# 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.**

# Homeostasis

= maintainance of stable conditions in the internal body environment

*Maintainance of Constant Volume and Composition of Body Fluids*

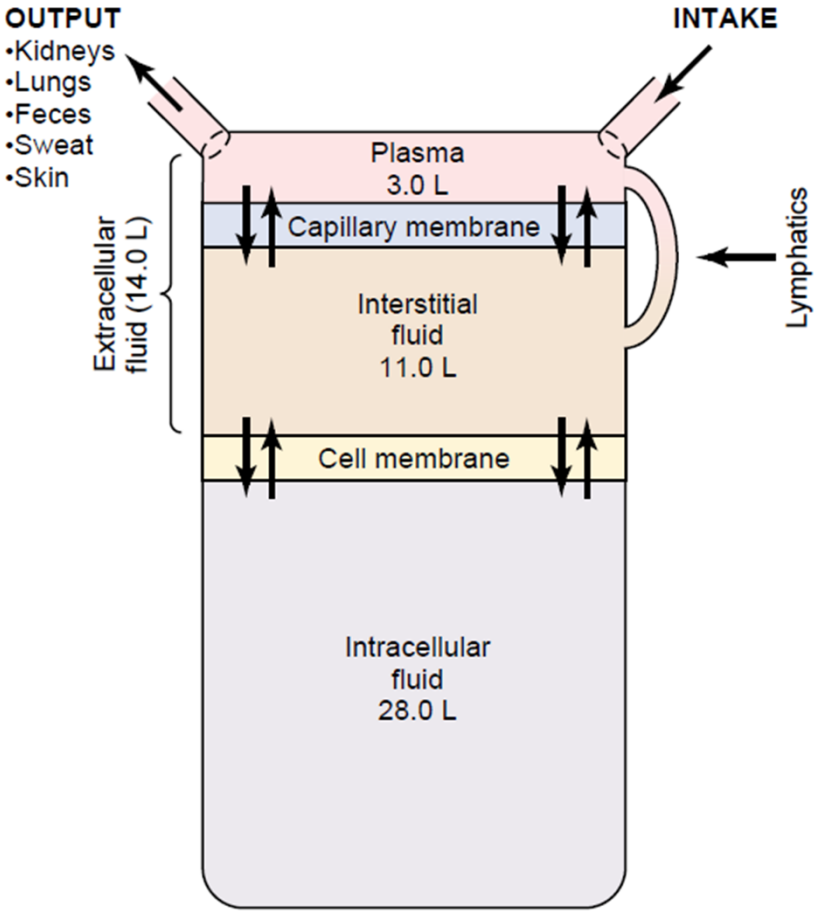
*Maintainance of Acid-Base Balance*

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

# Body Fluids – Types and Volumes

## Compartments

60 % of the body weight in total




5 % of the body weight

15 % of the body weight

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

40 % of the body weight

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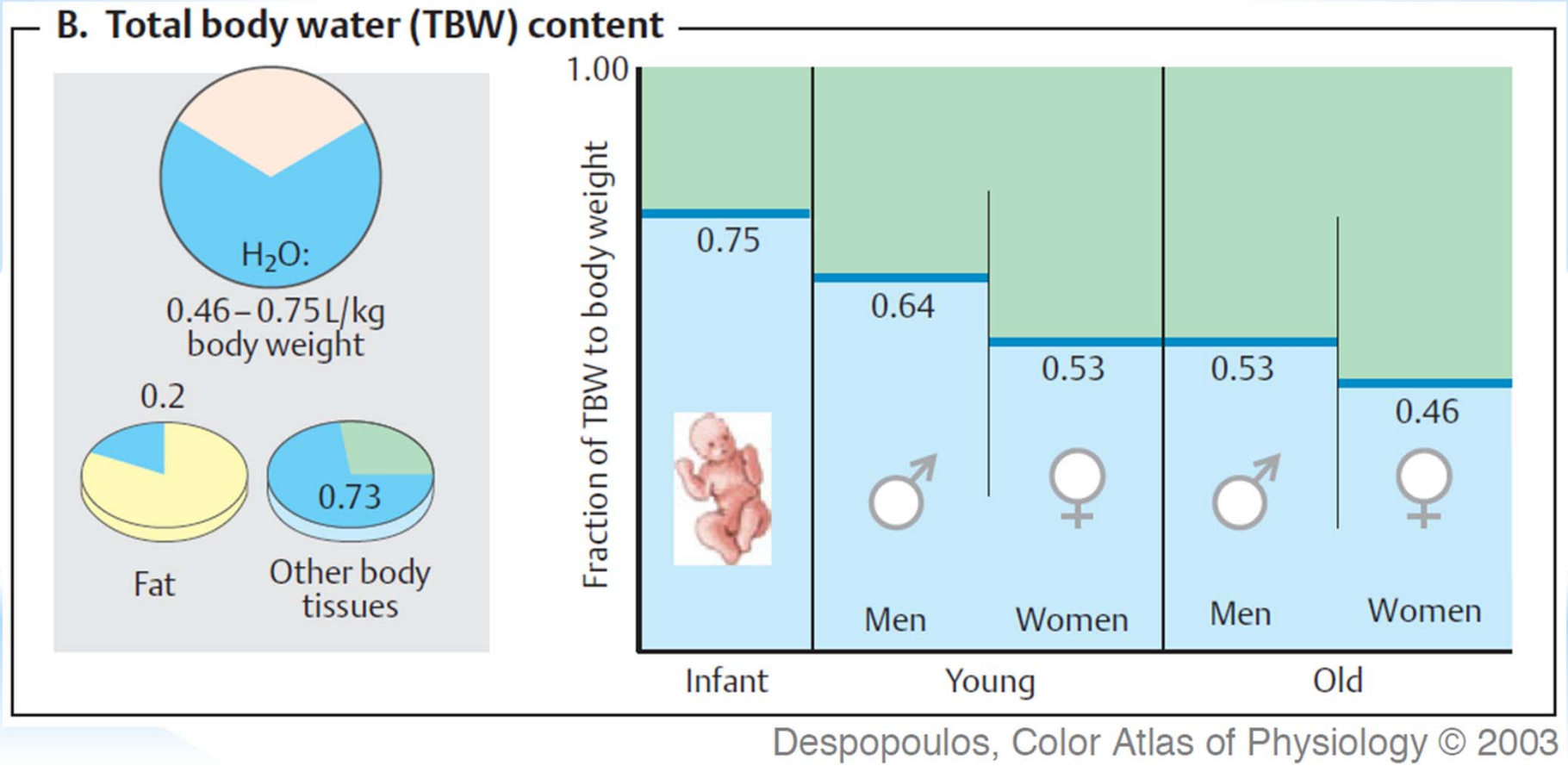
# Body Fluids – Types and Volumes

## Changes with aging

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# Body Fluids – Types and Volumes

*Balance between Input and Output of Fluid*

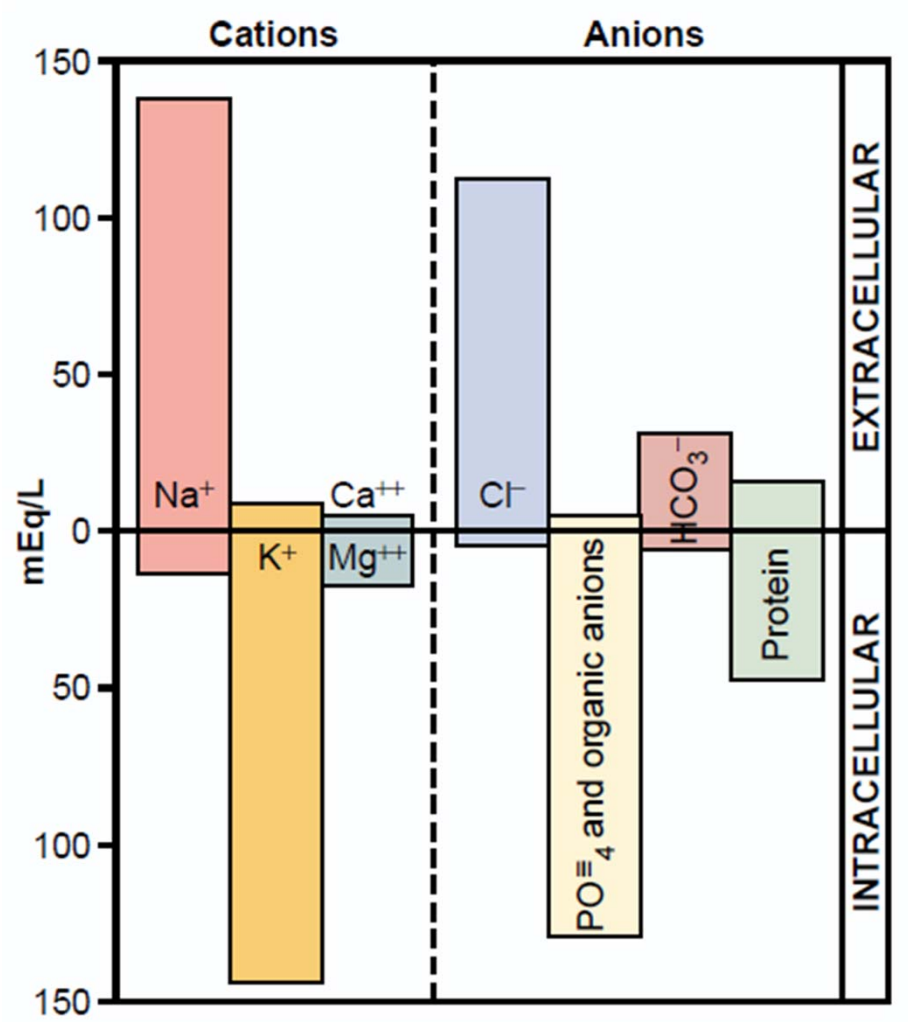
**Daily Intake and Output of Water (ml/day)**

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

*Guyton & Hall. Textbook of Medical Physiology*

# Body Fluids – Composition

## *ECF vs. ICF*

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# Body Fluids – Composition

*plasma vs. ISF*

| | Plasma (mOsm/L $H_2O$) | Interstitial (mOsm/L $H_2O$) |
|---|---|---|
| $Na^+$ | 142 | 139 |
| $K^+$ | 4.2 | 4.0 |
| $Ca^{++}$ | 1.3 | 1.2 |
| $Mg^+$ | 0.8 | 0.7 |
| $Cl^-$ | 108 | 108 |
| $HCO_3^-$ | 24 | 28.3 |
| $HPO_4^-$, $H_2PO_4^-$ | 2 | 2 |
| $SO_4^-$ | 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 |

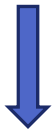
*Guyton & Hall. Textbook of Medical Physiology*

# Body Fluids – Composition

**osmolality** 285 mosm/kg $H_2O$

↑ ↑ 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*

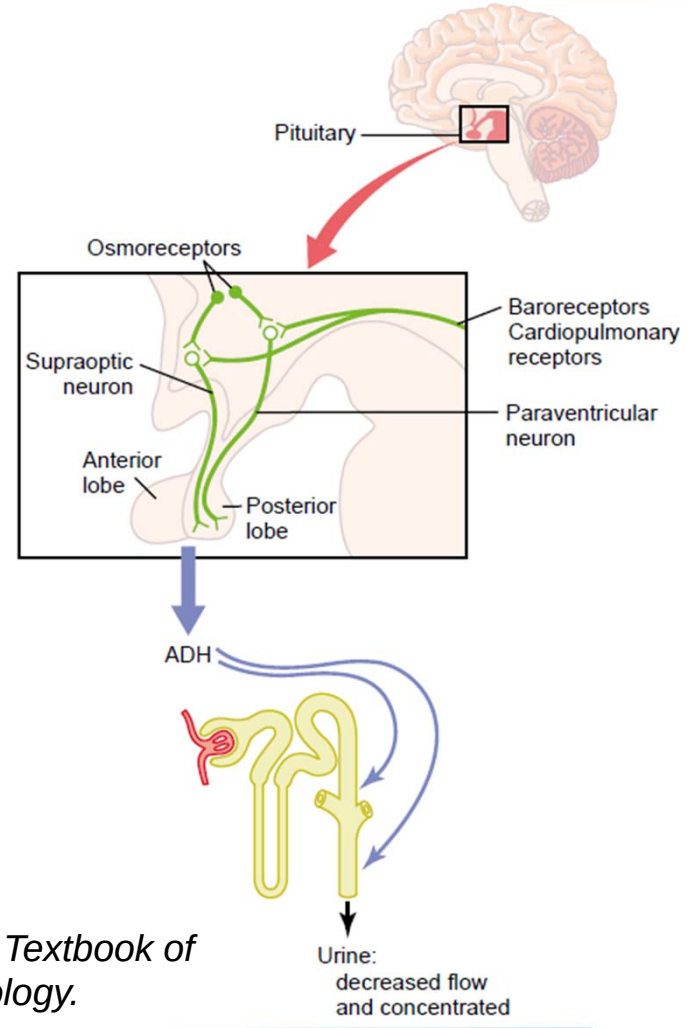
*(vasopressin)*

- effects:

→ water reabsorption in kidneys (aquaporin 2)

→ control of blood pressure

→ ↑ glycogenolysis, mediator in the brain, ↑ secretion of ACTH in adenohypophysis

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# Humoral Regulation of Body Fluids

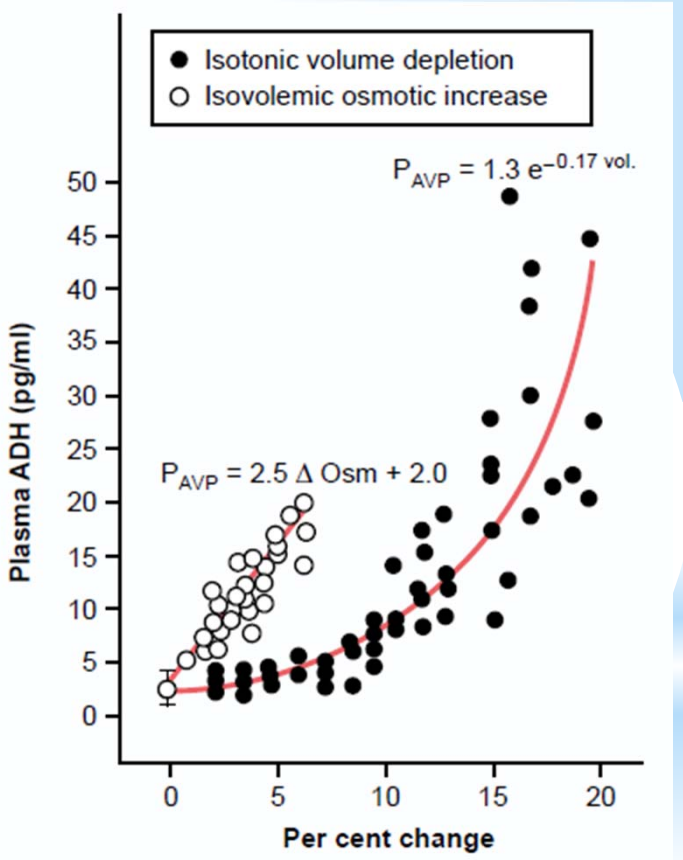
## *Antidiuretic Hormone*

*(vasopressin)*

- regulation of secretion:

↑
- ↑ osmolality
- ↓ volume of ECF
- pain, emotions, stress (surgical), physical exertion; standing
- nausea, vomitting
- angiotensine II
- morphin, nicotine, barbiturates, …

↓
- ↓ osmolality, ↑ volume of ECF
- alcohol; antagonists of opioids

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# 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 $Na^+/K^+$-ATPase
  - ↑ number of amiloride-inhibited $Na^+$-channels
  - ↑ activity of $H^+$-pump
  - ↑ activity of $Na^+/H^+$-antiport

# Humoral Regulation of Body Fluids

## *Aldosteron*

- the most important steroid with the mineralocorticoid effect

- effects:

→↑ $Na^+$ reabsorption (urine, sweat, saliva, gastric juice)
→↑ $K^+$ urine excretion, ↑ acidity of urine (exchange for $Na^+$)
→↑ $K^+$ content and ↓ $Na^+$ 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 ↑ plasmatic concentration of $K^+$ and ↓ $Na^+$ (lower sensitivity)
  - renin-angiotensine-aldosteron system
  - atrial natriuretic peptide
  - other hormones od adenohypophysis (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 cirhosis, 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)

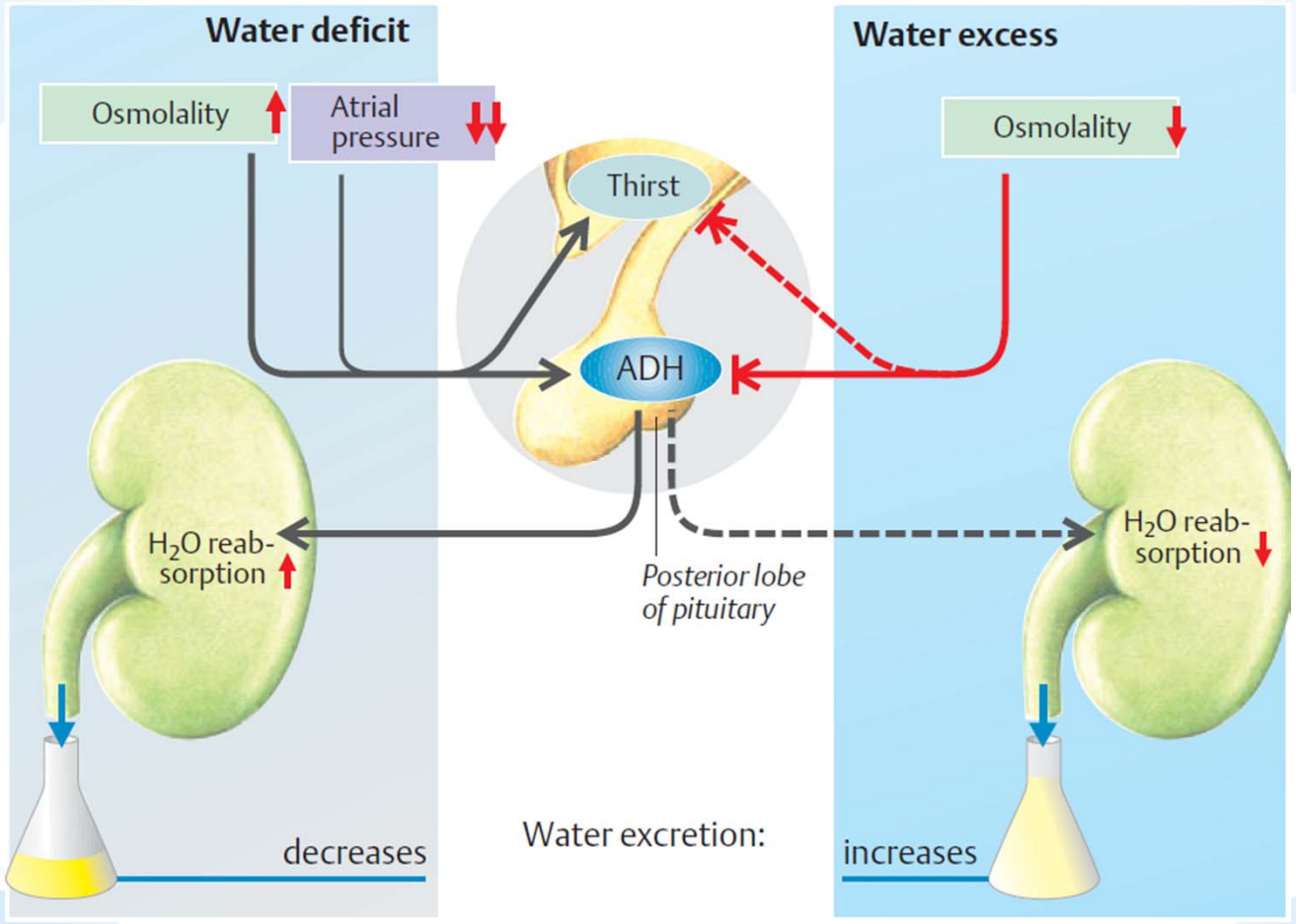
- effects (through ↑ cGMP): → ↓ **BP** (also through the brain stem)
  - → natriuresis
  - → ↓ reactivity of vascular smooth muscles for vasocontrictive substances
  - → inhibition of renin secretion, ↓ reactivity of *zona glomerulosa* for stimuli ↑ aldosteron secretion
  - → inhibition of ADH secretion → ↑ water excretion

- regulation of its secretion:
  - ↑ - ↑ ECF volume
  - ↓ - ↓ CVP at orthostasis

# Humoral Regulation of Body Fluids

## *Water Homeostasis*

water intoxication

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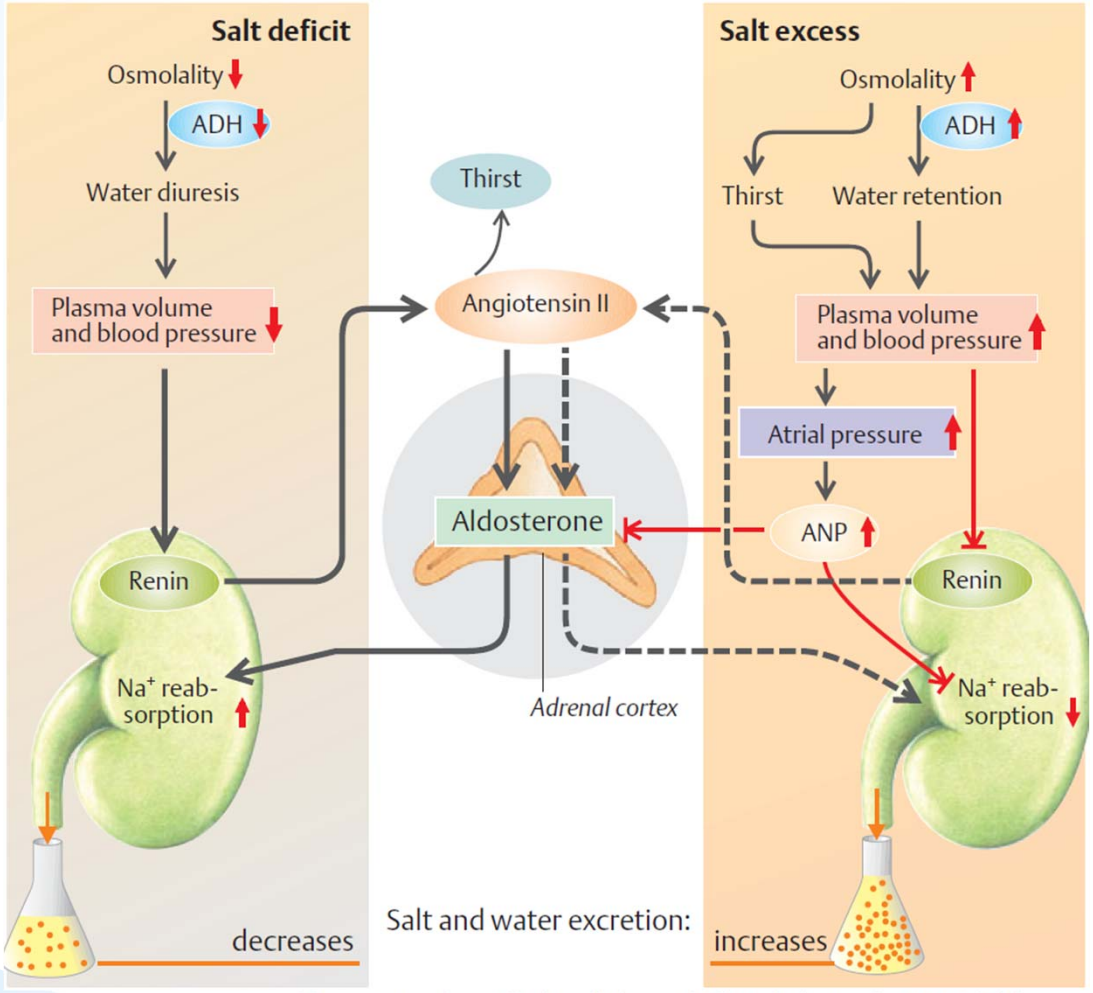
# Humoral Regulation of Body Fluids

## *Salt Homeostasis*

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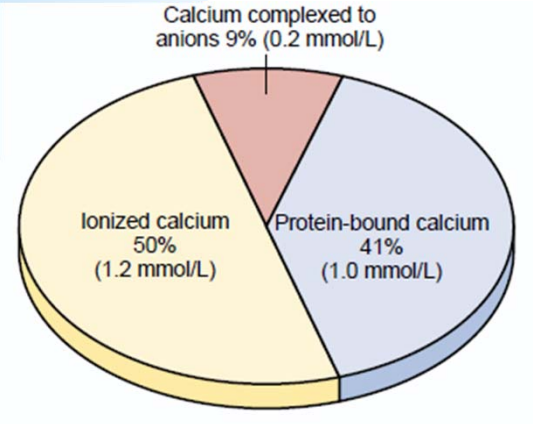
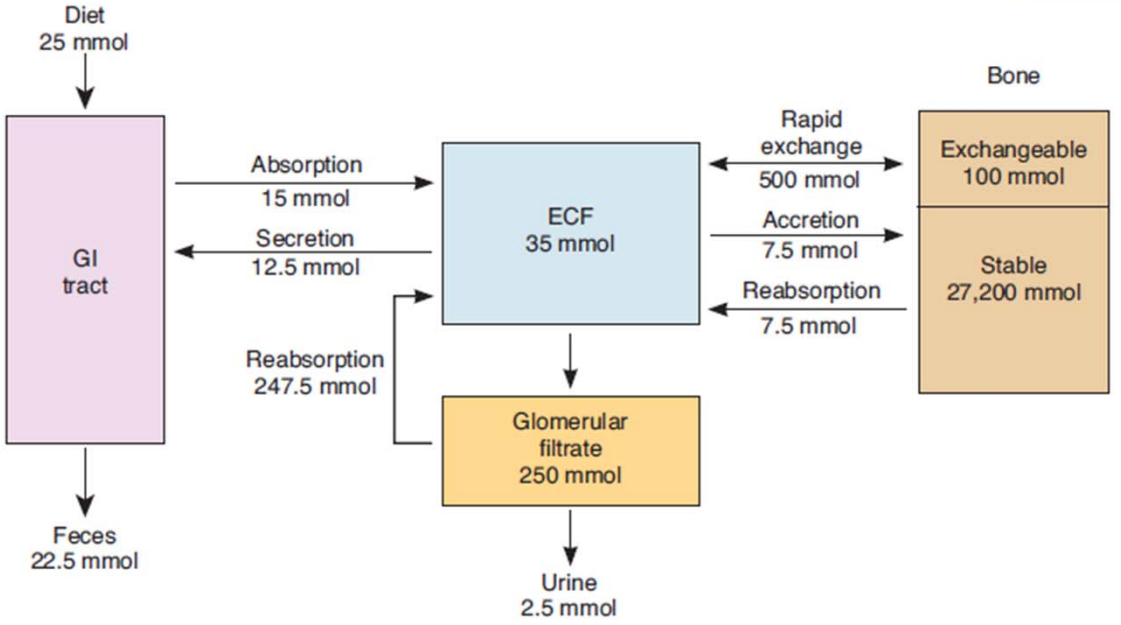
# Humoral Regulation of Body Fluids

## *Calcium in the Body*




*Guyton & Hall. Textbook of Medical Physiology.*




*Ganong´s Review of Medical Physiology*

hypocalcemia

hypercalcemia

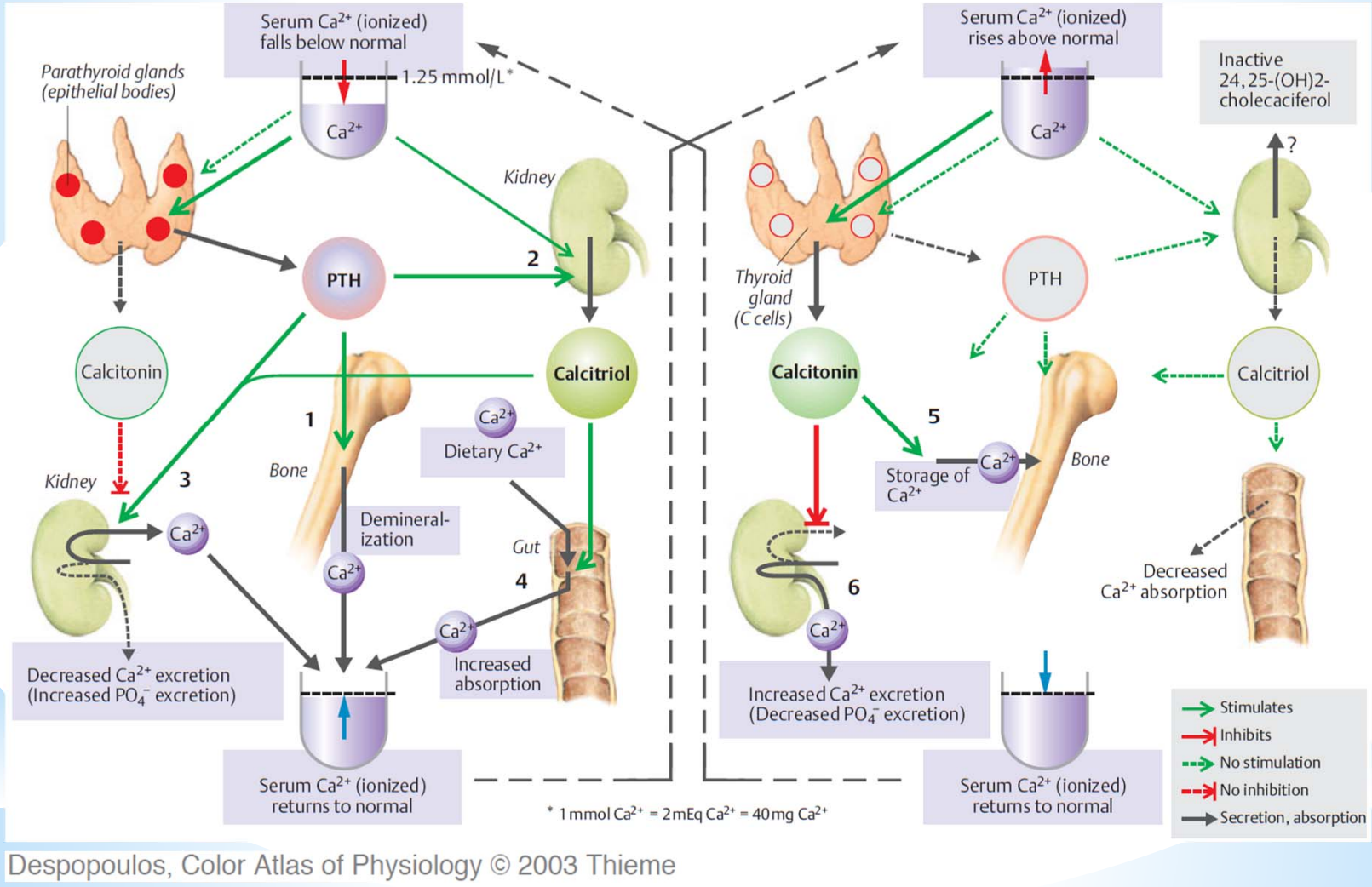
# Humoral Regulation of Body Fluids

## *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 $H^+$:

     buffer + $H^+$ $\rightleftharpoons$ H - buffer

     $\uparrow[H^+]$ direction to the right favoured till free buffer is available

     $\downarrow[H^+]$ direction to the left favoured, $H^+$ released

2) Lungs
   - fast regulation (minutes even hours)
   - elimination of $CO_2$ from the body ($H_2CO_3 \rightarrow H_2O + CO_2$)

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 $HCO_3^-$ still filtered in the glomerulus

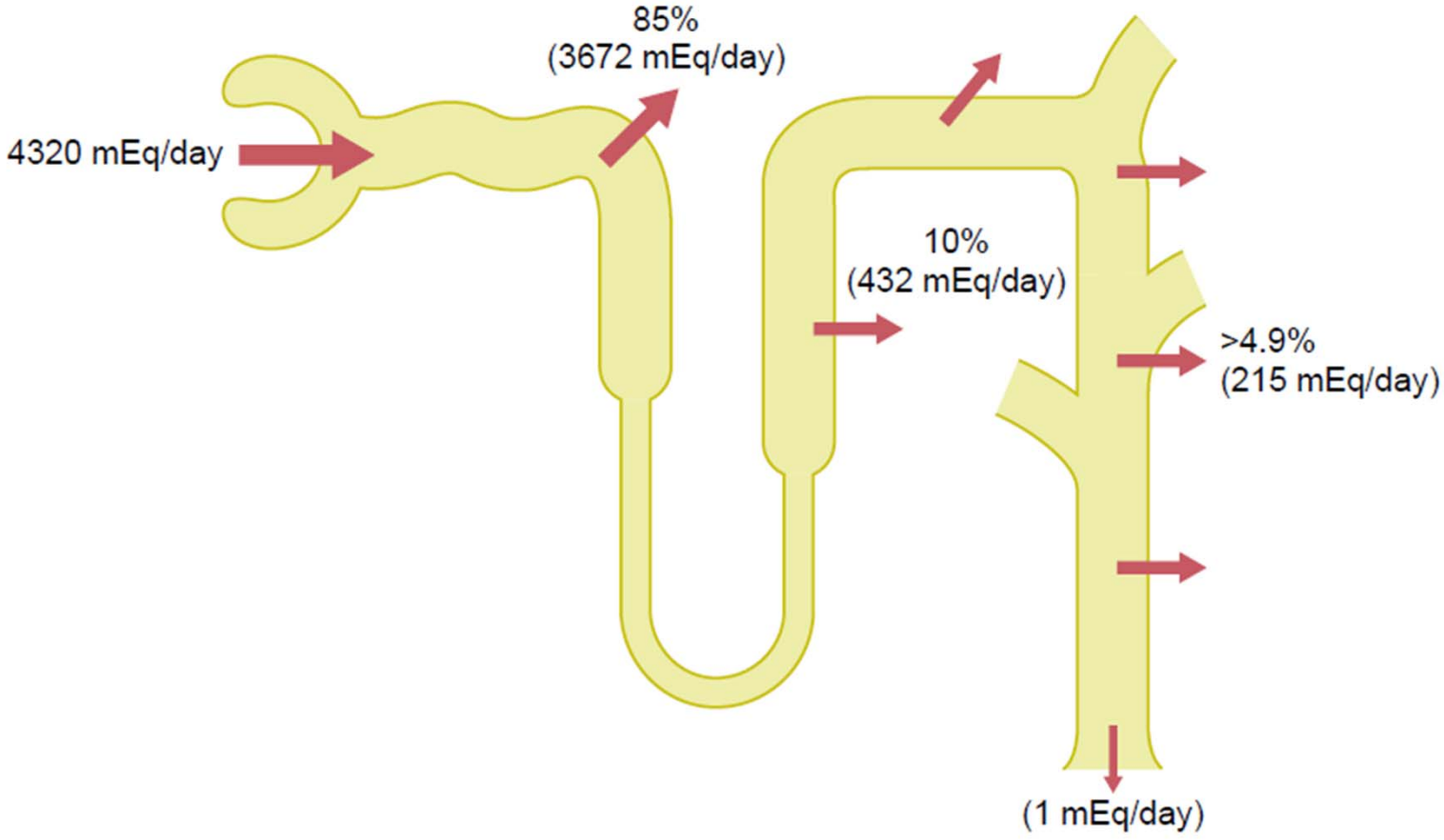
  GFR 180 l/day, $[HCO_3^-]_{plasma}$ 24 mEq/l $\rightarrow$ 4320 mEq $HCO_3^-$ filtered per day – almost all ordinarily reabsorbed
- a high amount of $H^+$ still secreted in renal tubules

  about 80 mEq of non-volatile acids are formed in the course of metabolic processes per day – have to be excreted by kidneys
- filtered $HCO_3^-$ / secreted $H^+$

# Acid-Base Balance and its Regulation

*Regulation of Acid-Base Balance by Kidneys*

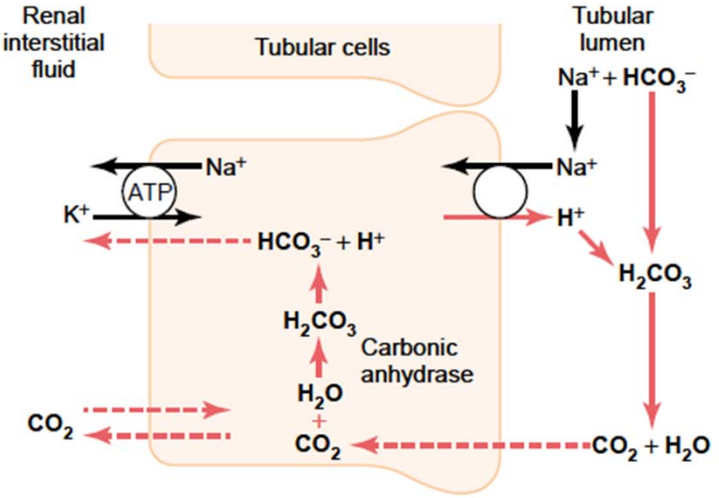
1) Secretion of $H^+$
2) Reabsorption of $HCO_3^-$



# 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:

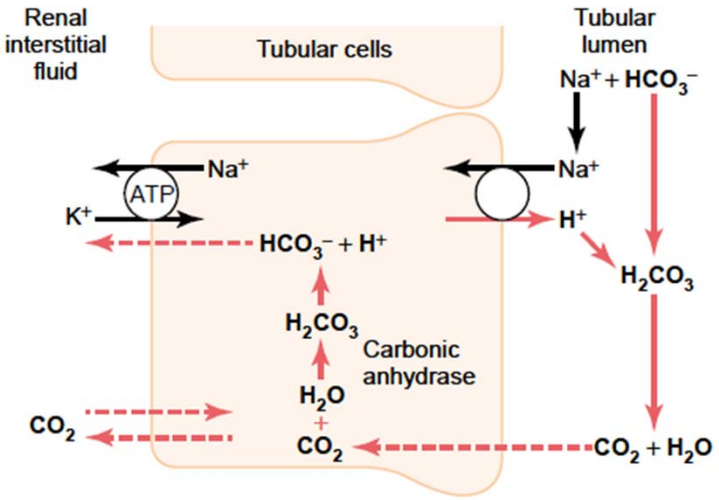
- $Na^+$-$HCO_3^-$ co-transport
  (the proximal tubule)
- $Cl^-$-$HCO_3^-$ exchanger
  (the end of proximal tubule and the following parts of tubulus except for the thin loop of Henle)

# Acid-Base Balance and its Regulation

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

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

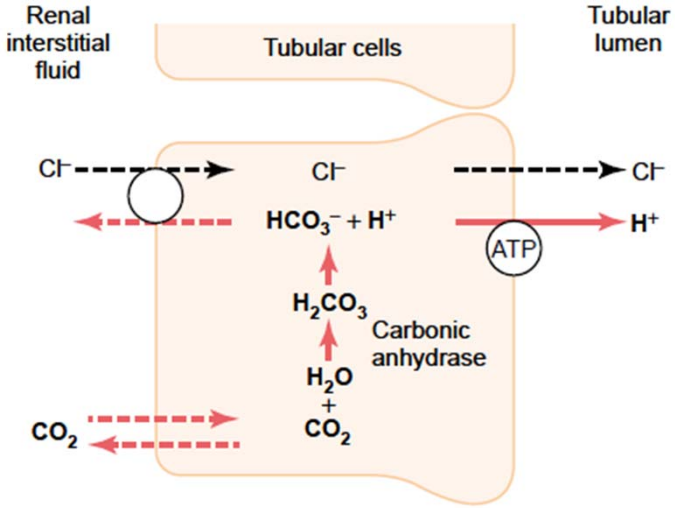
- in the proximal tubule, thick loop of Henle and at the beginning of the distal tubule




$Na^+/H^+$-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)

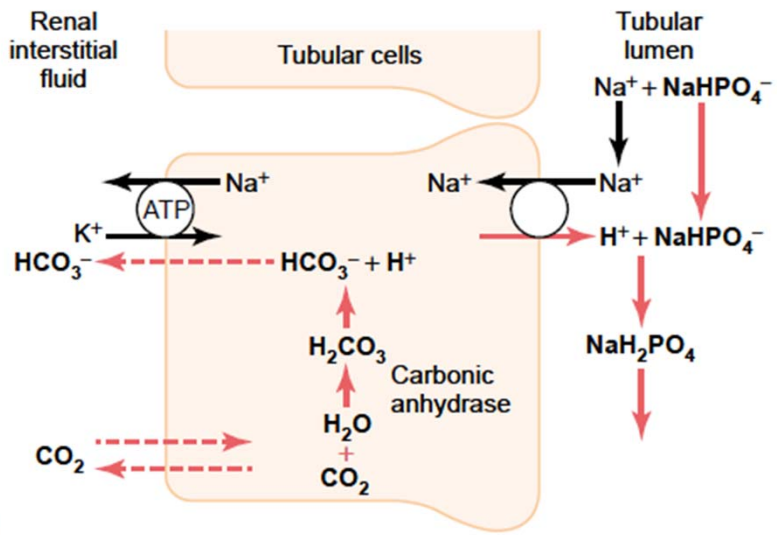
*acidification of urine*

# Acid-Base Balance and its Regulation

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

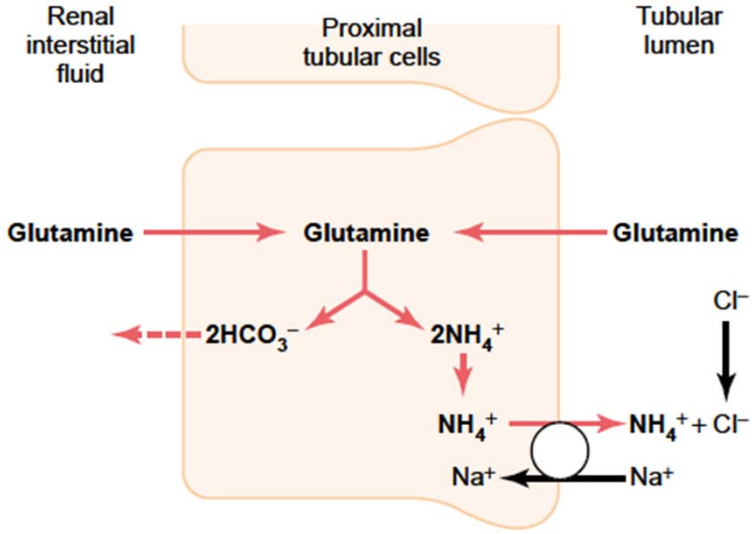
1) Secretion of $H^+$
2) Reabsorption of $HCO_3^-$
3) Production of $HCO_3^-$ *de novo*

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




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

❖ Ammonium buffer ($NH_3$, $NH_4^+$)



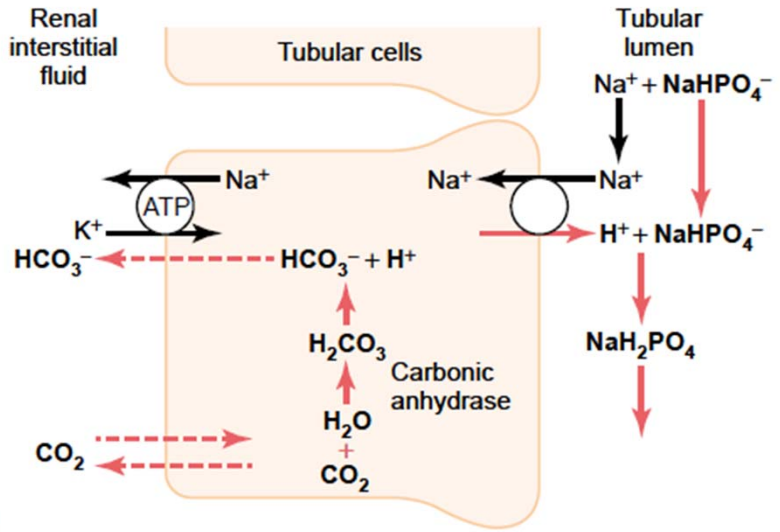

$NH_4^+$ originates from glutamine – the proximal tubule, thick ascending loop of Henle and distal tubule

# 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 ⇒ their concentration in the tubular fluid gradually rises

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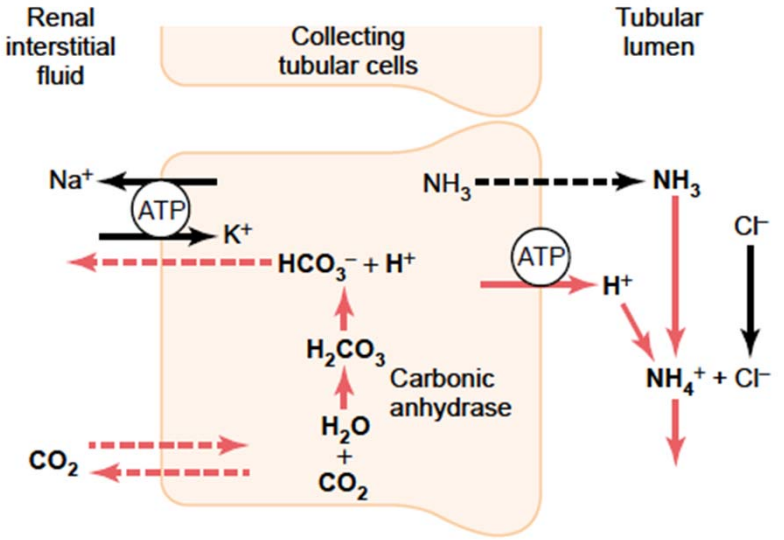



the collecting duct (permeable for $NH_3$ but far less for $NH_4^+$ - excreted by urine)

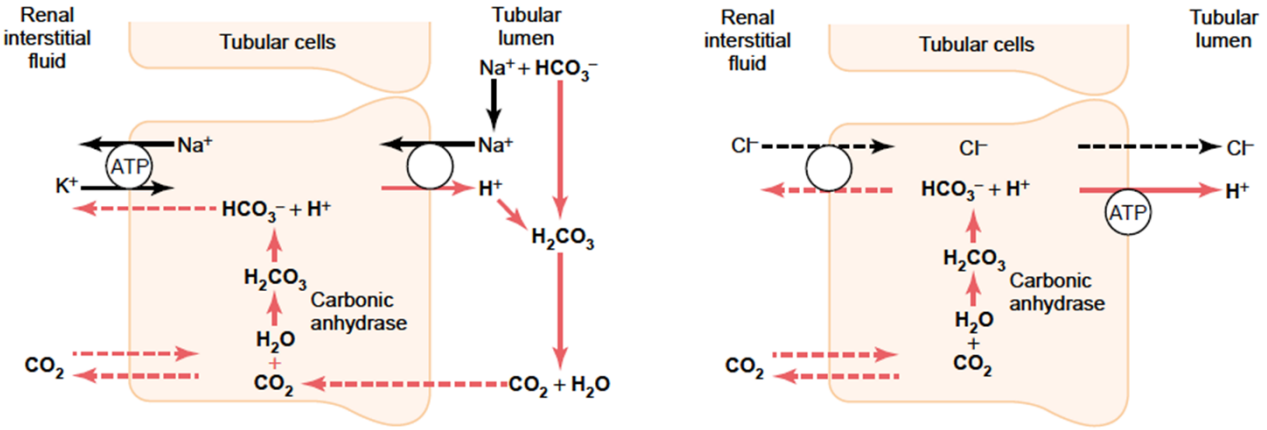
50% of $H^+$ secretion and $HCO_3^-$ formed *de novo*!

# Acid-Base Balance and its Regulation

*Regulation of Acid-Base Balance by Kidneys*

## Regulation of $H^+$ secretion

↑ - ↑ **$pCO_2$ in ECF** (respiratory acidosis; direct stimulation due to ↑ formation of $H^+$ in tubular cells)




- ↓ **pH in ECF** (respiratory or metabolic acidosis)
- ↑ **secretion of aldosteron** (stimulates $H^+$ 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 $H^+$ secretion

**Factors That Increase or Decrease $H^+$ Secretion and $HCO_3^-$ Reabsorption by the Renal Tubules**

| Increase $H^+$ Secretion and $HCO_3^-$ Reabsorption | Decrease $H^+$ Secretion and $HCO_3^-$ Reabsorption |
|---|---|
| ↑ $P_{CO_2}$ | ↓ $P_{CO_2}$ |
| ↑ $H^+$, ↓ $HCO_3^-$ | ↓ $H^+$, ↑ $HCO_3^-$ |
| ↓ Extracellular fluid volume | ↑ Extracellular fluid volume |
| ↑ Angiotensin II | ↓ Angiotensin II |
| ↑ Aldosterone | ↓ Aldosterone |
| Hypokalemia | Hyperkalemia |

RAS

↑ activity of $Na^+/H^+$ antiport

↑ activity of $H^+$ ATPase

↓

tendency to alkalosis

# Acid-Base Balance and its Regulation

*Regulation of Acid-Base Balance by Kidneys*

## Acidosis – correction by kidneys

$$\downarrow \; pH = 6.1 + \log \frac{HCO_3^-}{0.03 \times P_{CO2}} \; \downarrow$$

- metabolic acidosis: due to $\downarrow HCO_3^-$
  renal correction : $\downarrow HCO_3^-$ in ECF $\rightarrow \downarrow$ filtered $HCO_3^- \rightarrow$ complete reabsorption of $HCO_3^-$ + its formation *de novo* ($HCO_3^-$ not excreted) + $\uparrow H^+$ excretion $\rightarrow$ pH normalization
- respiratory acidosis: due to $\uparrow P_{CO2}$ (hypoventilation)
  renal correction: $\uparrow P_{CO2}$ in ECF $\rightarrow \uparrow P_{CO2}$ in tubular cells $\rightarrow \uparrow$ formation of $H^+$ and $HCO_3^-$ in tubular cells $\rightarrow \uparrow H^+$ secretion + $\uparrow HCO_3^-$ reabsorption $\rightarrow$ pH normalization

# Acid-Base Balance and its Regulation

*Regulation of Acid-Base Balance by Kidneys*

## Alkalosis – correction by kidneys

$$\uparrow \; pH = 6.1 + \log \frac{HCO_3^-}{0.03 \times P_{CO2}} \; \uparrow$$

- metabolic alkalosis: due to $\uparrow HCO_3^-$

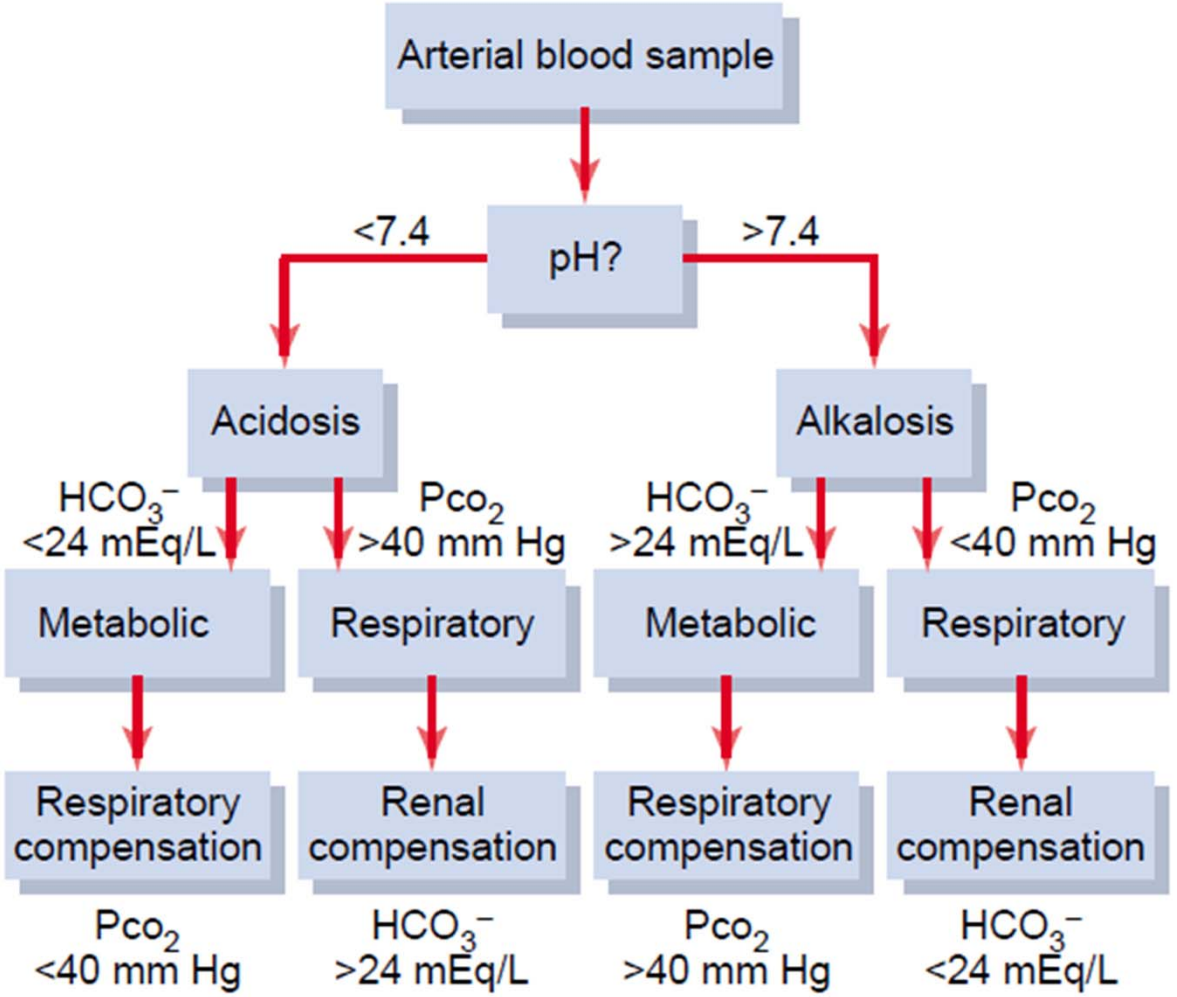
  renal correction: $\uparrow HCO_3^-$ in ECF $\rightarrow \uparrow$ filtered $HCO_3^- \rightarrow$ incomplete $HCO_3^-$ reabsorption (lack of H+) $\rightarrow \uparrow HCO_3^-$ excretion by urine $\rightarrow$ pH normalization

- respiratory alkalosis : due to $\downarrow P_{CO2}$ (hyperventilation)

  renal correction: $\downarrow P_{CO2}$ in ECF $\rightarrow \downarrow P_{CO2}$ in tubular cells $\rightarrow \downarrow$ formation of $H^+$ and $HCO_3^-$ in tubular cells $\rightarrow \downarrow H^+$ secretion + $\downarrow HCO_3^-$ reabsorption $\rightarrow$ pH normalization

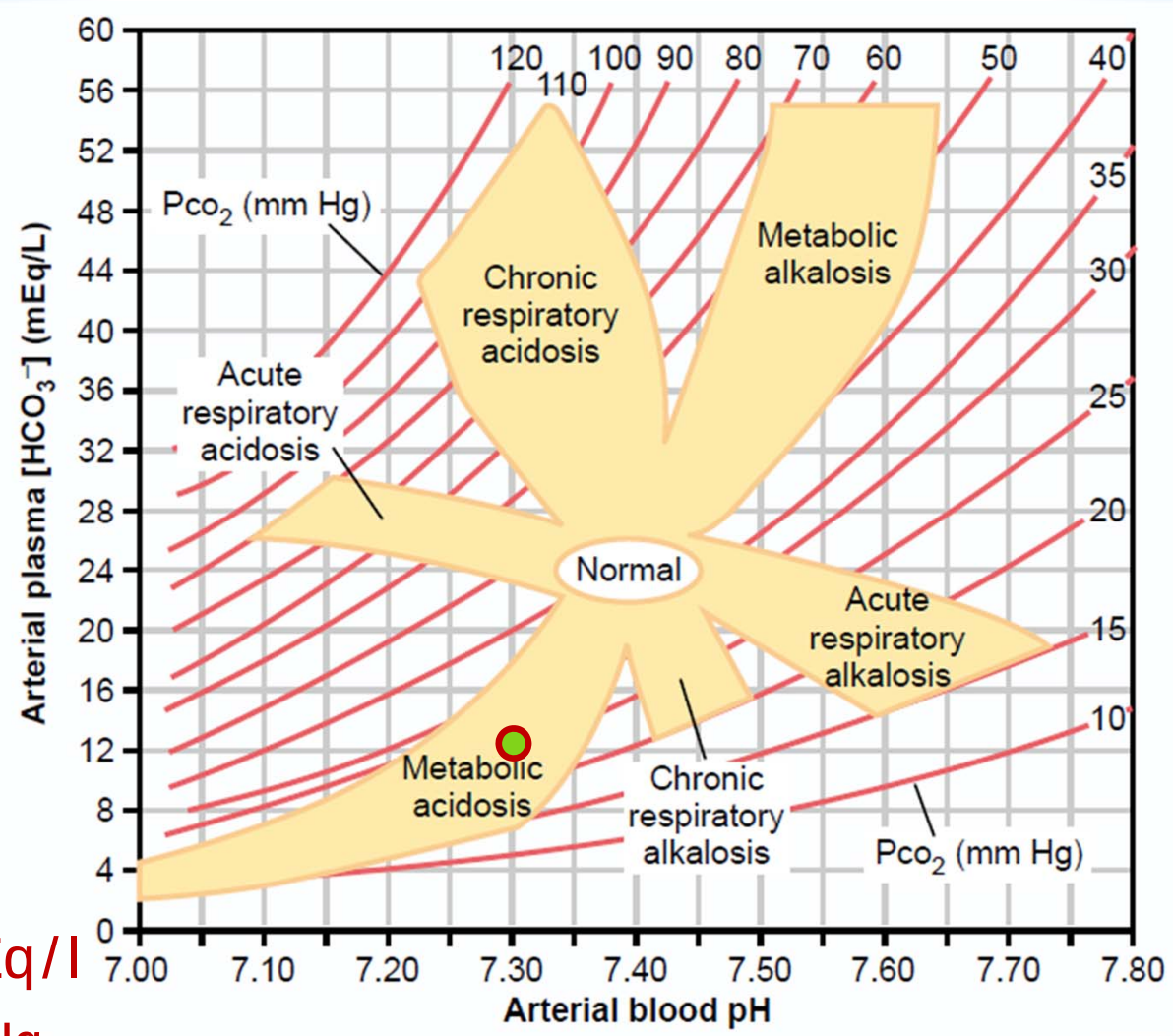
# Acid-Base Balance and its Regulation

## *Diagnostics*



# Acid-Base Balance and its Regulation

## *Diagnostics*




pH: 7,3

$HCO_3^-$: 12 mEq/l

$P_{CO2}$: 25 mmHg

# Acid-Base Balance and its Regulation

## *Diagnostics - Siggaard–Andersen nomogram*