

# Kidneys in regulation of homeostasis

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**This presentation includes only the most important terms and facts. Its content by itself is not a sufficient source of information required to pass the Physiology exam.**

A45. Kidney in regulation of homeostasis

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A3. Compartmentalization of body fluids

A4. Differences between intra- and extracellular fluids

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B84. Regulation of body fluid volume

B85. Regulation of constant osmotic pressure

B65. Formation and secretion of posterior pituitary hormones

B70. Adrenal cortex. Functions, malfunctions.

B74. Natriuretic peptides

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B73. Bone formation and resorption. Regulation of calcaemia.

A33. Homeostasis (acid-base balance)



# Homeostasis

= maintenance of stable conditions in the internal body environment

*Maintenance of Constant Volume and Composition of Body Fluids*

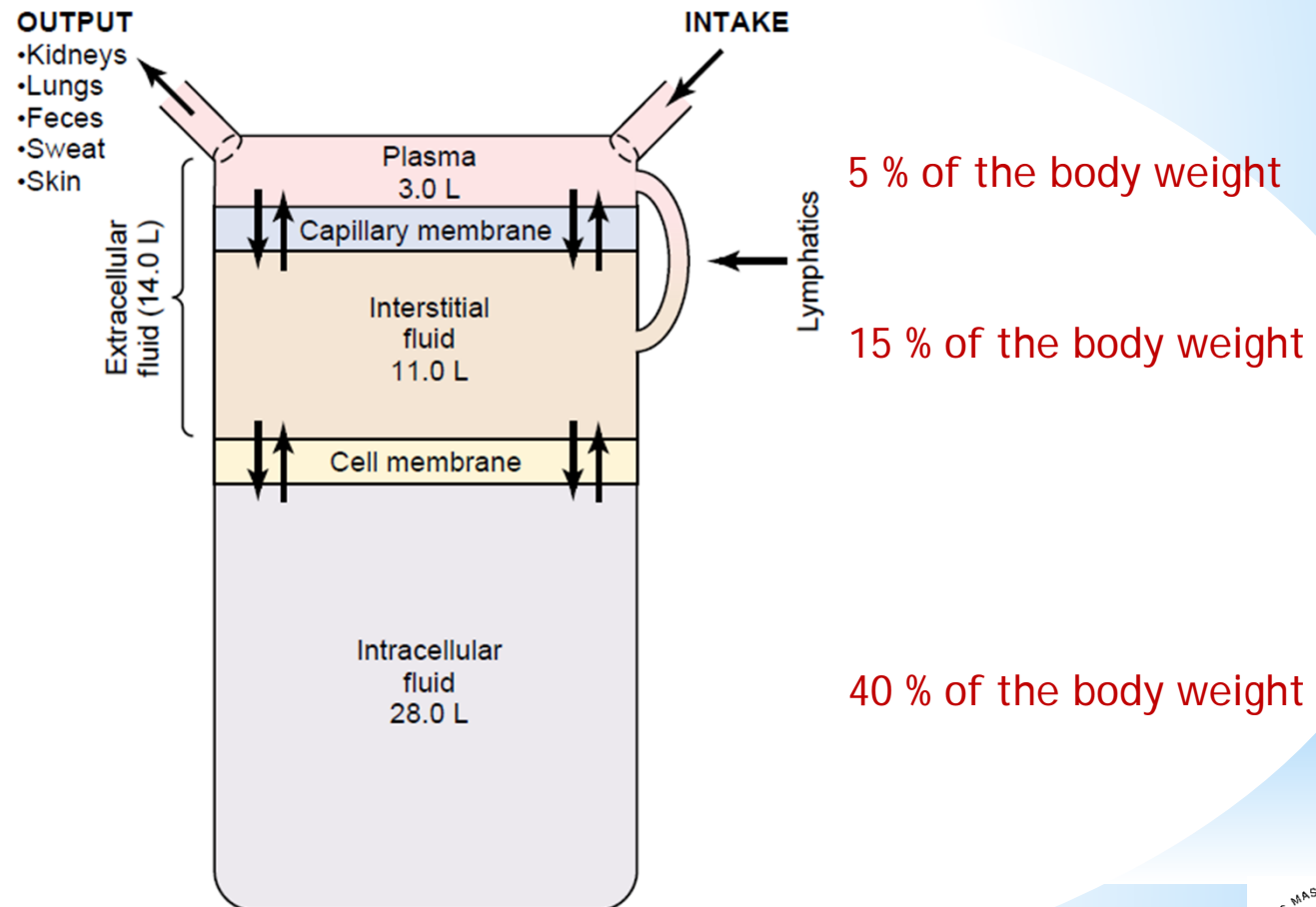
*Maintenance of Acid-Base Balance*

# **Constant Volume and Composition of Body Fluids - Regulation by Kidneys -**

# Body Fluids – Types and Volumes

## Compartments

60 % of the body weight in total



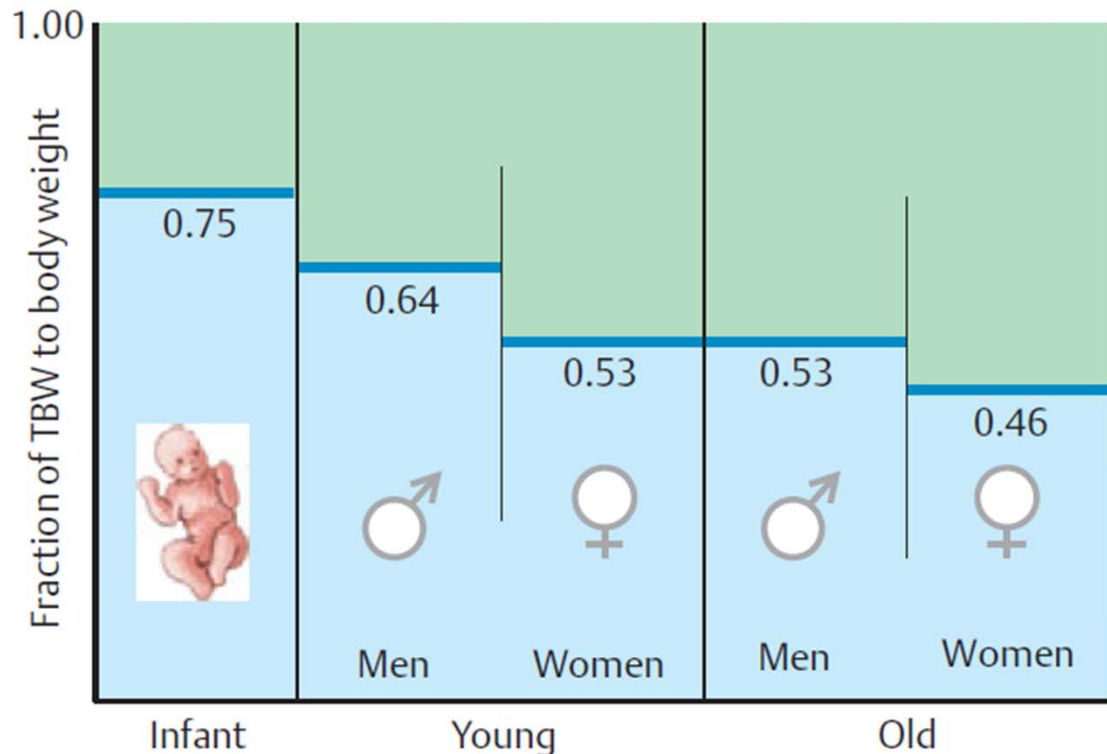
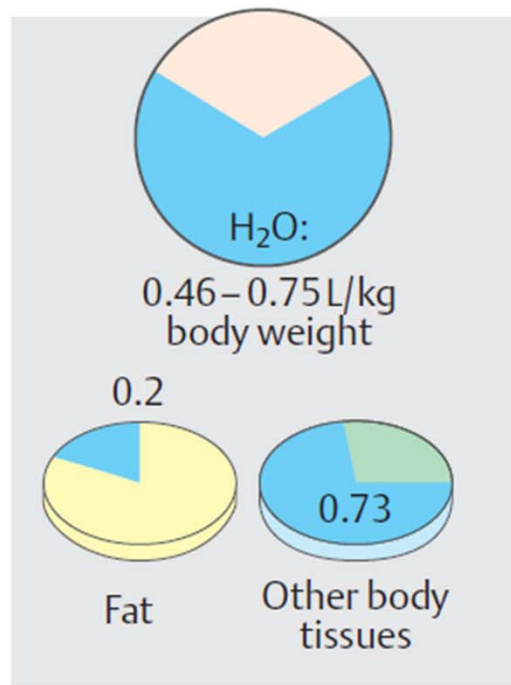
Transcellular fluid (1-2 l) - special type of ECF

*Guyton & Hall. Textbook of Medical Physiology*

# Body Fluids – Types and Volumes

## Changes with aging

### B. Total body water (TBW) content



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# Body Fluids – Types and Volumes

## *Balance between Input and Output of Fluid*

### Daily Intake and Output of Water (ml/day)

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	Normal	Prolonged, Heavy Exercise
<b>Intake</b>		
Fluids ingested	2100	?
From metabolism	<u>200</u>	<u>200</u>
Total intake	2300	?
<b>Output</b>		
Insensible—skin	350	350
Insensible—lungs	350	650
Sweat	100	5000
Feces	100	100
Urine	<u>1400</u>	<u>500</u>
Total output	2300	6600

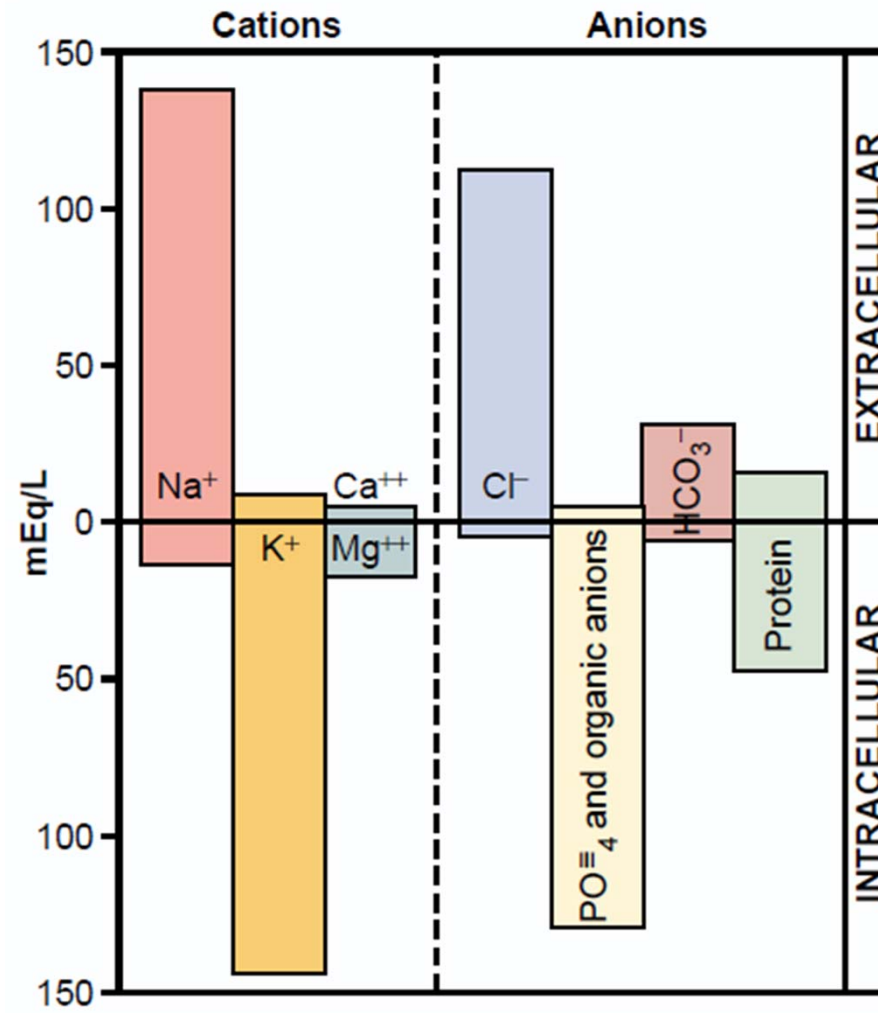
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*Guyton & Hall. Textbook of Medical Physiology*



# Body Fluids – Composition

*ECF vs. ICF*



*Guyton & Hall. Textbook of Medical Physiology*

# Body Fluids – Composition

## *plasma vs. ISF*

	Plasma (mOsm/L H <sub>2</sub> O)	Interstitial (mOsm/L H <sub>2</sub> O)
Na <sup>+</sup>	142	139
K <sup>+</sup>	4.2	4.0
Ca <sup>++</sup>	1.3	1.2
Mg <sup>+</sup>	0.8	0.7
Cl <sup>-</sup>	108	108
HCO <sub>3</sub> <sup>-</sup>	24	28.3
HPO <sub>4</sub> <sup>-</sup> , H <sub>2</sub> PO <sub>4</sub> <sup>-</sup>	2	2
SO <sub>4</sub> <sup>-</sup>	0.5	0.5
Phosphocreatine		
Carnosine		
Amino acids	2	2
Creatine	0.2	0.2
Lactate	1.2	1.2
Adenosine triphosphate		
Hexose monophosphate		
Glucose	5.6	5.6
Protein	1.2	0.2
Urea	4	4
Others	4.8	3.9

*Guyton & Hall. Textbook of Medical Physiology*



# Body Fluids – Composition

**osmolality** 285 mosm/kg H<sub>2</sub>O



↑ NaCl intake, loss of water → shrinking of cells



↓ NaCl intake, ↑ water input → cell edema



**Precise regulation of osmolality of ESF is necessary!**

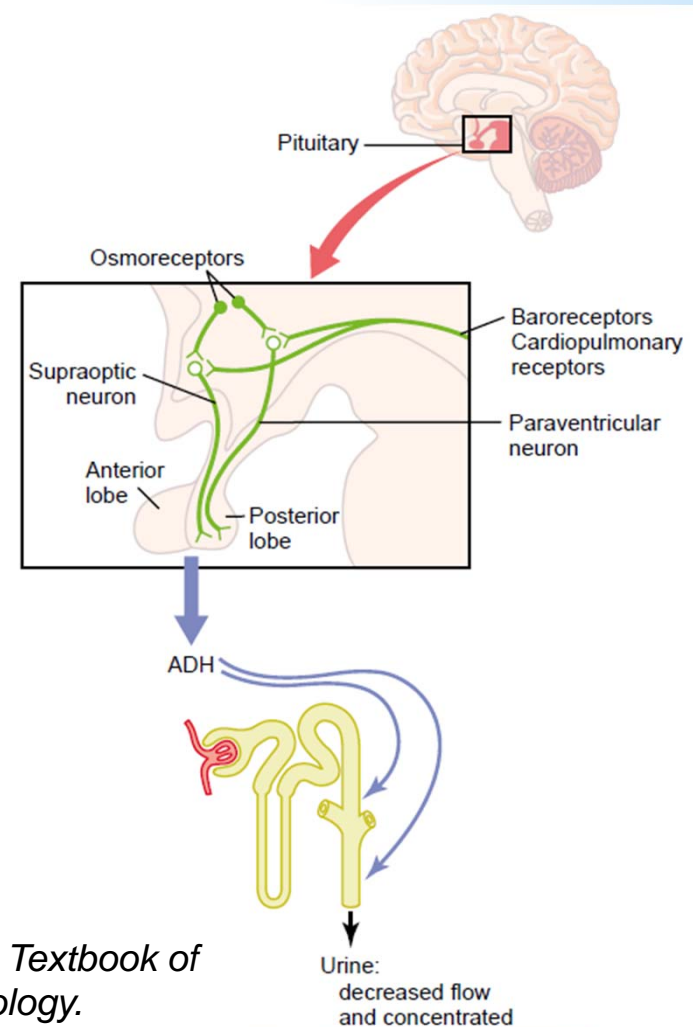
- **osmoreceptors**
- **kidneys** (target organ for the action of hormones below)
- **antidiuretic hormone**
- **aldosteron**
- **natriuretic peptides**

# Humoral Regulation of Body Fluids

## **Antidiuretic Hormone** (*vasopressin*)

### - effects:

- water reabsorption in kidneys (aquaporin 2)
- control of blood pressure
- ↑ glycogenolysis, mediator in the brain, ↑ secretion of ACTH in adenohypophysis



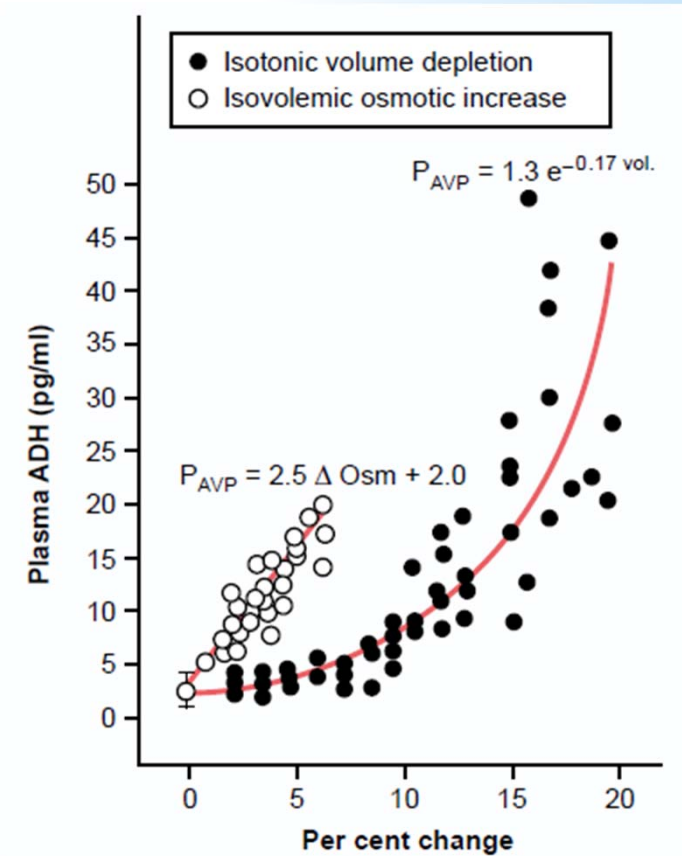
*Guyton & Hall. Textbook of Medical Physiology.*

# Humoral Regulation of Body Fluids

## **Antidiuretic Hormone** (*vasopressin*)

### - regulation of secretion:

- ↑ - ↑ osmolality
- ↓ volume of ECF
- pain, emotions, stress (surgical), physical exertion; standing
- nausea, vomiting
- angiotensin II
- morphine, nicotine, barbiturates, ...
- ↓ - ↓ osmolality, ↑ volume of ECF
- alcohol; antagonists of opioids



*Guyton & Hall. Textbook of Medical Physiology.*



# Humoral Regulation of Body Fluids

## ***Antidiuretic Hormone*** (*vasopressin*)

- pathology:

↑ SIADH

↓ *diabetes insipidus*

# Humoral Regulation of Body Fluids

## *Aldosteron*

- the most important steroid with the mineralocorticoid effect

- **mechanism of action:**

binding to the mineralocorticoid receptor

→ synthesis of proteins:

- namely **Na<sup>+</sup>/K<sup>+</sup>-ATPase**
- ↑ number of amiloride-inhibited **Na<sup>+</sup>-channels**
- ↑ activity of **H<sup>+</sup>-pump**
- ↑ activity of **Na<sup>+</sup>/H<sup>+</sup>-antiport**

# Humoral Regulation of Body Fluids

## *Aldosteron*

- the most important steroid with the mineralocorticoid effect

### - effects:

- ↑ Na<sup>+</sup> reabsorption (urine, sweat, saliva, gastric juice)
- ↑ K<sup>+</sup> urine excretion, ↑ acidity of urine (exchange for Na<sup>+</sup>)
- ↑ K<sup>+</sup> content and ↓ Na<sup>+</sup> content in muscle and brain cells



# Humoral Regulation of Body Fluids

## *Aldosteron*

- the most important steroid with the mineralocorticoid effect
- regulation of its secretion:
  - ACTH (transient effect)
  - direct stimulatory effect of  $\uparrow$  plasmatic concentration of  $K^+$  and  $\downarrow Na^+$  (lower sensitivity)
  - renin-angiotensine-aldosteron system
  - atrial natriuretic peptide
  - other hormones od adenohipophysis (maintenance of reactivity of *zona glomerulosa*)

# Humoral Regulation of Body Fluids

## *Aldosteron - Pathology*

### Primary hyperaldosteronism (Conn's syndrome)

- tumors of adrenal cortex which secretes aldosteron

### Secondary hyperaldosteronism

- patients with the congestive heart failure, nephrosis, liver cirrhosis, renal artery constriction, hypertension, with the salt-losing form of adrenogenital syndrome

### Hyporeninemic hypoaldosteronism

### Pseudohypoaldosteronism

# Humoral Regulation of Body Fluids

## *Atrial Natriuretic Peptide*

- one of natriuretic peptides (BNP – cardiac ventricles, CNP – brain)
- secreted by atrial cardiomyocytes, found also in the brain
- receptors
- short half-life

# Humoral Regulation of Body Fluids

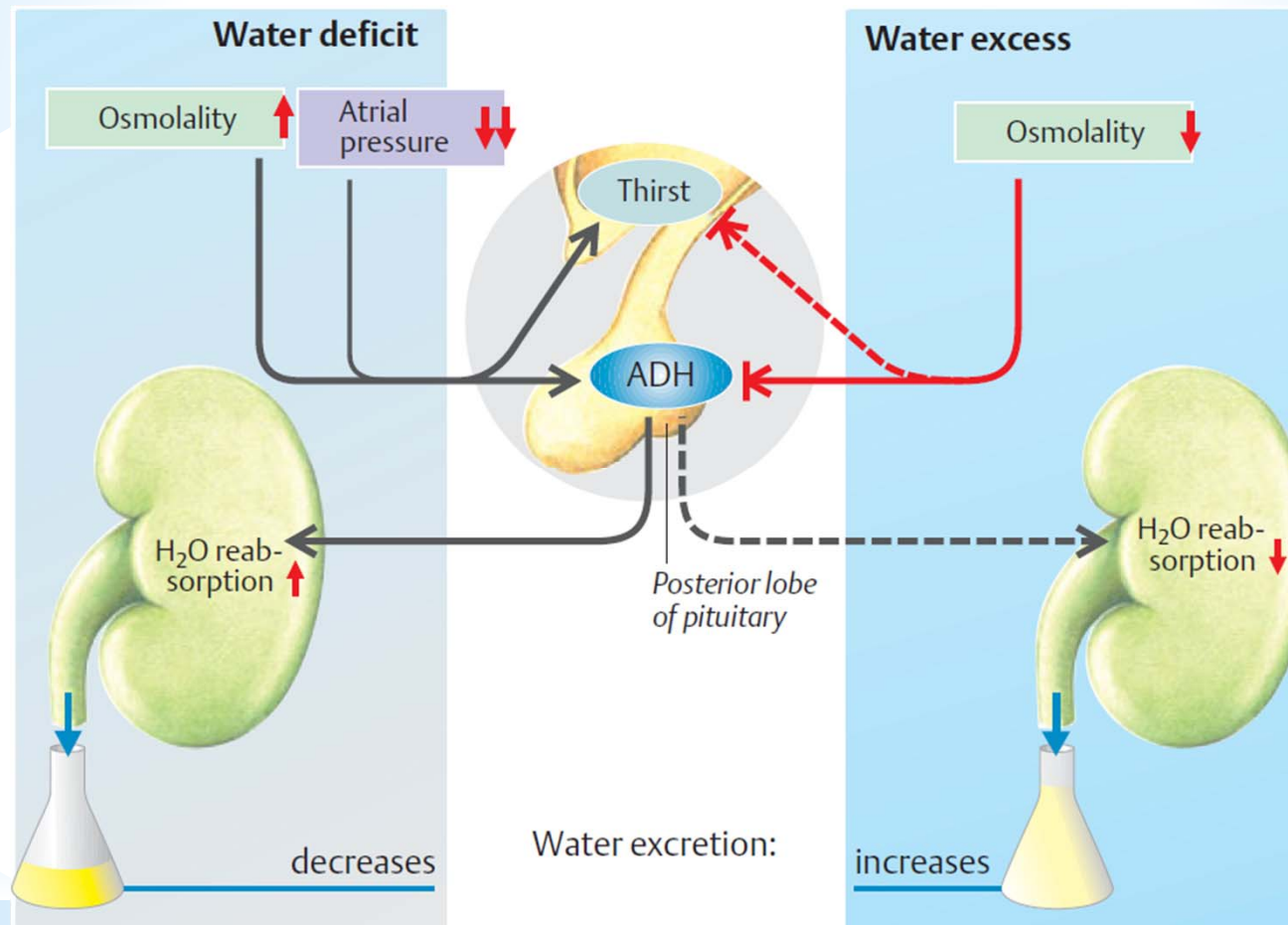
## *Atrial Natriuretic Peptide*

- one of natriuretic peptides (BNP – cardiac ventricles, CNP – brain)
- **effects (through  $\uparrow$  cGMP):  $\rightarrow \downarrow$  BP** (also through the brain stem)
  - $\rightarrow$  natriuresis
  - $\rightarrow \downarrow$  reactivity of vascular smooth muscles for vasoconstrictive substances
  - $\rightarrow$  inhibition of renin secretion,  $\downarrow$  reactivity of *zona glomerulosa* for stimuli  $\uparrow$  aldosteron secretion
  - $\rightarrow$  inhibition of ADH secretion  $\rightarrow \uparrow$  water excretion
- **regulation of its secretion:**
  - $\uparrow$  -  $\uparrow$  ECF volume
  - $\downarrow$  -  $\downarrow$  CVP at orthostasis

# Humoral Regulation of Body Fluids

## *Water Homeostasis*

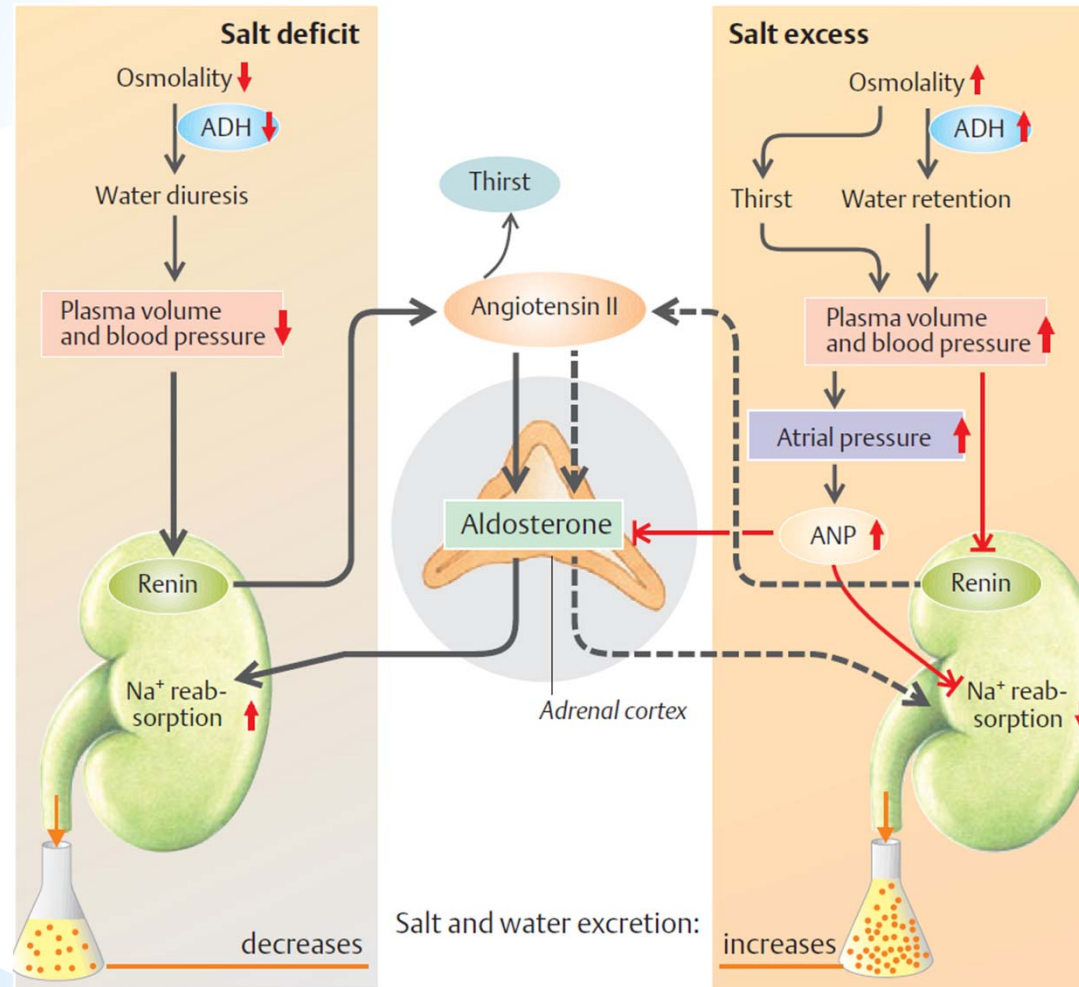
water intoxication



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# Humoral Regulation of Body Fluids

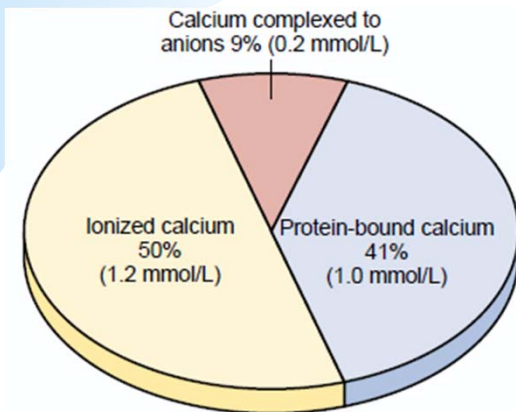
## *Salt Homeostasis*



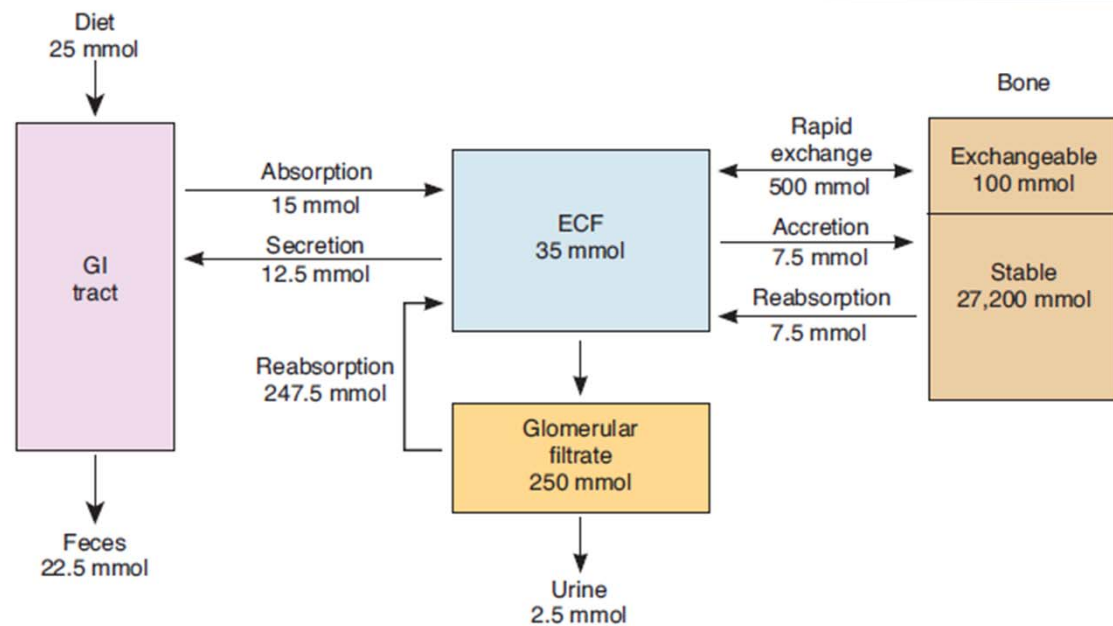
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# Humoral Regulation of Body Fluids

## Calcium in the Body



Guyton & Hall. Textbook of Medical Physiology.



Ganong's Review of Medical Physiology

hypocalcemia

hypercalcemia

# Humoral Regulation of Body Fluids

## *Hormonal Regulation of Calcemia*

*Parathormone*

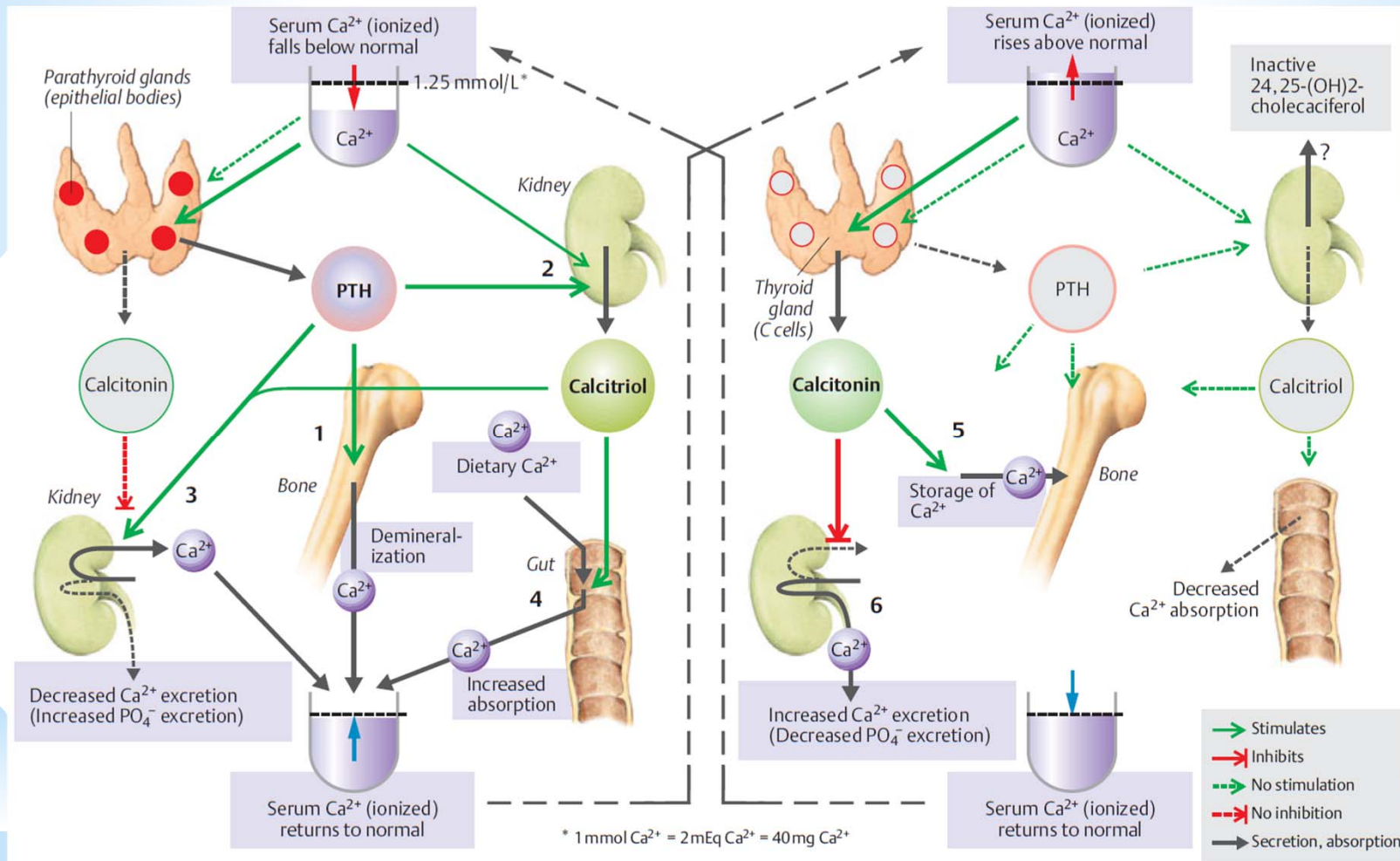
*Vitamin D*

*Calcitonin*



# Humoral Regulation of Body Fluids

## Hormonal Regulation of Calcemia



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# **Acid-Base Balance**

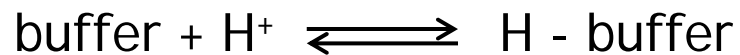
## **- Regulation by Kidneys -**

# Acid-Base Balance and its Regulation

Acid-base balance is regulated by:

## 1) Buffers

- fast regulation (seconds)
- pH changes attenuated by binding and release of H<sup>+</sup>:



↑[H<sup>+</sup>] direction to the right favoured till free buffer is available

↓[H<sup>+</sup>] direction to the left favoured, H<sup>+</sup> released

## 2) Lungs

- fast regulation (minutes even hours)
- elimination of CO<sub>2</sub> from the body ( $\text{H}_2\text{CO}_3 \rightarrow \text{H}_2\text{O} + \text{CO}_2$ )

## 3) Kidneys

- slower regulation (hours even days) but the most powerful
- elimination of acids and bases from the body

# Acid-Base Balance and its Regulation

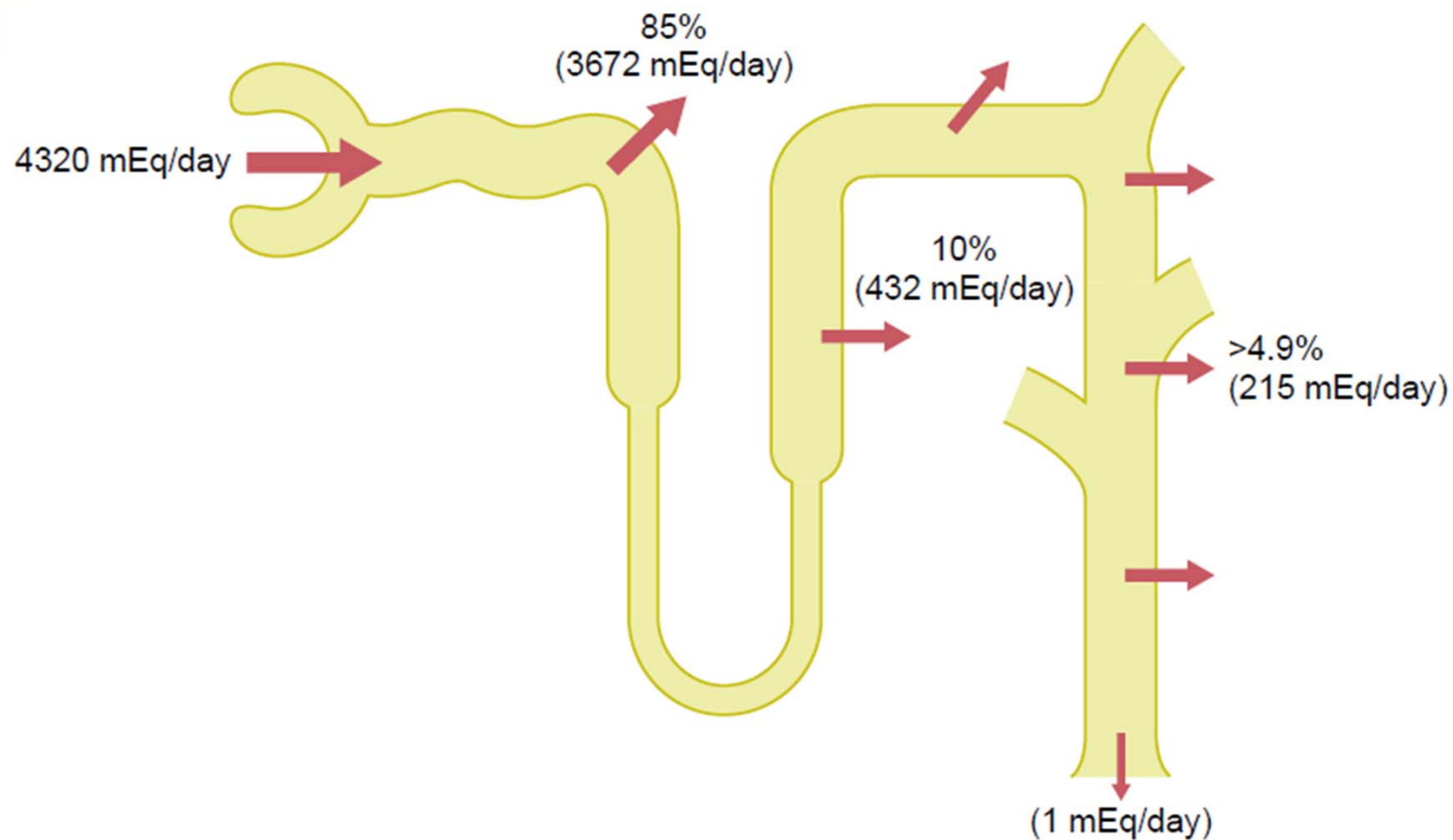
## *Regulation of Acid-Base Balance by Kidneys*

- by excretion of acid or alkalic urine
- a high amount of  $\text{HCO}_3^-$  still filtered in the glomerulus  
GFR 180 l/day,  $[\text{HCO}_3^-]_{\text{plasma}} 24 \text{ mEq/l} \rightarrow 4320 \text{ mEq HCO}_3^-$   
filtered per day - almost all ordinarily reabsorbed
- a high amount of  $\text{H}^+$  still secreted in renal tubules  
about 80 mEq of non-volatile acids are formed in the course of  
metabolic processes per day - have to be excreted by kidneys
- filtered  $\text{HCO}_3^-$  / secreted  $\text{H}^+$

# Acid-Base Balance and its Regulation

## *Regulation of Acid-Base Balance by Kidneys*

- 1) Secretion of  $H^+$
- 2) Reabsorption of  $HCO_3^-$

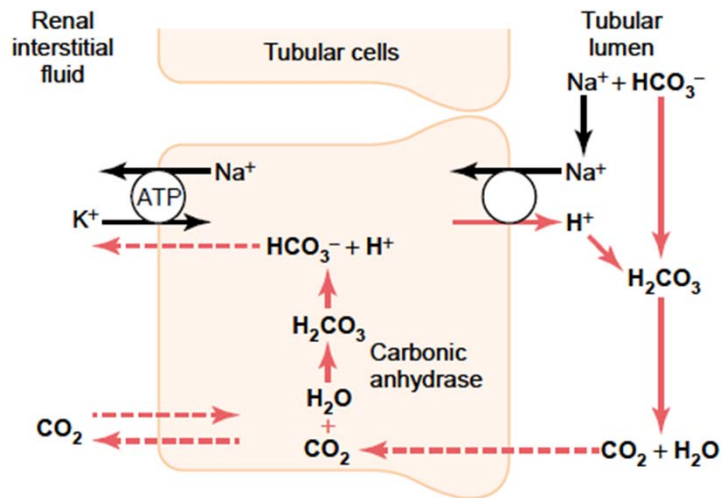


# Acid-Base Balance and its Regulation

## *Regulation of Acid-Base Balance by Kidneys*

- 1) Secretion of  $H^+$
- 2) Reabsorption of  $HCO_3^-$

❖ in the proximal tubule, thick loop of Henle and at the beginning of the distal tubule



$Na^+/H^+$ -antiport

*>90%  $HCO_3^-$  reabsorbed - only a slight acidification of the urine!*

Reabsorption of  $HCO_3^-$  across the basolateral membrane facilitated by:

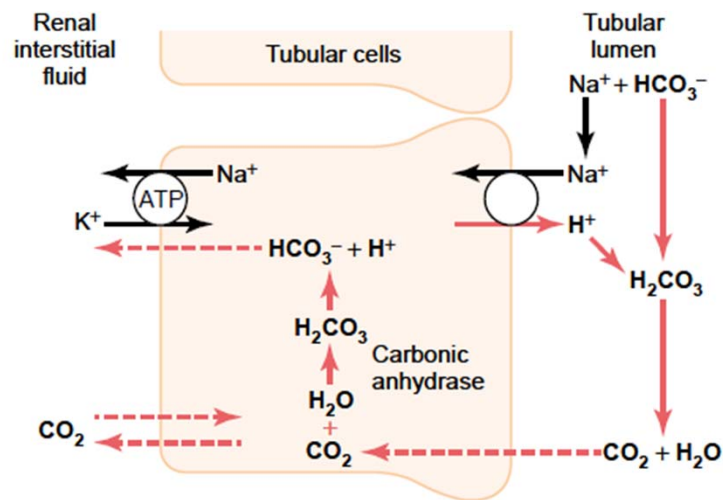
- $Na^+$ - $HCO_3^-$  co-transport (the proximal tubule)
- $Cl^-$ - $HCO_3^-$  exchanger (the end of proximal tubule and the following parts of tubulus except for the thin loop of Henle)

# Acid-Base Balance and its Regulation

## *Regulation of Acid-Base Balance by Kidneys*

- 1) Secretion of  $H^+$
- 2) Reabsorption of  $HCO_3^-$

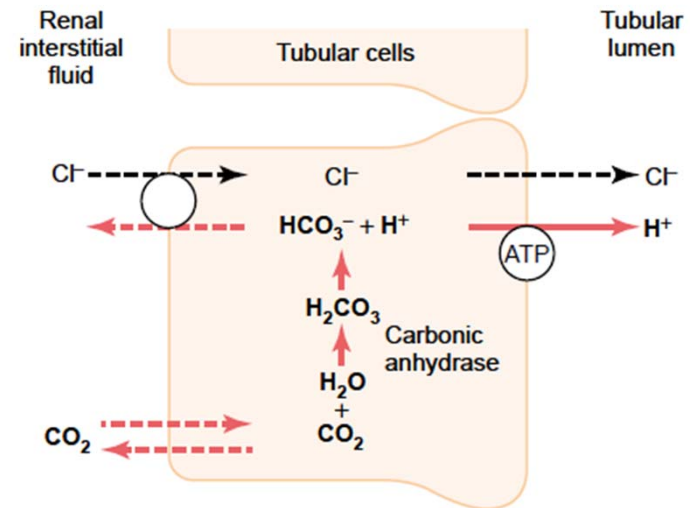
❖ in the proximal tubule, thick loop of Henle and at the beginning of the distal tubule



$Na^+/H^+$ -antiport

*>90%  $HCO_3^-$  reabsorbed - only a slight acidification of the urine!*

❖ in the final part of distal tubule and in the collecting duct



primary active transport of  $H^+$   
(intercalated cells)

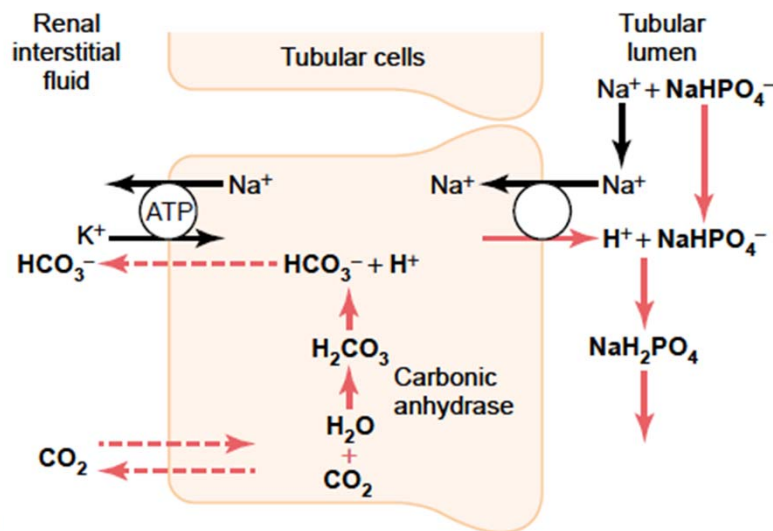
*acidification of urine*

# Acid-Base Balance and its Regulation

## *Regulation of Acid-Base Balance by Kidneys*

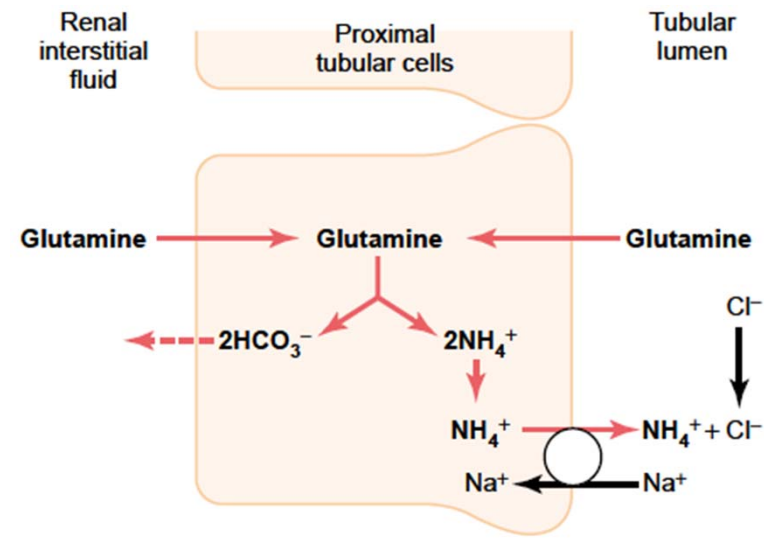
- 1) Secretion of  $H^+$
- 2) Reabsorption of  $HCO_3^-$
- 3) Production of  $HCO_3^-$  *de novo*

### ❖ Phosphate buffer ( $HPO_4^{2-}$ , $H_2PO_4^-$ )



$HPO_4^{2-}$  and  $H_2PO_4^-$  are reabsorbed less than water  $\Rightarrow$  their concentration in the tubular fluid gradually rises

### ❖ Ammonium buffer ( $NH_3$ , $NH_4^+$ )



$NH_4^+$  originates from glutamine - the proximal tubule, thick ascending loop of Henle and distal tubule

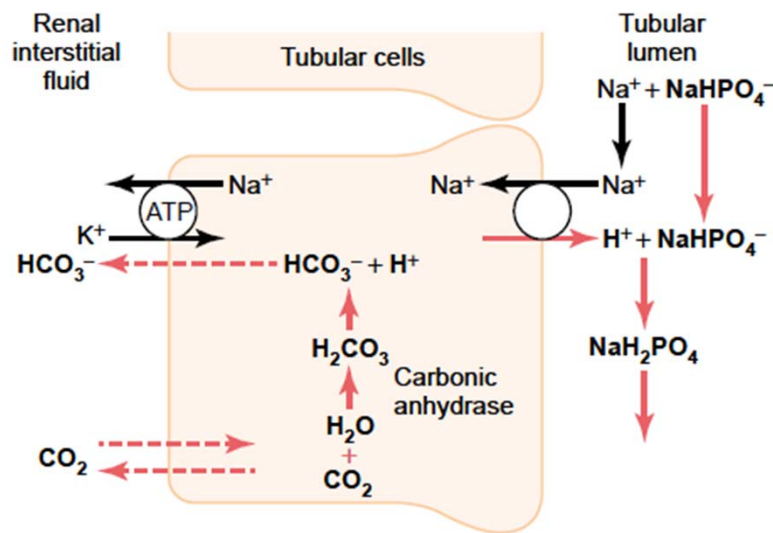


# Acid-Base Balance and its Regulation

## *Regulation of Acid-Base Balance by Kidneys*

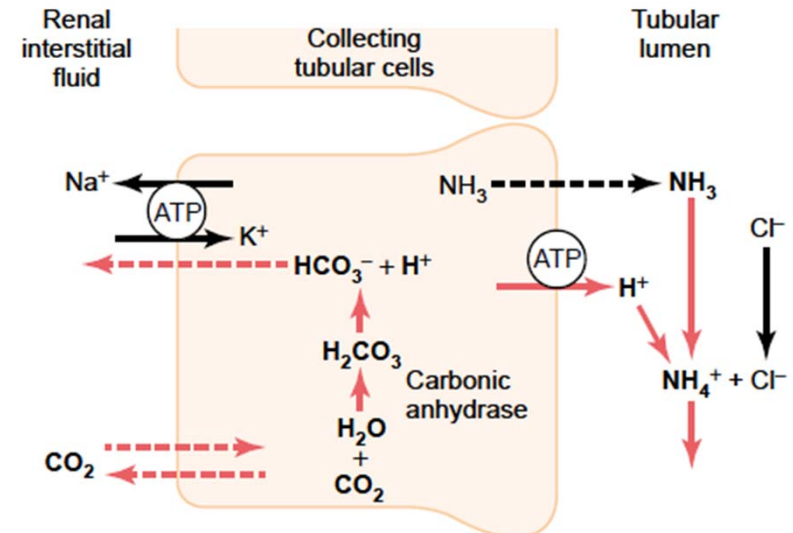
- 1) Secretion of  $H^+$
- 2) Reabsorption of  $HCO_3^-$
- 3) Produkce nového  $HCO_3^-$

### ❖ Phosphate buffer ( $HPO_4^{2-}$ , $H_2PO_4^-$ )



$HPO_4^{2-}$  and  $H_2PO_4^-$  are reabsorbed less than water  $\Rightarrow$  their concentration in the tubular fluid gradually rises

### ❖ Ammonium buffer ( $NH_3$ , $NH_4^+$ )



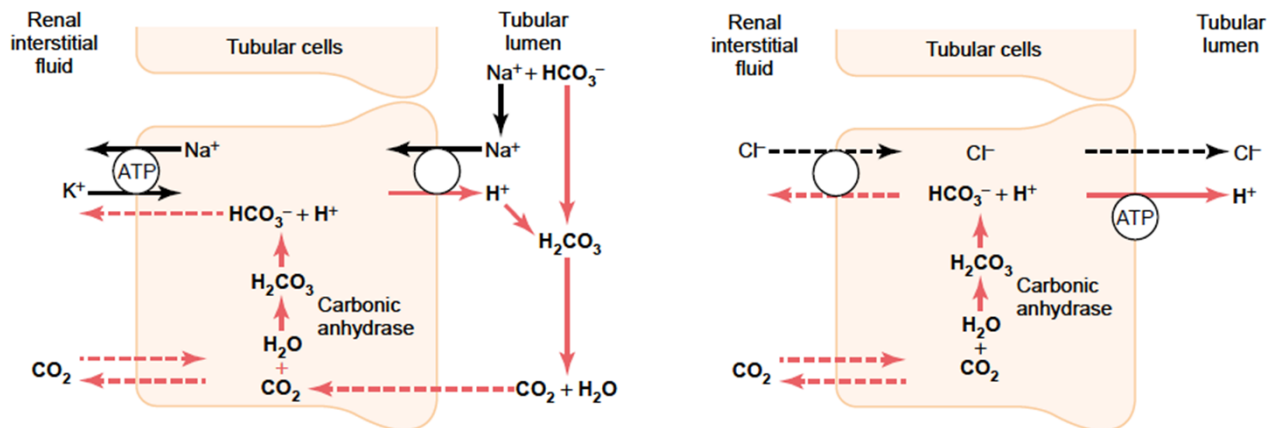
the collecting duct (permeable for  $NH_3$  but far less for  $NH_4^+$  - excreted by urine)  
50% of  $H^+$  secretion and  $HCO_3^-$  formed *de novo!*

# Acid-Base Balance and its Regulation

## *Regulation of Acid-Base Balance by Kidneys*

### Regulation of H<sup>+</sup> secretion

- ↑ - ↑ pCO<sub>2</sub> in ECF (respiratory acidosis; direct stimulation due to ↑ formation of H<sup>+</sup> in tubular cells)



- ↓ pH in ECF (respiratory or metabolic acidosis)
- ↑ secretion of aldosterone (stimulates H<sup>+</sup> secretion in intercalated cells of collecting ducts; Conn's syndrome - alkalosis)

# Acid-Base Balance and its Regulation

## *Regulation of Acid-Base Balance by Kidneys*

### Regulation of H<sup>+</sup> secretion

#### Factors That Increase or Decrease H<sup>+</sup> Secretion and HCO<sub>3</sub><sup>-</sup> Reabsorption by the Renal Tubules

##### Increase H<sup>+</sup> Secretion and HCO<sub>3</sub><sup>-</sup> Reabsorption

↑ PCO<sub>2</sub>

↑ H<sup>+</sup>, ↓ HCO<sub>3</sub><sup>-</sup>

↓ Extracellular fluid volume

↑ Angiotensin II

↑ Aldosterone

Hypokalemia

RAS

##### Decrease H<sup>+</sup> Secretion and HCO<sub>3</sub><sup>-</sup> Reabsorption

↓ PCO<sub>2</sub>

↓ H<sup>+</sup>, ↑ HCO<sub>3</sub><sup>-</sup>

↑ Extracellular fluid volume

↓ Angiotensin II

↓ Aldosterone

Hyperkalemia

↑ activity of Na<sup>+</sup>/H<sup>+</sup> antiport

↑ activity of H<sup>+</sup> ATPase

tendency to alkalosis

# Acid-Base Balance and its Regulation

## *Regulation of Acid-Base Balance by Kidneys*

### Acidosis - correction by kidneys

$$\downarrow \text{pH} = 6.1 + \log \frac{\text{HCO}_3^-}{0.03 \times P_{\text{CO}_2}} \downarrow$$

- **metabolic acidosis:** due to  $\downarrow \text{HCO}_3^-$   
**renal correction :**  $\downarrow \text{HCO}_3^-$  in ECF  $\rightarrow$   $\downarrow$  filtered  $\text{HCO}_3^- \rightarrow$  complete reabsorption of  $\text{HCO}_3^-$  + its formation *de novo* ( $\text{HCO}_3^-$  not excreted) +  $\uparrow \text{H}^+$  excretion  $\rightarrow$  pH normalization
- **respiratory acidosis:** due to  $\uparrow P_{\text{CO}_2}$  (hypoventilation)  
**renal correction:**  $\uparrow P_{\text{CO}_2}$  in ECF  $\rightarrow$   $\uparrow P_{\text{CO}_2}$  in tubular cells  $\rightarrow$   $\uparrow$  formation of  $\text{H}^+$  and  $\text{HCO}_3^-$  in tubular cells  $\rightarrow$   $\uparrow \text{H}^+$  secretion +  $\uparrow \text{HCO}_3^-$  reabsorption  $\rightarrow$  pH normalization

# Acid-Base Balance and its Regulation

## *Regulation of Acid-Base Balance by Kidneys*

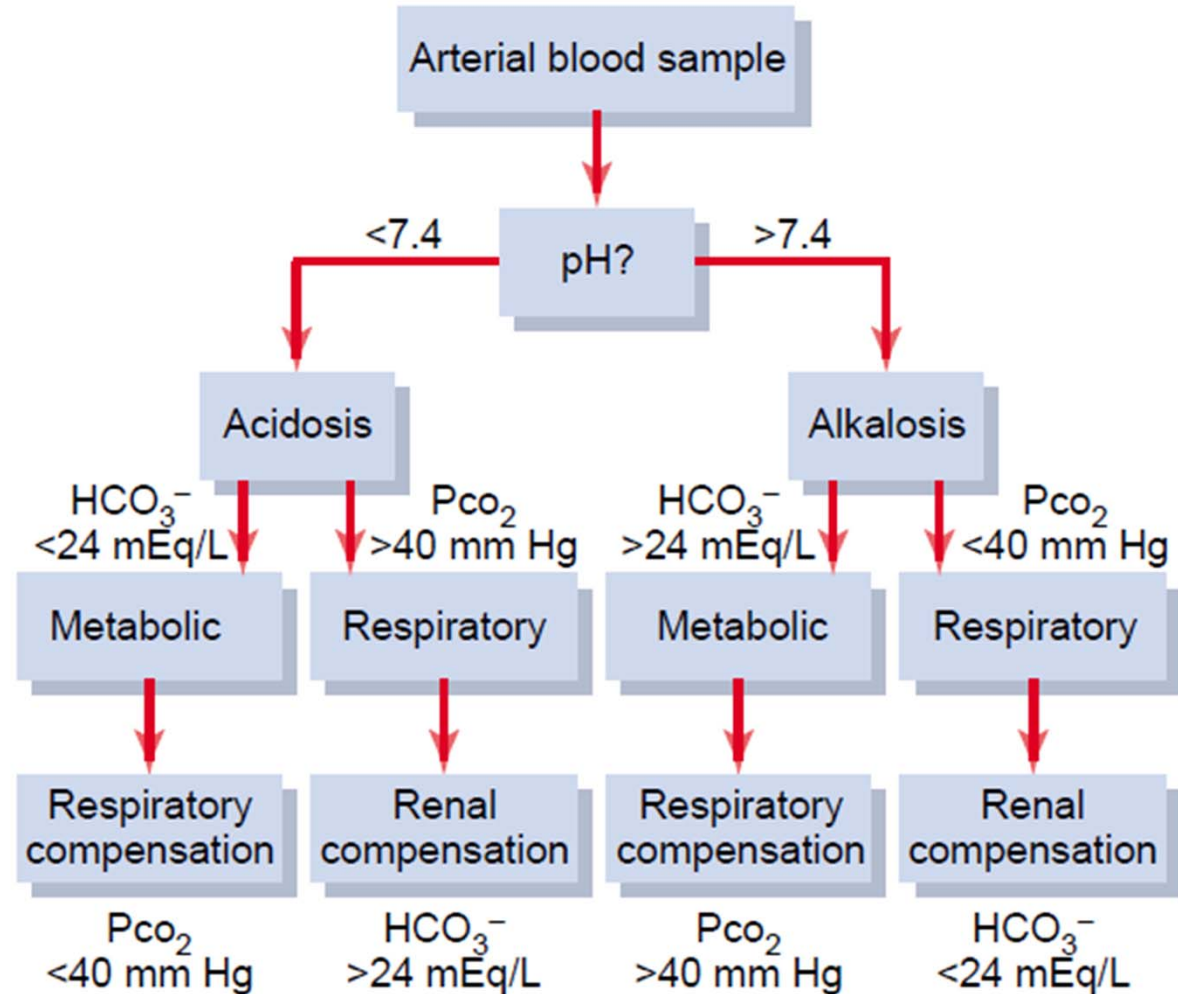
### Alkalosis - correction by kidneys

$$\uparrow \text{pH} = 6.1 + \log \frac{\text{HCO}_3^-}{0.03 \times P_{\text{CO}_2}} \uparrow$$

- **metabolic alkalosis:** due to  $\uparrow \text{HCO}_3^-$   
**renal correction:**  $\uparrow \text{HCO}_3^-$  in ECF  $\rightarrow$   $\uparrow$  filtered  $\text{HCO}_3^-$   $\rightarrow$  incomplete  $\text{HCO}_3^-$  reabsorption (lack of  $\text{H}^+$ )  $\rightarrow$   $\uparrow \text{HCO}_3^-$  excretion by urine  $\rightarrow$  pH normalization
- **respiratory alkalosis :** due to  $\downarrow P_{\text{CO}_2}$  (hyperventilation)  
**renal correction:**  $\downarrow P_{\text{CO}_2}$  in ECF  $\rightarrow$   $\downarrow P_{\text{CO}_2}$  in tubular cells  $\rightarrow$   $\downarrow$  formation of  $\text{H}^+$  and  $\text{HCO}_3^-$  in tubular cells  $\rightarrow$   $\downarrow \text{H}^+$  secretion +  $\downarrow \text{HCO}_3^-$  reabsorption  $\rightarrow$  pH normalization

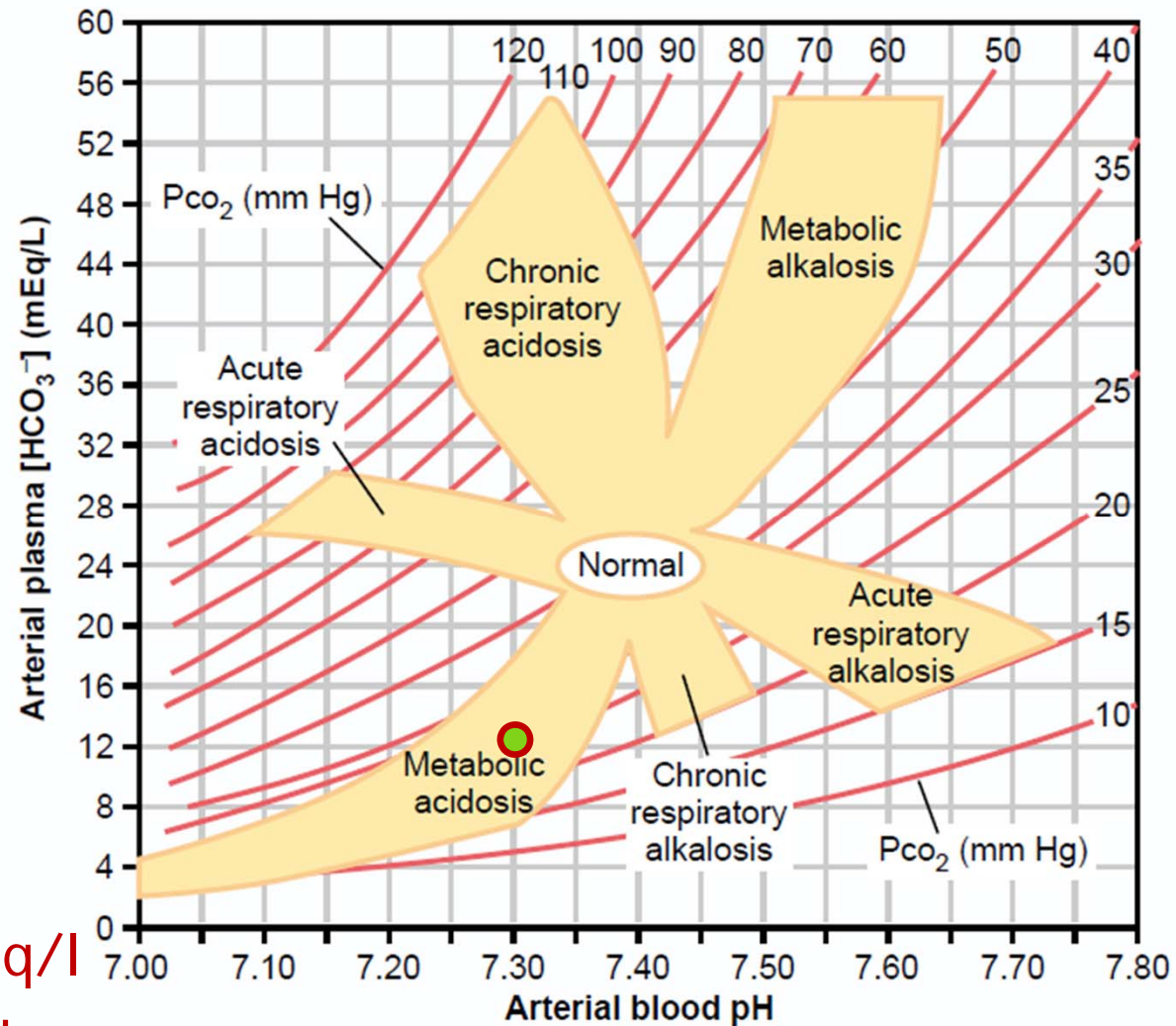
# Acid-Base Balance and its Regulation

## *Diagnostics*



# Acid-Base Balance and its Regulation

## *Diagnostics*



pH: 7,3

$HCO_3^-$ : 12 mEq/l

$P_{CO_2}$ : 25 mmHg

# Acid-Base Balance and its Regulation

## *Diagnostics - Siggaard-Andersen nomogram*

