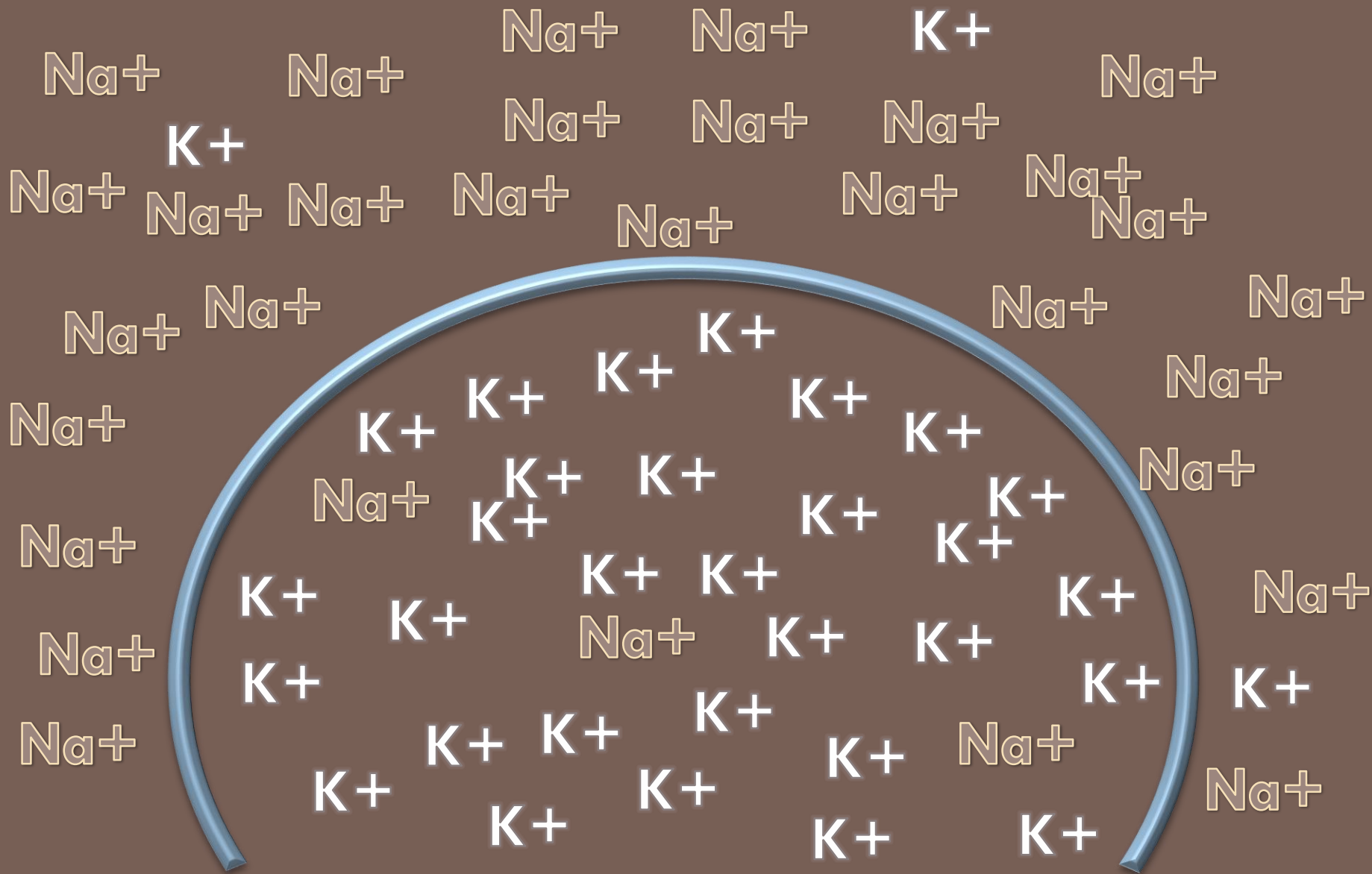
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**CALCIO**

**1 mEq è uguale a:**

- **1 mg di idrogeno,**
- **23 mg di Na,**
- **39 mg di K,**
- **20 mg di Ca,**
- **35 mg di Cl.**



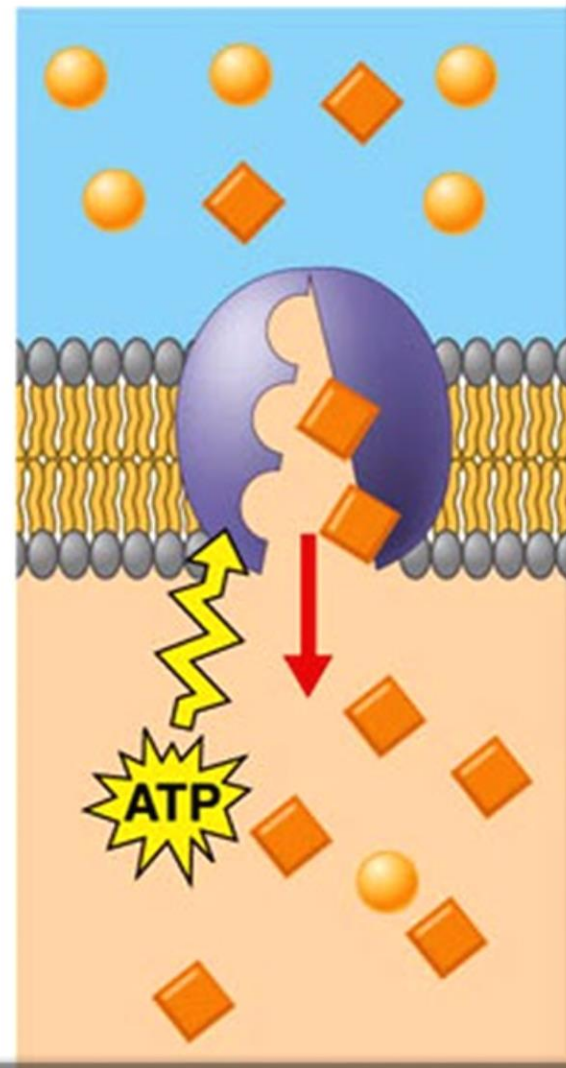
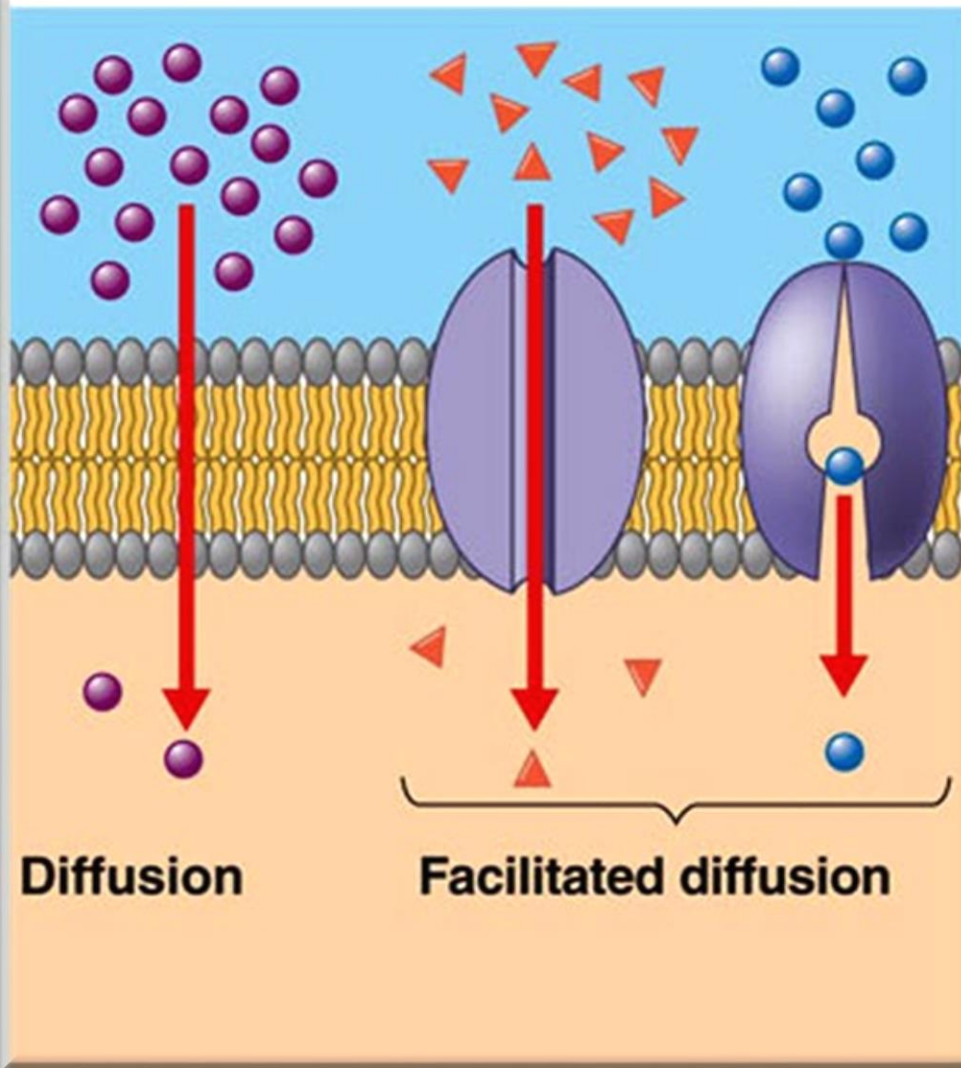


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# NATRIEMIA/POTASSIEMIA

## Passive transport

## Active transport

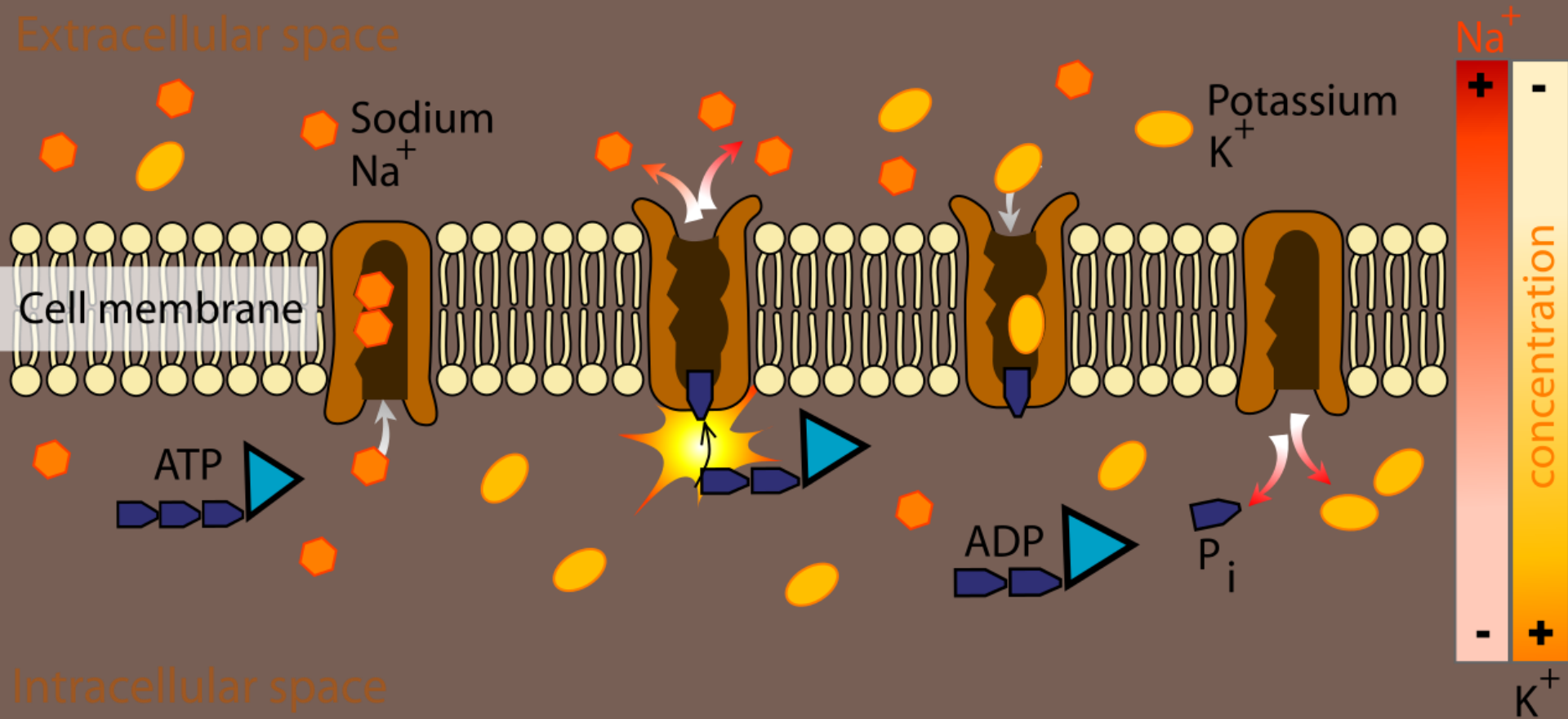


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TRASPORTO  $\text{Na}^+/\text{K}^+$



Extracellular space



Intracellular space



Carmelo Libetta

POMPA Na<sup>+</sup>/K<sup>+</sup> ATPasi

Na<sup>+</sup>



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Sodio e Acqua



Quantita' di sodio corporeo



Quantita'

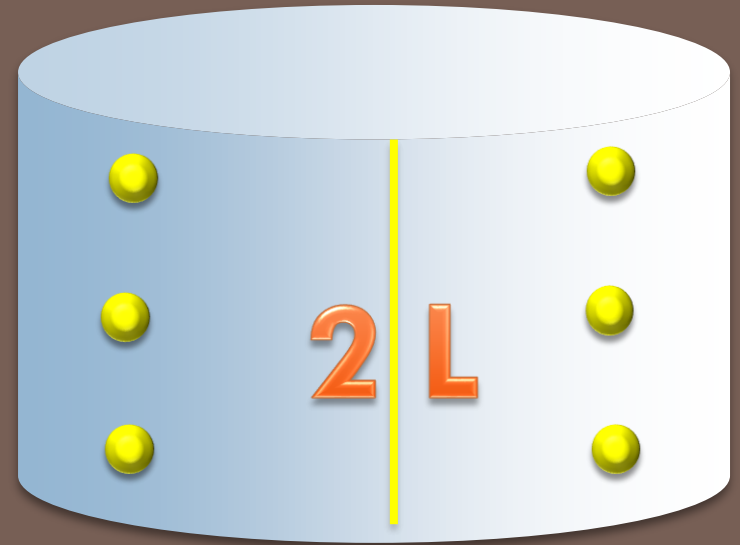
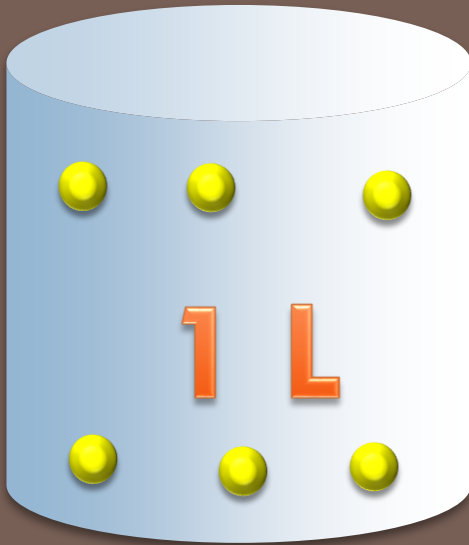
Sodiemia

Concentrazione



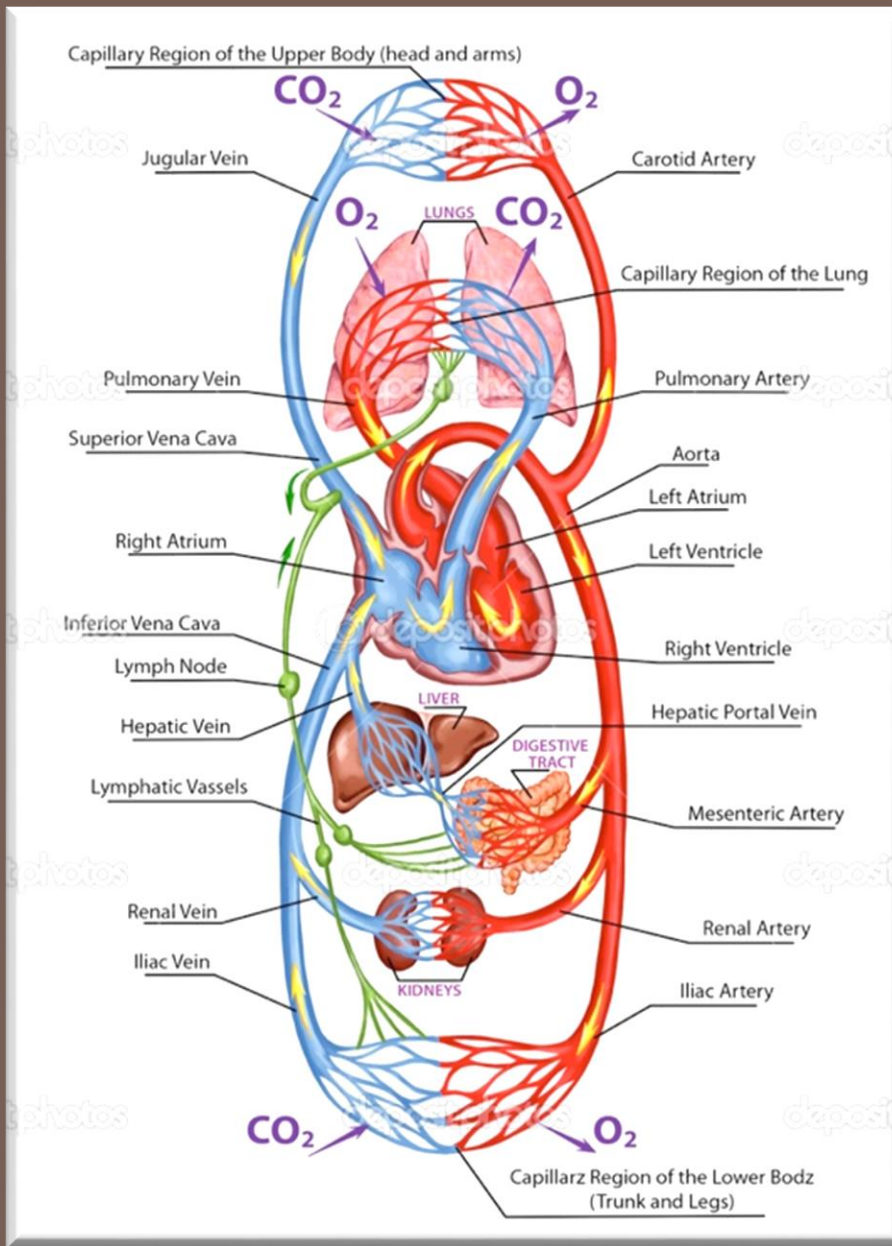
Carmelo  
Libetta

SODIO



Carmelo  
Libetta

SODIEMIA



Carmelo  
Libetta

# VOLEMIA

**Il volume circolante effettivo (VCE):**  
quella parte della volemia che  
produce la pressione arteriosa e  
quindi la perfusione dei tessuti.

**500 ml**

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**VOLEMIA EFFICACE**

- VEC

- VOLEMIA

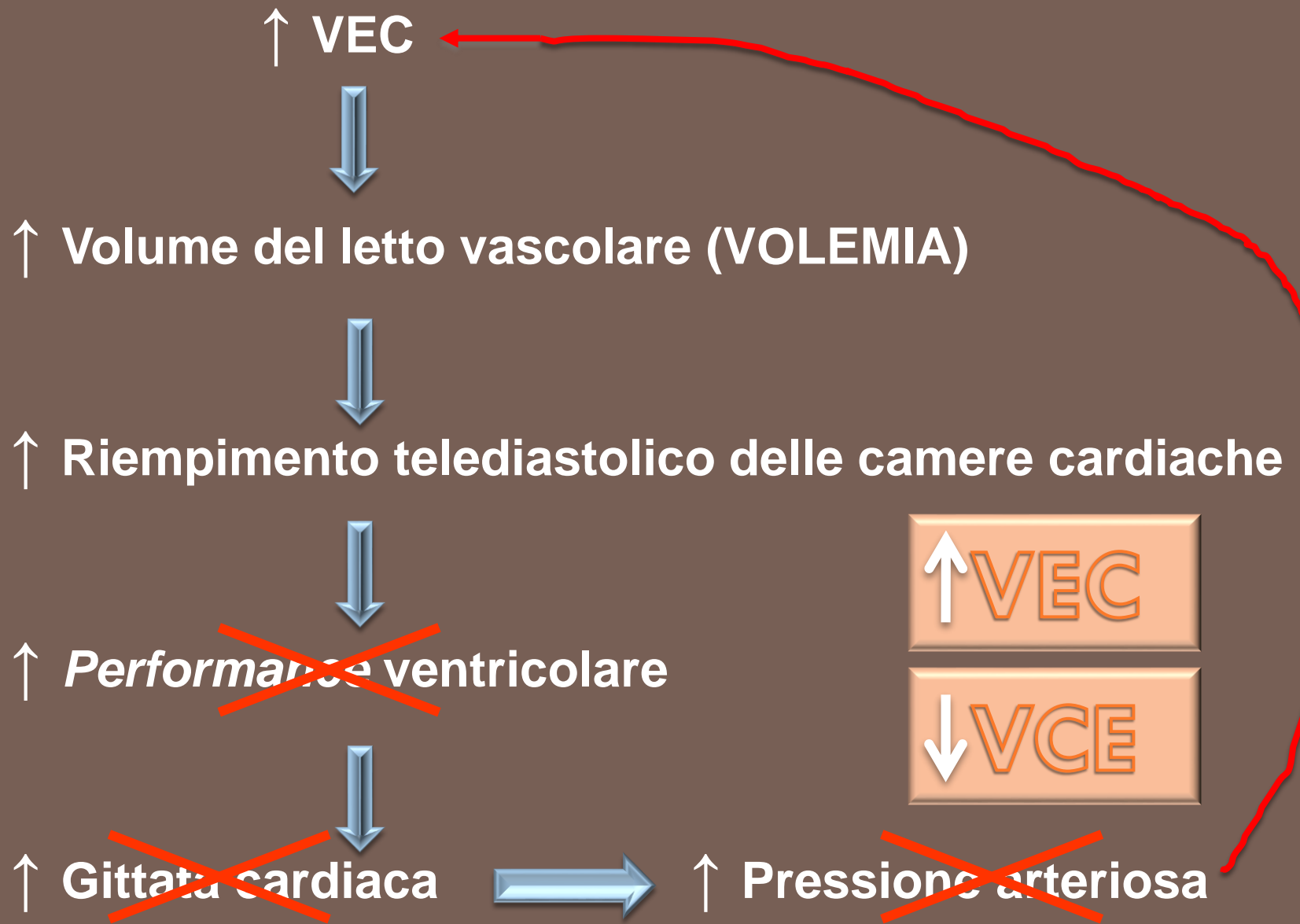
- Riempimento telediastolico cardiaco

- Gittata cardiaca



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VCE



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Libetta

# Scompenso cardiaco

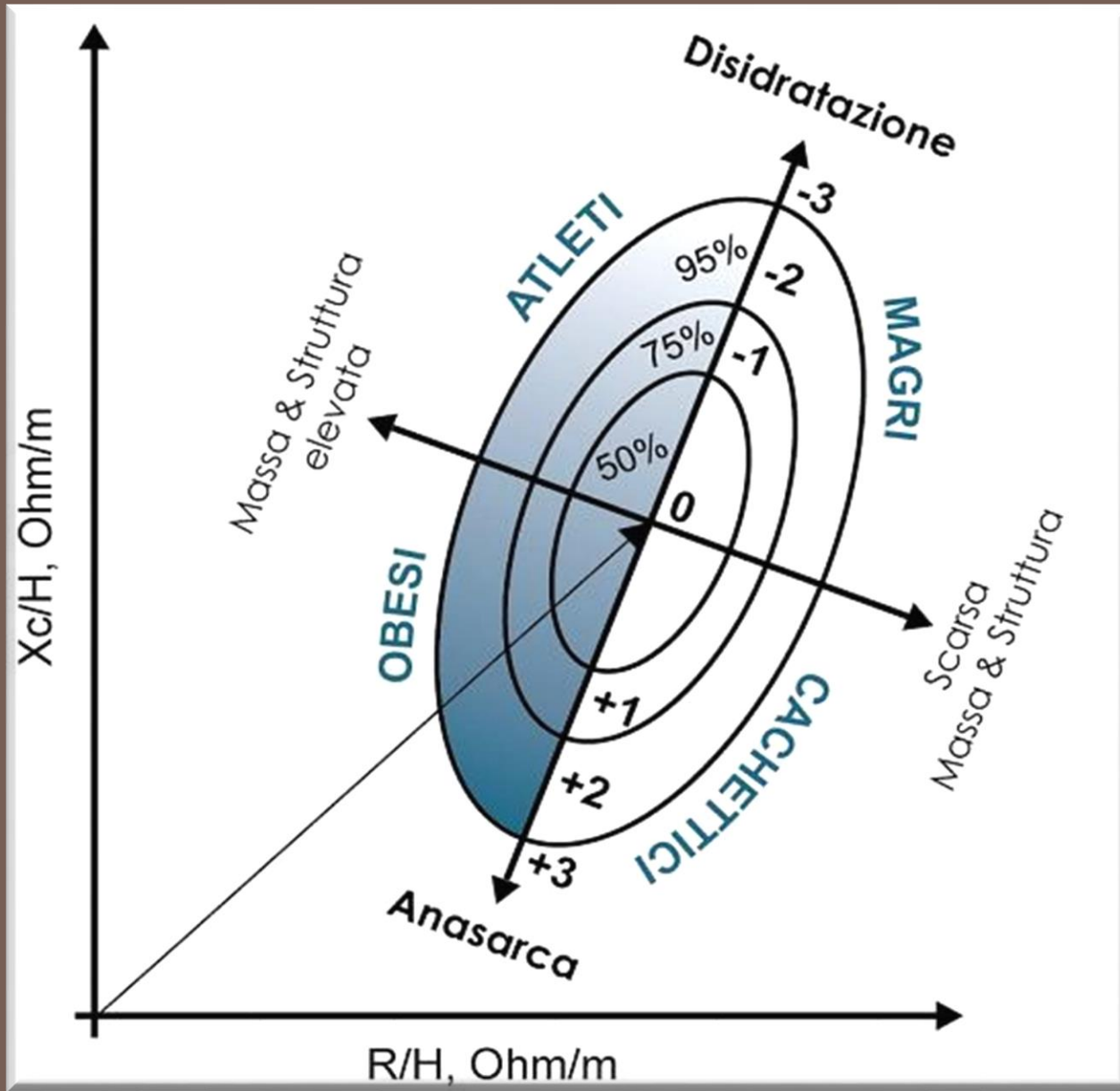


VALUTAZIONE CLINICA  
DEL VEC

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Libetta

SODIO/VEC



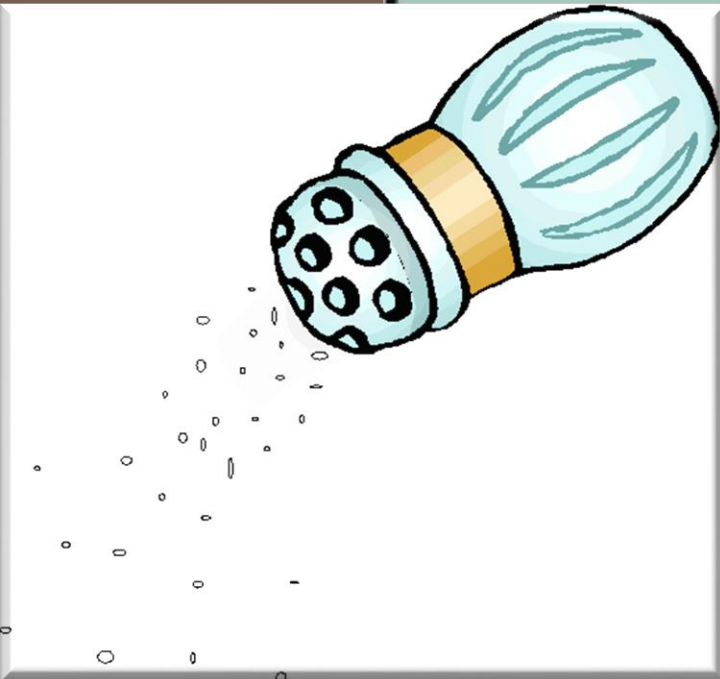


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BIOIMPEDENZIOMETRIA







“I’m wrapping it tightly to keep the ankle from swelling.”



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ESPANSIONE DEL VEC

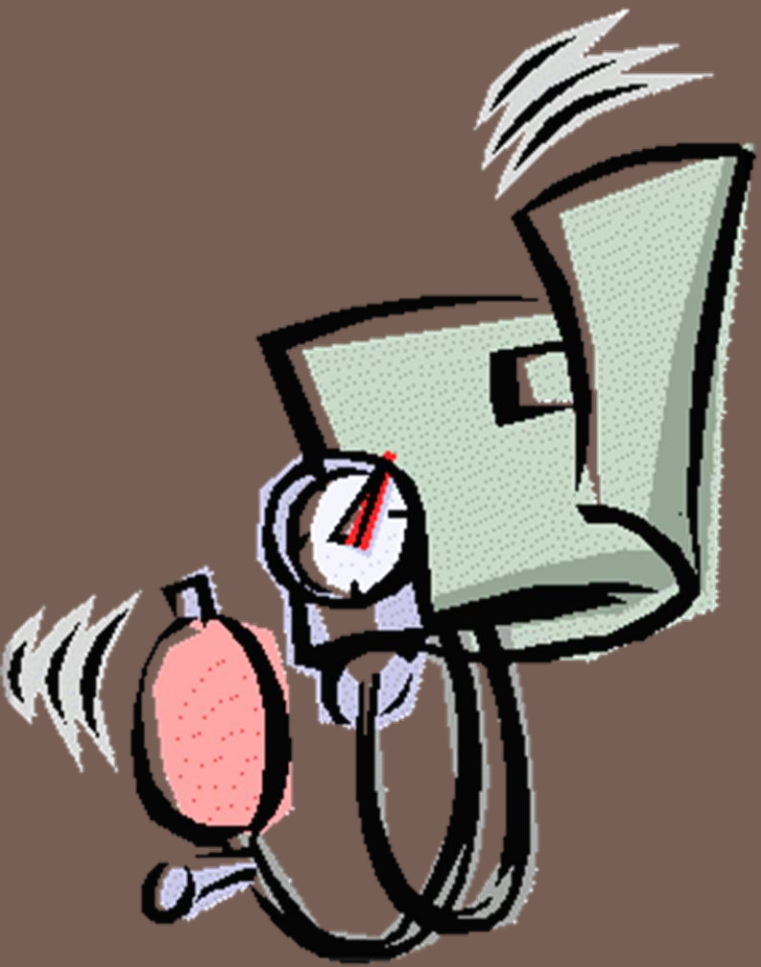
**DOTTORE HO  
I PIEDI GONFI**



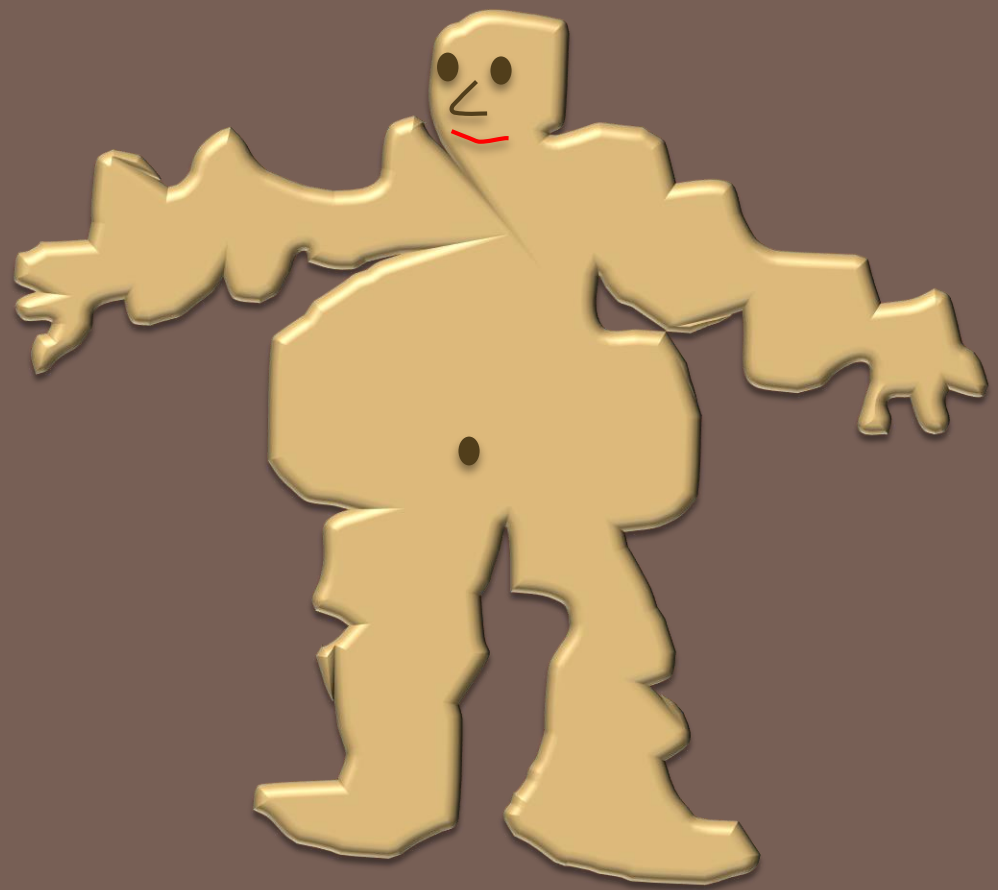
**Carmelo  
Libetta**

**ESPANSIONE VEC**





**IPERTENSIONE**

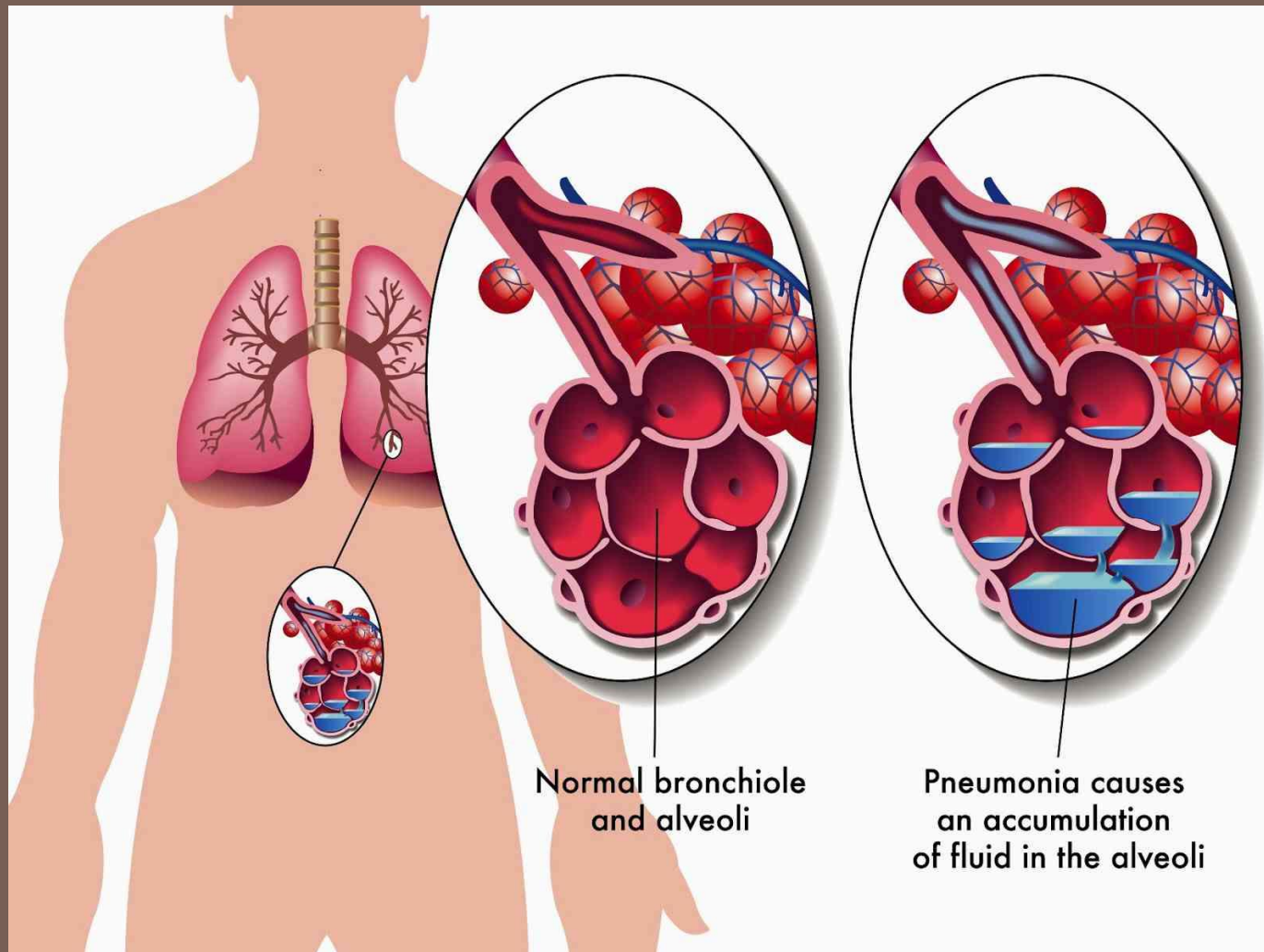


**EDEMA**



**Carmelo  
Libetta**

**SEGNI DI ESPANSIONE DEL VEC**

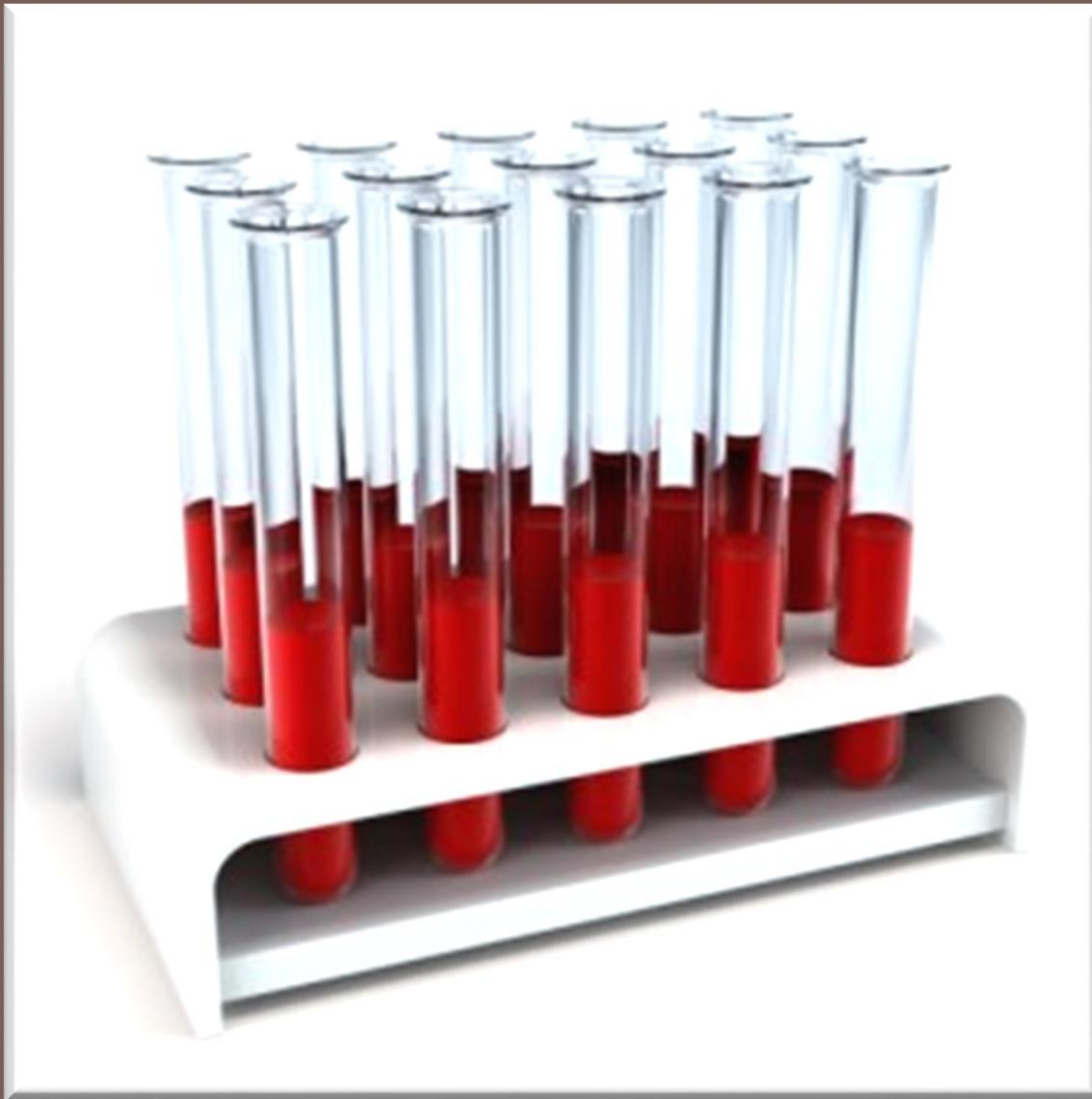


# EDEMA POLMONARE

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SEGNI DI ESPANSIONE DEL VEC





○ **Ht**

○ **GR**

○ **PT**



**Carmelo  
Libetta**

**EMODILUIZIONE**

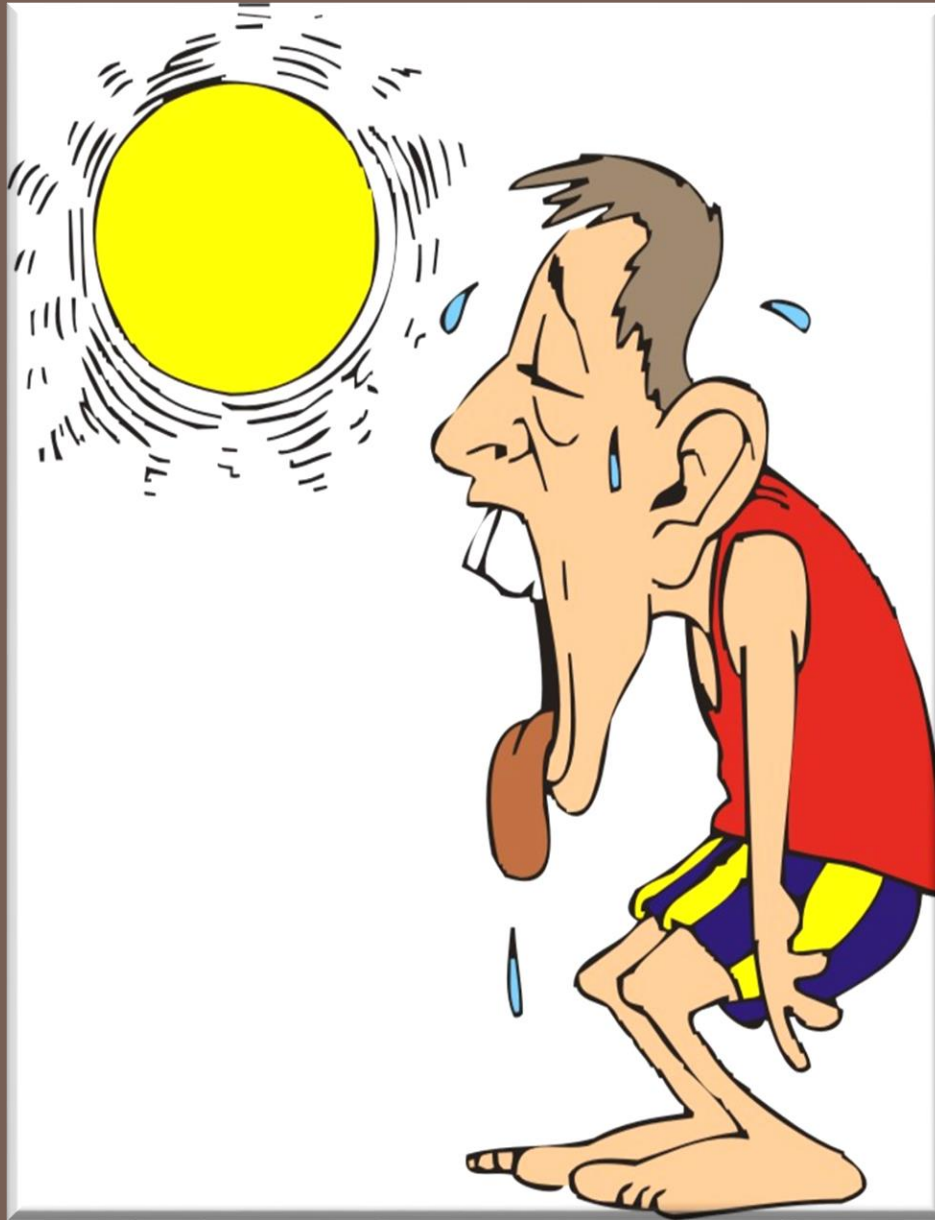


**DIURETICI**



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TERAPIA ESPANSIONE VEC



Carmelo  
Libetta

DEPLEZIONE VEC



**Rolling Stone**

copertinefb

## Solchi trasversali

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SEGNI CLINICI DI DEPLEZIONE







## Secchezza cutanea



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Libetta

SEGNI CLINICI DI DEPLEZIONE

AGII



ADH



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SEGNI CLINICI



PA<sub>s</sub> -20 mmHg



PA<sub>d</sub> -10 mmHg



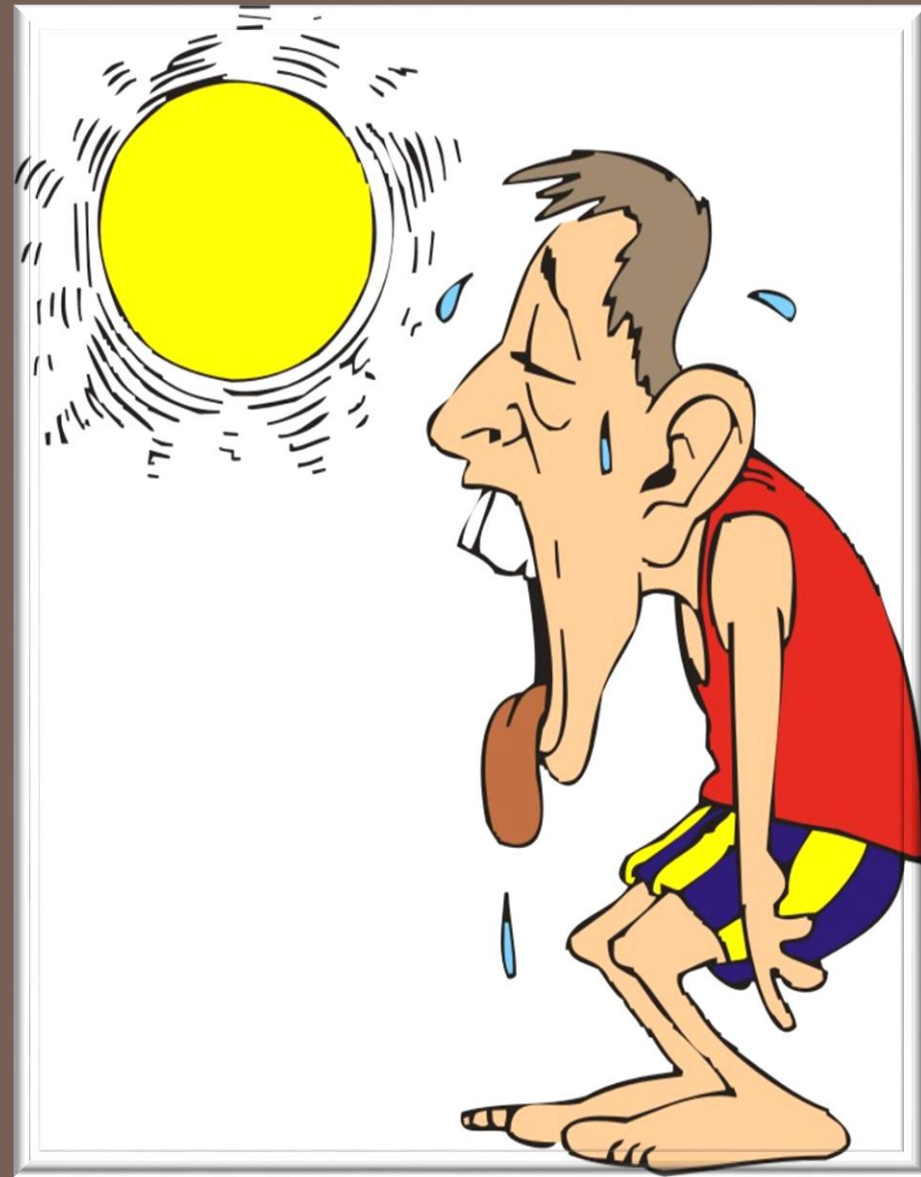
Ipotensione  
ortostatica



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Libetta

SEGNI CLINICI DI DEPLEZIONE

- OLIGURIA
- SPOSSATEZZA
- IRRITAZIONE



Carmelo  
Libetta

ALTRI SINTOMI





○ **Ht**

○ **GR**

○ **PT**



**Carmelo  
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**EMOCONCENTRAZIONE**



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TERAPIA DEPLEZIONE VOLUME

**Carico filtrato di Na<sup>+</sup>: 180 l/die × 140 mmol/l = 25200 mmol/die**

**Riassorbimento renale:**

- 1) 67% dal TCP;**
- 2) 25% dal TAS dell'ansa di Henle;**
- 3) 4% dal TCD;**
- 4) > 3% dal dotto collettore.**

**FE < 1% del carico filtrato**



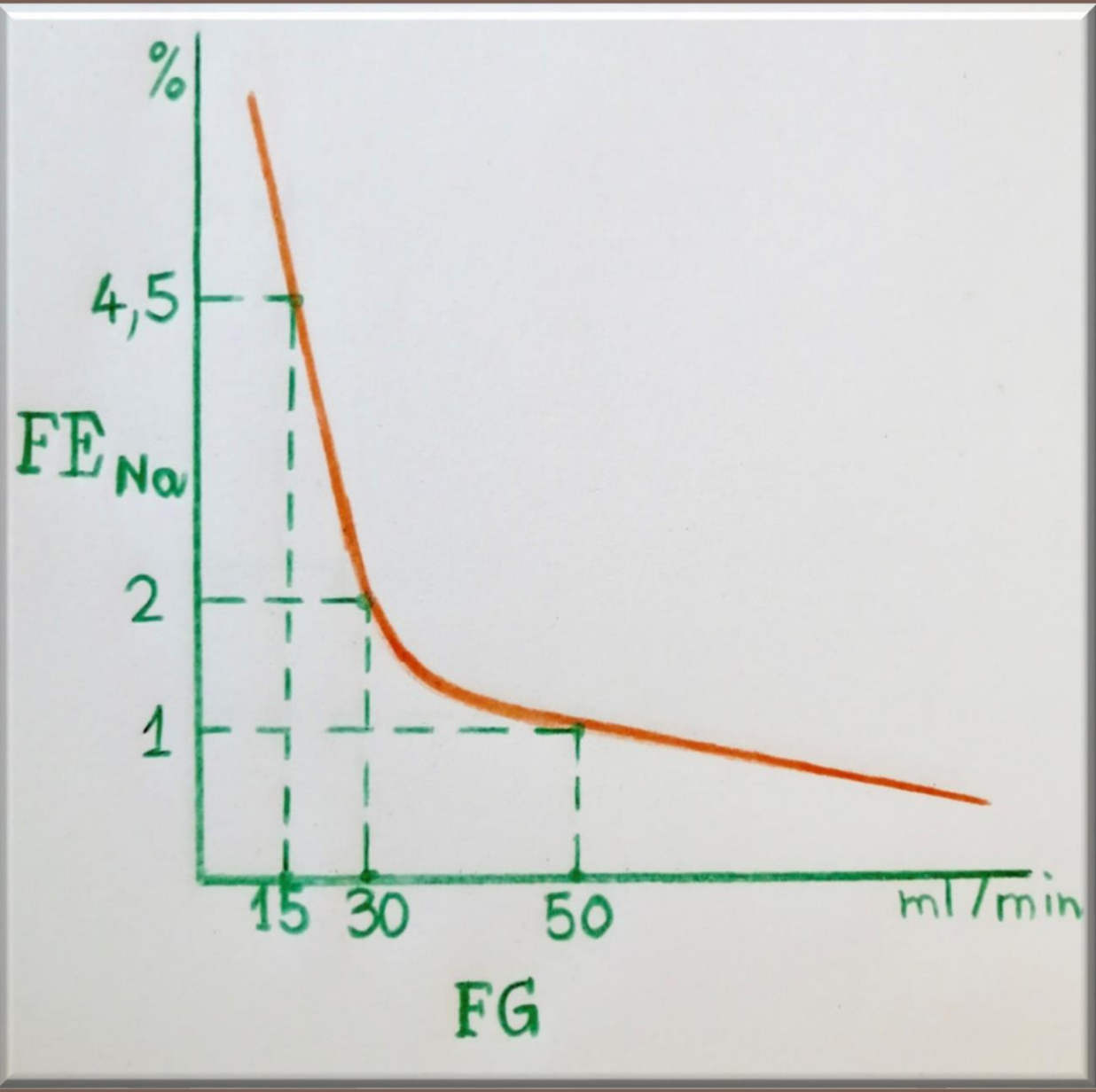
$$FE_{Na} = \frac{U_{Na} \times P_{Cr}}{P_{Na} \times U_{Cr}} \times 100$$



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FRAZIONE ESCRETA Na<sup>+</sup>



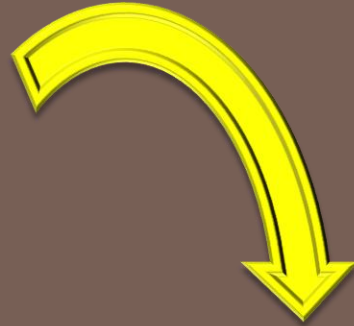


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Libetta

Fe Na<sup>+</sup> e FG



VCE



Bilancio  
Sodico



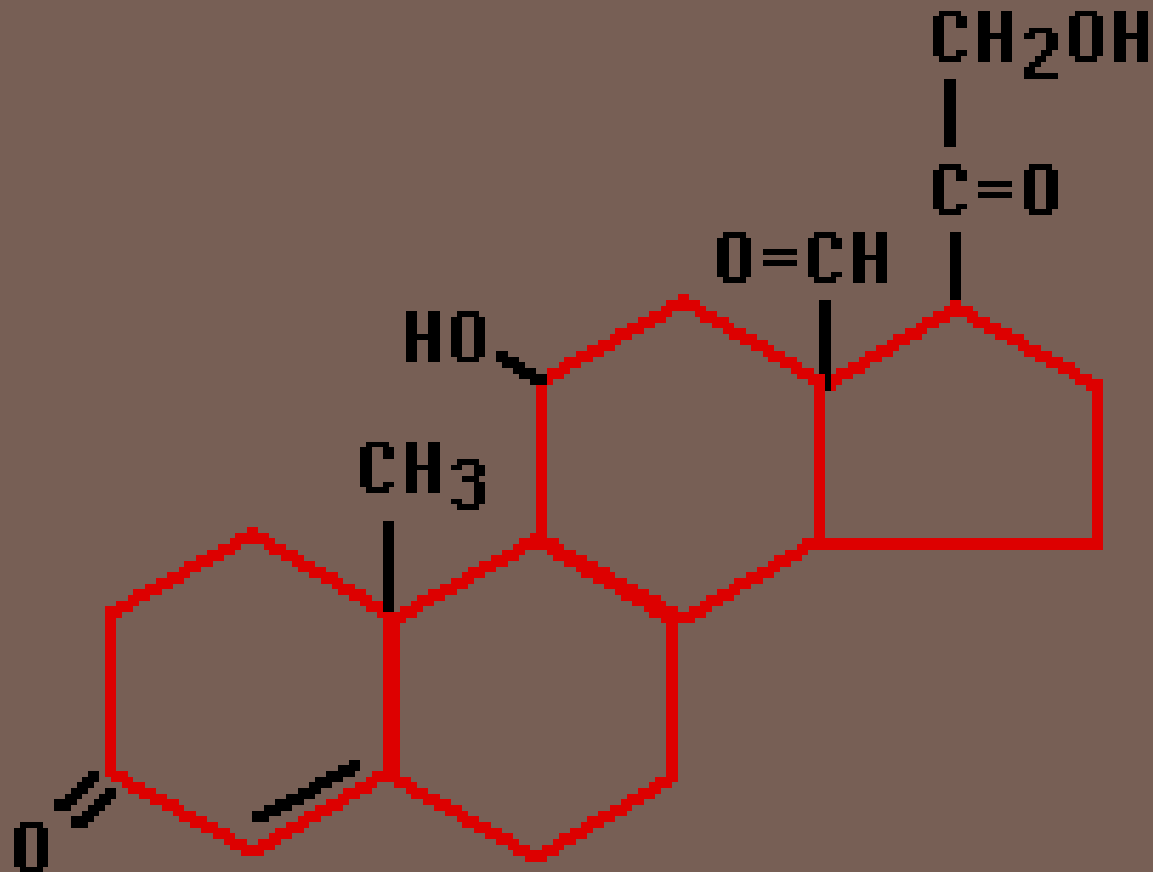
Carmelo  
Libetta

Volemia e Bilancio del sodio



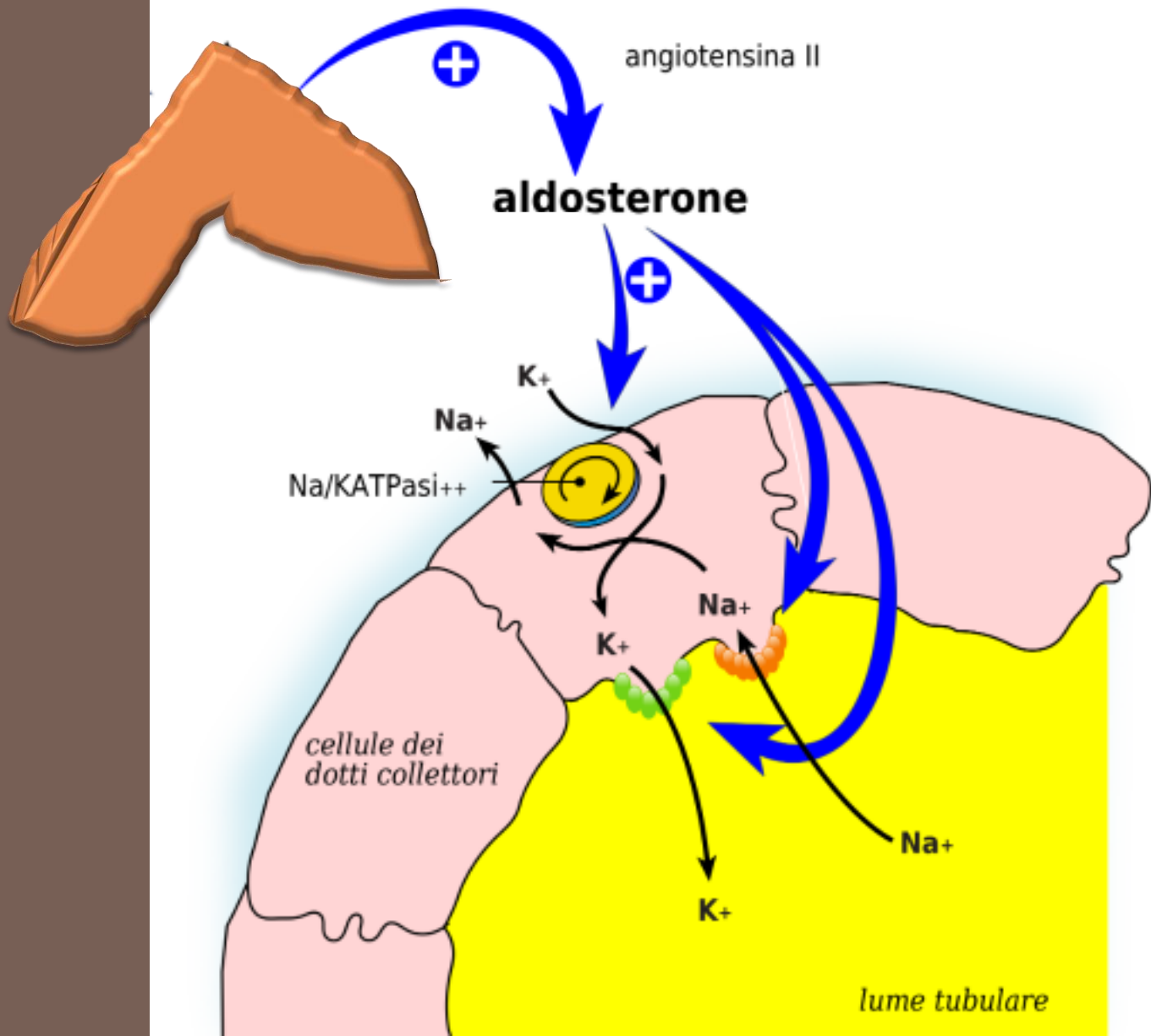
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BILANCIO SODICO



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Libetta

# ALDOSTERONE

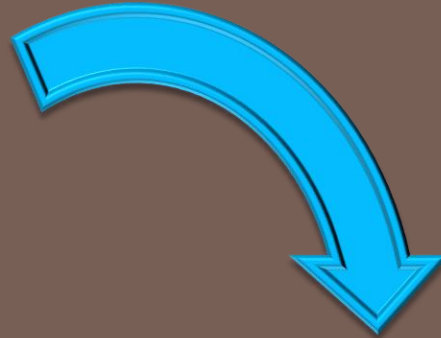


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# ALDOSTERONE



Osmolalità



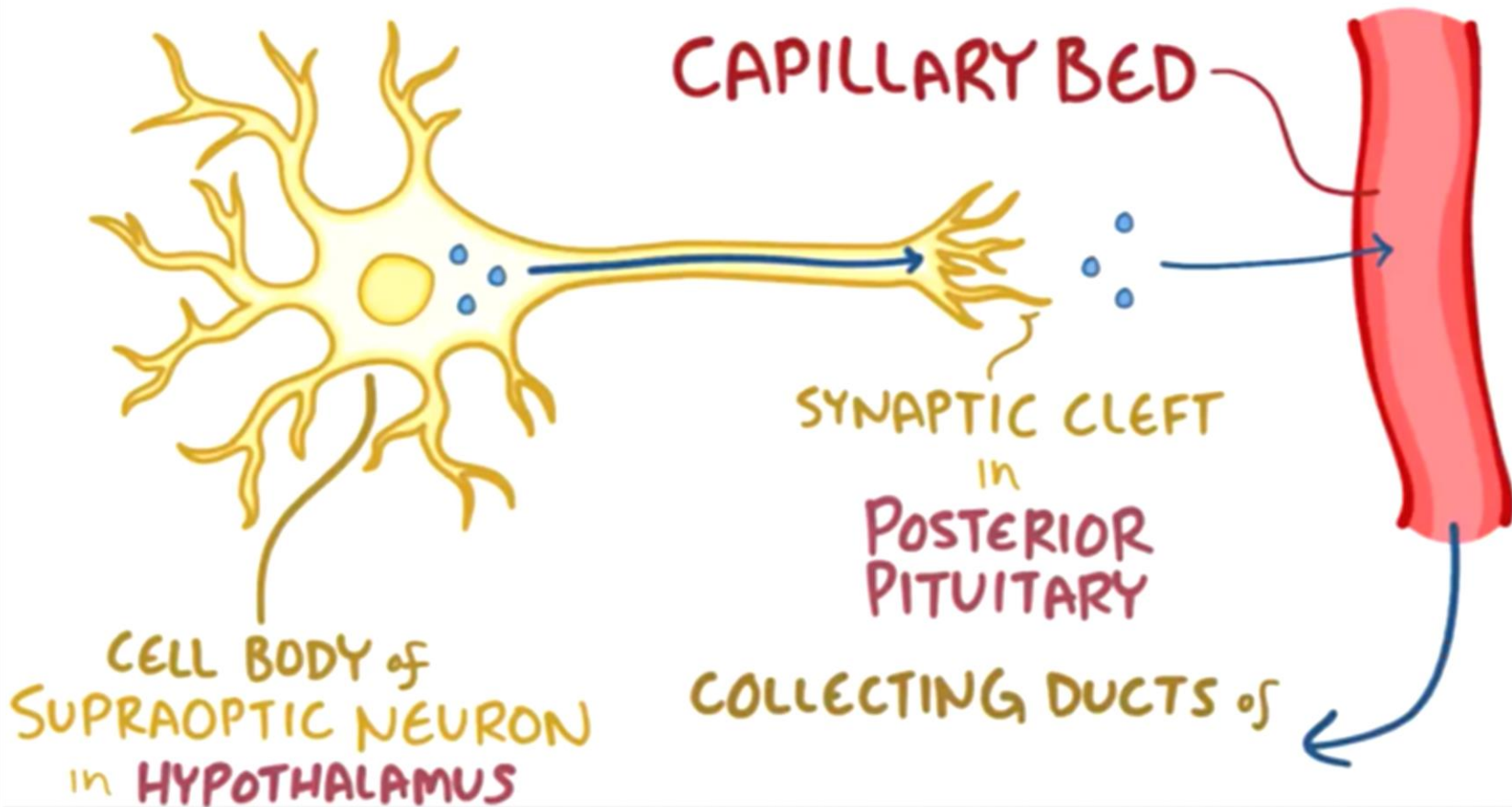
**Bilancio  
Idrico**



Carmelo  
Libetta

Rene e Bilancio dell'acqua

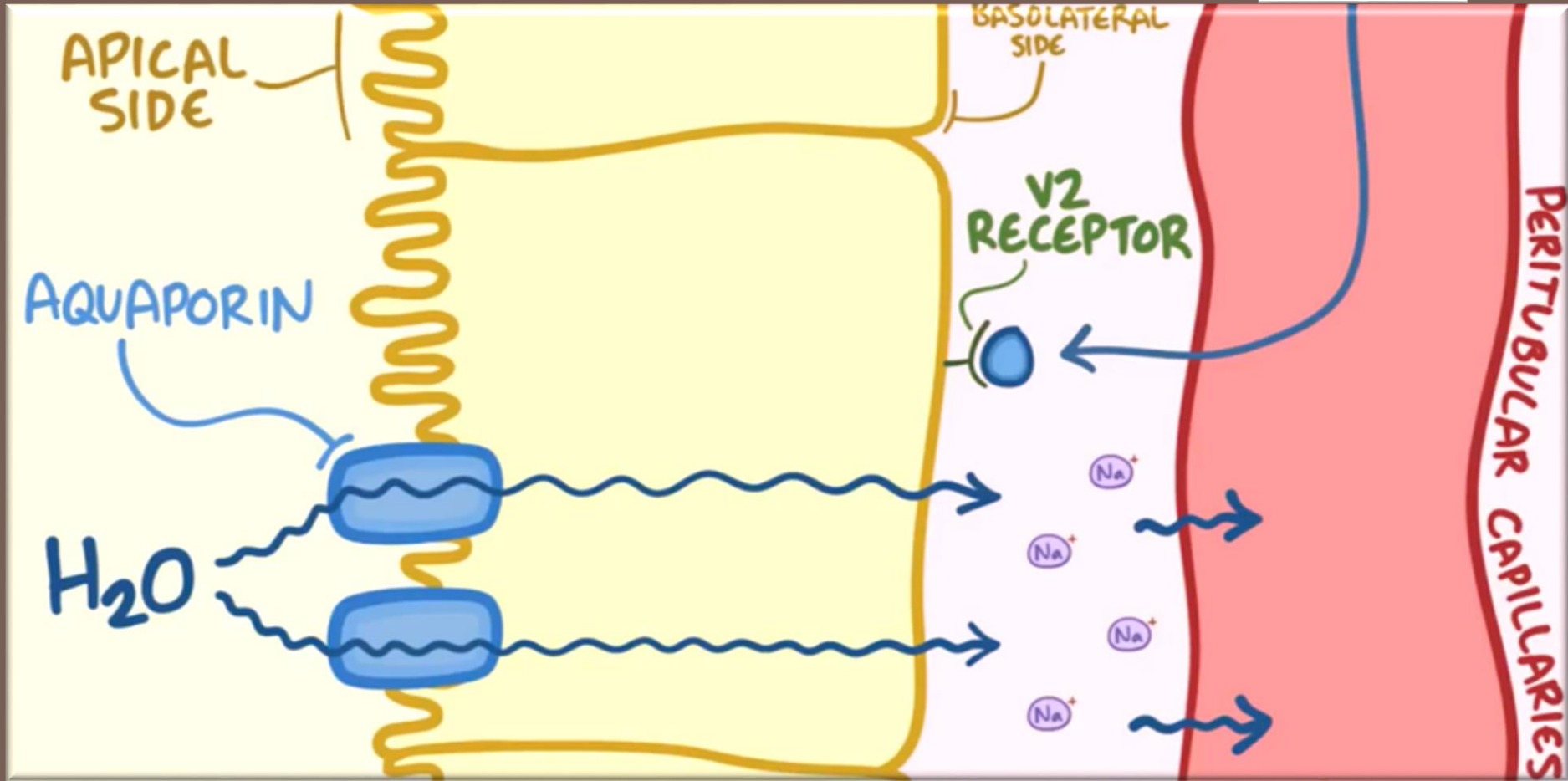
# ADH ~ PEPTIDE HORMONE



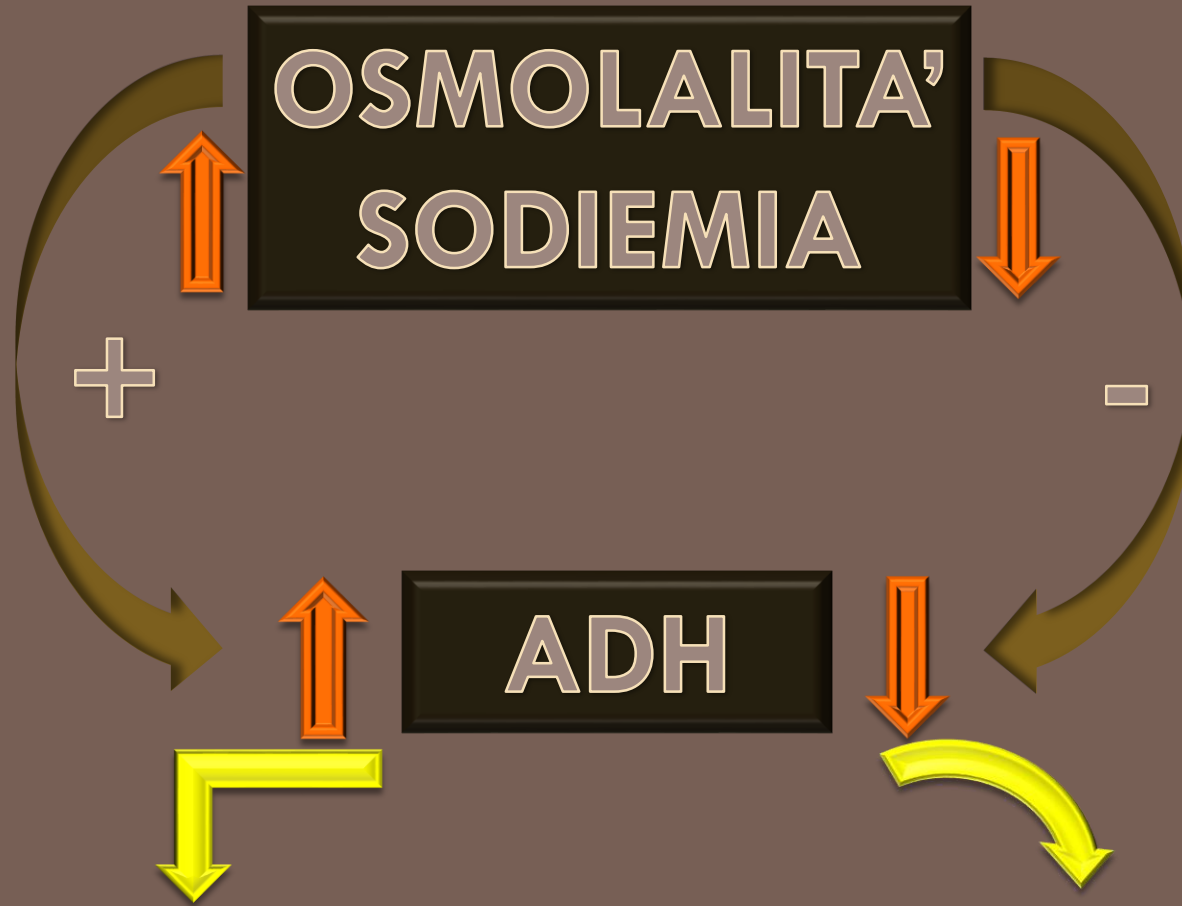
Carmelo  
Libetta

Rene e Bilancio dell'acqua









Ritenzione di H<sub>2</sub>O

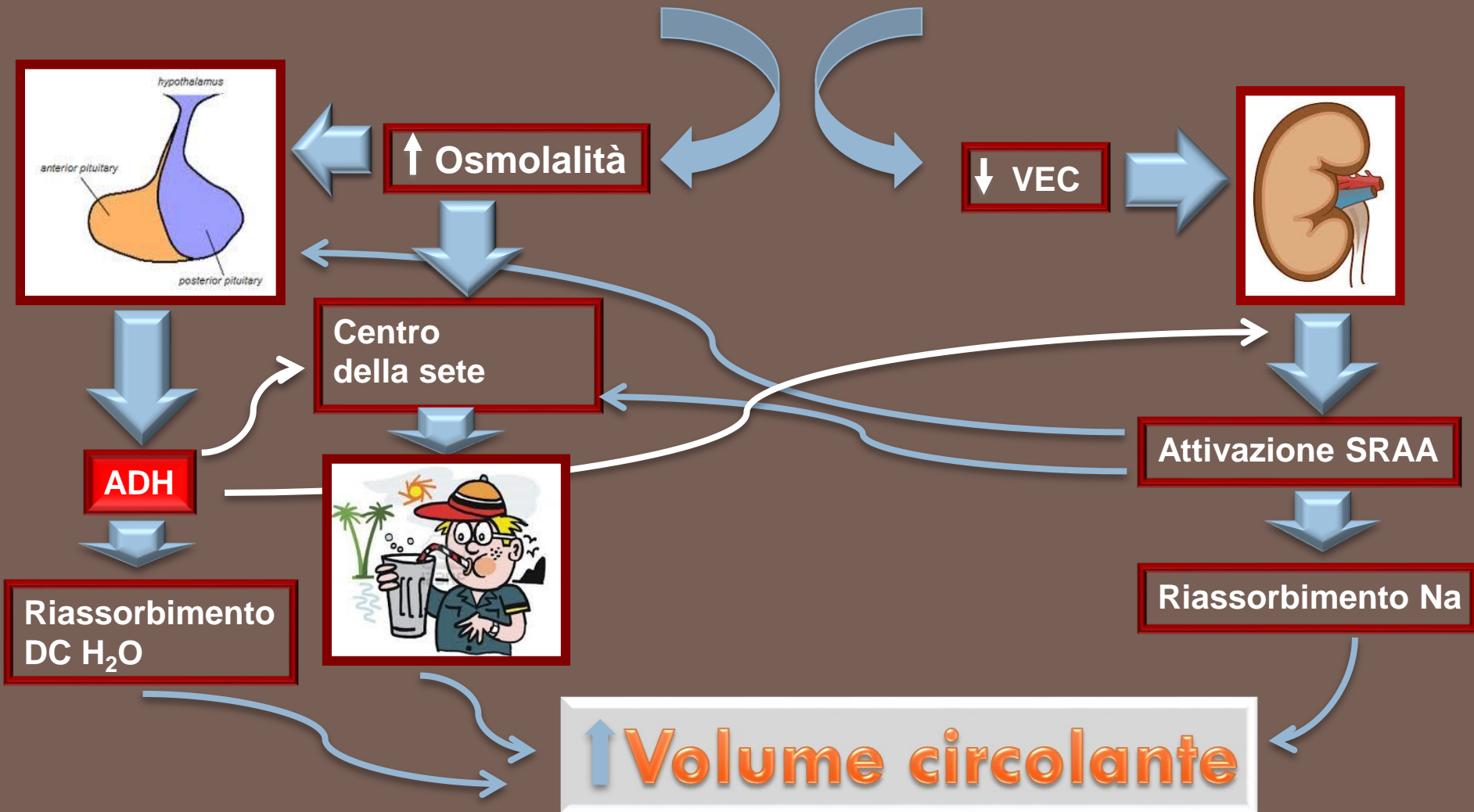
Eliminazione di H<sub>2</sub>O

Carmelo  
Libetta

BILANCIO H<sub>2</sub>O



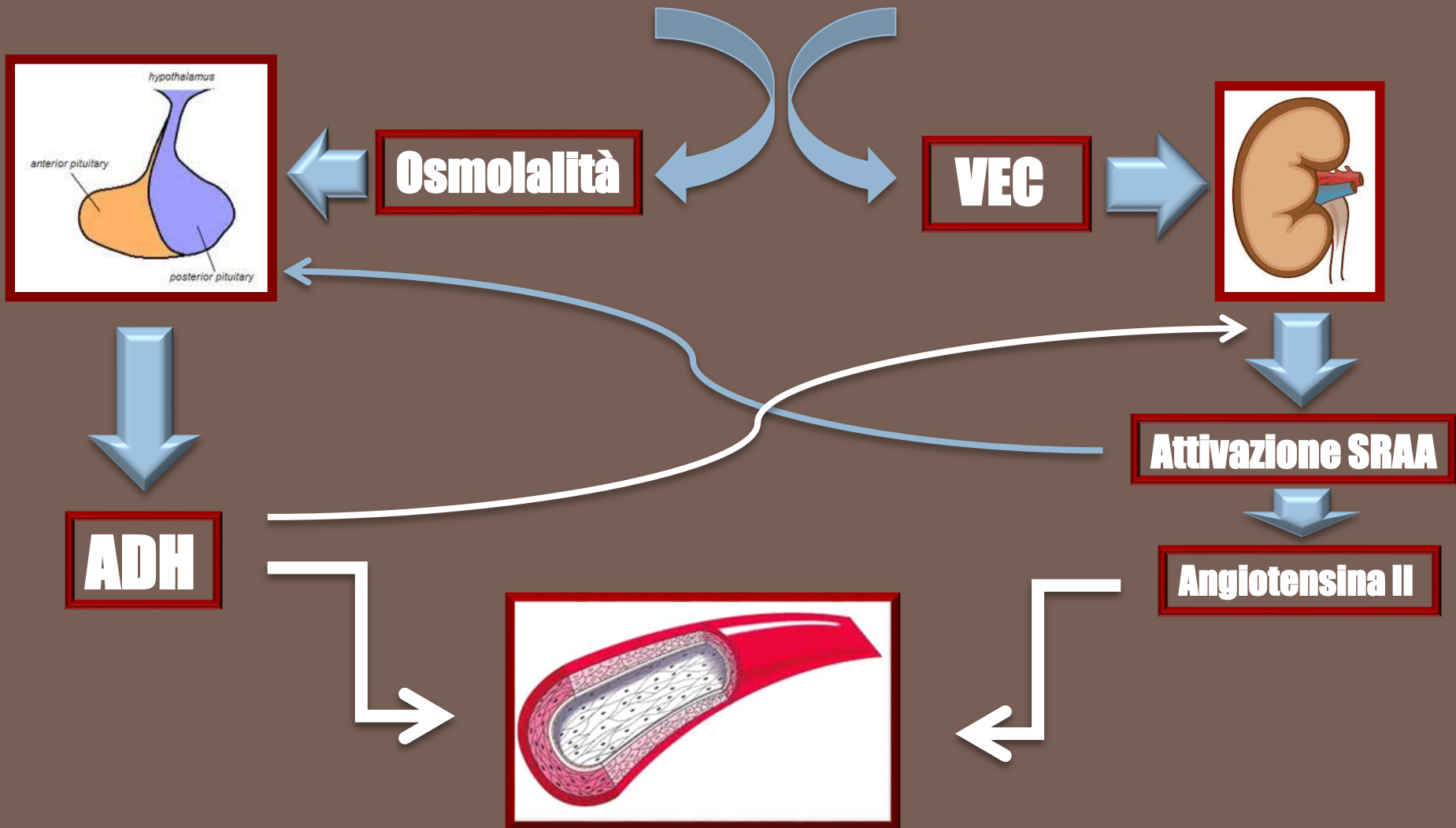
# DISIDRATAZIONE



Carmelo  
Libetta

Sistema integrato ADH / SRAA

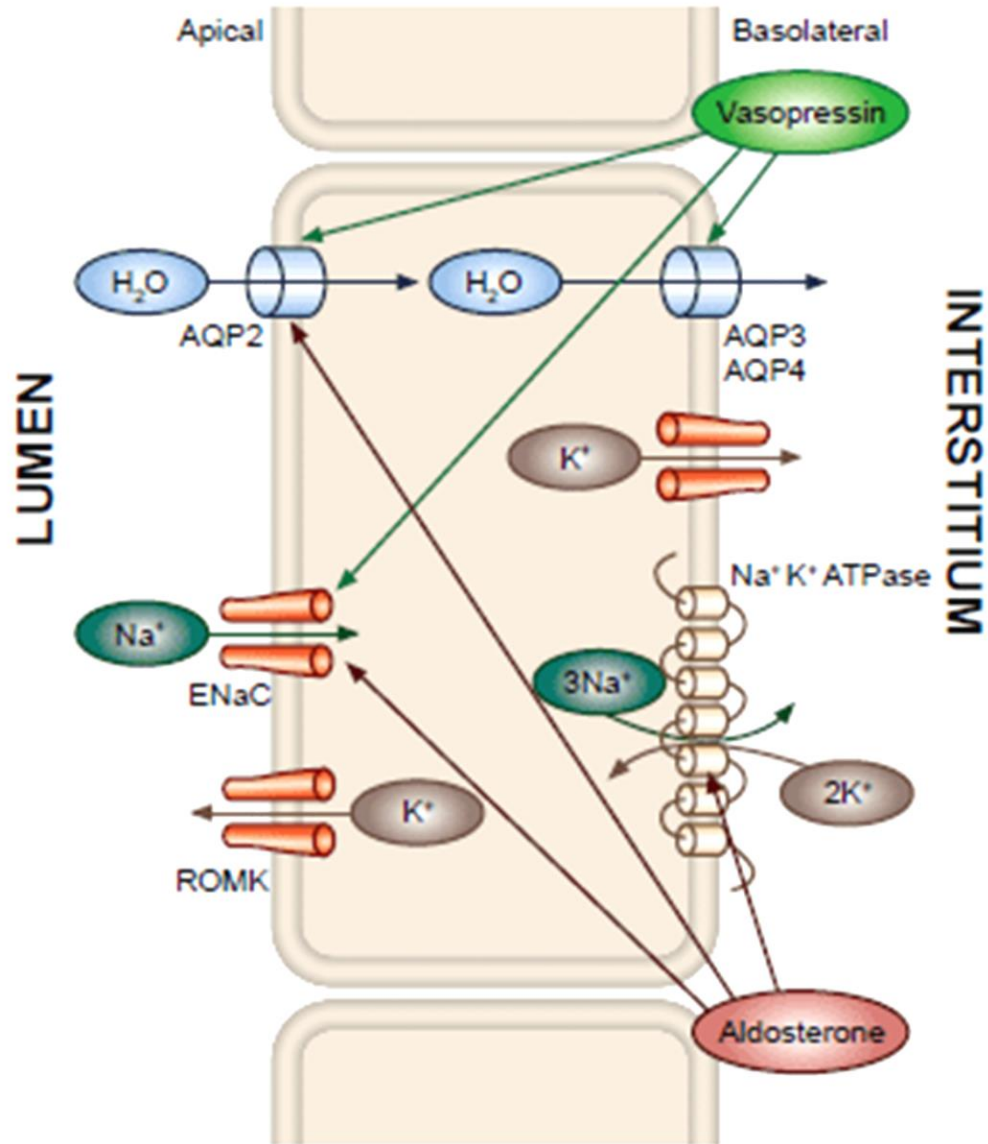
# DISIDRATAZIONE



Carmelo Libetta

Sistema integrato ADH / SRAA

# Cellule Principali



# Tubulo Collettore

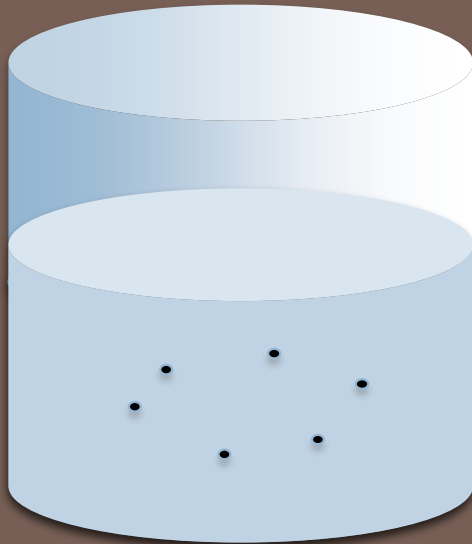


Carmelo  
Libetta

## ALDOSTERONE/ADH

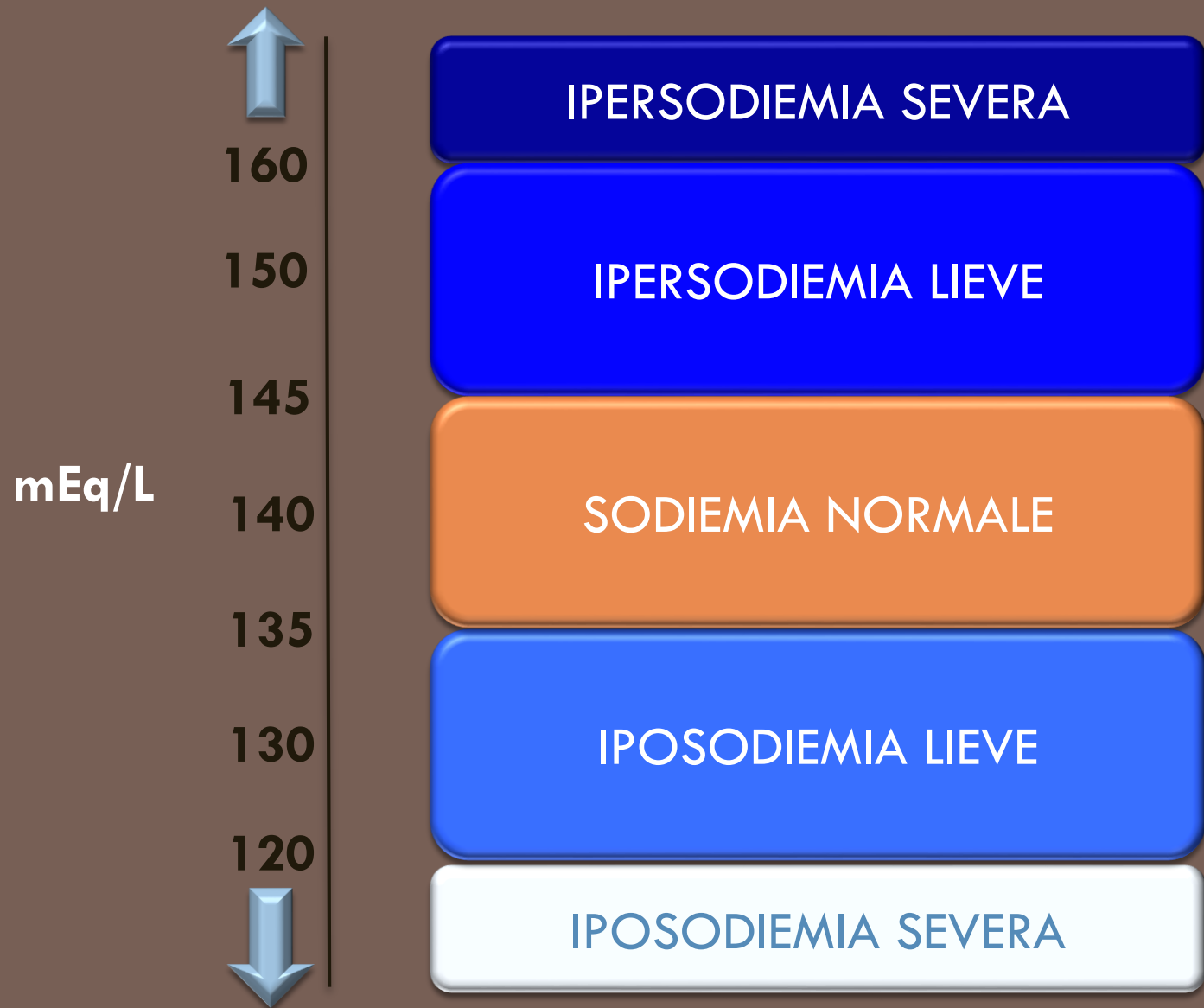


# ALTERAZIONI DELLA CONCENTRAZIONE DEL SODIO



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ALTERAZIONI SODIEMIA



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# Alterazioni SODIEMIA



# #Hyponatraemia



**EXPLAINED!**

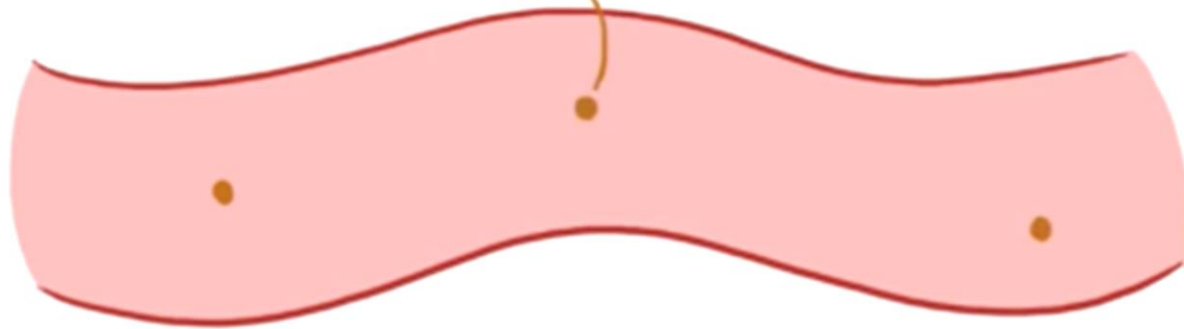


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Libetta

Iponatriemia

# HYPONATREMIA

LOW SODIUM in the BLOOD  
(Na<sup>+</sup>)



BELOW 135 mEq



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## IPONATRIEMIA



## ESCLUDERE STATI NON IPOOSMOLARI

- IPONATRIEMIA  
IPEROSMOLARE
- PSEUDO-IPONATRIEMIA

Osmolalità

Valutazione dello  
STATO VOLEMICO

$\text{Na}_{\text{urinario}}$

DIAGNOSI

Carmelo  
Libetta

IPOSODIEMIA



# Osmolalità



Carmelo  
Libetta

Iponatriemia

**Alta OSM**



**Iperosmolare**

**Bassa OSM**



**Iponatriemia vera**

**Normale OSM**



**Pseudo-iponatiemia**



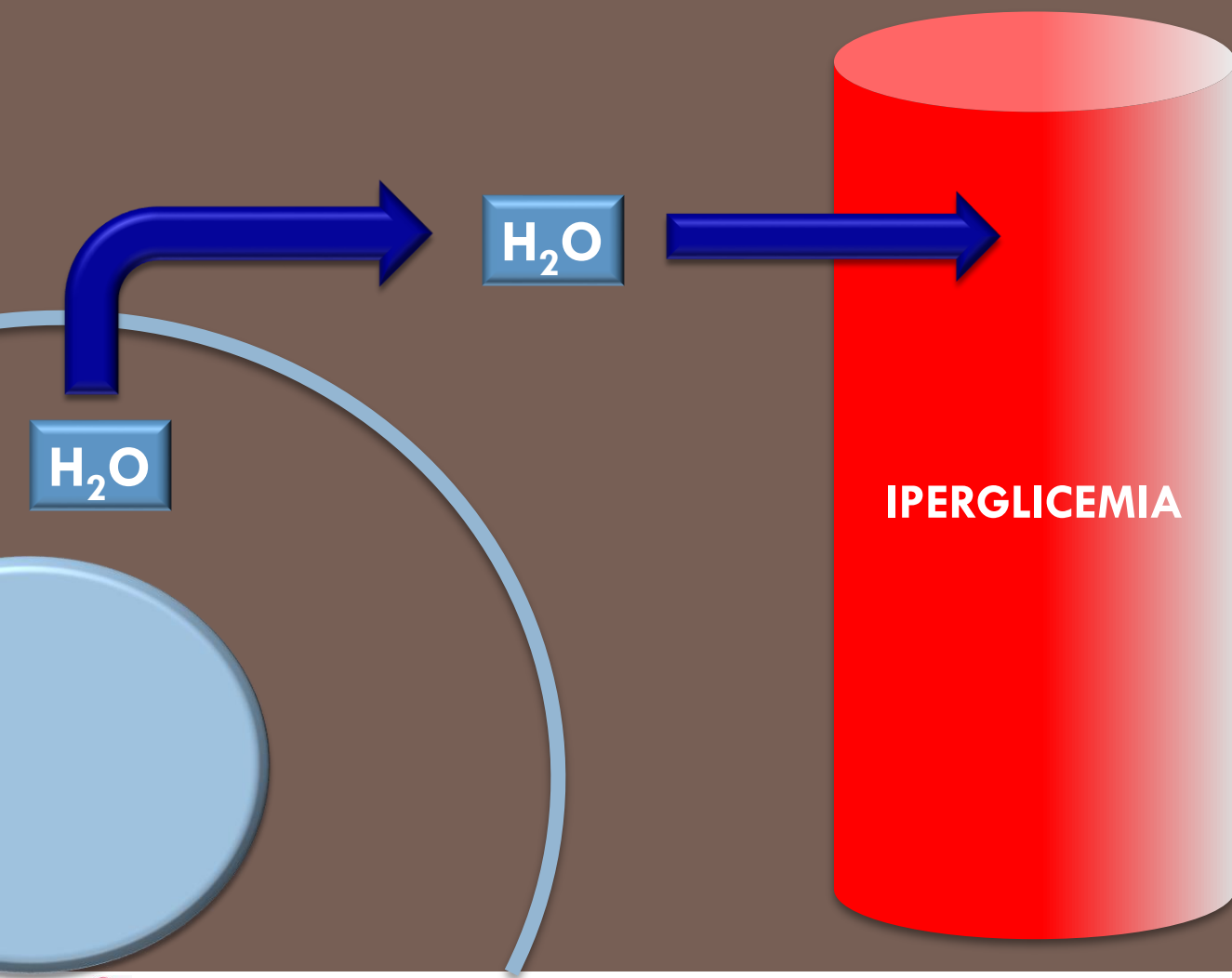
**Perdita di Na<sup>+</sup>**

**Ritenzione di H<sub>2</sub>O**



**Carmelo  
Libetta**

**IPONATRIEMIA**



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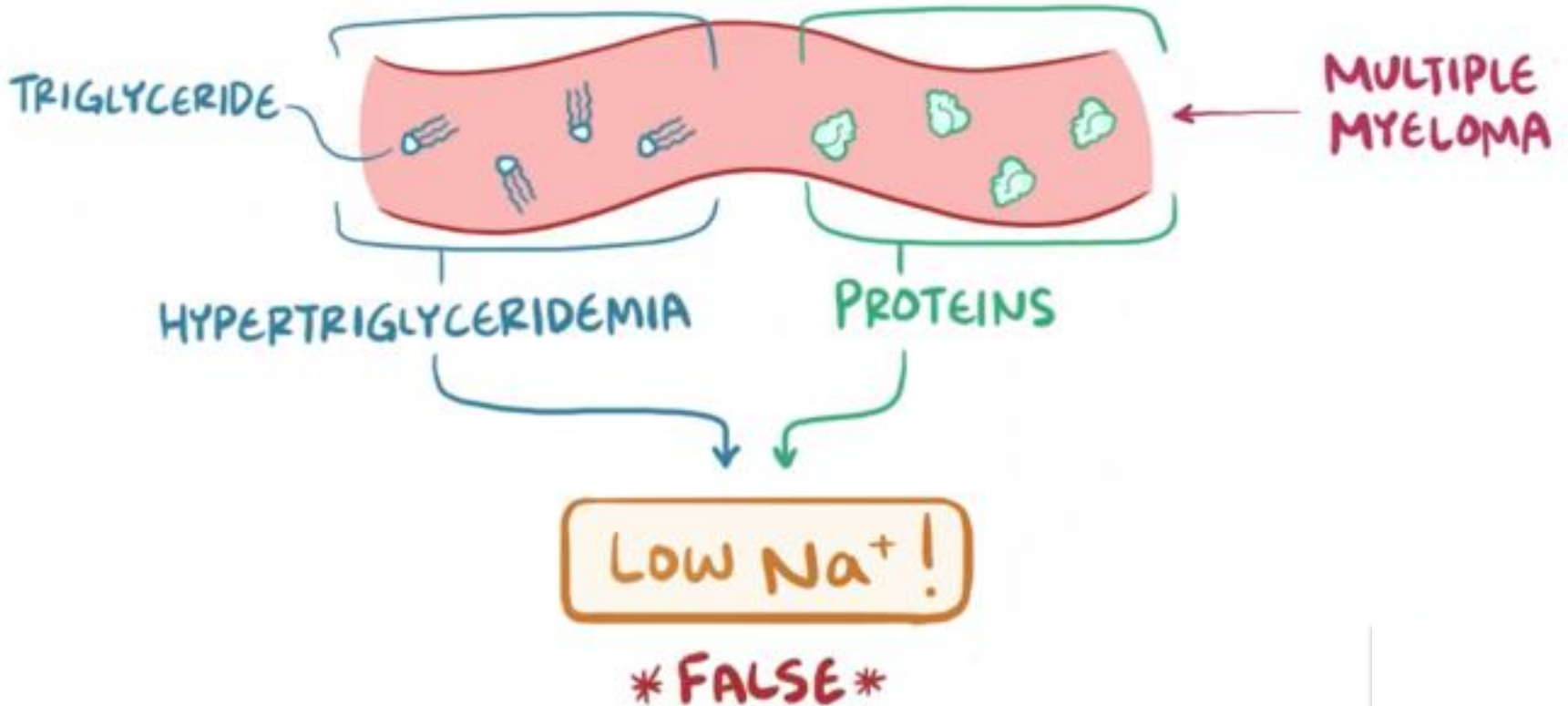
IPONATRIEMIA IPEROSMOLARE

# FALSE HYPONATREMIA

(PSEUDO-)

\*NORMAL  $\text{Na}^+$

\*NORMAL  $\text{H}_2\text{O}$



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IPOSODIEMIA NORMO-OSMOLARE

**IPOSODIEMIA VERA**

**IPOSODIEMIA  
IPO-OSMOLARE**



**Carmelo  
Libetta**

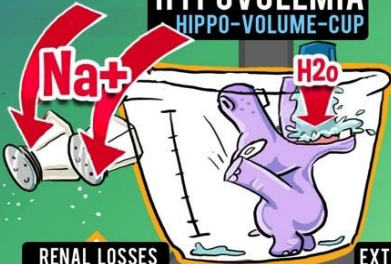
**IPOSODIEMIA**

# HYPONATREMIA

HIPPO-SALT-SHAKER



## HYPOVOLEMIA HIPPO-VOLUME-CUP



## HYPERVOLEMIA HIKER-SALT-SHAKER



## EUVOLEMIA EVEN-VOLUME-CUP

# VEC

RENAL LOSSES  
KIDNEY LOSS



EXTRARENAL LOSSES  
OUTSIDE KIDNEY LOSS



DIURETICS  
DIE-ROCKET



DIARRHEA  
TOILET



MINERALCORTICOID  
DEFICIENCY  
MINERALS BROKEN



VOMITING  
VOMIT



RENAL TUBULAR ACIDOSIS  
KIDNEY TUBA ACIDIC-LEMON



PANCREATITIS  
PANCREAS-ON-FIRE



CEREBRAL SALT  
WASTING  
BRAIN WASTING SALT



POOR INTAKE  
EMPTY SALT-SHAKER



TEA AND TOAST  
TEA AND TOAST



PSYCHOGENIC POLYDIPSIA  
POLLY-DIPPER



CHRONIC MALNUTRITION  
(RESET OSMOSTAT)  
CRONE WITH NUTRITIONAL-MALLET



SIADH  
INAPPROPRIATE ANT-TIE  
DIE-ROCKET



BEER POTOMANIA  
BEER POT



NEPHROTIC SYNDROME  
NERD-FROG



CARDIAC FAILURE  
DEAD HEART



CIRRHOSIS  
C-ROSES LIVER



ACUTE RENAL FAILURE  
DEAD ACUTE-ANGLE KIDNEY



CHRONIC RENAL FAILURE  
DEAD CRONE KIDNEY



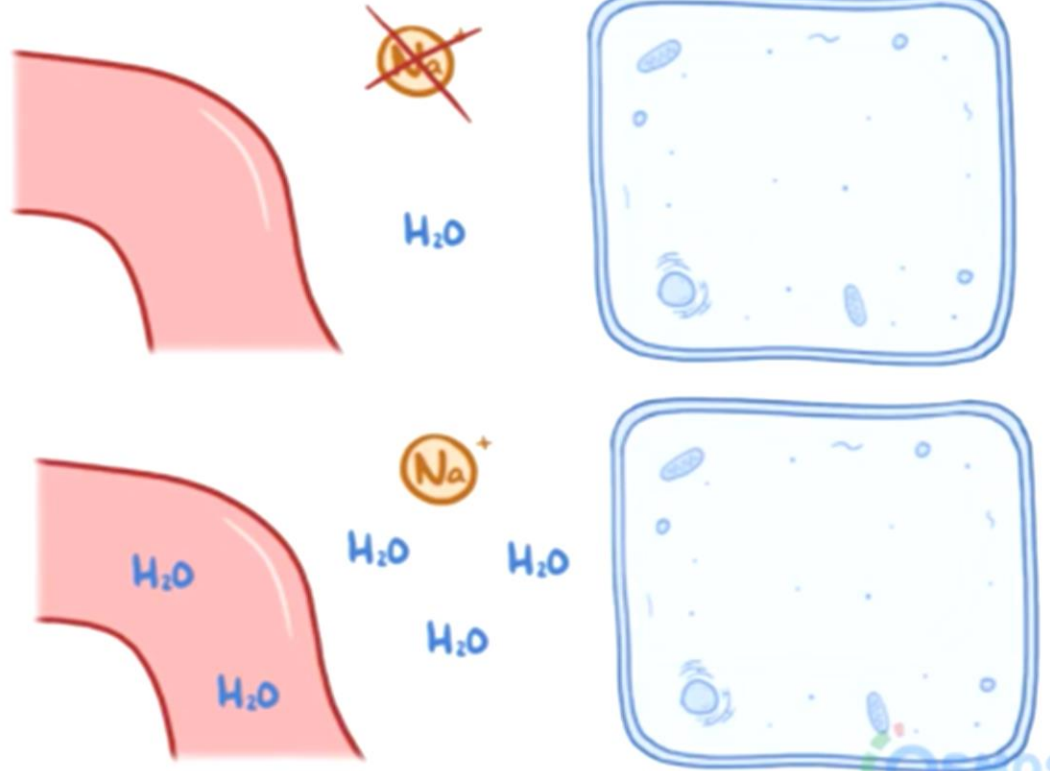
# HYPONATREMIA

\* LOW CONCENTRATION \*

\* **LOSING MORE SODIUM** than **WATER**

OR

\* **GAINING MORE WATER** than **SODIUM**



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Composizione fluidi corporei



**PERDITA DI Na<sup>+</sup>**

**↓ VEC**

**Perdite Extrarenali**

- Vomito
- Diarrea
- Ustioni

**Sodiuria <20 mEq/L**

**Perdite Renali**

- Eccesso diuretici
- Nefrop. perdita di Na<sup>+</sup>
- Diuresi osmotica
- Iposurrenalismo

**Sodiuria >80 mEq/L**



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**IPONATRIEMIA/IPOVOLEMIA**

**IPONATRIEMIA**



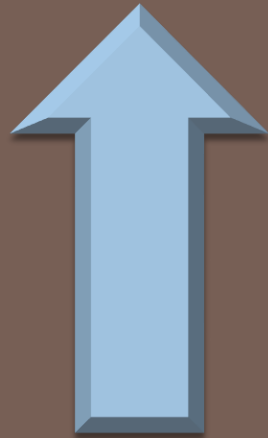
**EUVOLEMIA**



- SIADH
- Polidipsia
- Birra



$H_2O$



ADH

IPONATRIEMIA



↑ VEC



- Sindr. Nefrosica
- Scomp. Cardiaco
- Cirrosi epatica

$Na^+$



ALD



Carmelo Libetta

IPONATRIEMIA/IPERVOLEMIA

**Na<sup>+</sup> > 125 mEq/L**



**Il paziente non lamenta sintomi particolari**

**Na<sup>+</sup> < 125 mEq/L**



**Inappetenza  
Nausea, Vomito  
Cefalea  
Irritabilità  
Alterazioni del tono dell'umore  
Deficit dell'attenzione  
Confusione  
Disorientamento  
Disturbi dell'andatura  
Cadute  
Aumentato rischio di fratture e ridotta densità minerale ossea  
Crampi muscolari  
Letargia**

**Na<sup>+</sup> < 110 mEq/L**



**Intensa astenia  
Sonnolenza  
Depressione dei riflessi  
Paralisi di tipo bulbare o pseudobulbare  
Convulsioni  
Erniazione del tronco encefalico  
Coma  
Arresto respiratorio**

**Carmelo  
Libetta**

**SINTOMI IPONATRIEMIA**



# SYMPTOMS

\* NAUSEA, VOMITING, MUSCLE CRAMPS

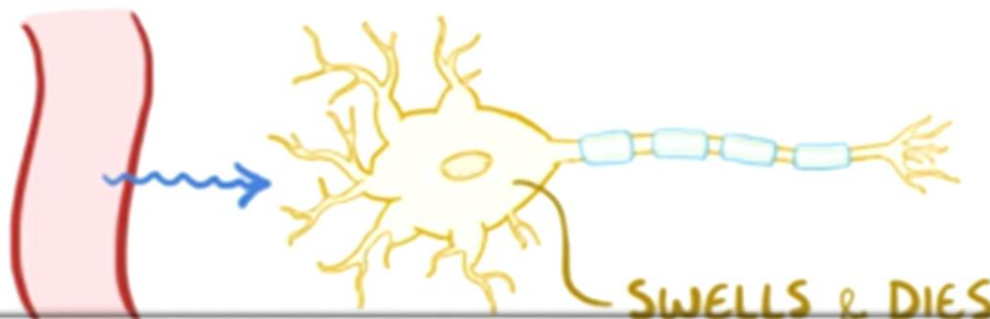
~ SEVERE ( $< 120 \text{ mEq/L}$ ) ~

\* CEREBRAL EDEMA

↳ CONFUSION, COMA, DEATH

↳ INCREASED INTRACRANIAL PRESSURE → ISCHEMIA

↳ HERNIATION → RESPIRATORY FAIL'

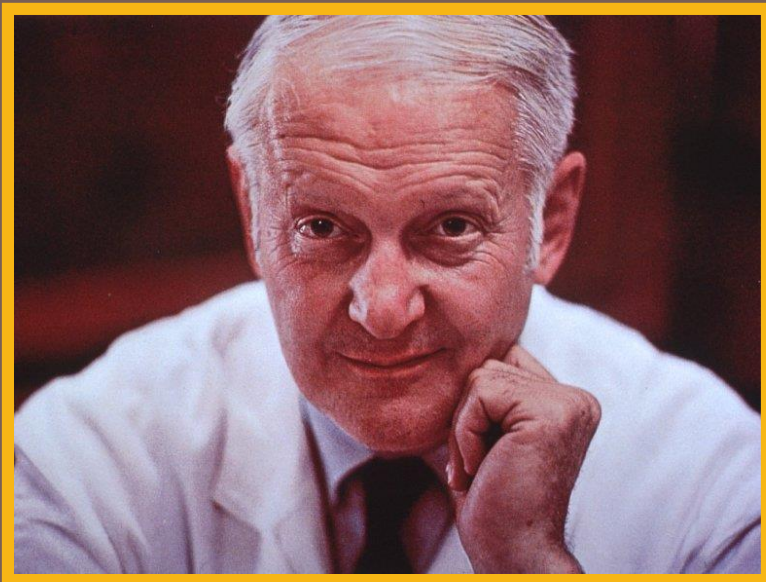


# SIADH

Sindrome da inappropriata secrezione ADH



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**F. C. Bartter**



**W. B. Schwartz**



**Carmelo  
Libetta**

**1957**

# A Syndrome of Renal Sodium Loss and Hyponatremia Probably Resulting from Inappropriate Secretion of Antidiuretic Hormone\*

WILLIAM B. SCHWARTZ, M.D., † WARREN BENNETT, M.D.,‡ SIDNEY CURELOR, M.D.§

*Boston, Massachusetts*

and FREDERIC C. BARTTER, M.D.

*Bethesda, Maryland*

with comments by

WILLIAM B. SCHWARTZ AND JOSEPH G. VERBALIS

Reprinted from *Am. J. Med.* 23: 529–542, 1957

This paper is a report of studies of two patients with bronchogenic carcinoma in whom hyponatremia developed as the result of unexplained failure of renal sodium conservation. The data indicate that sustained inappropriate secretion of antidiuretic hormone was probably responsible for the disorder of sodium metabolism. The physiologic abnormality appears to be analogous to that which can be produced by the continuous administration of pitressin® and water to normal subjects.

## CASE REPORTS

**CASE 1.** W.A., a sixty-year old hat cleaner, complained of coughing up bright red blood for the previous six weeks, and loss of 15 pounds of weight. On physical examination, he was well nourished. The blood pressure was 120/70 mm. Hg. There was marked clubbing of the fingers and toes which the patient said had been present all his life. Physical and neurologic examination was otherwise within normal limits.

Initial routine laboratory studies revealed no abnormalities



## AUTHOR COMMENTARY

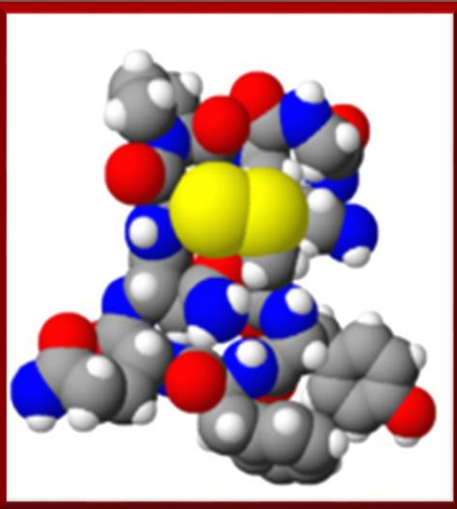
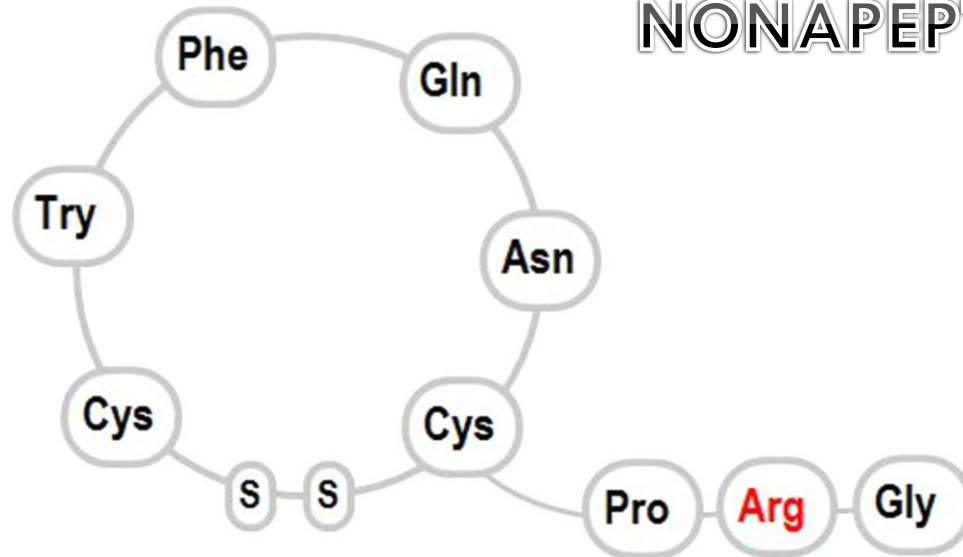
William B. Schwartz

*University of Southern California  
Los Angeles, California*

In 1955, a patient with bronchogenic carcinoma was admitted to the New England Medical Center with a puzzling syndrome of severe, unexplained hyponatremia and renal salt wasting. His BP was normal, and there was no evidence



# NONAPEPTIDE

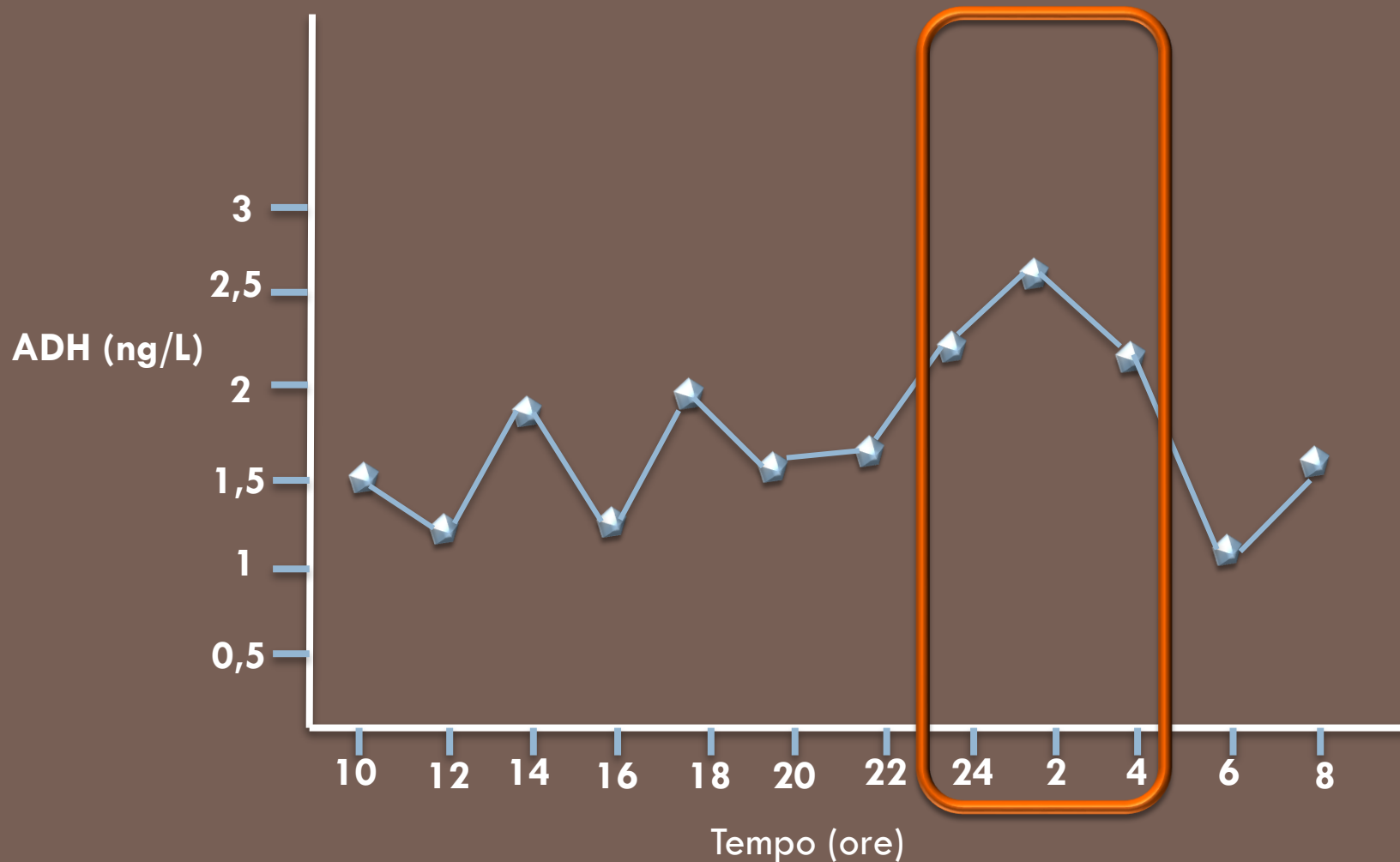


vn: 1,5-6 ng/L

Carmelo  
Libetta

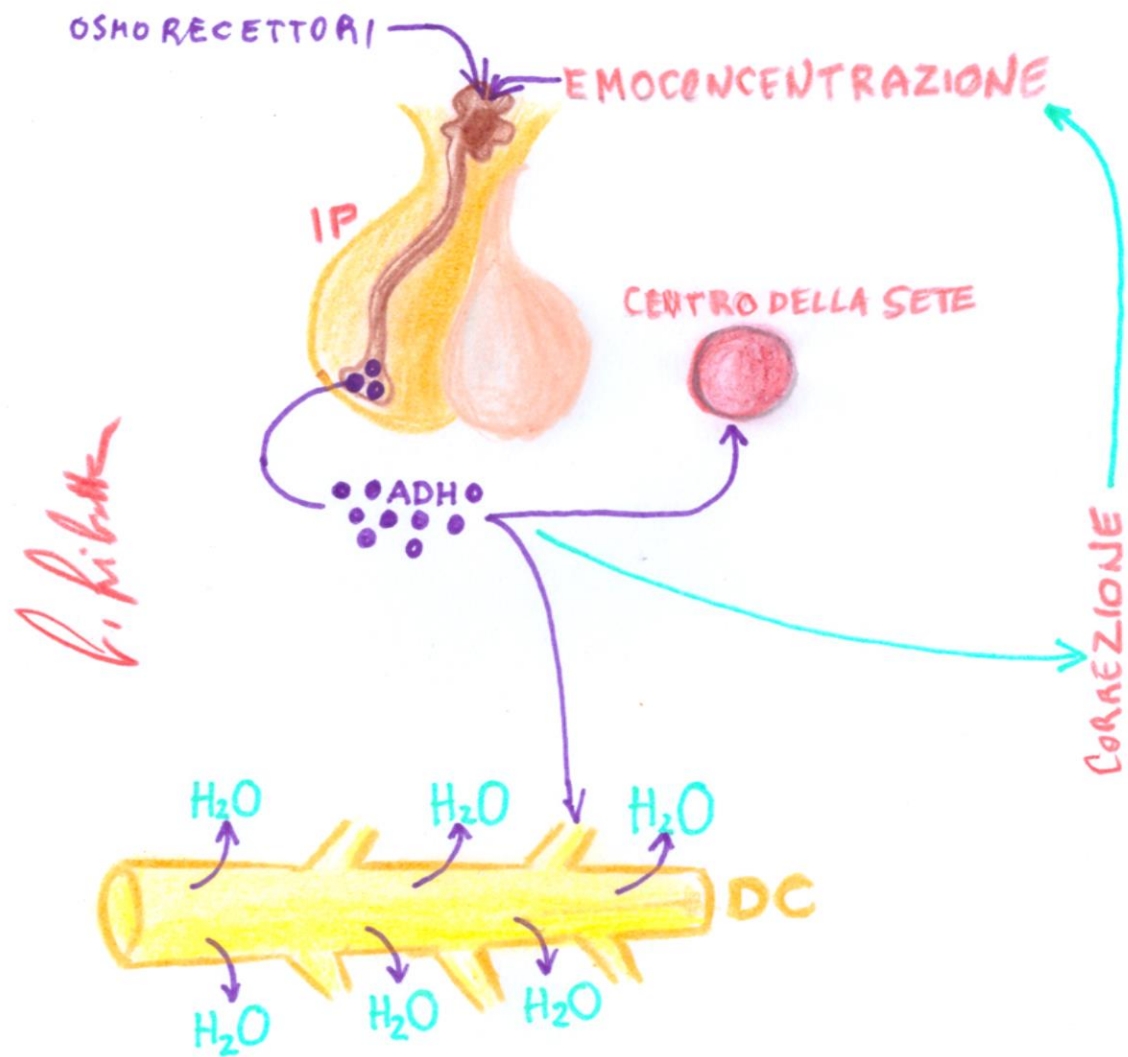
ADH





Carmelo  
Libetta

Ciclo circadiano



Carmelo  
Libetta

ADH



## ESPRESSIONE

## AZIONE

### ○ V1a

cellule muscolari vasi	→	vasocostrizione
cardiomiociti	→	iperplasia
piastrine	→	aggregazione
macula densa	→	SRAA

### ○ V2

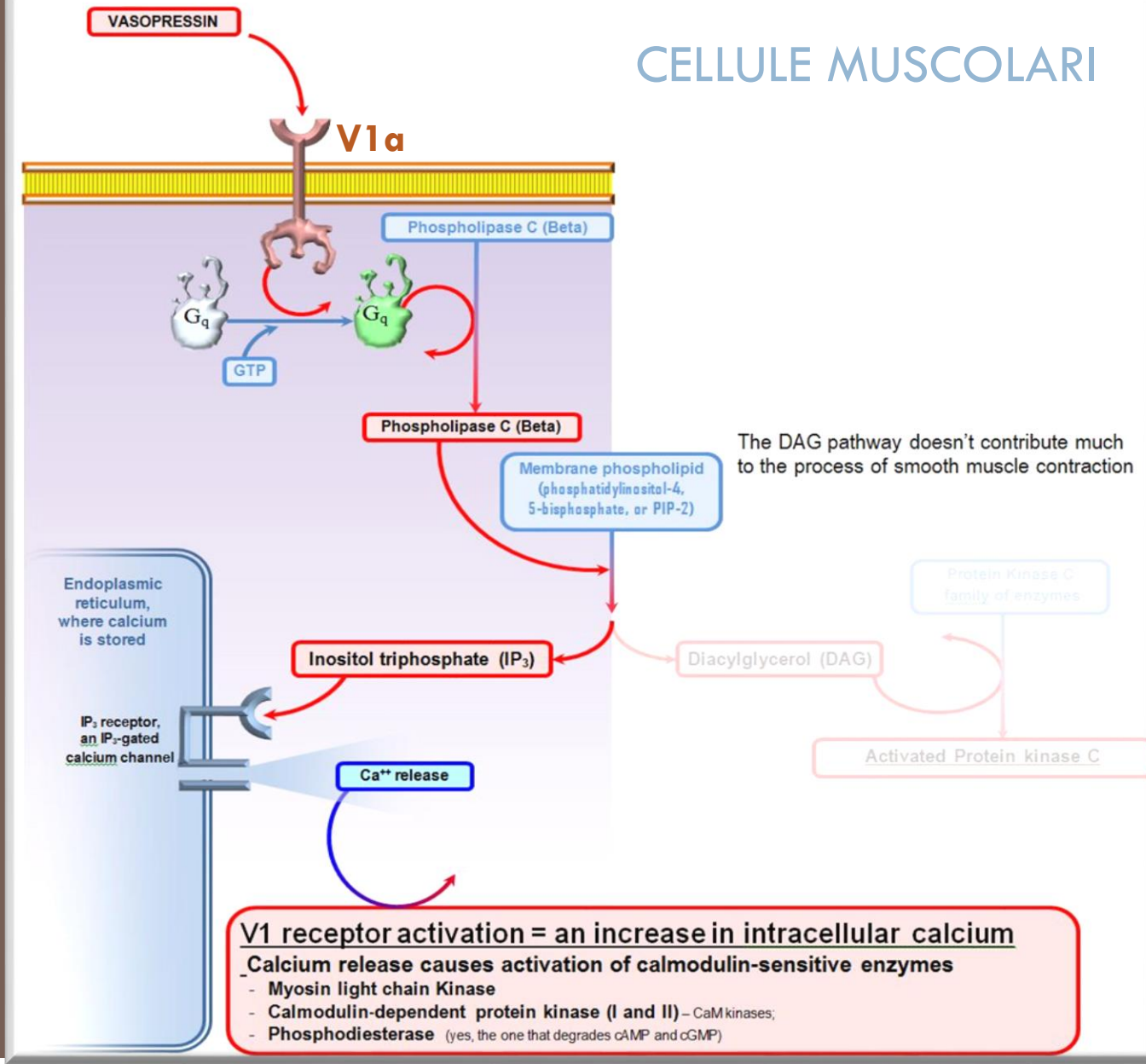
dotto collettore nefrone	→	ritenzione H <sub>2</sub> O
--------------------------	---	-----------------------------

### ○ V3

ipofisi anteriore	→	ACTH
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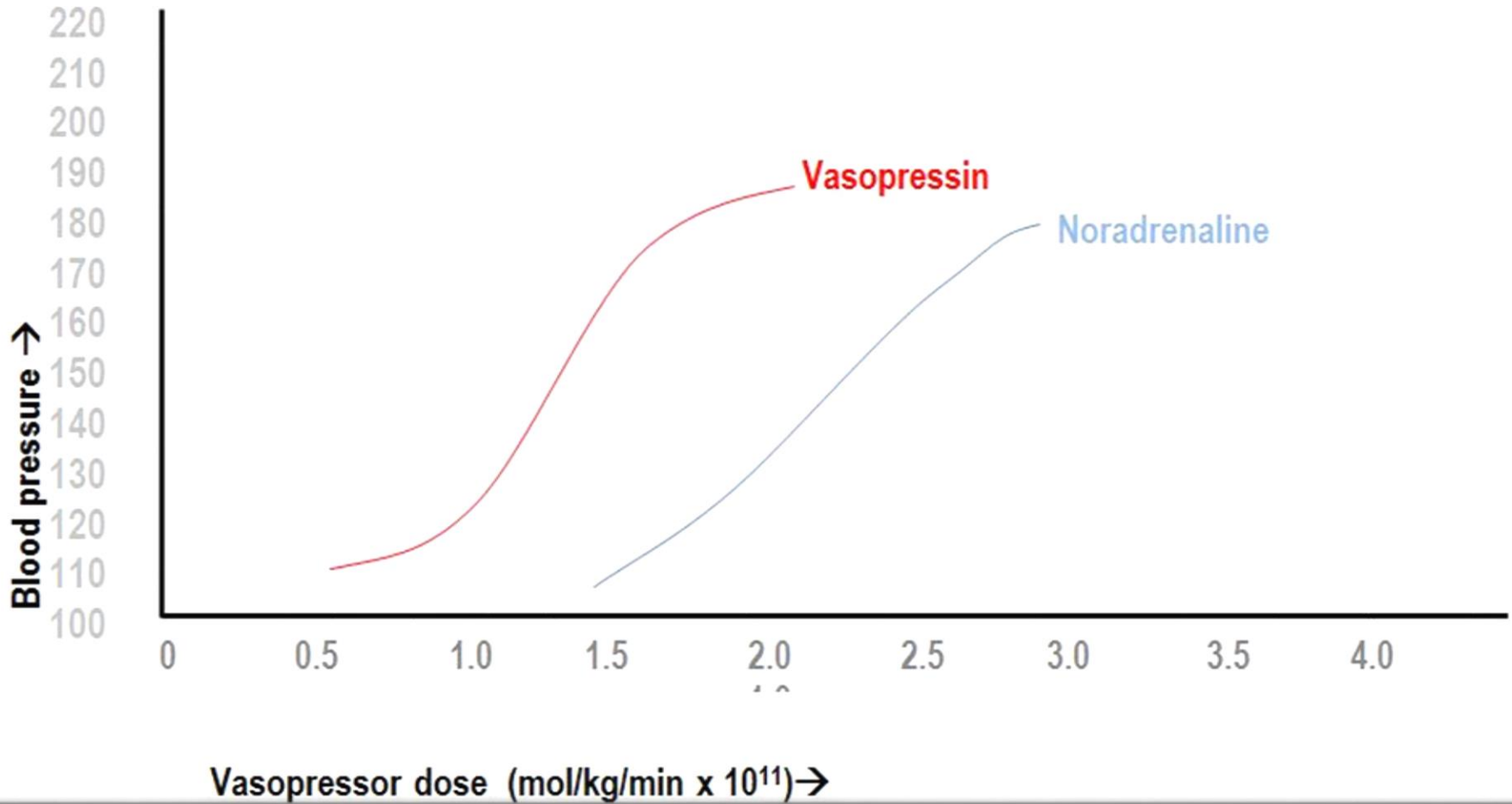
# CELLULE MUSCOLARI



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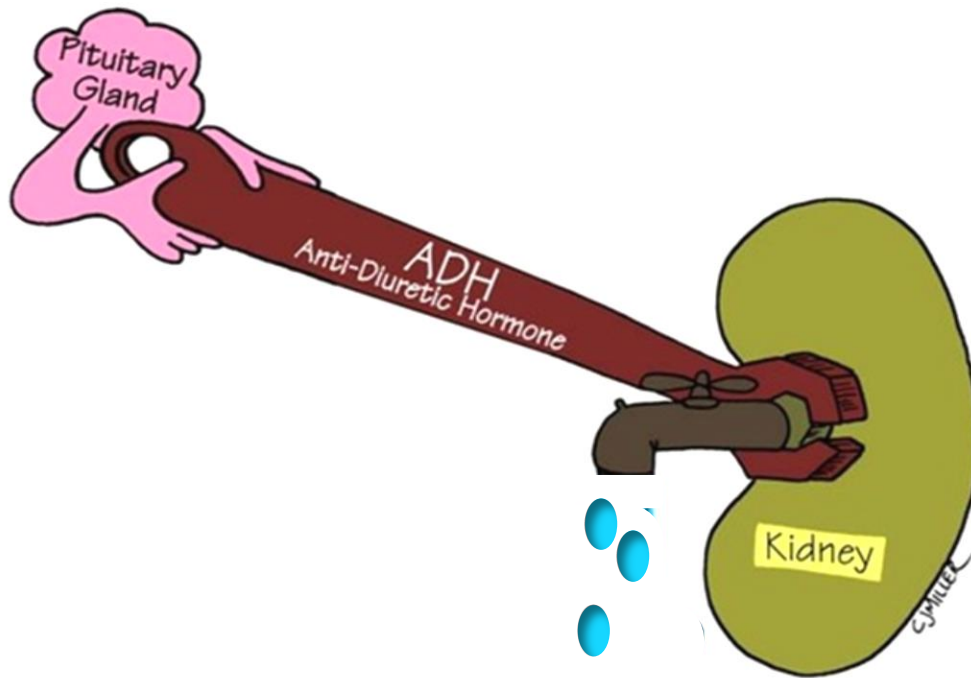
ADH/V1





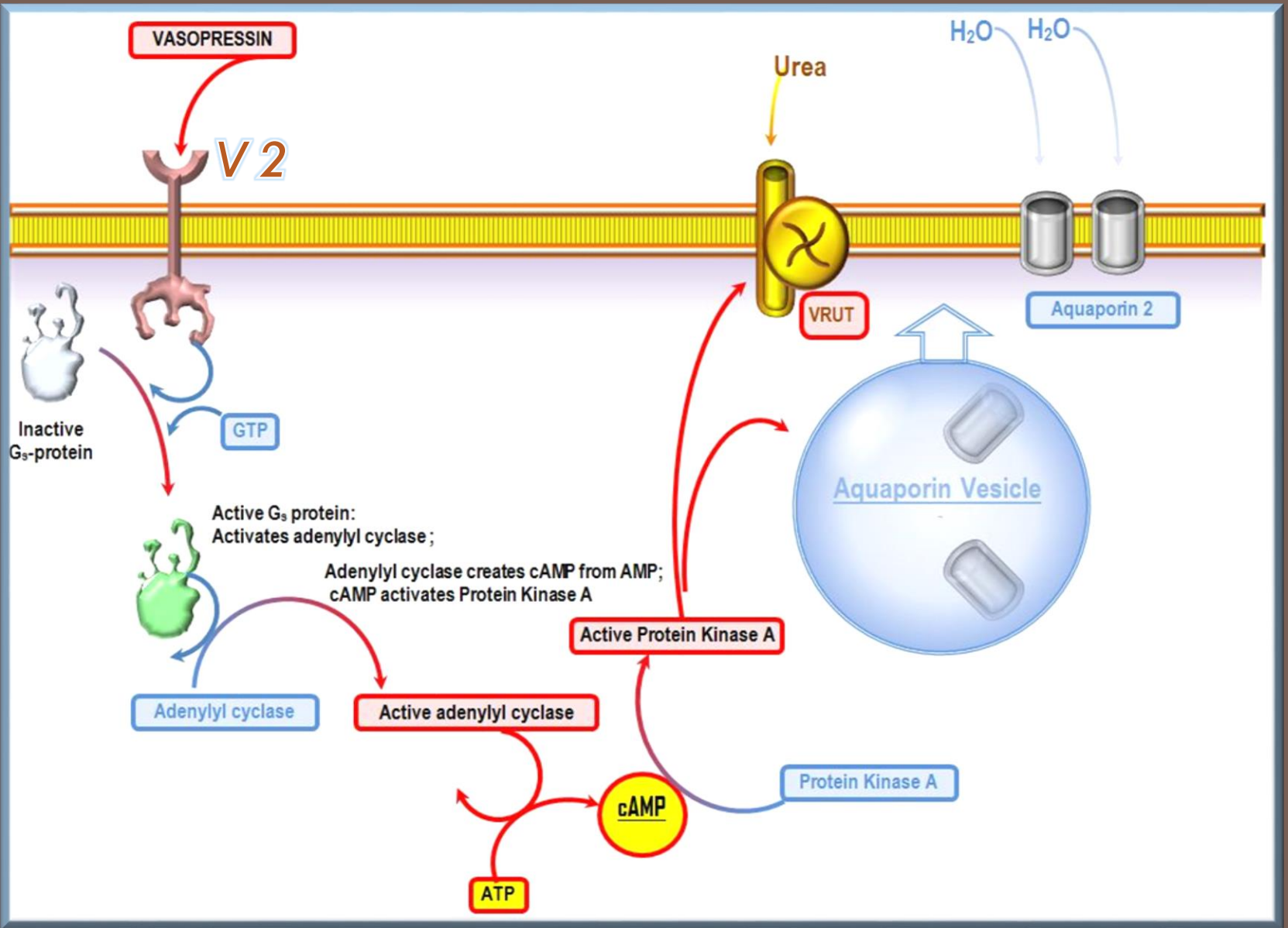
Carmelo  
Libetta

PA/ADH



Carmelo  
Libetta

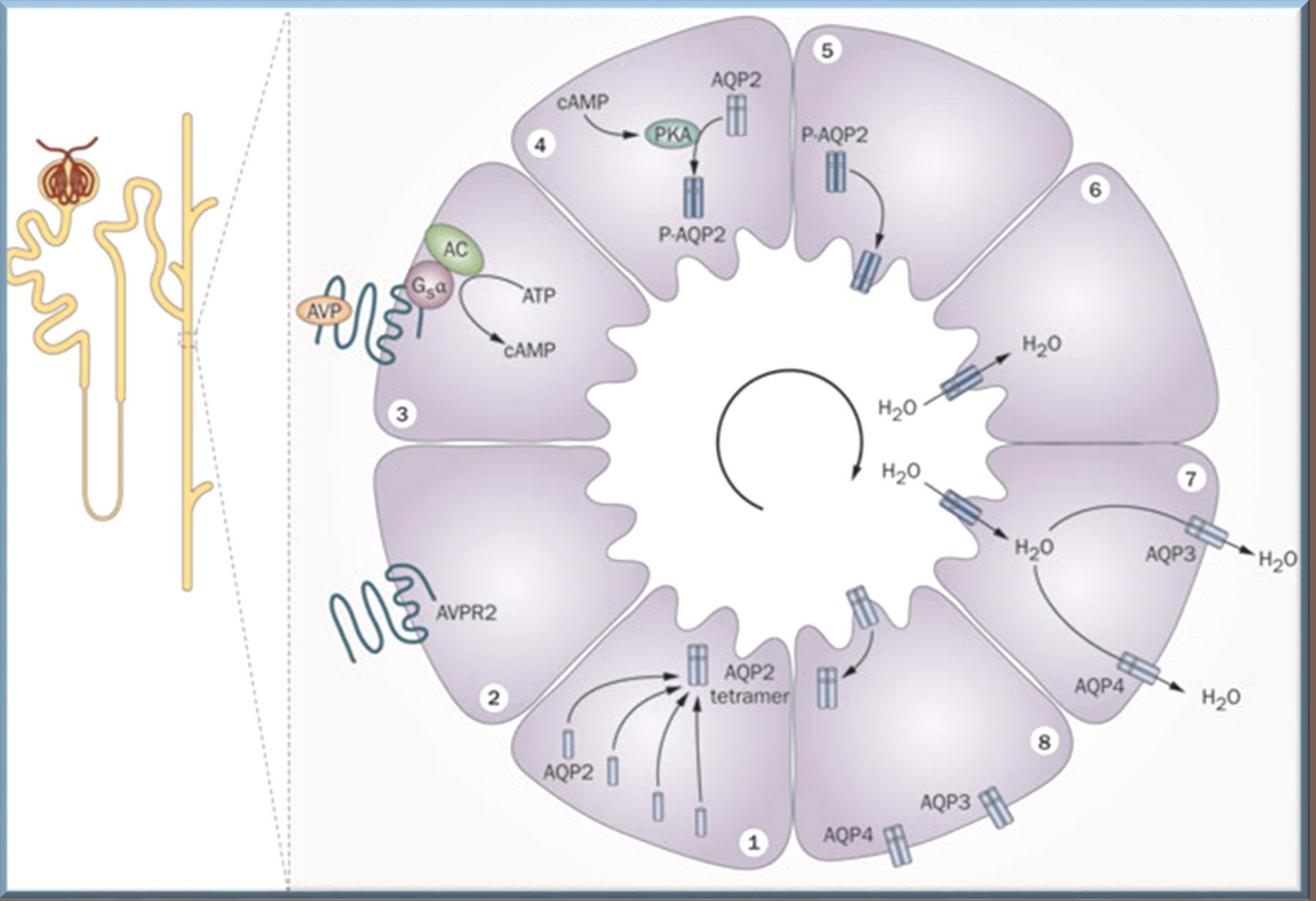
Idraulico



Carmelo  
Libetta

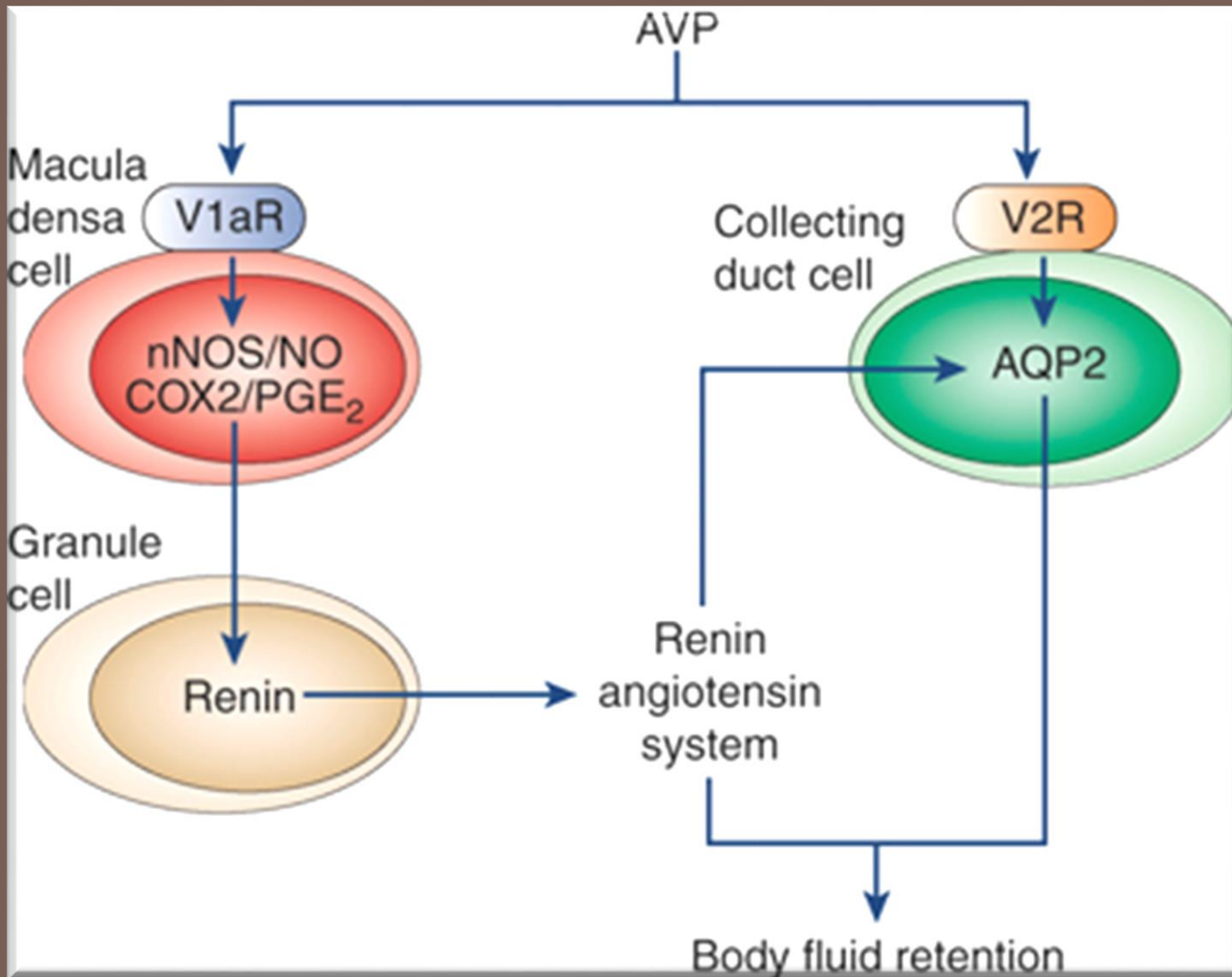
ADH/V2





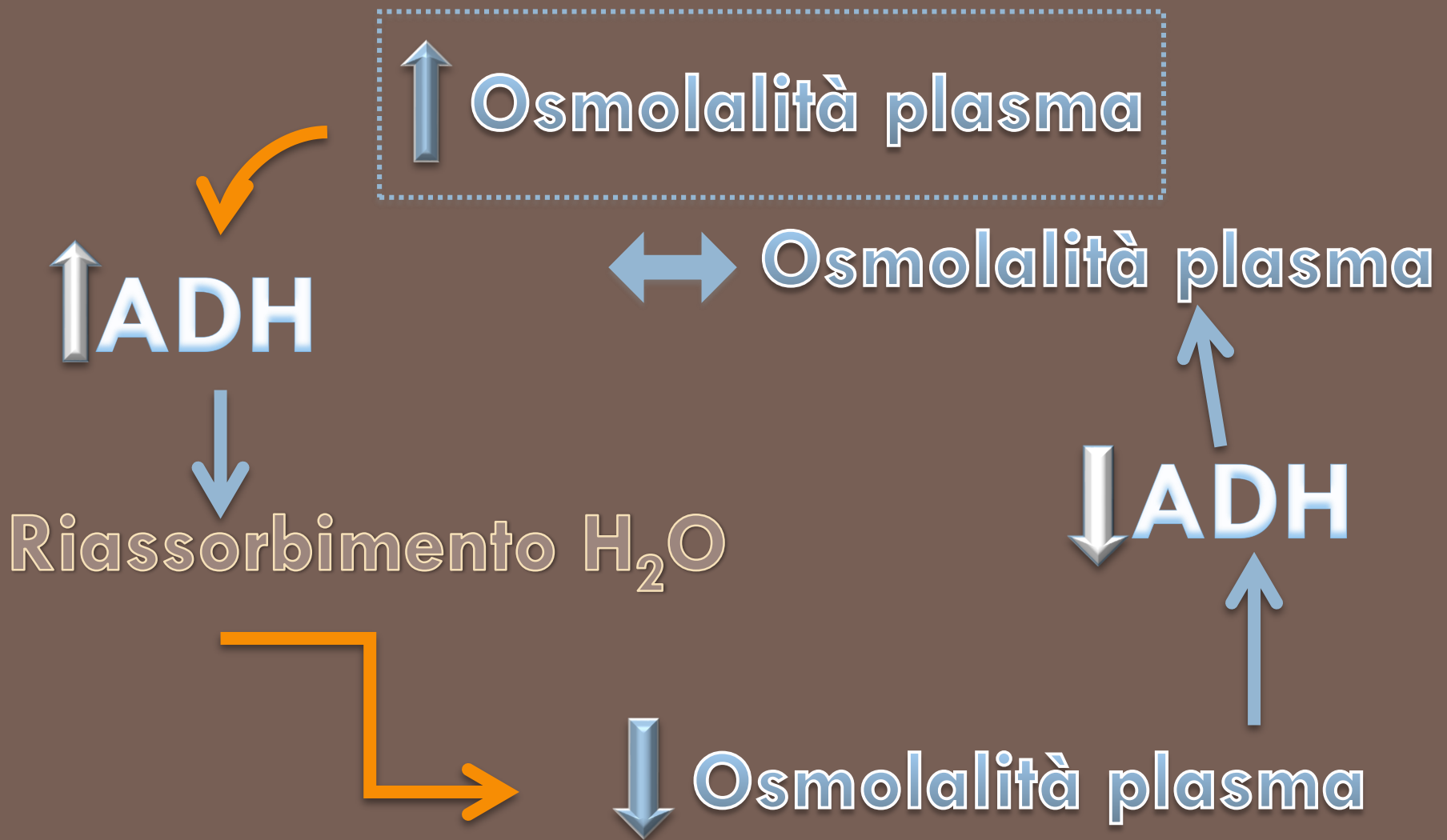
Carmelo  
Libetta

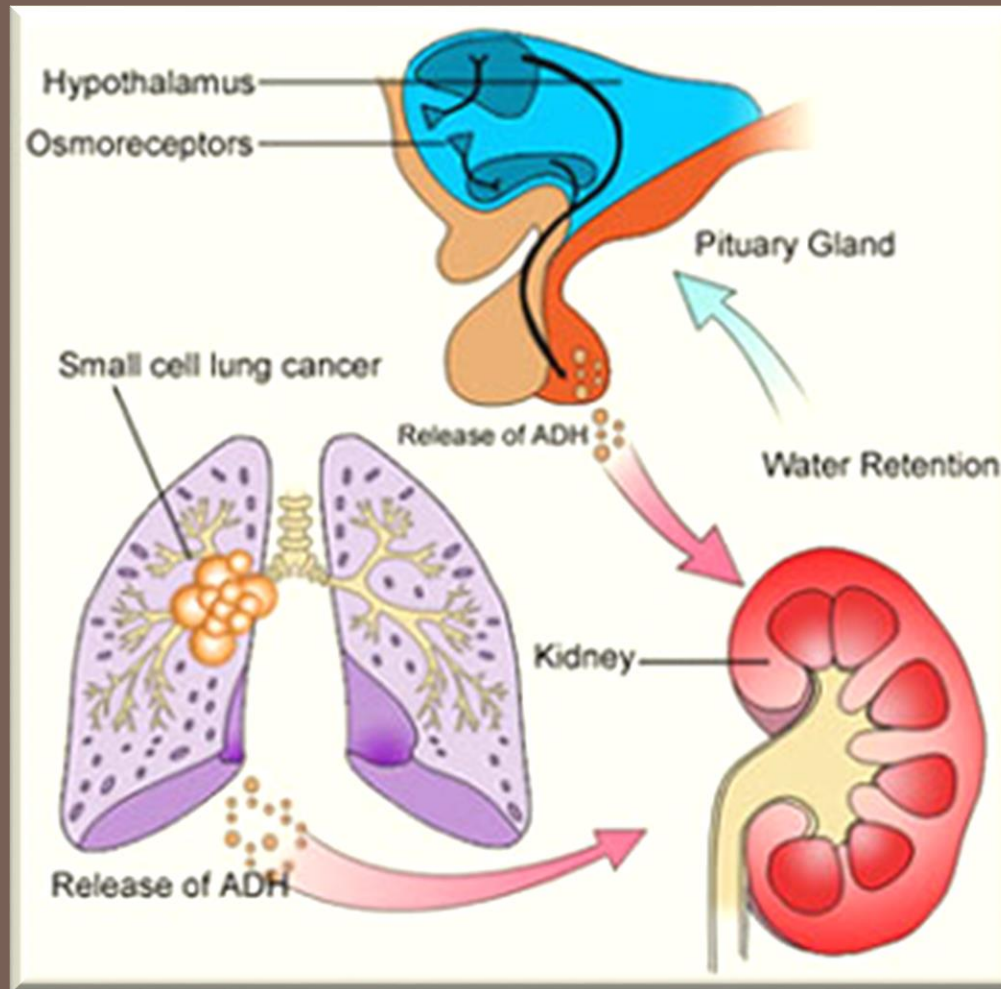
# Antidiuresi



**Carmelo  
Libetta**

# Sistema Integrato ADH/AII





Carmelo  
Libetta

# Eziologia SIADH

<ul style="list-style-type: none"> <li>● Antidepressivi           <ul style="list-style-type: none"> <li>Triciclici (amitriptilina, desipramina, protriptilina)</li> <li>Inibitori selettivi del reuptake della serotonina</li> <li>Inibitori delle monoaminossidasi</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>● Antidiabetici           <ul style="list-style-type: none"> <li>Clorpropamide</li> <li>Tolbutamide</li> <li>Rosiglitazone</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>● Antipsicotici           <ul style="list-style-type: none"> <li>Fenotiazine (tioridazina, trifluoperazina)</li> <li>Butirrofenoni (aloperidolo)</li> <li>Aripiprazolo</li> <li>Clozapina ? (rare segnalazioni in passato; dati più recenti indicano, viceversa, la possibilità di miglioramento dell'iponatremia nel paziente schizofrenico con polidipsia psicogena)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>● Antibiotici           <ul style="list-style-type: none"> <li>Trimetoprim-sulfametossazolo</li> <li>Ciprofloxacina</li> <li>Cefoperazone/sulbactam</li> <li>Rifabutina</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>● Antiepilettici           <ul style="list-style-type: none"> <li>Carbamazepina, oxcarbazepina</li> <li>Valproato di sodio</li> <li>Lamotrigina</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>● Miscellanea           <ul style="list-style-type: none"> <li>Antinfiammatori non steroidei (inibitori della sintesi di prostaglandine)</li> <li>Oppiacei</li> <li>Tramadolo</li> <li>Nicotina</li> <li>Clofibrato</li> <li>ACE-inibitori</li> <li>Amiodarone, lorcainide, propafenone</li> <li>Amlodipina</li> <li>MDMA (ecstasy)</li> <li>Teofillina</li> <li>Imatinib</li> <li>Sibutramina</li> <li>Inibitori di pompa protonica (omeprazolo)</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>● Agenti antineoplastici           <ul style="list-style-type: none"> <li>Vincristina, vinblastina (raro)</li> <li>Cisplatino (frequente), carboplatino (raro)</li> <li>Ciclofosfamida iv, melfalan, ifosfamida</li> <li>Metotrexato</li> <li>Interferone-alfa e gamma</li> <li>Levamisolo</li> <li>Pentostatina</li> <li>Anticorpi monoclonali</li> </ul> </li> </ul>	



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Libetta**

**Farmaci e SIADH**



Carmelo  
Libetta

DIAGNOSI

# 1. Osmolalità plasmatica ridotta ( $<275\text{mOsm/Kg}$ )

# 2. Osmolalità urinaria $>$ di quella sierica

**Tabella 9** Criteri per la diagnosi di SIAD.

Criteri essenziali	Criteri aggiuntivi
$P_{\text{osm}} < 275 \text{ mosm/kg H}_2\text{O}$	Uricemia $< 4 \text{ mg/dL}$
$U_{\text{osm}} > 100 \text{ mosm/kg H}_2\text{O}$	Azotemia $< 10 \text{ mg/dL}$
Euvolemia	Mancata risposta all'infusione di soluzione salina allo 0,9%
$\text{Na}^+$ urinario $> 40 \text{ mmol/L}$	Correzione con restrizione idrica

# 4. Euvolemia

# 5. Miglioramento iponatriemia dopo restrizione di $\text{H}_2\text{O}$



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Criteri maggiori

# EMODILUIZIONE

- Livelli di azotemia  $< 20$  mg/dl
- Livelli di uricemia  $< 3$  mg/dl

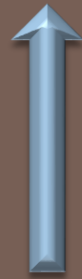


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Criteria secondari



~~SAFH~~

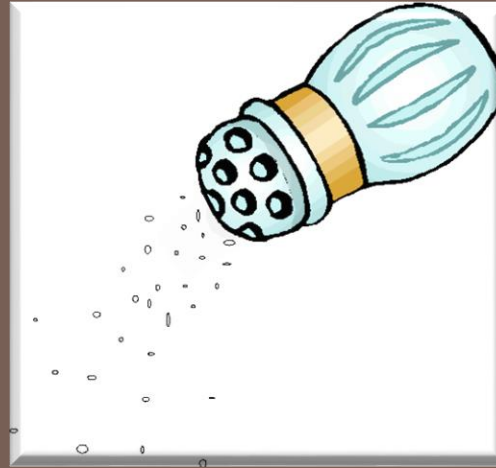


Eliminare la causa



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TERAPIA



# IPOSODIEMIA



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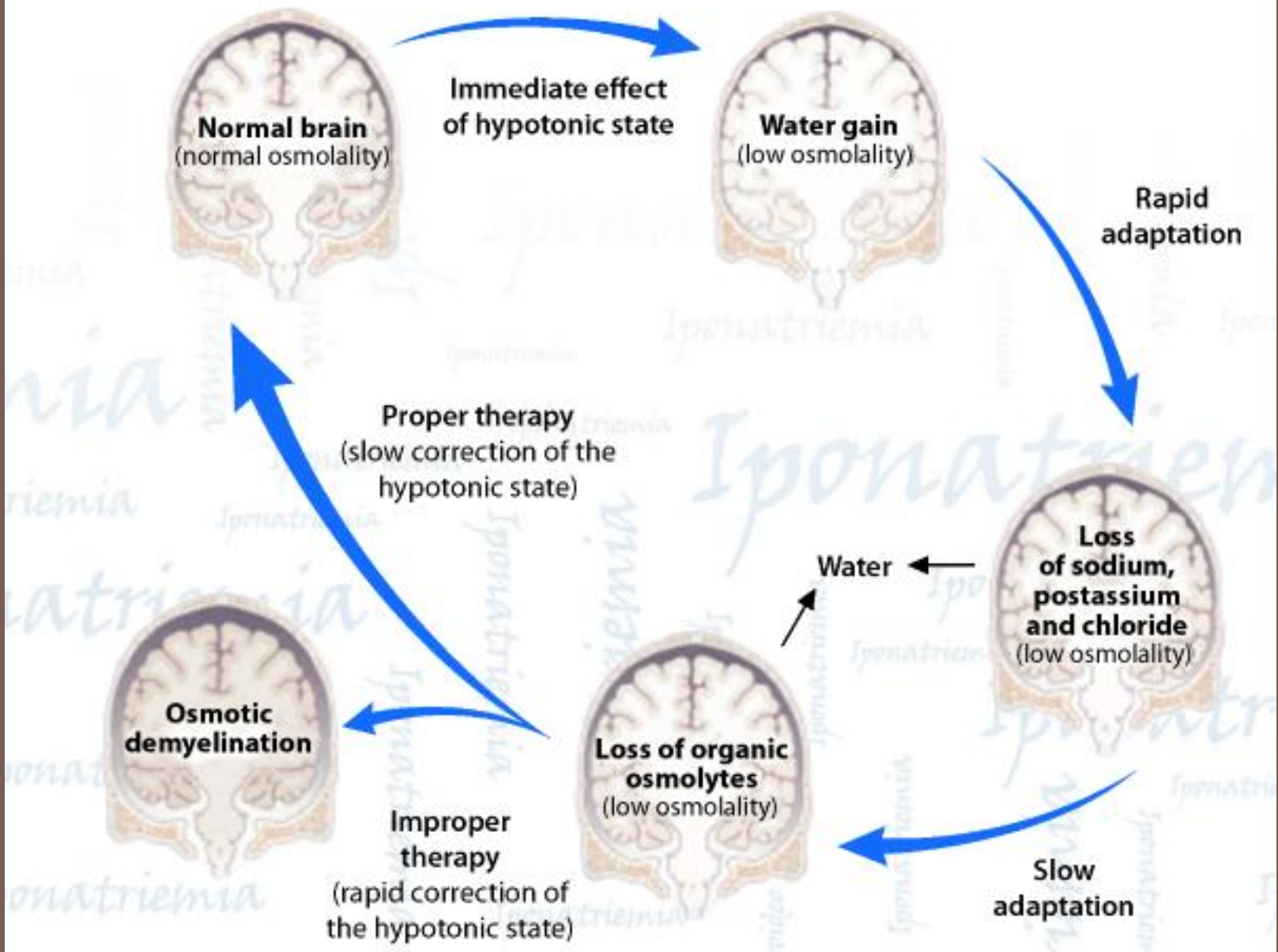
## TERAPIA

**PRIMUM NON NOCERE**



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Libetta

Mielinosi pontina



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Libetta

# Mielinosi pontina

# TREATMENT ~ DEPENDS on CAUSE

\* SIADH → FLUID RESTRICTION

\* HYPOVOLEMIA → MORE FLUID

\* SEVERE HYPONATREMIA

↳ HYPERTONIC SALINE

\* CAREFUL to AVOID CEREBRAL  
PONTINE MYELINOLYSIS



- ❖ **Restrizione idrica (500 ml/die)**
- ❖ **Infusione di soluzione fisiologica**
- ❖ **DIURETICI**

**Sodiemia 134-120 mEq/L**



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**Iponatriemia asintomatica**

- ◆ **Forme acute 8-10 mEq/L/24 h**
- ◆ **Forme croniche < 3 mEq/L/24 h**

**Controllo sodiemia ogni 4 ore**

**Sodiemia < 120 mEq/L**

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**Correzione sodiemia**

◆ Soluzioni saline ipertoniche (3%)

◆ Restrizione idrica (< 500 ml/die)

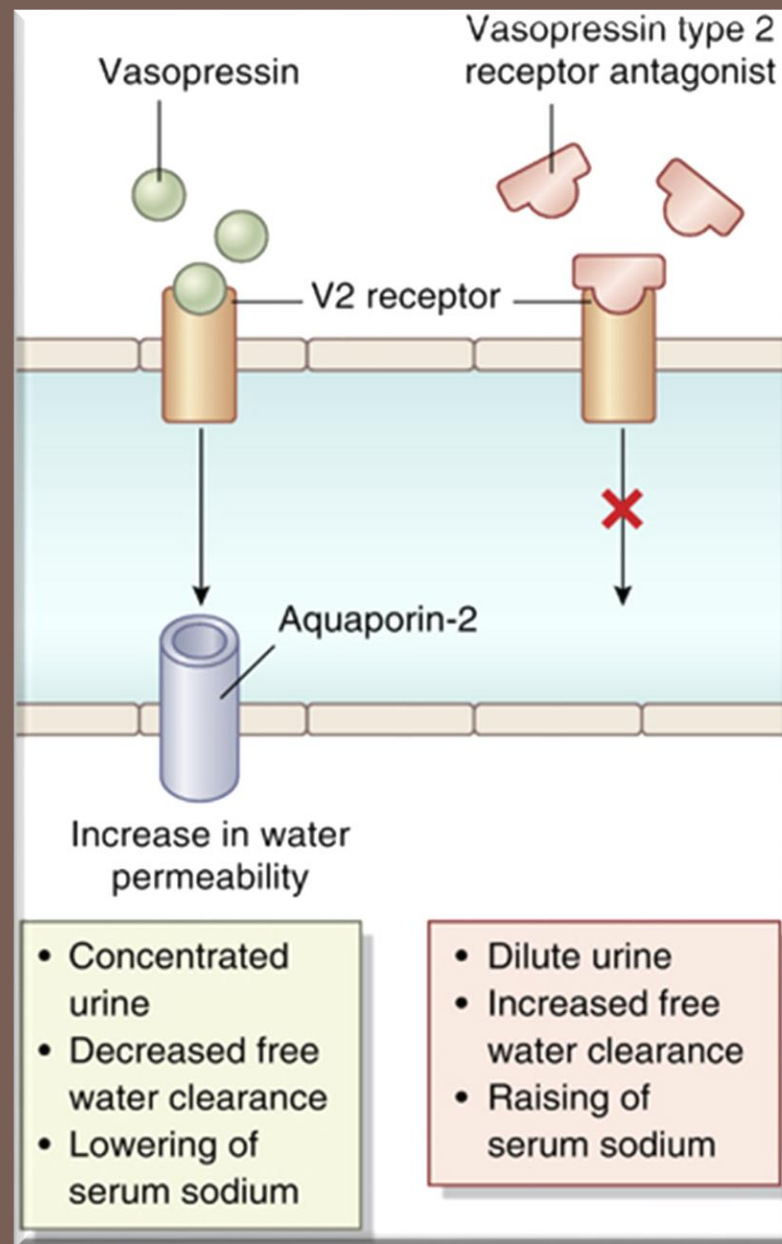
◆ VAPTANI



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Iponatriemia sintomatica





**Carmelo  
Libetta**

**VAPTANI**



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Libetta

IPERNATRIEMIA

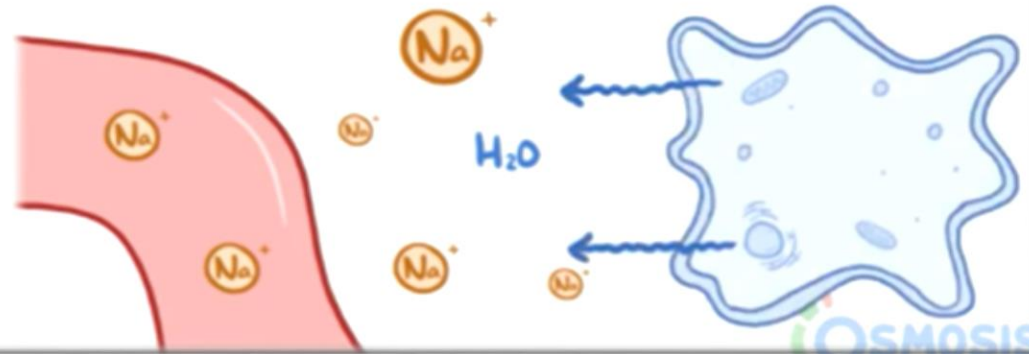
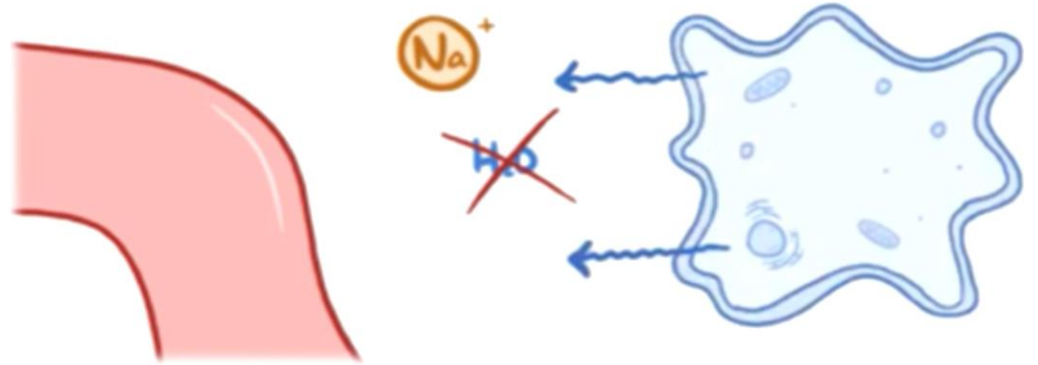
# HYPERNATREMIA

\* HIGH CONCENTRATION \*

\* **LOSING MORE WATER** than **SODIUM**

OR

\* **GAINING MORE SODIUM** than **WATER**



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IPERNATRIEMIA

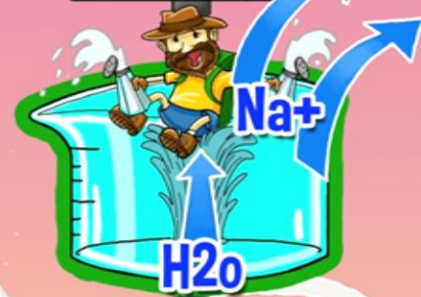
# HYPERNATREMIA HIKER SALT SHAKER



## HYPOVOLEMIA HIPPO-VOLUME-CUP



## HYPERTONIC HIKER VOLUME-CUP



## EUVOLEMIA EVEN-VOLUME-CUP



## PRIMARY HYPERALDOSTERONISM HIKER-ALDO-STEREO



## CUSHING'S SYNDROME CUSHION



## HYPERTONIC SALINE HIKER-TONIC SALINE-SAIL



## BICARBONATE BI-CAR-BOMBS



## SALT TABLETS SALT-SHAKER TABLETS



### RENAL LOSS KIDNEY LOSS



### EXTRARENAL LOSS OUTSIDE OF KIDNEY LOSS



### RENAL LOSS KIDNEY LOSS



### EXTRARENAL LOSS OUTSIDE OF KIDNEY LOSS



### LOOP DIURETICS LOOP-HEN DIE-ROCKET



### EXCESS SWEATING SWEATY-SWEATBAND



### OSMOTIC DIURETICS WATER DIE-ROCKET



### DIARRHEA TOILET



### DIABETES INSIPIDUS DYED-BEAD SIPPI-CUP



### INSENSIBLE LOSSES INCENSE EVAPORATION



### BURNS BURNED-GUY



### HYPODIPSIA HIPPO-DIPPER



# Ipovolemia

Extrarenale

Sudorazione  
Diarrea  
Ustioni

$\text{Na}^+\text{U} < 20 \text{ mEq/L}$

Renale

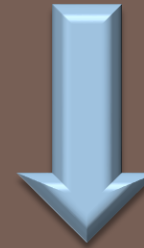
Diuresi osmotica  
Diuretici

$\text{Na}^+\text{U} > 80 \text{ mEq/L}$

# Euvolemia

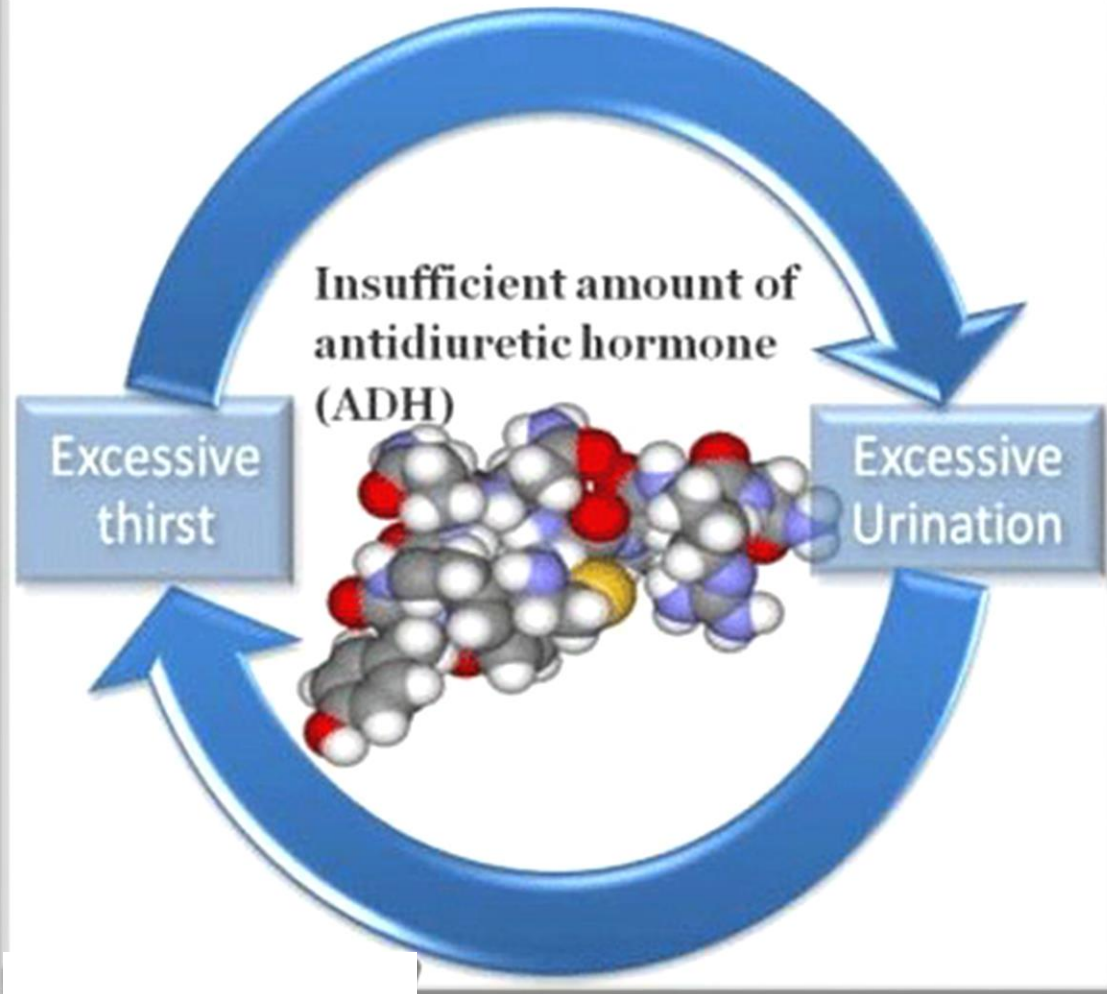


Diabete  
Insipido



- Perdite insensibili
- Ipodipsia





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# DIABETE INSIPIDO



Centrale

Deficit ADH

Nefrogenico

Mancaanza recettori V2

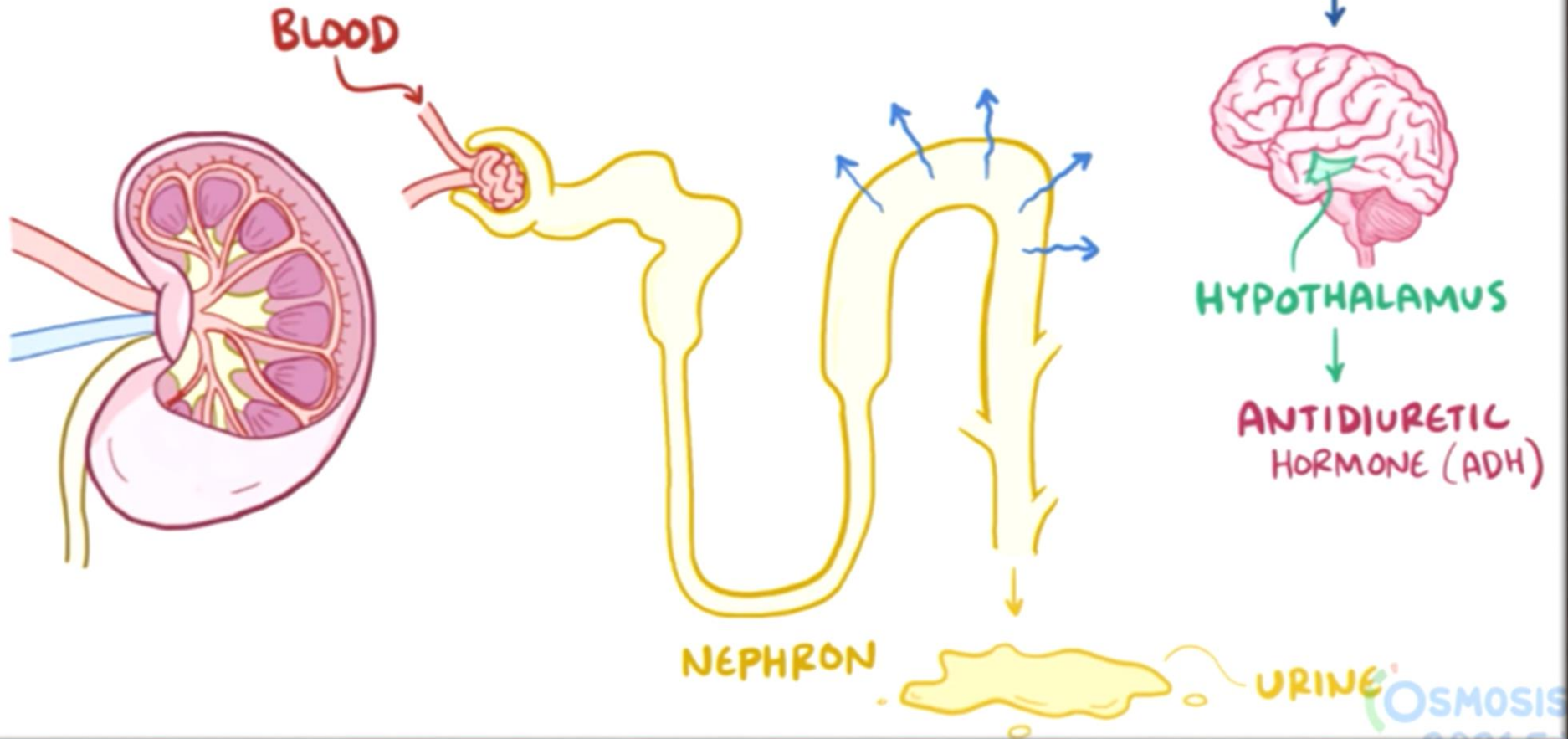


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DIABETE INSIPIDO



# CAUSES ~ WATER LOSS



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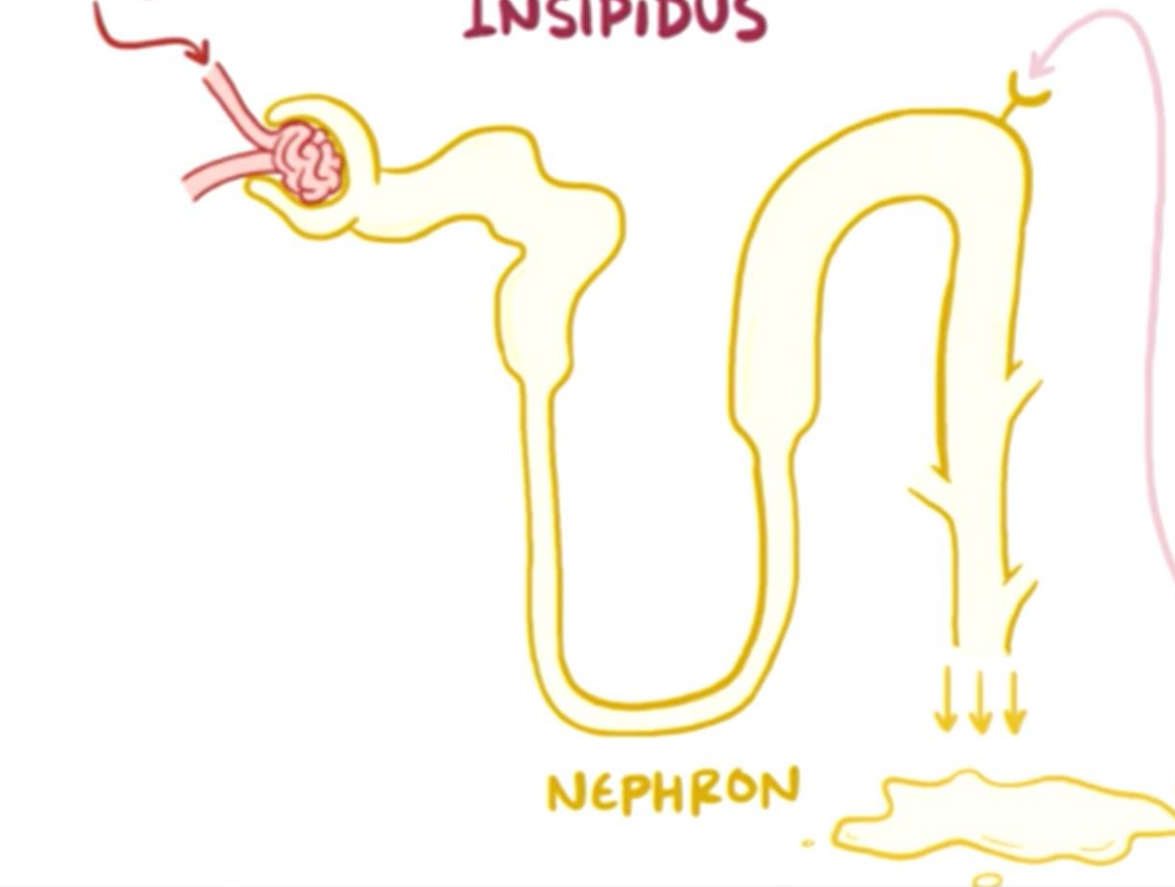
**CENTRALE**

# CAUSES ~ WATER LOSS

\* CENTRAL DIABETES  
INSIPIDUS

DEHYDRATION

BLOOD



HYPOTHALAMUS

ANTIDIURETIC  
HORMONE (ADH)

NEPHRON

URINE: DILUTE



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CENTRALE

Forme idiopatiche: forme più frequenti causate dalla mutazione del **gene neurofisina 2**.

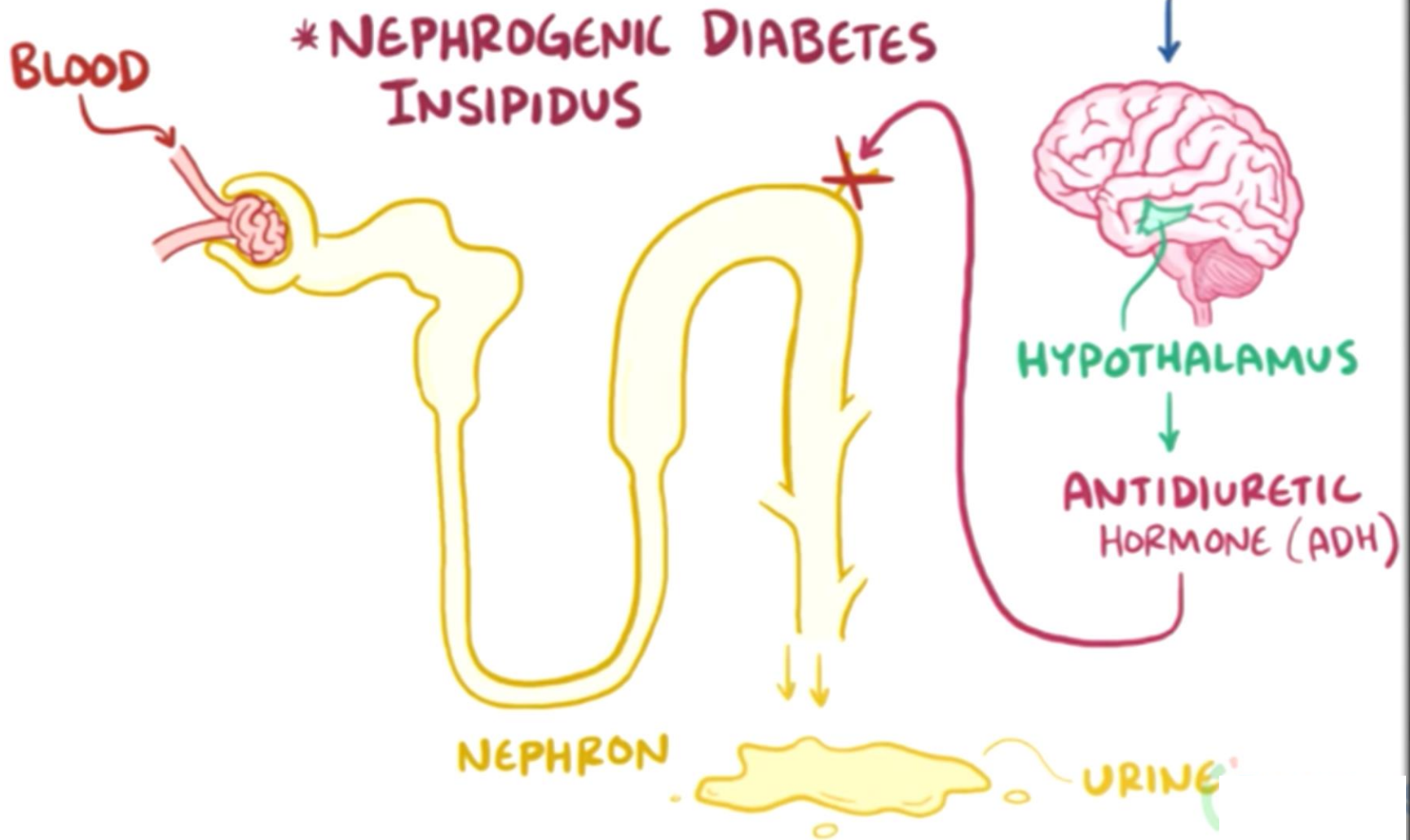
Forme acquisite: secondarie a traumi o ad interventi chirurgici interessanti la regione ipotalamo-ipofisaria.



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EZIOLOGIA D.I. Centrale

# CAUSES ~ WATER LOSS



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D. I. NEFROGENICO

- **Nefrogenico**, per difetto di azione del ADH, raro:
  - forma congenita in due varianti:
    - recessivo legato al cromosoma X, gene mutante Xq28 che codifica per i recettori di tipo 2 della vasopressina
    - autosomico recessivo, gene che codifica per l'acquaporina 2, a livello dei tubuli collettori renali
  - forme secondarie a danni tubulari, ipokaliemia, ipercalcemia, farmaci.



## Sintomi

- Poliuria
- Polidipsia

## Alterazioni

- PS urine  $< 1010$
- Uosm bassa  $<$  plasmatica



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DIABETE INSIPIDO

# Prova Desmopressina

SI

Centrale

NO

Nefrogenico

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Diagnosi differenziale



**Centrale**

**Desmopressina**

**Nefrogenico**

- Dieta basso contenuto Na
- Diuretici tiazidici



**Carmelo  
Libetta**

**TERAPIA DIABETE INSIPIDO**



# Ipervolemia



- Carico Salino (Na, HCO<sub>3</sub>)
- Sindrome di CONN
- Iperaldosteronismo secondario



# CAUSES ~ SODIUM GAIN



\* **INTRAVENOUS**

↳ TOO MUCH, TOO FAST



\* **DIET**

↳ TOO MUCH SALT



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IPERVOLEMIA/IPERNATRIEMIA

## Sintomi

- Iperensione
- Affaticamento muscolare

## Alterazioni

- Ipernatremia
- Ipokaliemia
- Alcalosi metabolica
- Renina bassa (Iperaldo)  
Alta (secondario)



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# IPERALDOSTERONISMO

## Primitivo

- Resezione chirurgica adenoma
- Spironolattone

## Secondario

- Correzione Stenosi arteria renale
- Sindrome edemigena



## SNC

- Letargia
- Irrequietezza
- Convulsioni

## Altri

- Sete
- Febbre
- Mucose secche

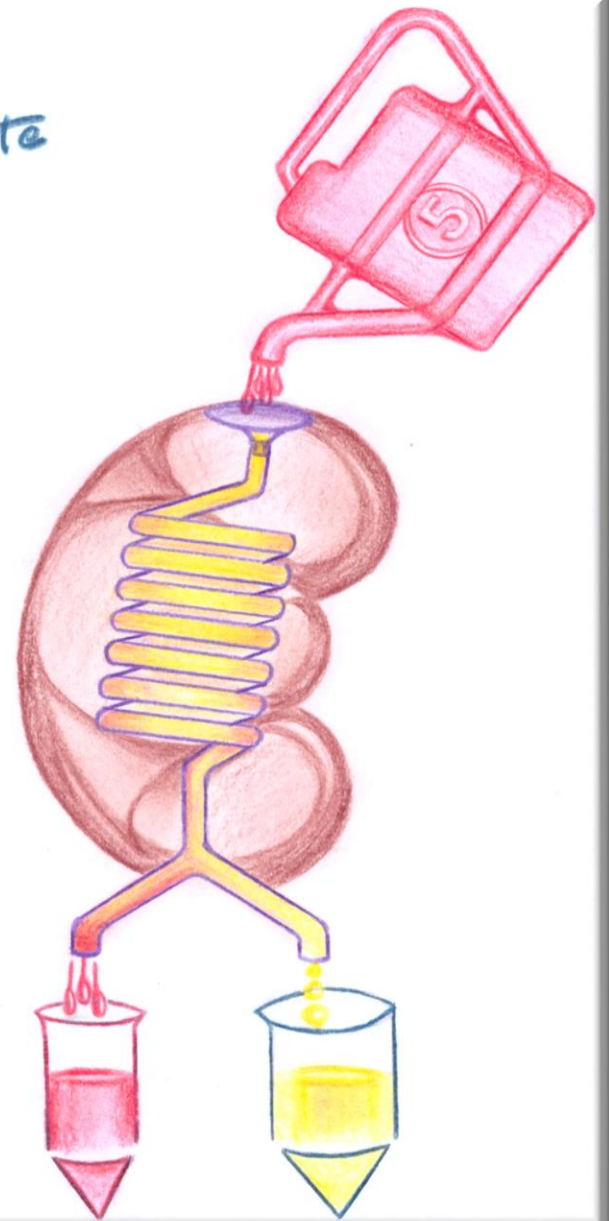


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Sintomi Ipernatremia

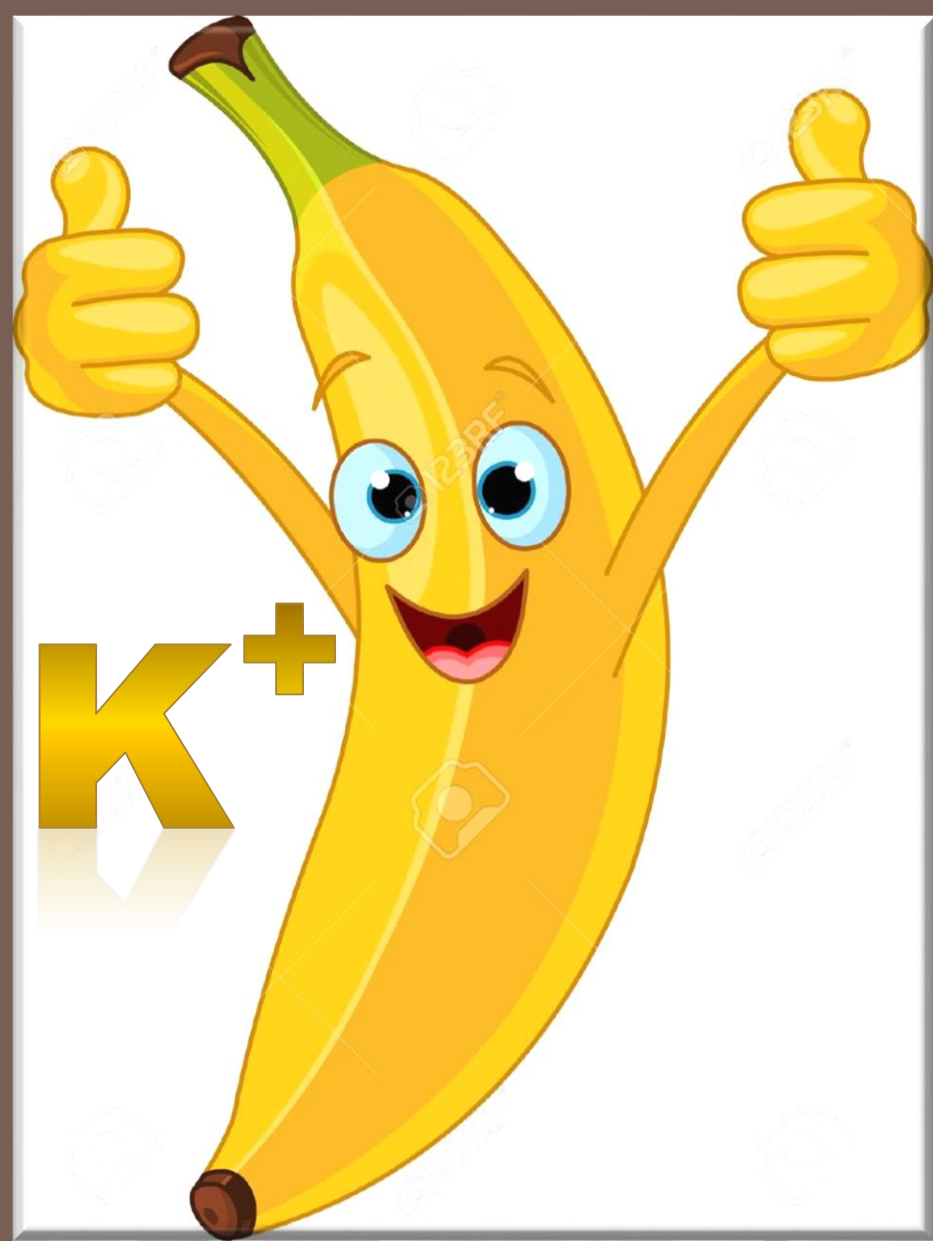
THE END

*C. Libetta*



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Libetta

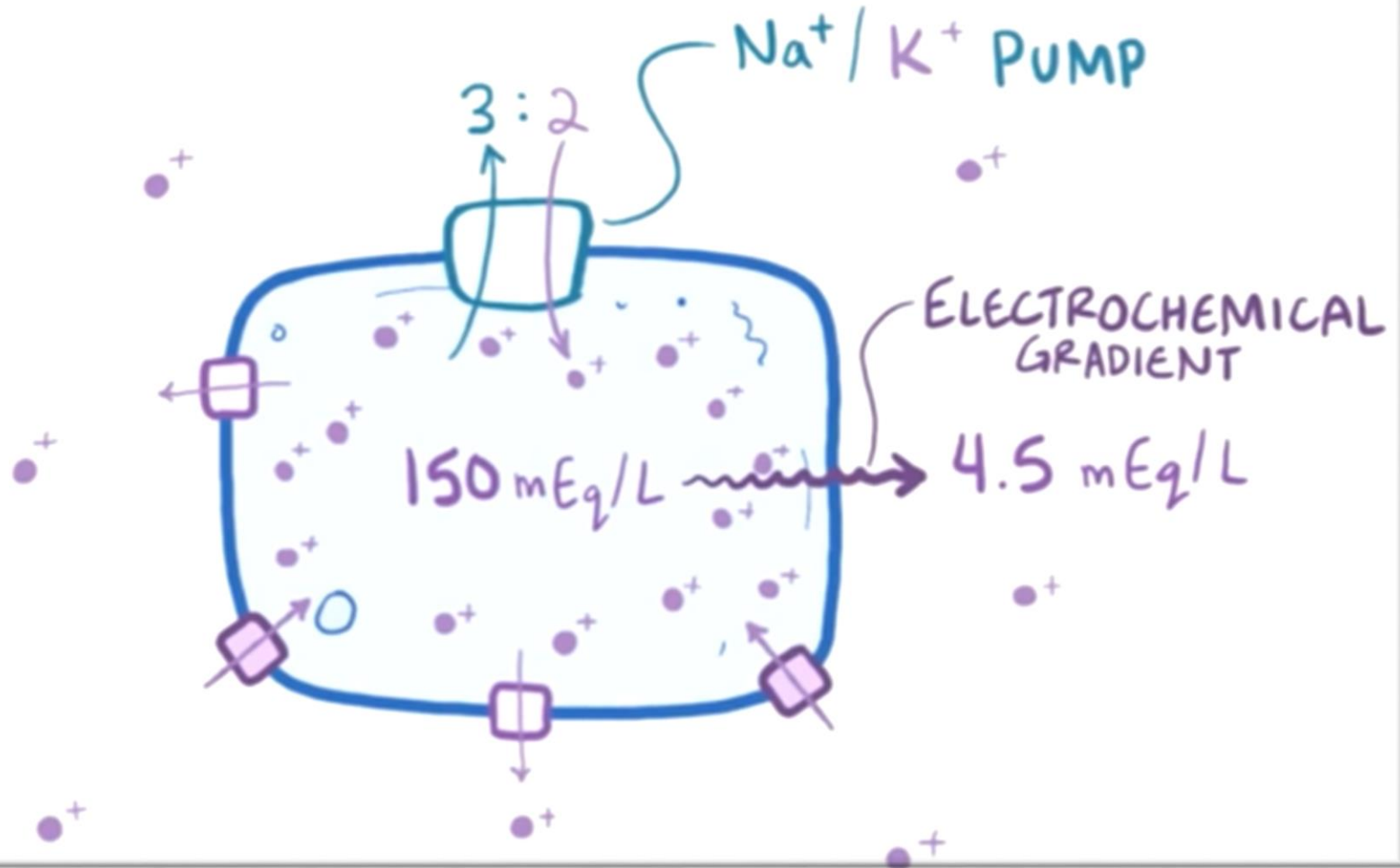
Chapter 3°



Carmelo  
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POTASSIEMIA

# INTERNAL K<sup>+</sup> BALANCE



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POTASSIEMIA



**[K<sup>+</sup>] extracellulare: 4.5 mEq/l**

**[K<sup>+</sup>] intracellulare: 140 mEq/l**

**In un uomo di 70 kg:**

**❖ 3920 mEq intracellulari**

**❖ 69 mEq extracellulari**



**Carmelo  
Libetta**

**DISTRIBUZIONE POTASSIO**



**Bone**  
50 mEq/L



**Muscle**  
2650 mEq/L

**Normal K<sup>+</sup> range**  
3.5–5.5 mEq/L

Daily dietary K<sup>+</sup> intake  
100 mEq/L

Extracellular fluid  
70 mEq/L

Normal K<sup>+</sup> excretion  
100 mEq/L

**Gut (10%)**

**Kidneys (90%)**

**Liver**  
250 mEq/L

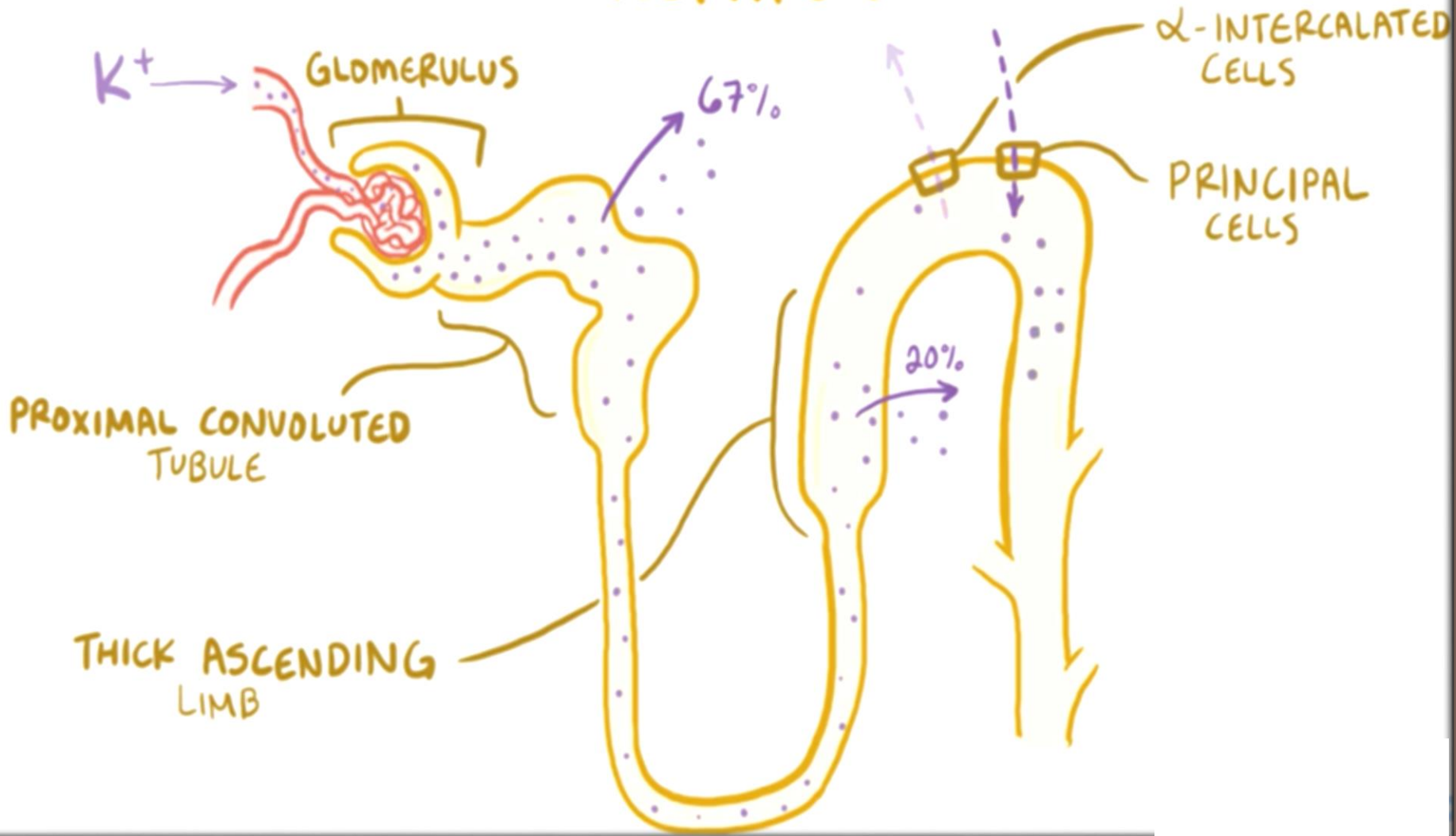
**Erythrocytes**  
250 mEq/L

# OMEOSTASI POTASSIO

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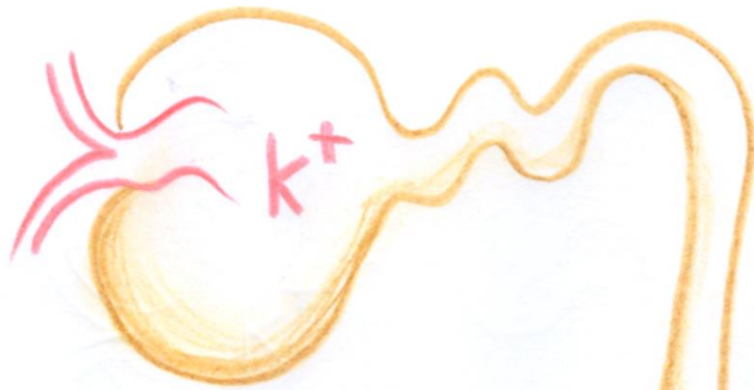
# NEPHRON



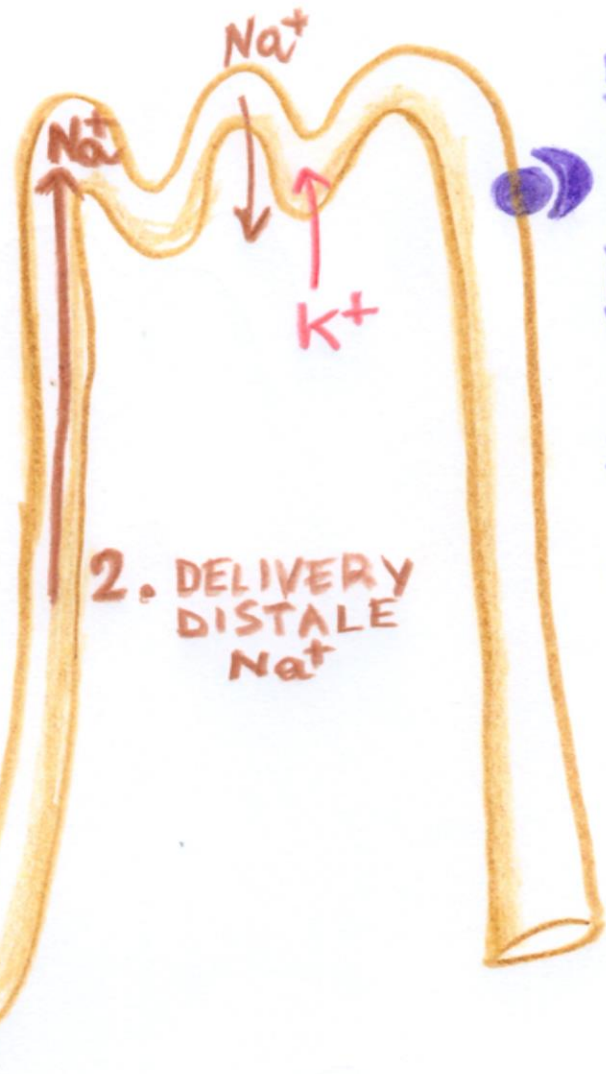
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POTASSIEMIA





1.  $K^+$  Filtrato



2. DELIVERY  
DISTALE  
 $Na^+$

3. ALDOSTERONE

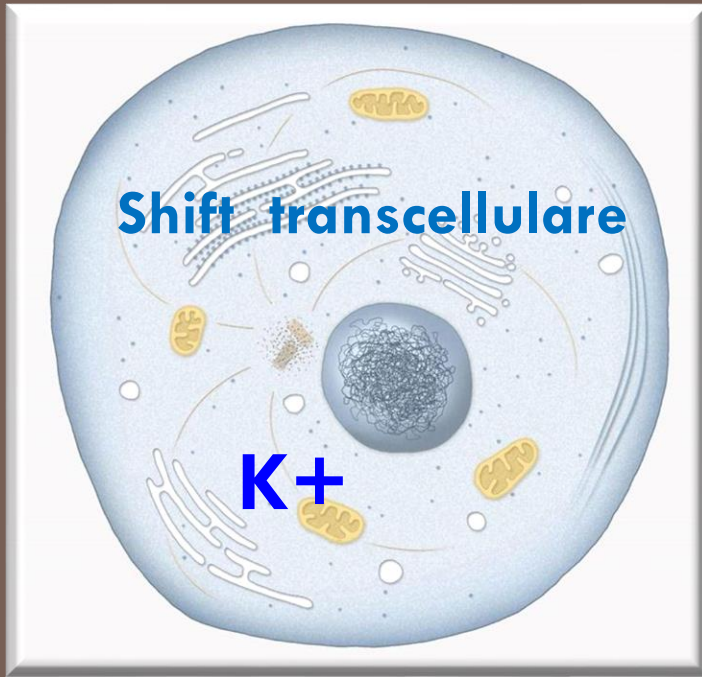
C. Libetta



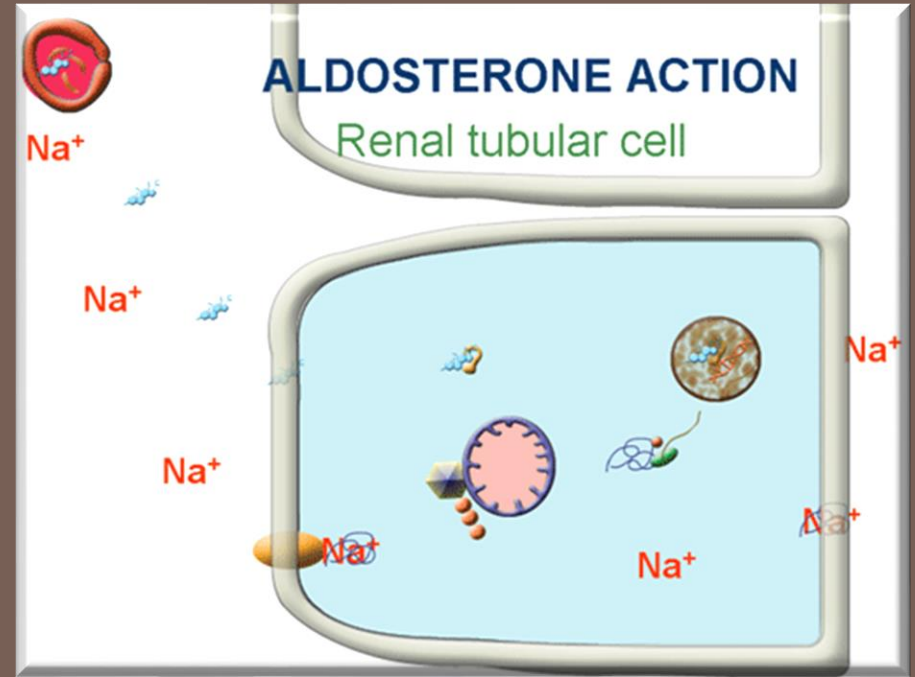
Carmelo  
Libetta

Determinanti Escrezione Potassio

# 1) Regolazione $K^+$ LIC/LEC



# 2) Regolazione Escrezione $K^+$



$H^+$   $K^+$

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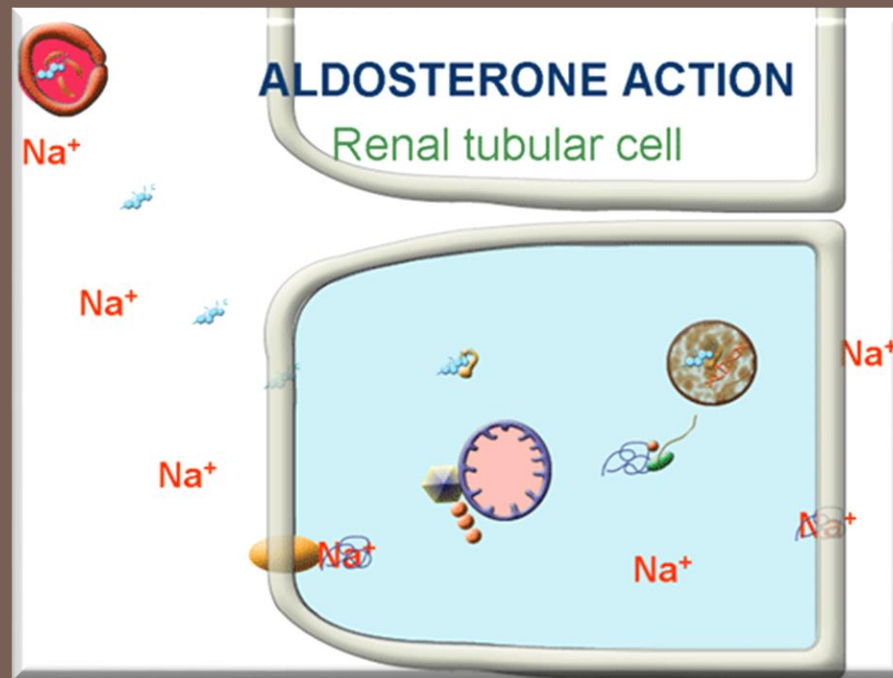
REGOLAZIONE POTASSIEMIA

# 1) ACUTO



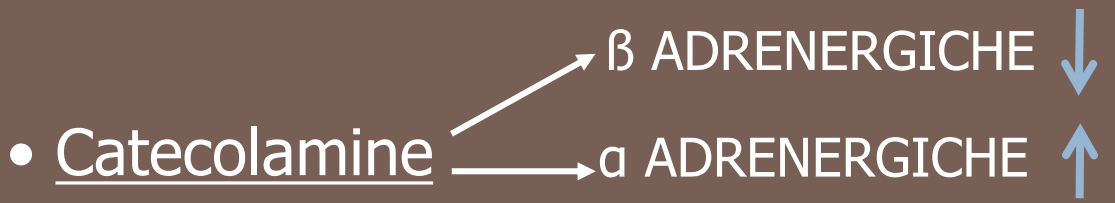
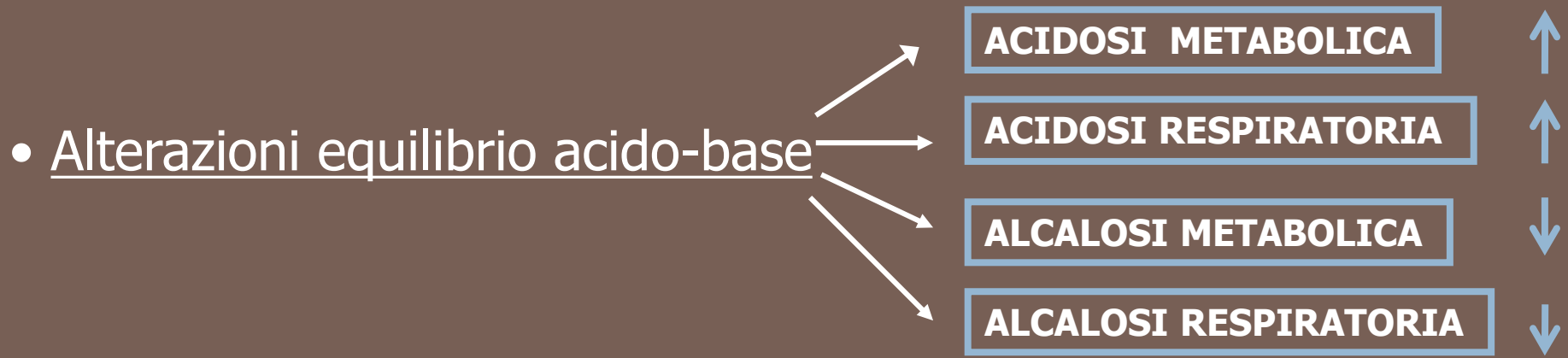
H<sup>+</sup> K<sup>+</sup>

# 2) CRONICO



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REGOLAZIONE POTASSIEMIA



↑ Uscita K+

↓ Entrata K+

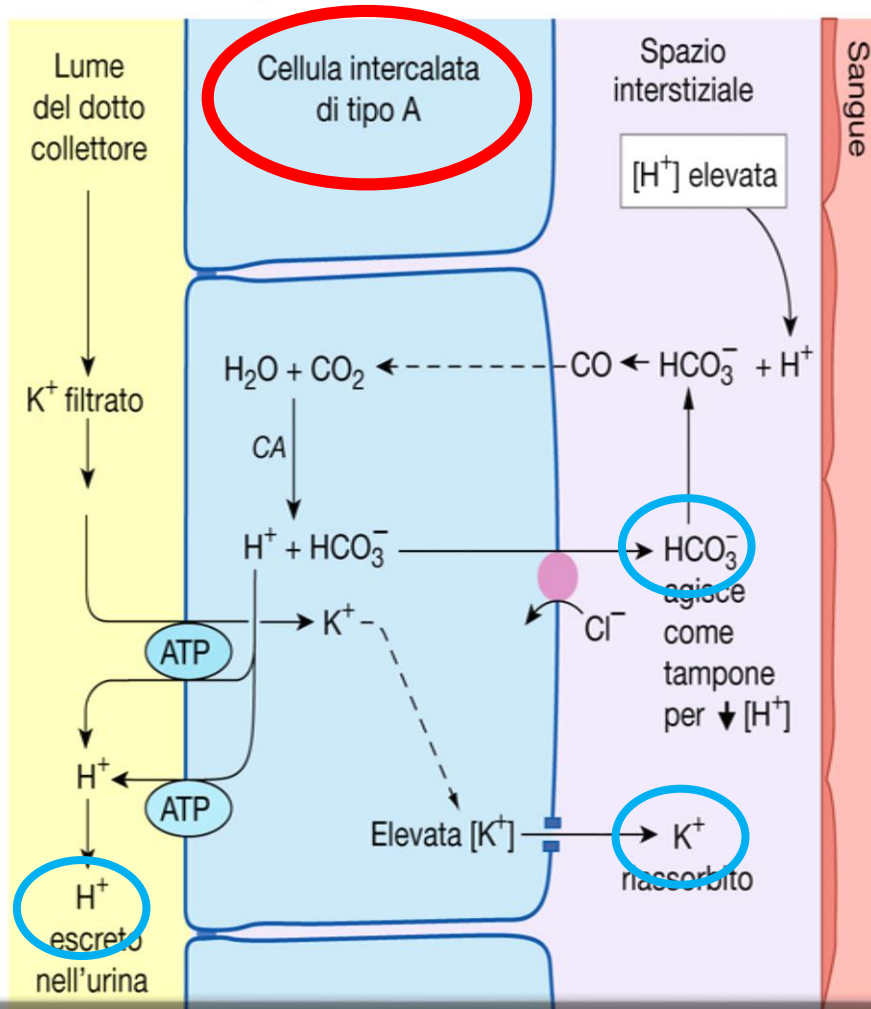


Carmelo Libetta

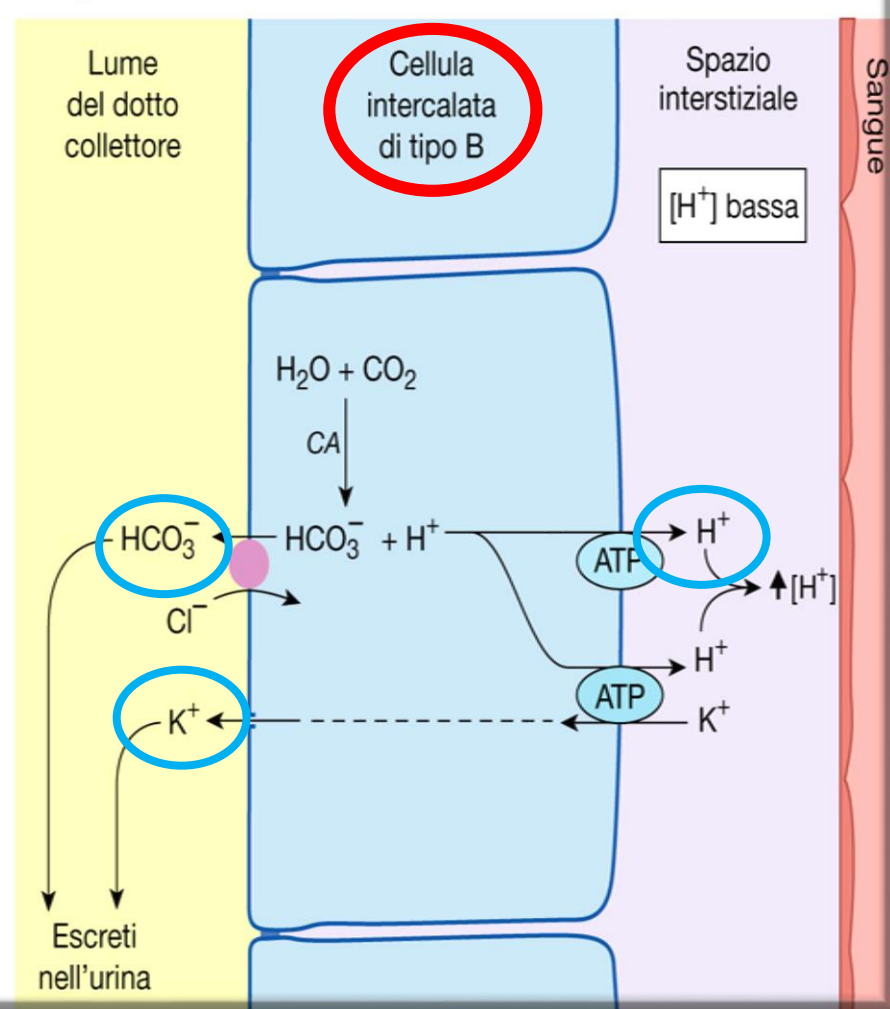
# Shift trans-cellulare

# CELLULE INTERCALATE DC

(a) Le cellule intercalate di tipo A agiscono in corso di acidosi.  
 $H^+$  è escretto;  $HCO_3^-$  e  $K^+$  sono riassorbiti.



(b) Le cellule intercalate di tipo B agiscono in corso di alcalosi.  
 $HCO_3^-$  e  $K^+$  sono escreti;  $H^+$  è riassorbito.

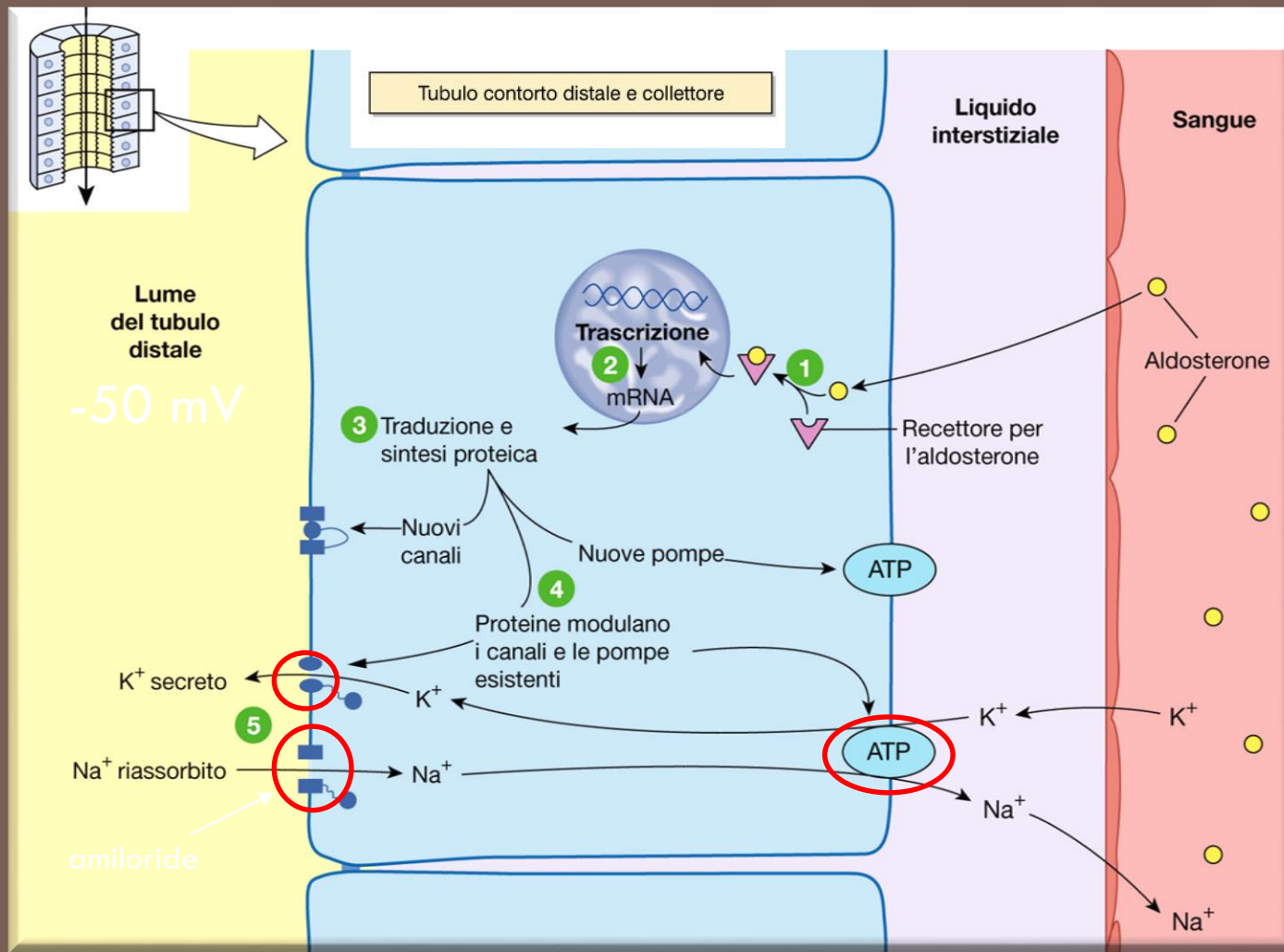


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POTASSIEMIA ACIDOSI/ALCALOSI



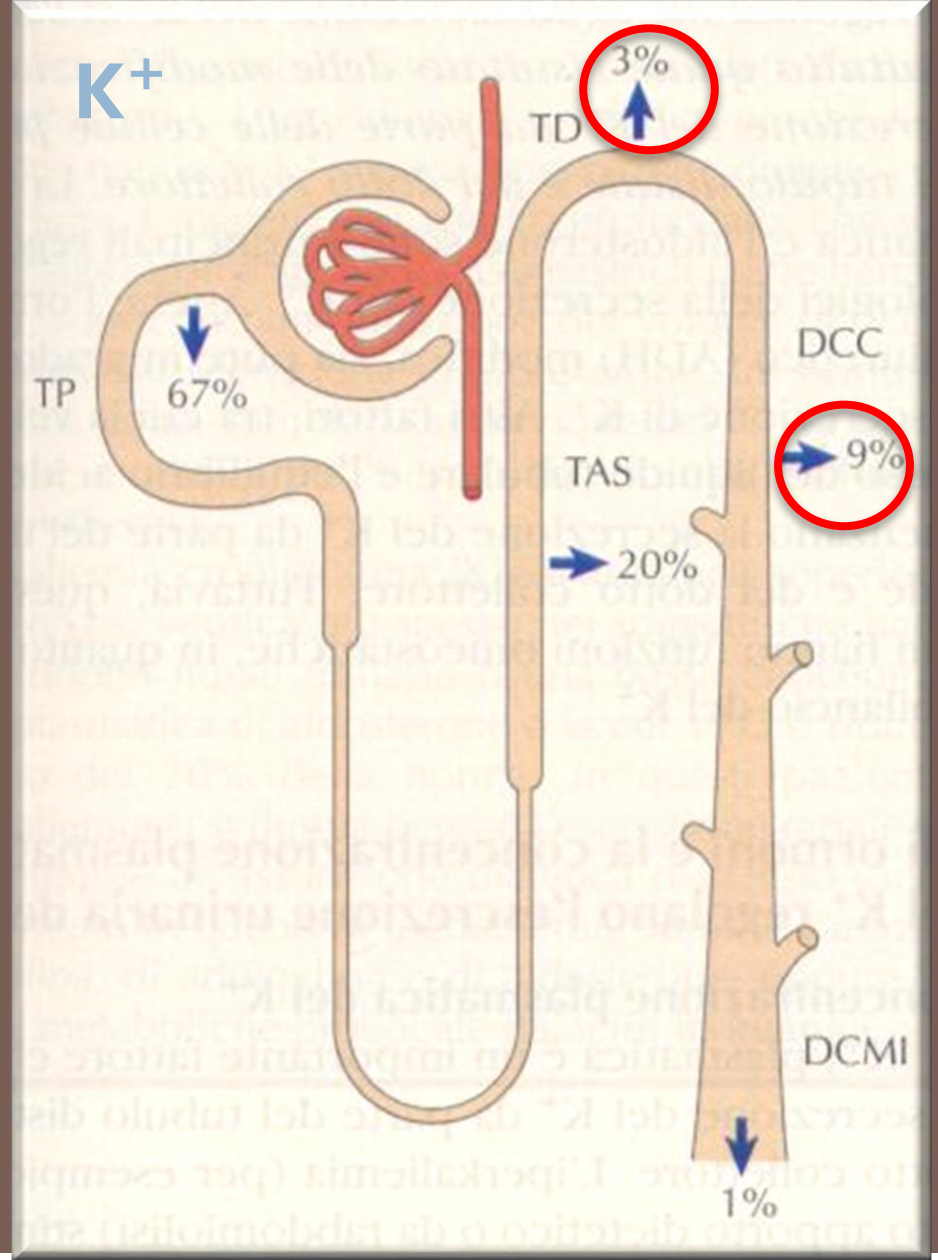




**Carmelo Libetta**

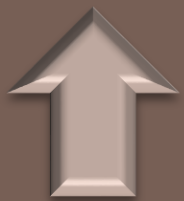
# ALDOSTERONE

↓ Aldosterone

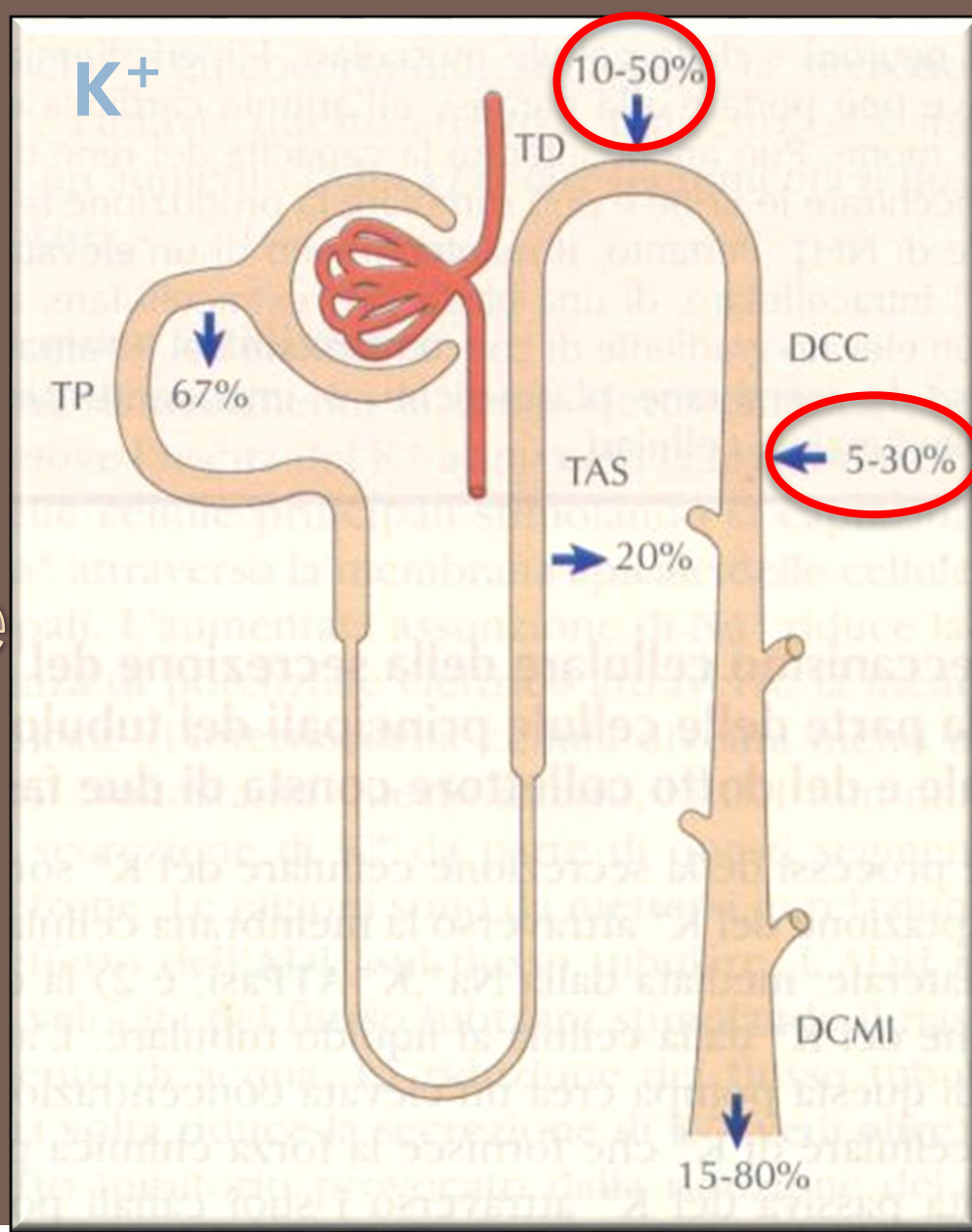


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IperKaliemia



Aldosterone

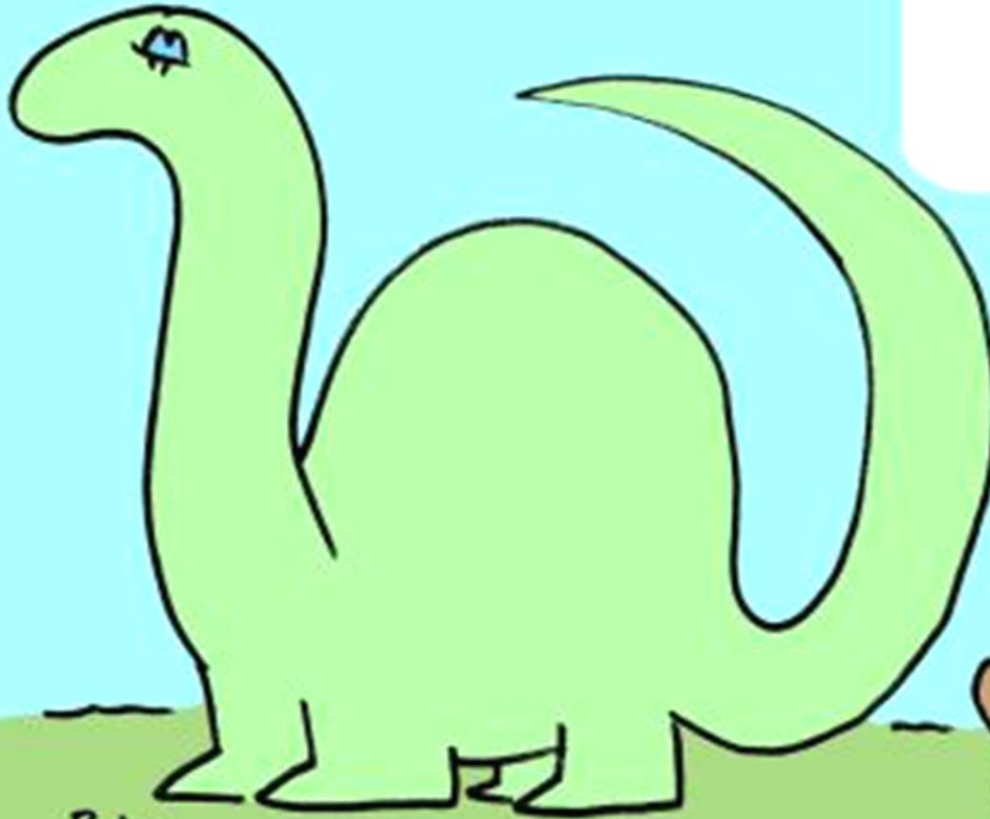


Carmelo Libetta

IpoKaliemia

# IPO-K<sup>+</sup>

ARE YOU SURE  
THEY'RE A GOOD  
SOURCE OF  
POTASSIUM?



B2/00



Carmelo  
Libetta

## IPOPOTASSIEMIA

**POOR POTASSIUM INTAKE  
NO BANANA INTAKE**



# **HYPOKALEMIA HIPPO-BANANA**

**SWEAT LOSS  
SWEATY-SWEATBAND**



**GASTROINTESTINAL LOSSES  
GI-GUY**



**VOMITING  
VOMIT**



**DIARRHEA  
TOILET**



**PANCREATIC FISTULAE  
PANCREAS FIST-TUNNEL**



**INCREASED ENTRY INTO CELLS  
UP-ARROW ENTRY INTO CELL**



**MEDICATIONS  
MED-BOTTLES**



**INSULIN  
INSECT-SYRINGES**



**EPINEPHRINE  
EPI-PEN**



**BETA AGONIST  
BETA-FISH-DRAGONIST**



**THEOPHYLLINE  
TEE-OFF-FELINE**



**METABOLIC FACTORS  
METAL-BALLS**



**INCREASED EXTRACELLULAR PH  
UP-ARROW PH-STRIP OUTSIDE CELL**



**HYPOTHERMIA  
HIPPO-THERMOMETER**



**INCREASED RBC PRODUCTION  
UP-ARROW RBC'S**



**HYPOKALEMIC PERIODIC PARALYSIS  
HIPPO-BANANA IN WHEELCHAIR**



**URINARY LOSSES  
URINAL LEAKING**



**MEDICATIONS  
MED-BOTTLES**



**DIURETICS  
DIE-ROCKET**



**AMPHOTERICIN B  
AMPHIBIAN-TERMIATOR BEE**



**CISPLATIN  
C-SPAN REPORTER**



**DISEASES  
DISEASED-GUY**



**EXCESS MINERALOCORTICOIDS  
PILE OF MINERALS**



**BARRTER SYNDROME  
BUTTER**



**GITELMAN SYNDROME  
GUITAR-MAN**



**DIABETIC KETOACIDOSIS (DKA)  
DYED-BEAD-PANCREAS WITH KEY-TO-ACIDIC LEMON**



**RENAL TUBULAR ACIDOSIS  
KIDNEY TUBA WITH ACIDIC-LEMON**



**METABOLICFACTORS  
METAL-BALLS**



**HYPOMAGNESEMIA  
HIPPO-MAGAZINE**



**INCREASED BLOOD PH  
UP-ARROW RBC PH-STRIP**



# HYPOKALEMIA ~ TOO LITTLE in BLOOD

## EXTERNAL BALANCE SHIFT

\* INCREASED  $K^+$  EXCRETION

↳ DECREASE in BLOOD

$K^+$   
(50-150 mEq/L)



KIDNEYS  
(MOST)



GI TRACT



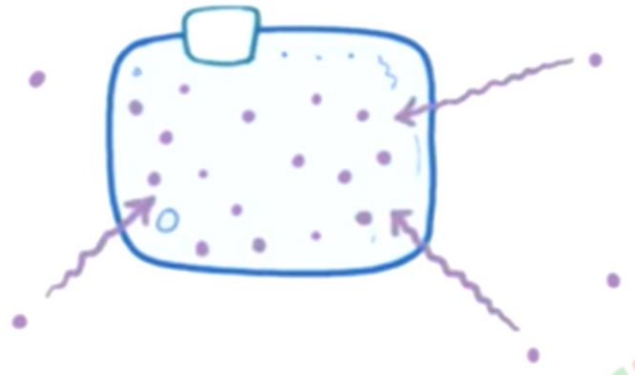
SWEAT



## INTERNAL BALANCE SHIFT

\*  $K^+$  MOVES INTO CELLS

↳ DECREASE in BLOOD



Carmelo  
Libetta

# IPOKALIEMIA

# IPOPOTASSIEMIA

Perdite renali

Perdite extrarenali

Shift  $K^+$  all'interno della cellula



Carmelo  
Libetta

Eziologia

## DIURETICS

- \* LOOP DIURETICS
- \* THIAZIDE DIURETICS

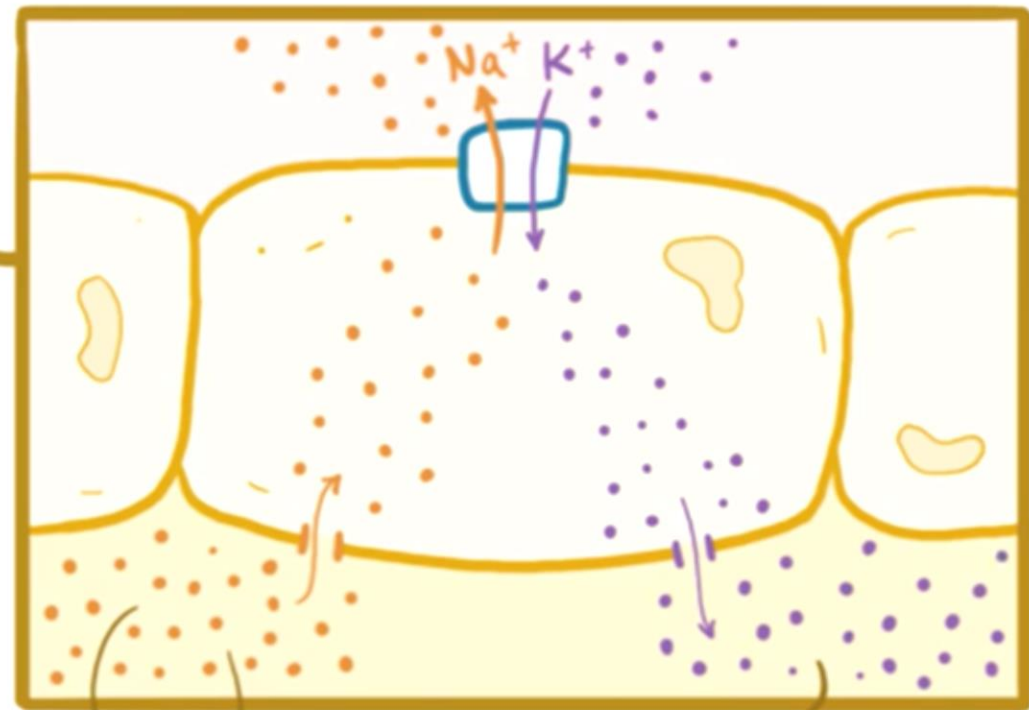


INHIBITS UPSTREAM  
 $\text{Na}^+$  REABSORPTION



MORE  $\text{Na}^+$  DOWNSTREAM

PRINCIPAL  
CELLS



MORE  
WATER

LOW  $\text{K}^+$

Carmelo  
Libetta

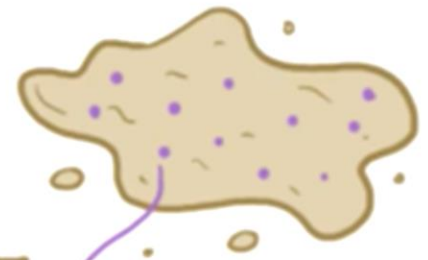
IPO-K/perdite renali



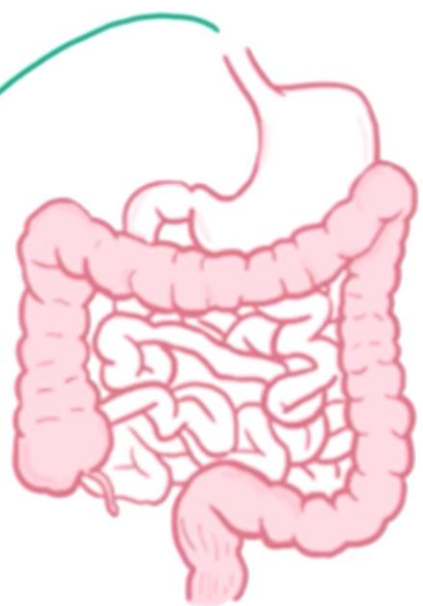
# EXTERNAL BALANCE SHIFT ~ LOSS of GASTROINTESTINAL SECRETIONS

## DIARRRHEA

\* from INFECTIONS, INFLAMMATORY BOWEL DISEASES, & LA



MORE DIRECT LOSS



## VOMITING



DIRECT LOSSES: MINIMAL STOMACH ACID LOST

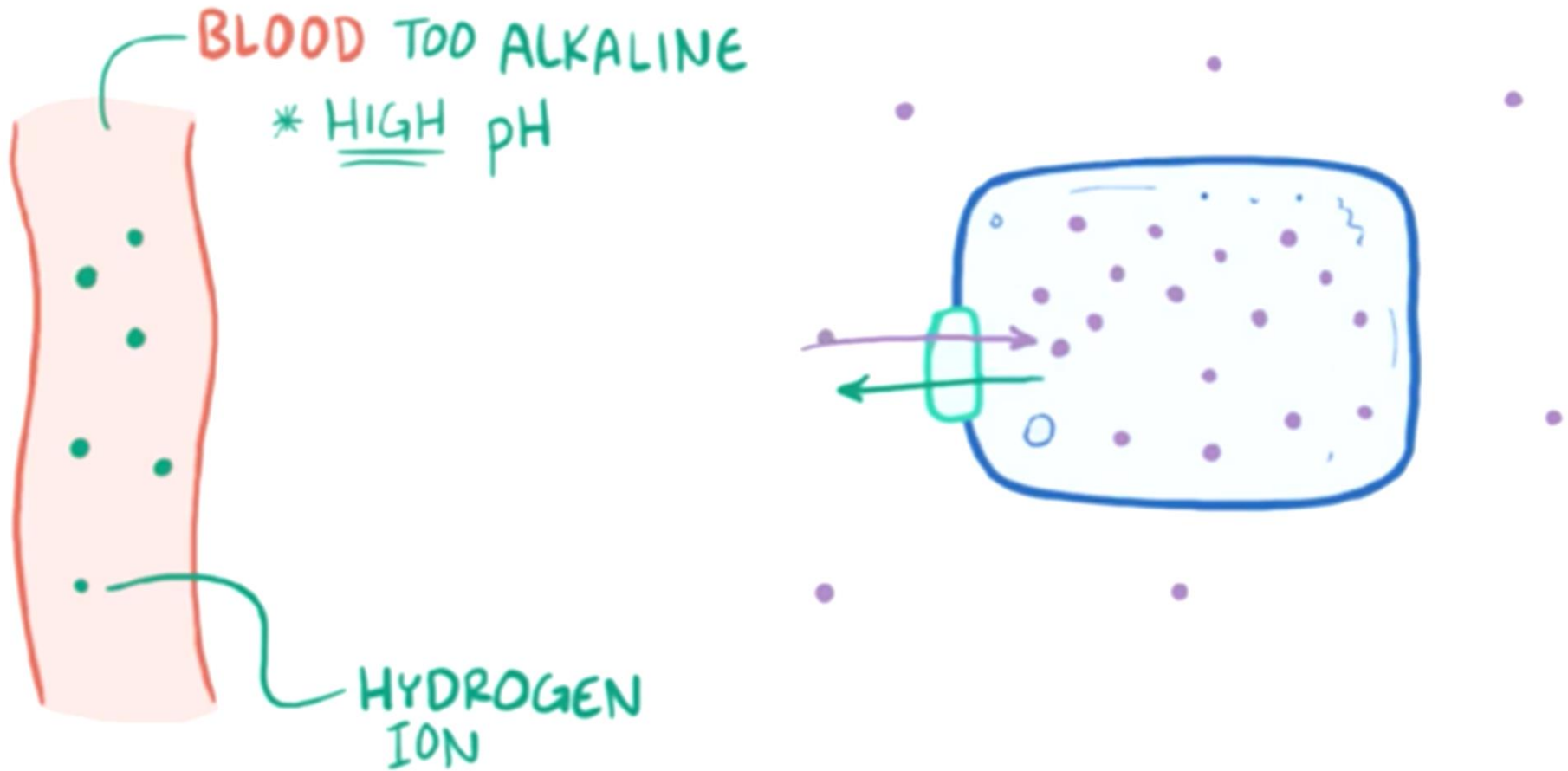
METABOLIC ALKALOSIS

Carmelo Libetta

Perdite extrarenali



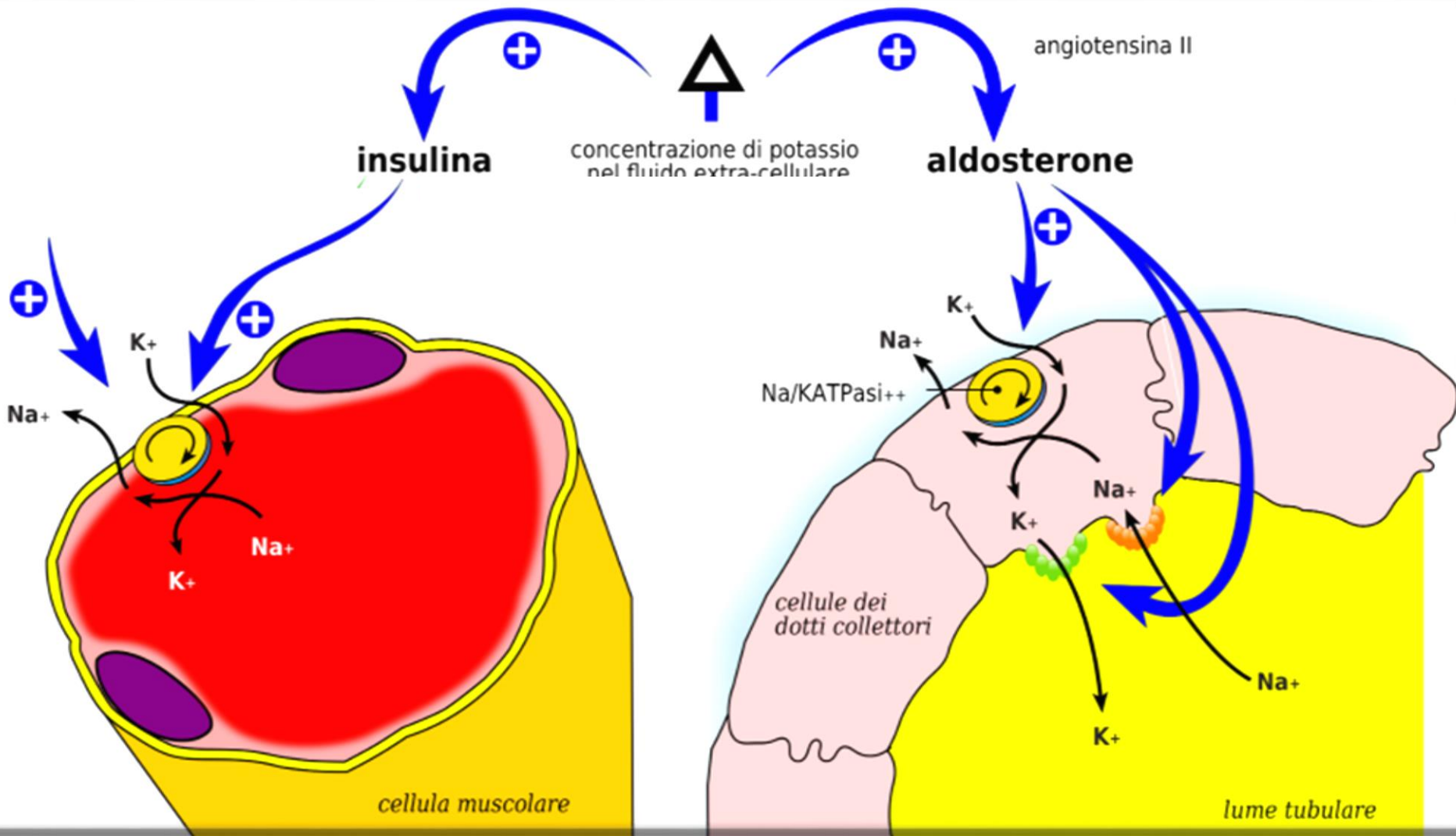
# INTERNAL BALANCE SHIFT ~ ALKALOSIS



Carmelo  
Libetta

IPO-K / Shift





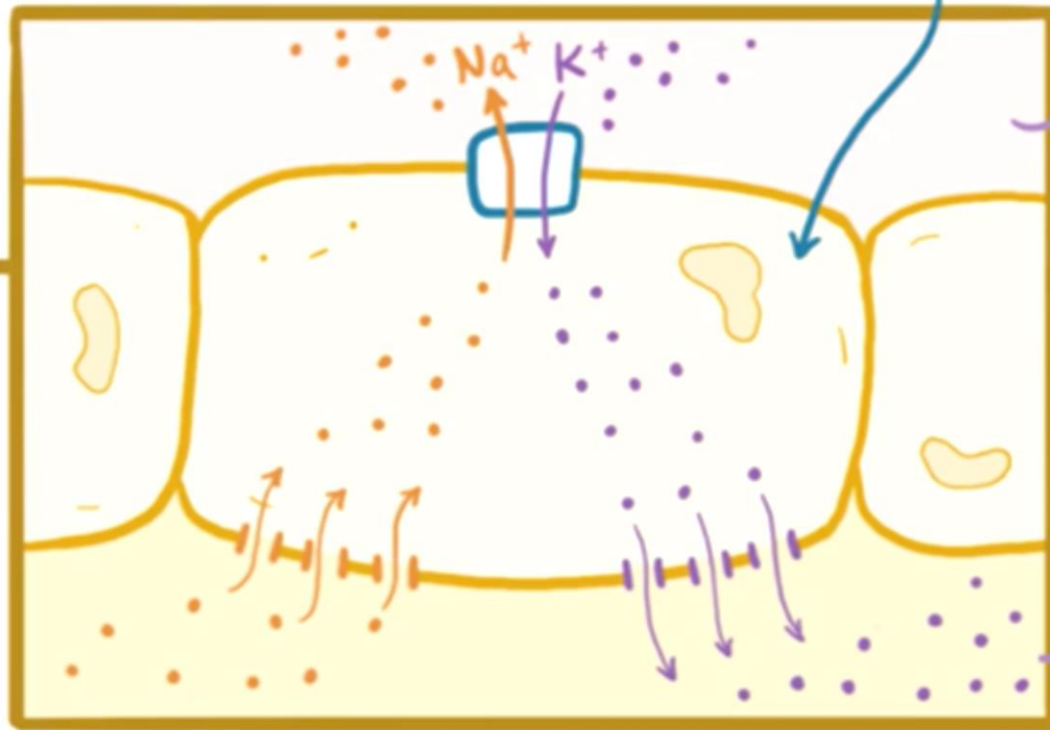
Carmelo  
Libetta

Ormoni e IPO-K<sup>+</sup>

# HYPERALDOSTERONISM

↑↑ ALDOSTERONE C[C@]12CC[C@@H]3[C@H]([C@@H]1CC[C@@H]2O)CCC4=CC(=O)CC[C@]34C

PRINCIPAL CELLS



LESS K<sup>+</sup> RETAINED

MORE K<sup>+</sup> EXCRETED

Carmelo Libetta

# HYPERALDOSTERONISMO



Alcalosi

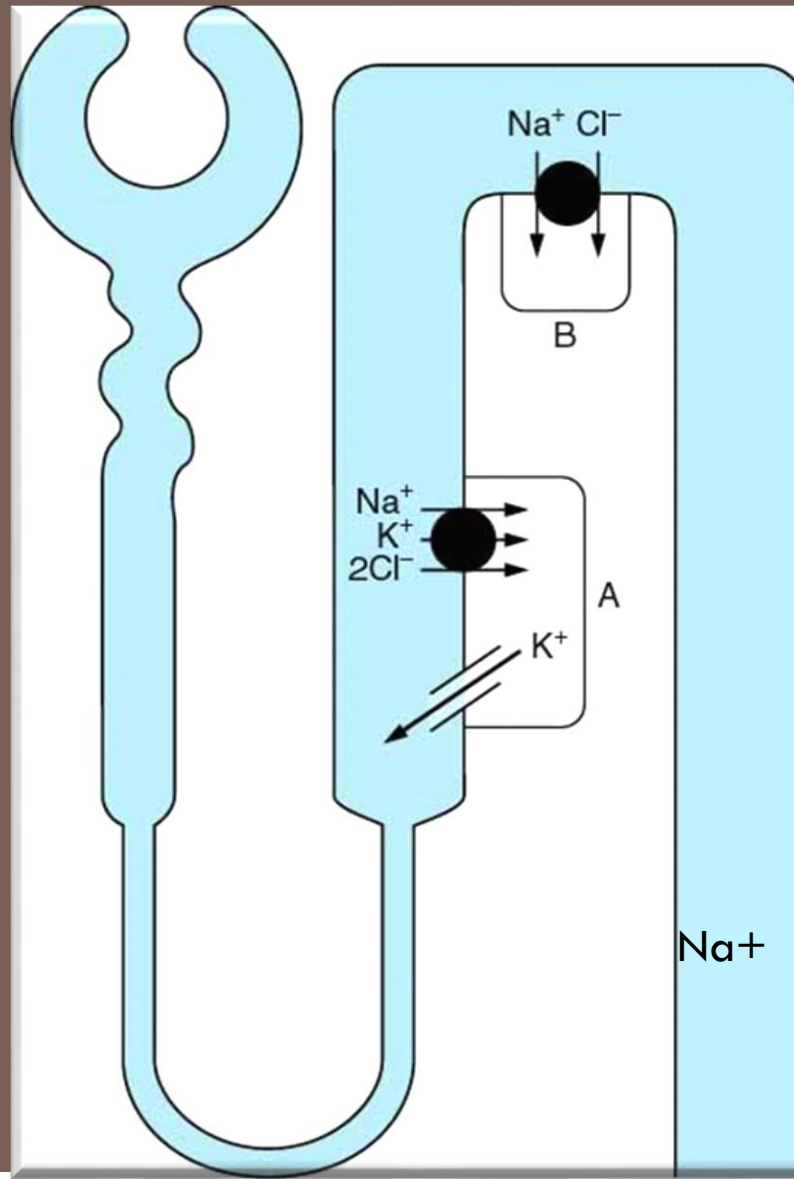
Iperinsulinismo

Beta-agonisti



Carmelo  
Libetta

Shift cellulare



Gitelman's Syndrome  
 Hypokalemia  
 Metabolic alkalosis  
 ↑ Renin/aldosterone  
 Hypocalciuria  
 Normotension  
 Hypomagnesemia  
 Age at diagnosis >6 yr  
 Mild growth retardation

Bartter's Syndrome  
 Hypokalemia  
 Metabolic alkalosis  
 ↑ Urinary PGE  
 ↑ Renin/aldosterone  
 Normotension  
 Hypercalciuria  
 Nephrocalcinosis  
 Age at diagnosis: infancy  
 Premature birth/growth retardation

Carmelo  
 Libetta

Perdite renali



## Muscolo scheletrico

- Debolezza
- Mialgie
- Crampi
- Parestesie
- Paralisi
- Dolore
- Aumento CPK, LDH, mioglobina
- Insuff. ventilatoria

## Muscolo liscio

- Ileo paralitico
- Stipsi
- Distensione addominale
- Anoressia
- Vomito



Approximate Serum K<sup>+</sup>  
(mEq/L)



1. **Onde T appiattite**

2. **Depressione ST**

3. **Onda U prominente**

Carmelo  
Libetta

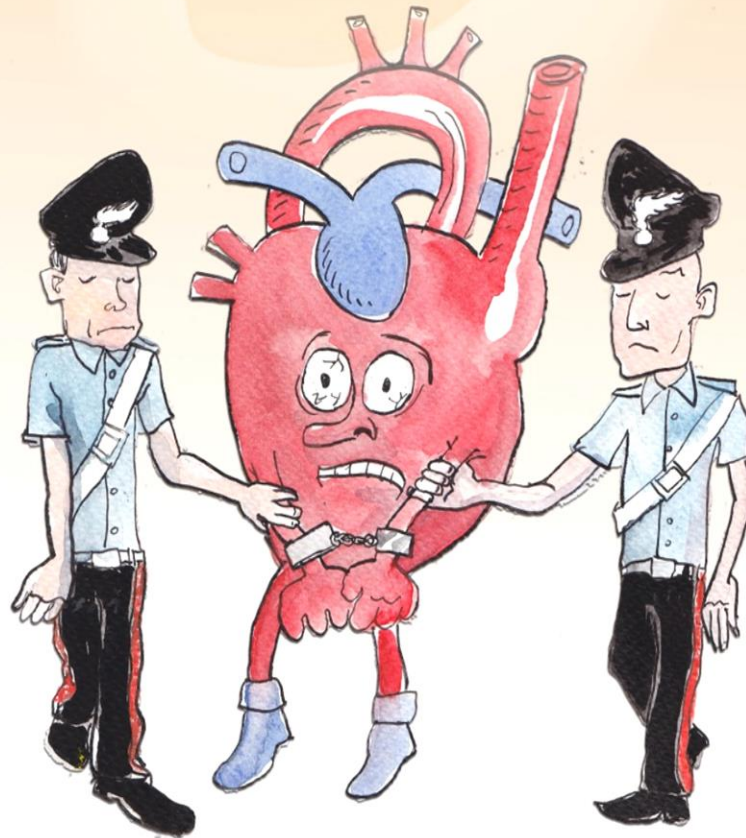
Alterazioni ECG





FIBRILLAZIONE VENTRICOLARE  
ARRESTO IN SISTOLE

# Arresto Cardiaco



ASS  CUORE

Associazione Cesenate per la lotta  
contro le Malattie di Cuore

Testi di Flavio Tartagni - Disegni di Valentino Menghi

ONLUS D.lgs. 460/1997

Carmelo  
Libetta

Alterazioni ECG



- **K<sup>+</sup> IN VENA**

- **NELLE FORME CON ALCALOSI:  
CORREZIONE**



Carmelo  
Libetta

**TERAPIA**

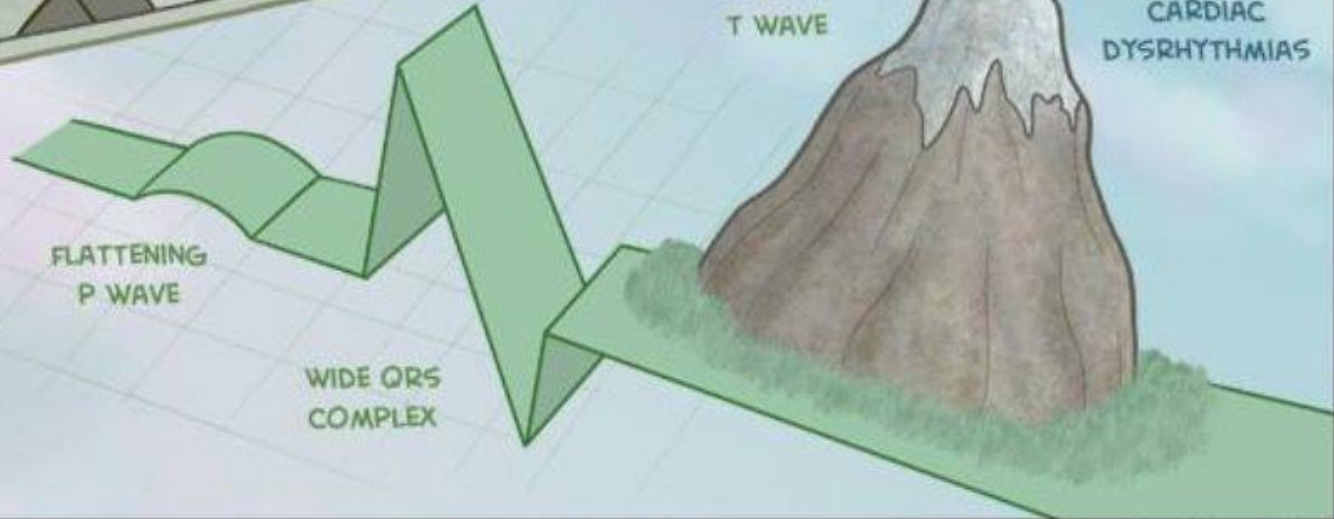
# HYPERKALEMIA

A SERUM POTASSIUM CONCENTRATION GREATER THAN **FIVE** INDICATES HYPERKALEMIA, INDEED.

TREATMENT: CALCIUM, INSULIN, ALBUTEROL, KAYEXALATE, DIURESIS, DIALYSIS



INTESTINAL COLIC, DIARRHEA, MUSCLE WEAKNESS, PARALYSIS



Carmelo Libetta

# HYPERKALIEMIA



INTERNAL

BALANCE SHIFT ~

CELL LYSIS

\* SEVERE BURNS, RHABDO



Carmelo  
Libetta

PSEUDO IPERPOTASSIEMIA



- **ALTERATA ESCREZIONE RENALE DI  $K^+$**

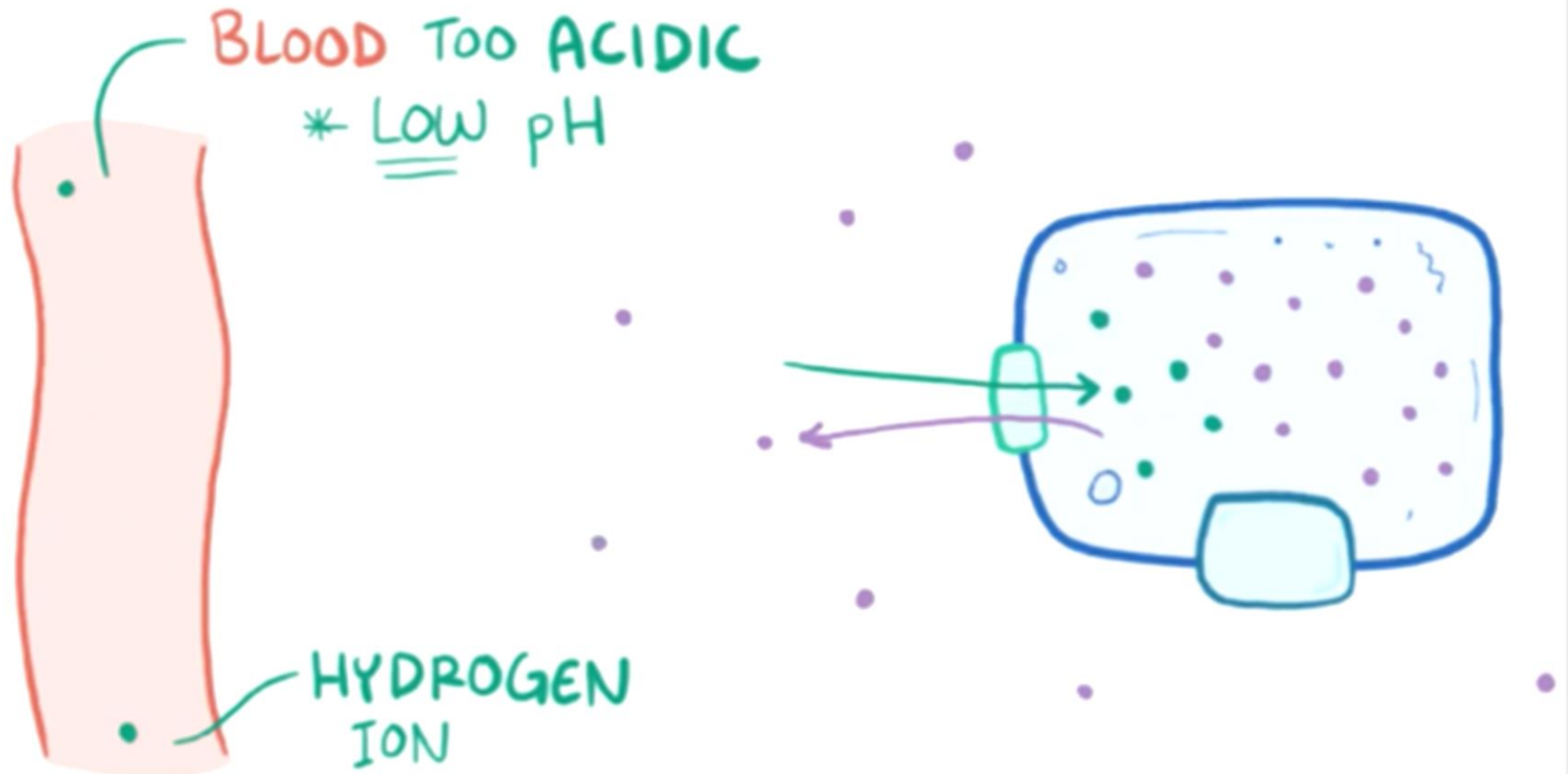
**DA FARMACI**

**MRC**

- ◆ **SHIFT  $K^+$  ALL'ESTERNO DELLA CELLULA (ACIDOSI)**
- ◆ **Morbo di ADDISON (ipoaldosteronismo)**
- ◆ **IPO-INSULINISMO**
- ◆ **Necrosi Muscolare (rabbdomiolisi)**
- ◆ **DA AUMENTATA DISTRUZIONE DEI LEUCOCITI  
(nelle forme neoplastiche)**



# INTERNAL BALANCE SHIFT ~ ACIDOSIS



Carmelo  
Libetta

ACIDOSI/POTASSIEMIA



- **DIURETICI RISPARMIATORI DI POTASSIO**
- **INIBITORI SRAA**
- **SUPPLEMENTAZIONI DI K**

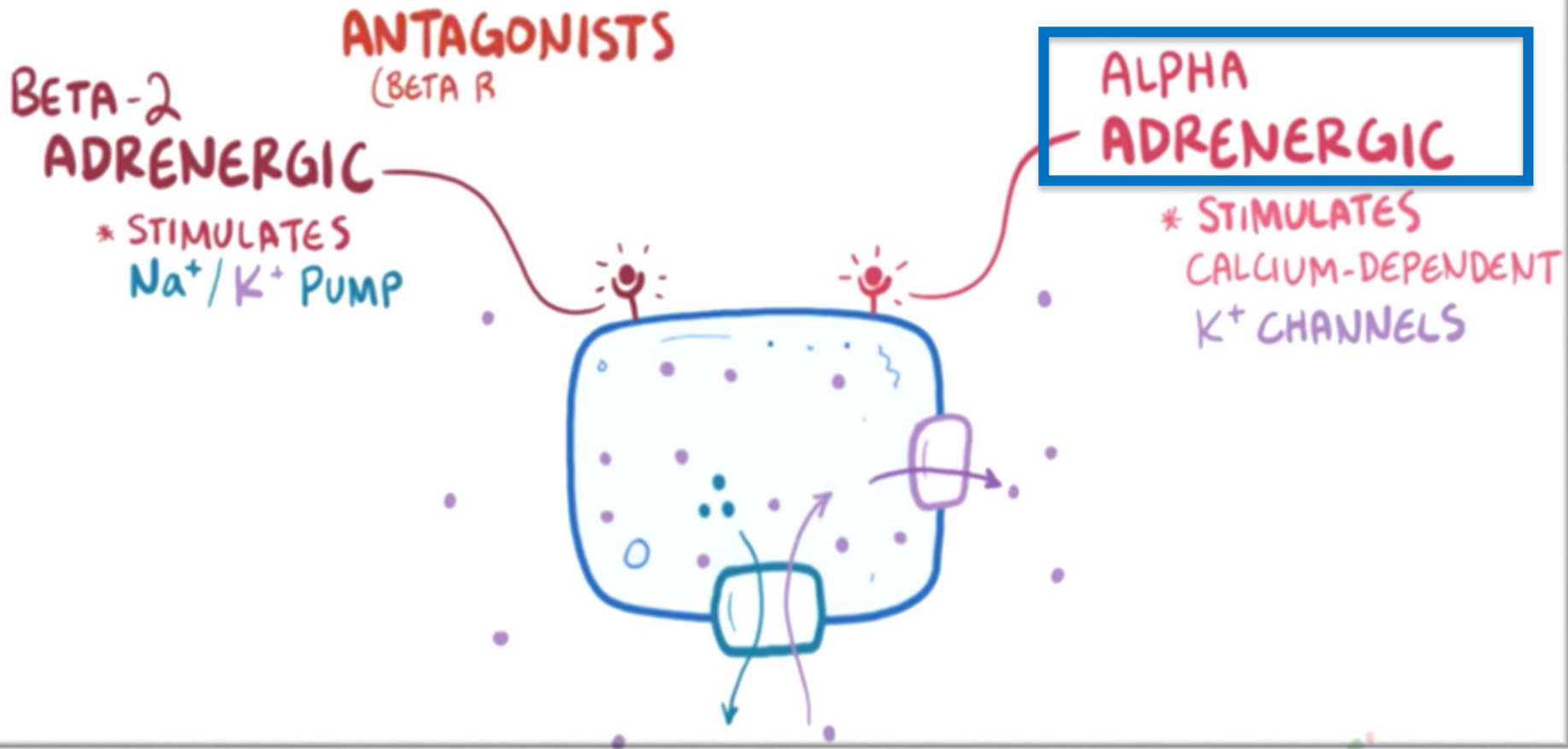


Carmelo  
Libetta

**IPERKALIEMIA IATROGENA**



INTERNAL  
BALANCE SHIFT ~ CERTAIN  
CATECHOLAMINES



Carmelo  
Libetta

POTASSIEMIA



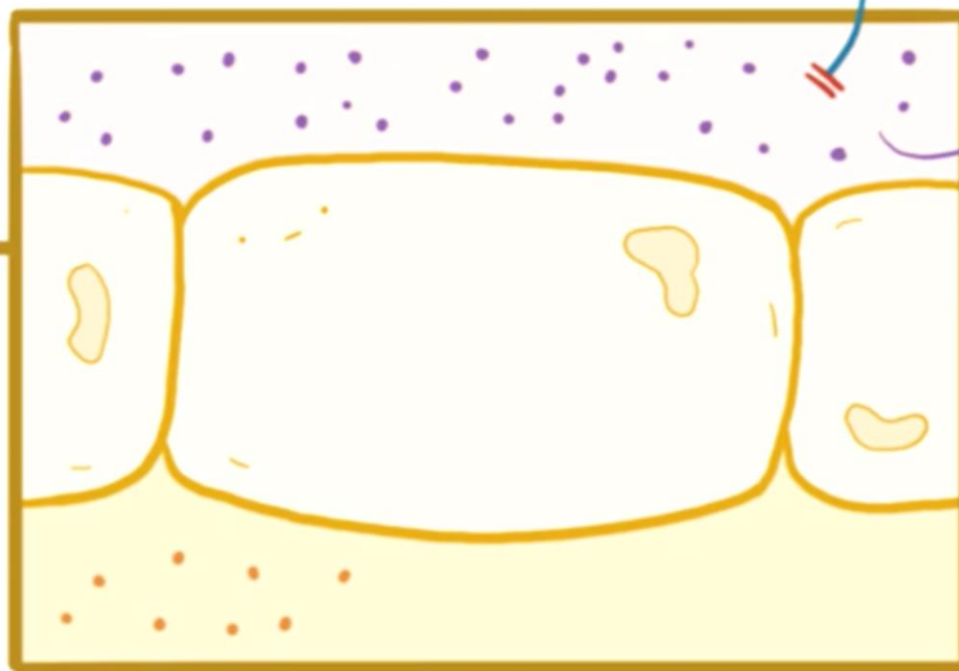
DRUGS

**HYPOALDOSTERONISM** (ADRENAL INSUFFICIENCY)

~~ALDOSTERONE~~



PRINCIPAL  
CELLS



HYPERKALEMIA



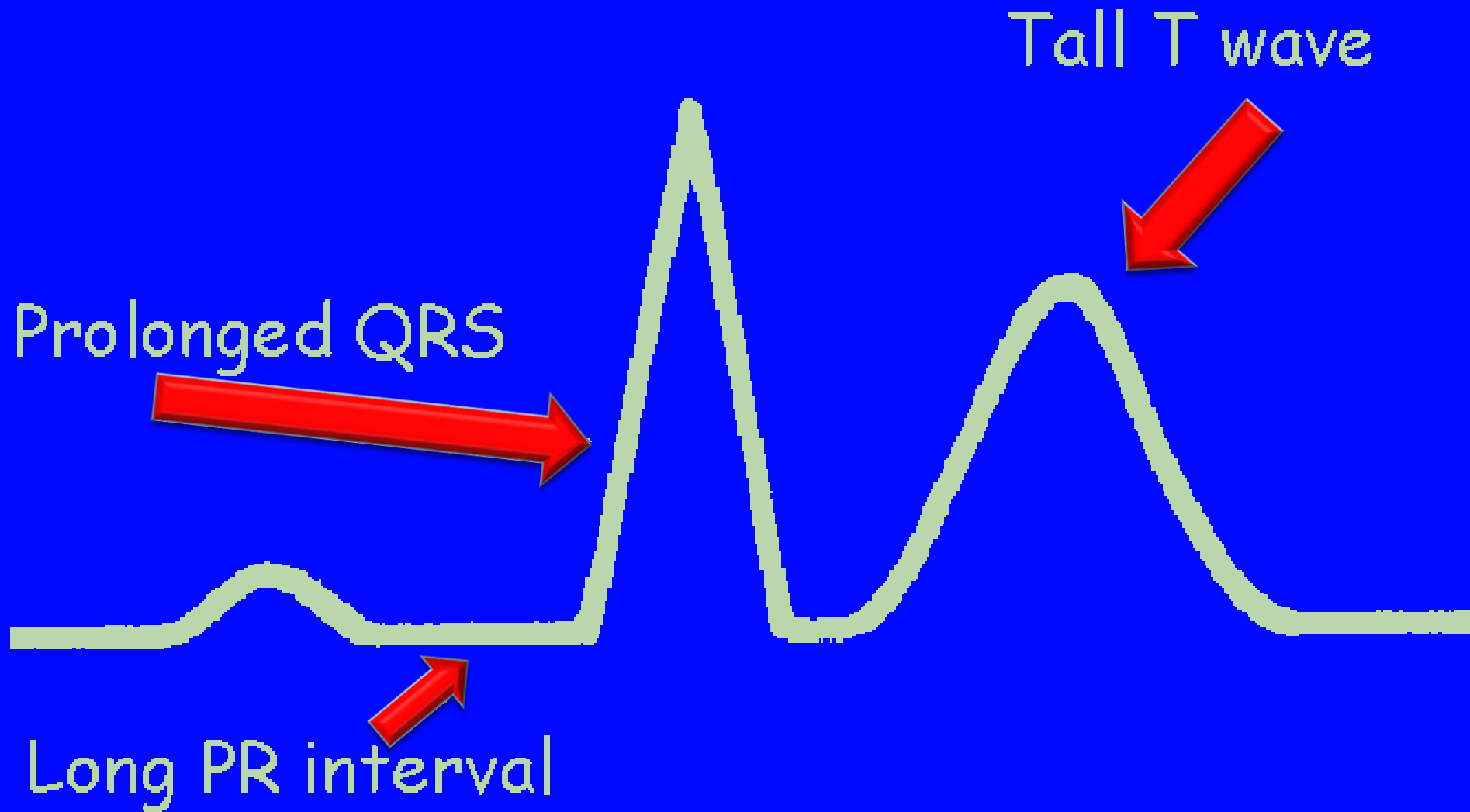
Carmelo  
Libetta

POTASSIEMIA

# HYPERKALEMIA ↑

- \* Muscle Twitches → Cramps → Paresthesia
- \* Irritability & Anxiety
- \* ↓ BP
- \* EKG Changes
- \* Dysrhythmias - Irregular Rhythm
- \* Abdominal Cramping
- \* Diarrhea



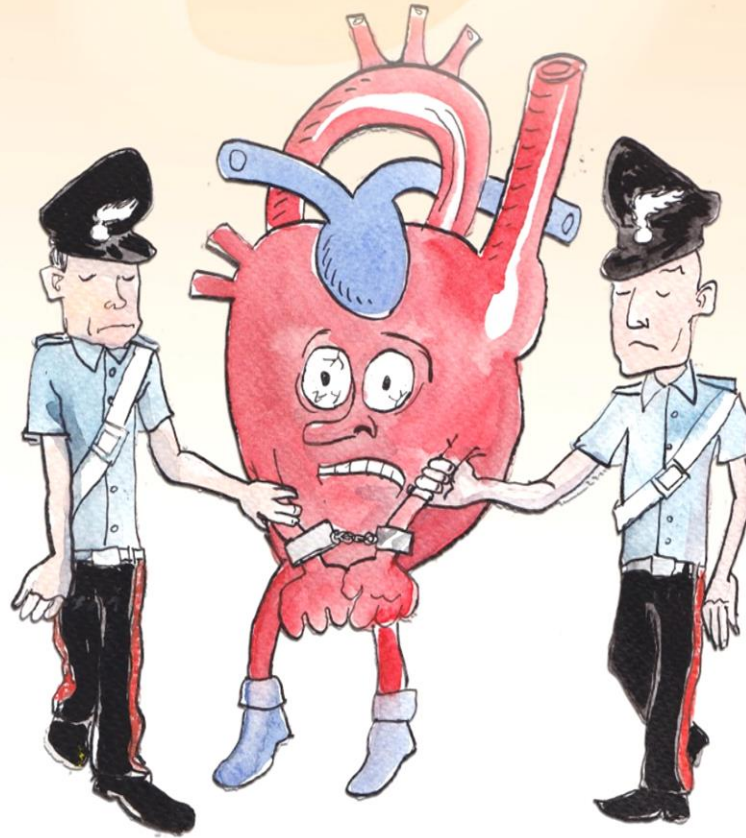


Carmelo  
Libetta

Alterazioni ECG

FIBRILLAZIONE VENTRICOLARE  
ARRESTO IN DIASTOLE

# Arresto Cardiaco



ASS  CUORE

Associazione Cesenate per la lotta  
contro le Malattie di Cuore

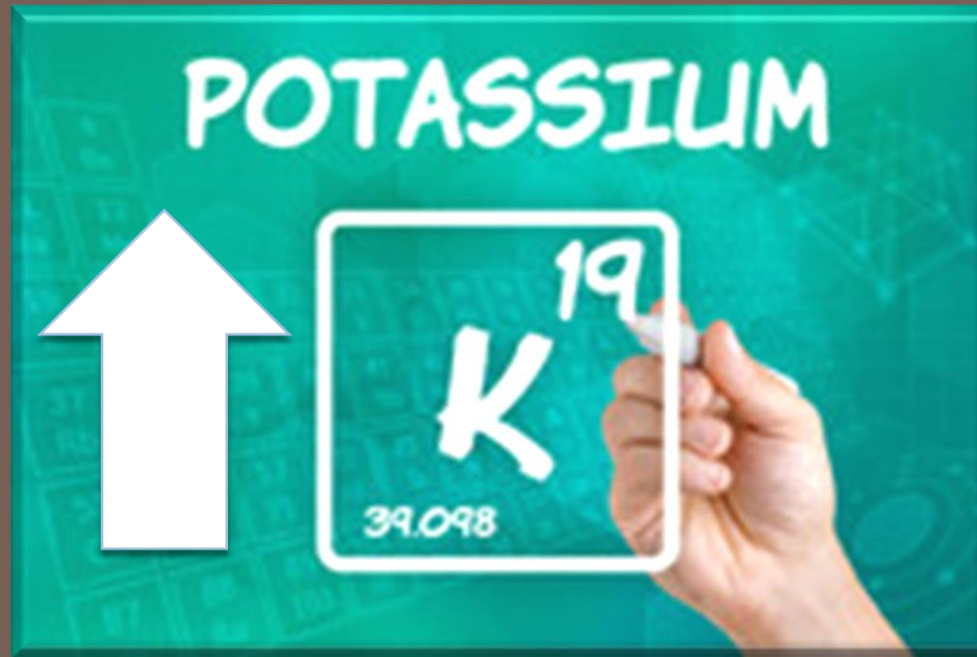
Testi di Flavio Tartagni - Disegni di Valentino Menghi

ONLUS D.lgs. 460/1997

Carmelo  
Libetta

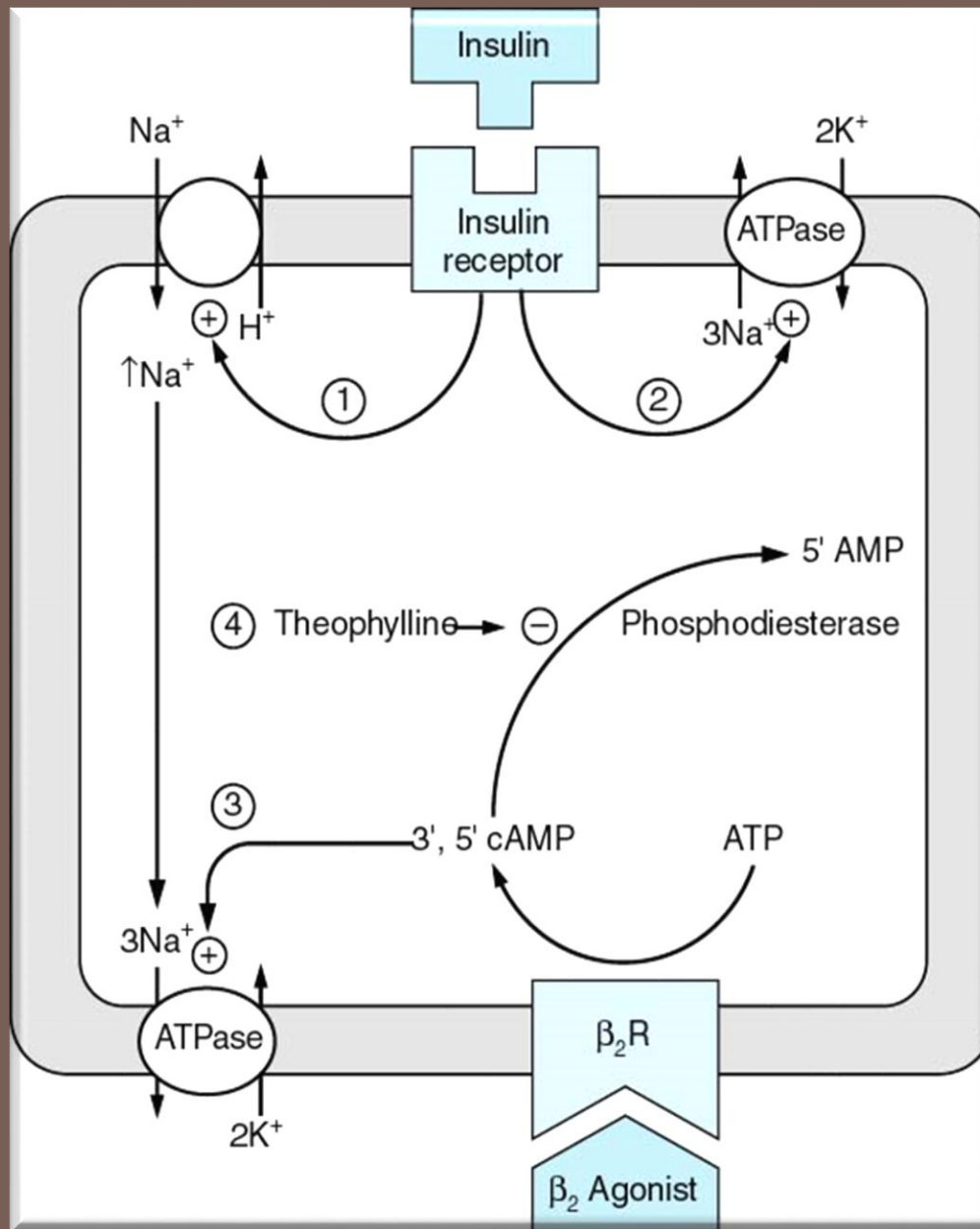
## Alterazioni ECG





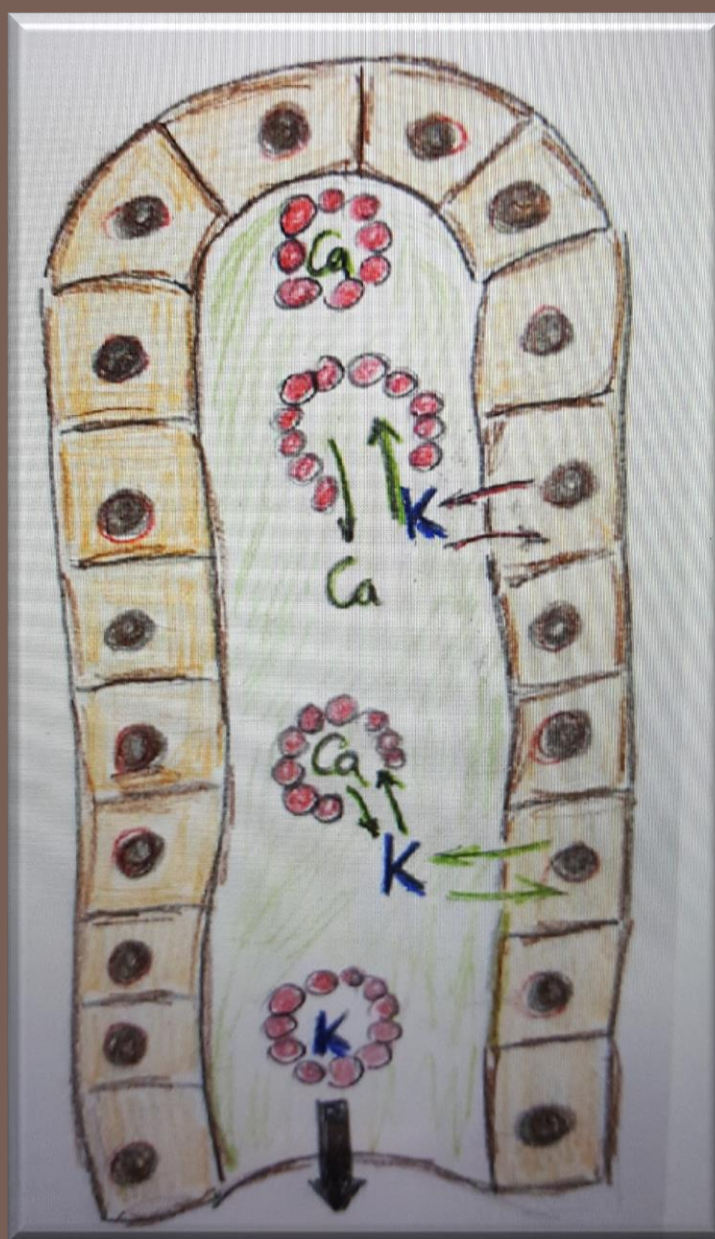
Carmelo  
Libetta

TERAPIA



Carmelo  
Libetta

Correzione iperpotassiemia



**SODIO  
POLISTIRENSULFONATO**

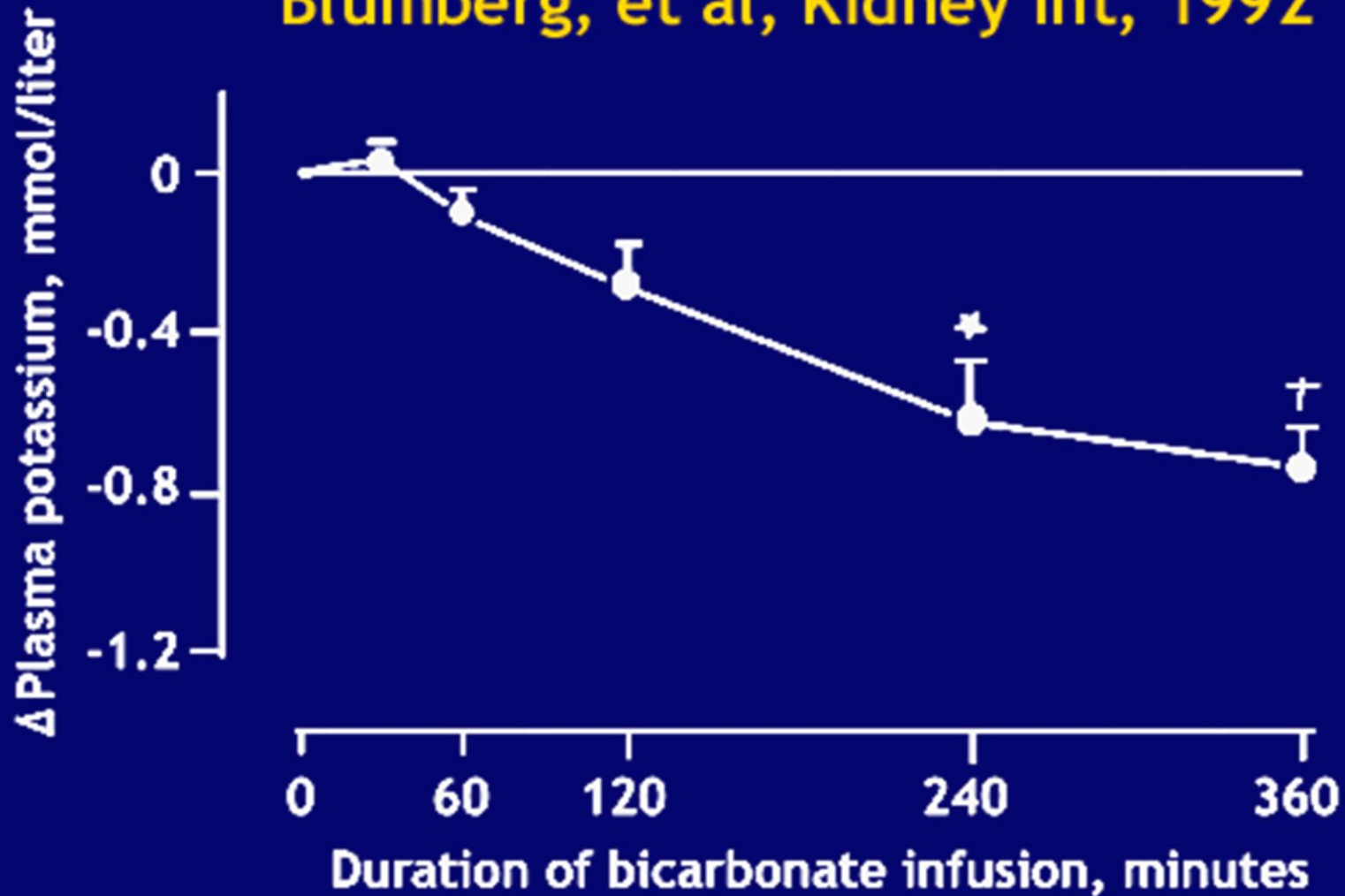


**Carmelo  
Libetta**

**RESINE A SCAMBIO IONICO**



## Blumberg, et al, Kidney Int, 1992



Carmelo  
Libetta

IPER K<sup>+</sup>/ACIDOSI METABOLICA

THE END



Carmelo  
Libetta

Chapter 3°