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

A3. Compartmentalization of body fluids
A4. Differences between intra- and extracellular fluids

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

B73. Bone formation and resorption. Regulation of calcaemia.

A33. Homeostasis (acid-base balance)

Homeostasis

= maintainance of stable conditions in the internal body environment

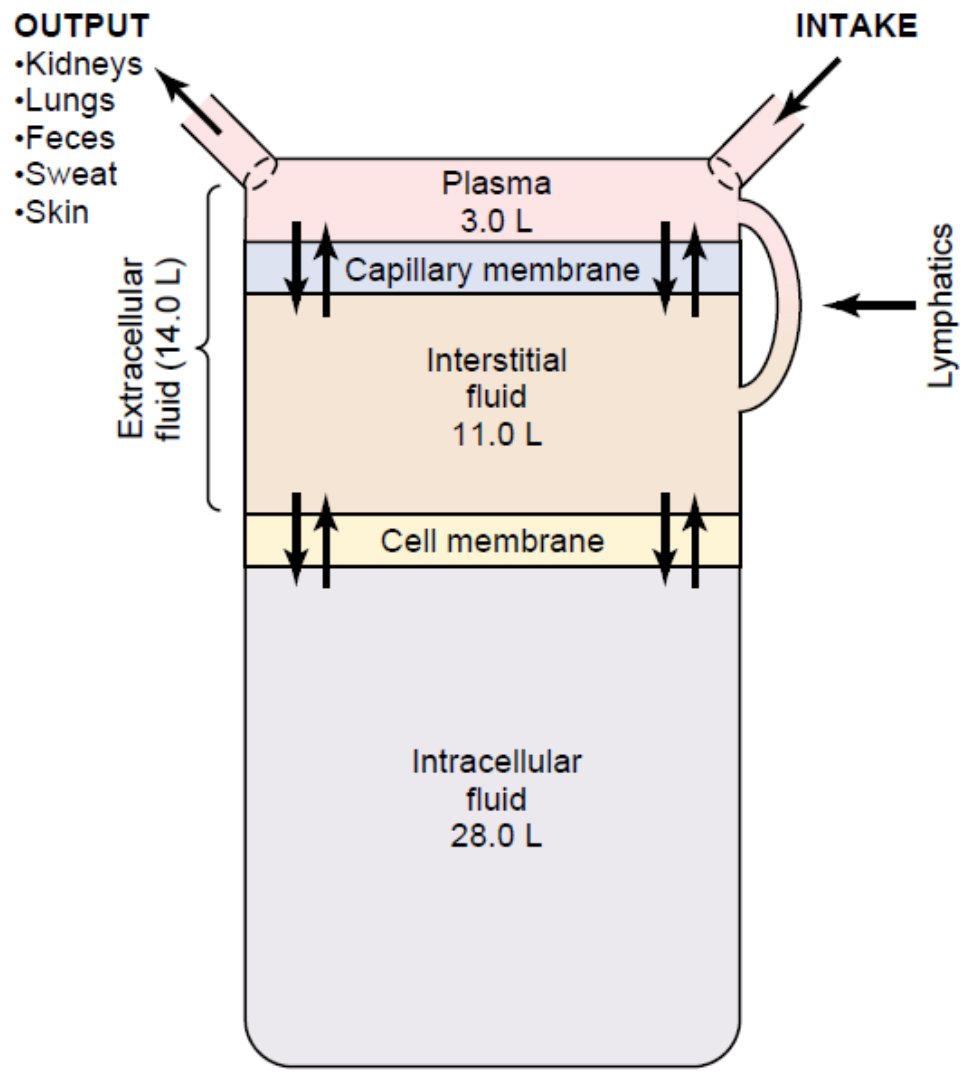
Maintainance of Constant Volume and Composition of Body Fluids

Maintainance of Acid-Base Balance

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

Body Fluids – Types and Volumes

Body fluids occupy ~60% of the body weight.



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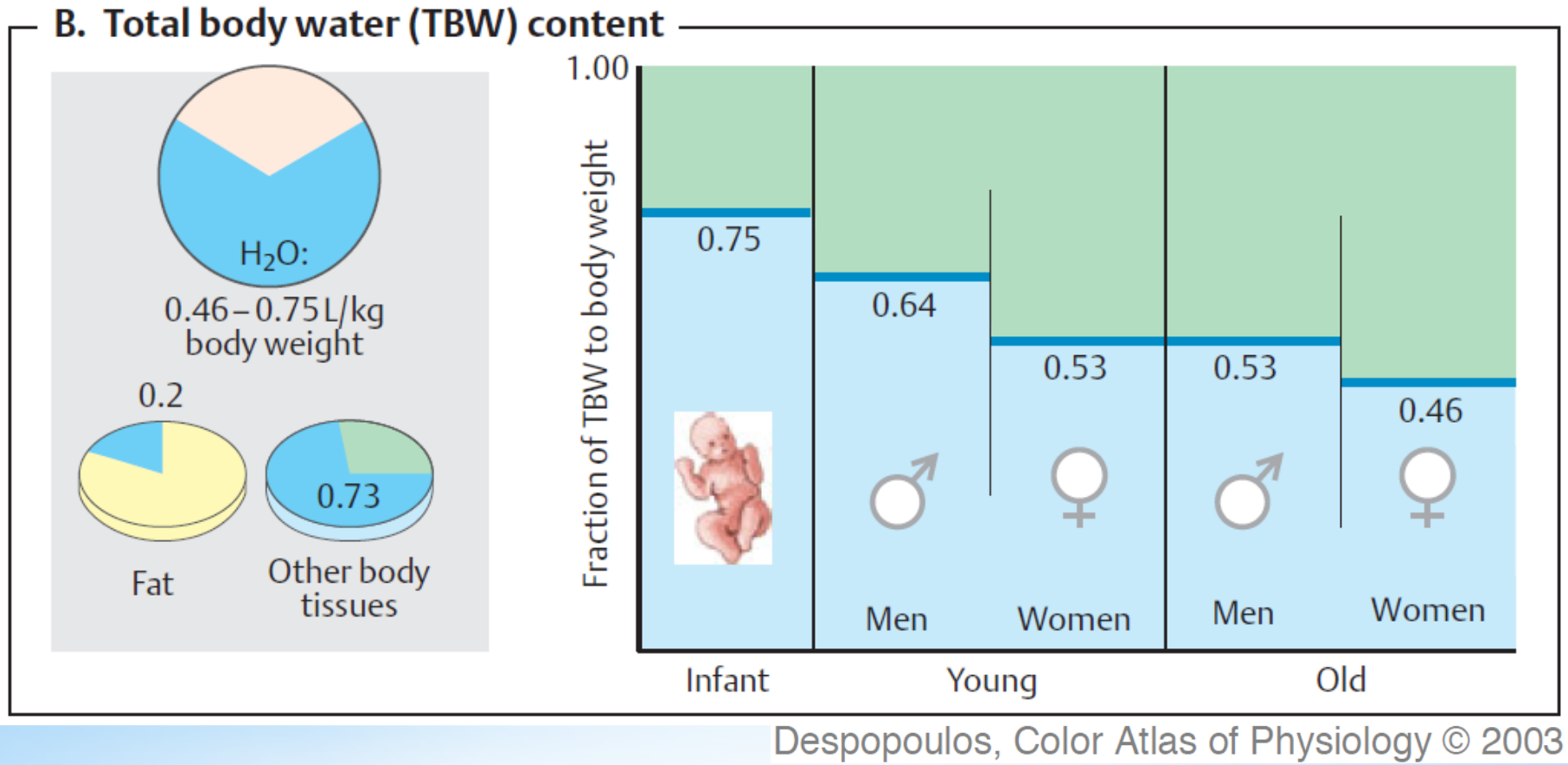
Body Fluids – Types and Volumes



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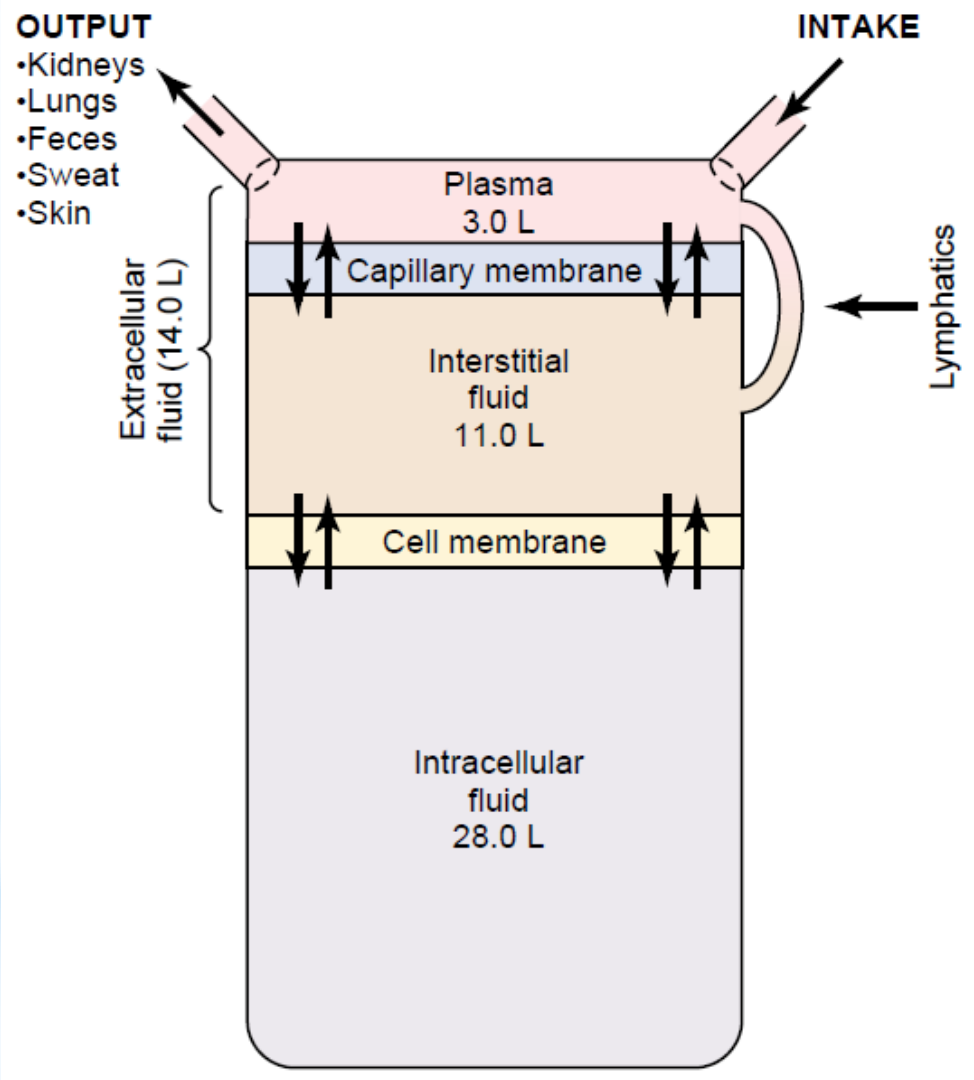
Body Fluids – Types and Volumes

Body fluids occupy ~60% of the body weight.

Transcellular fluid (1-2 l) – special type of ECF. (peritoneal, pericardial, synovial, cerebrospinal and intraocular fluid)



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5% of the body weight

15% of the body weight

40% of the body weight

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

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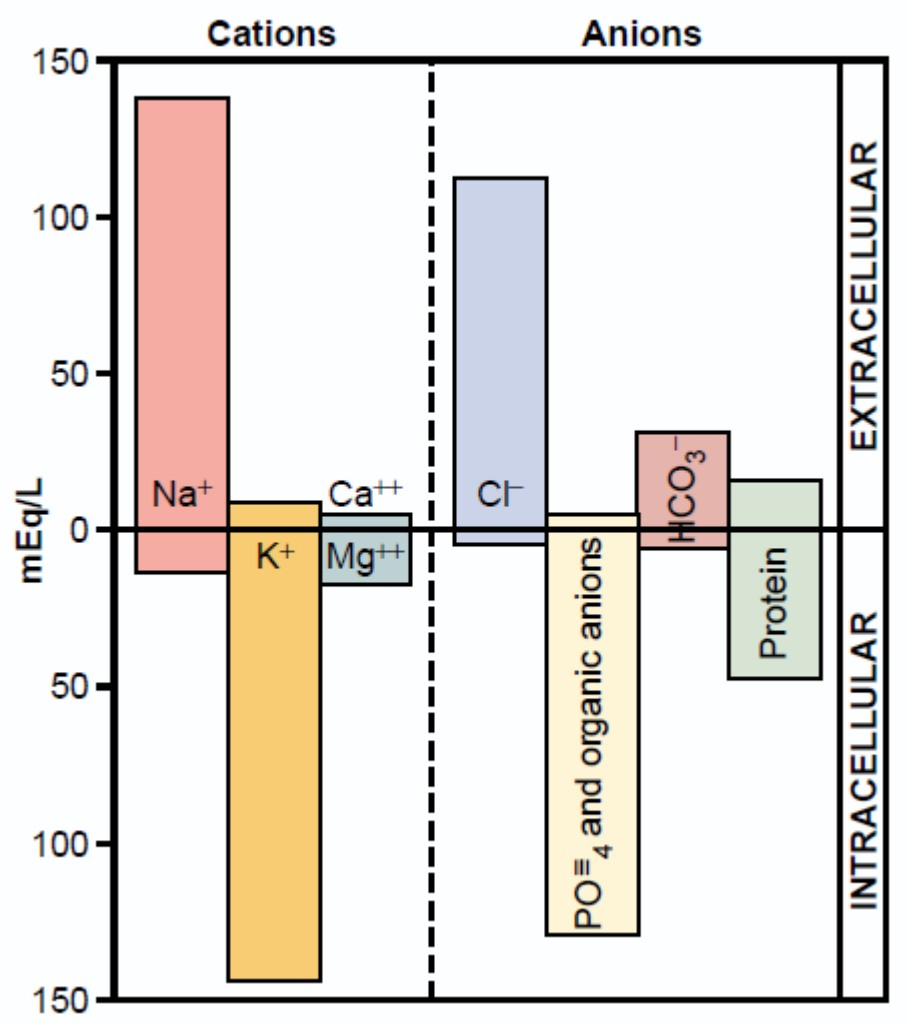
Body Fluids – Composition

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

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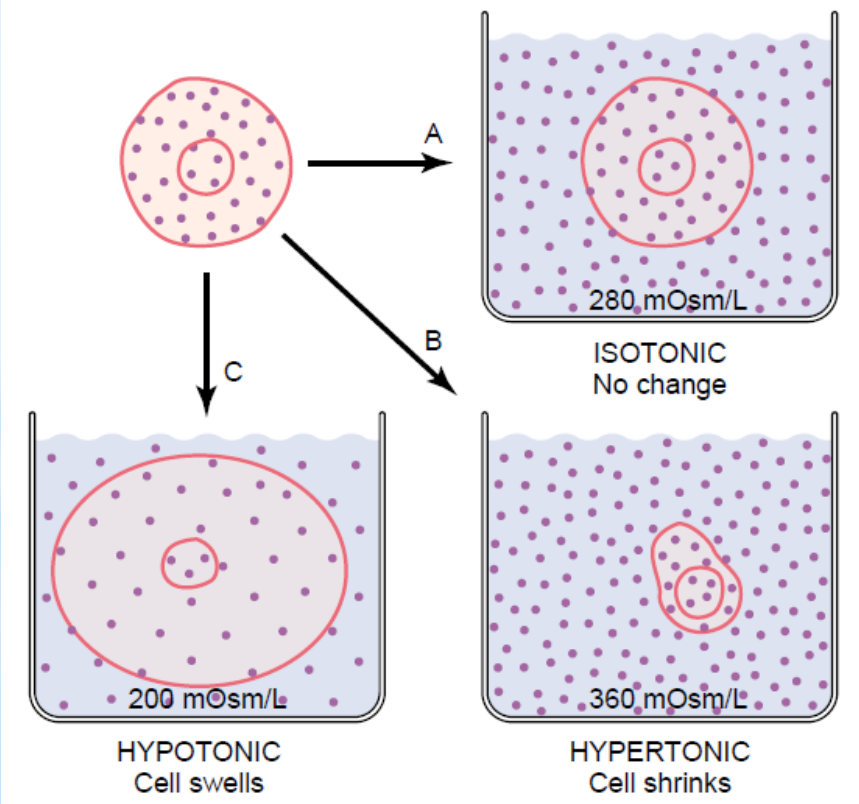
Body Fluids – Composition

osmolality 285 mosm/kg H_2O

↑ ↑ NaCl intake, loss of water → water leaves cells (shrinking of cells)

↓ ↓ NaCl intake, ↑ water input → water sucked into cells by osmosis (cell edema)



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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

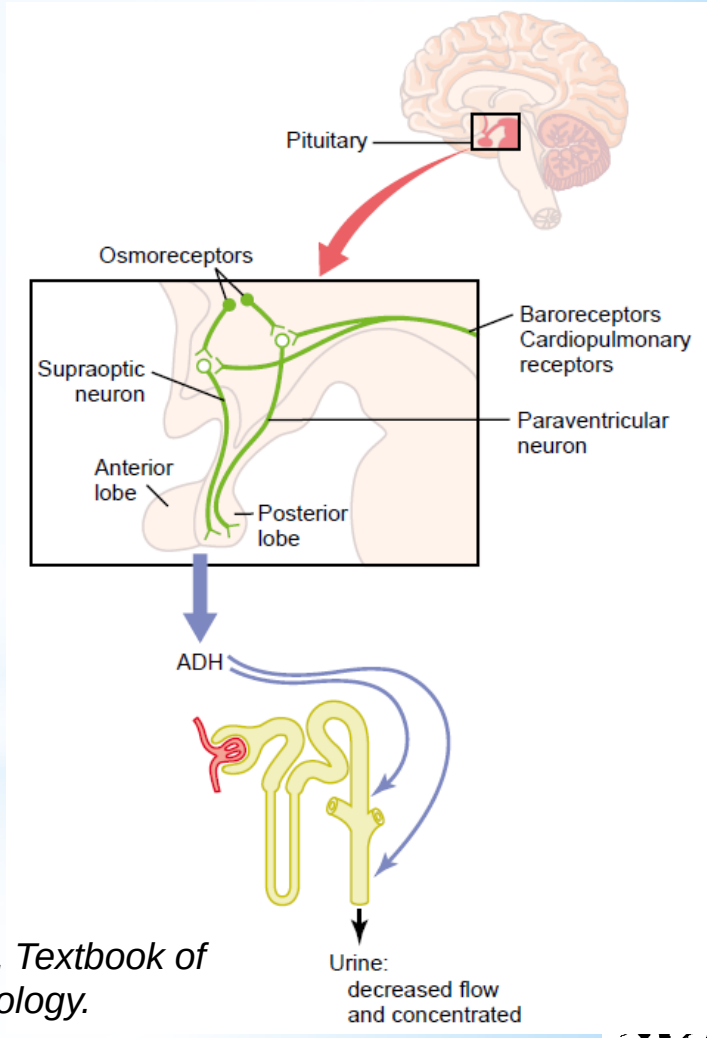
(vasopressin)

- effects:

→ water reabsorption in kidneys (collecting duct, aquaporin 2)

→ control of blood pressure (water reabsorption, vasoconstriction)

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



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Humoral Regulation of Body Fluids

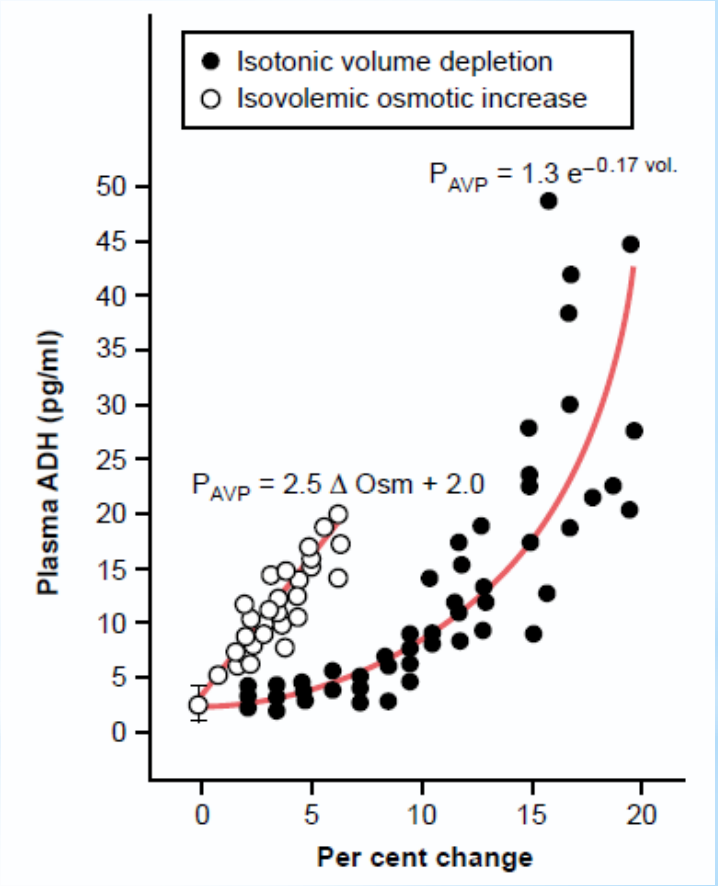
Antidiuretic Hormone

(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

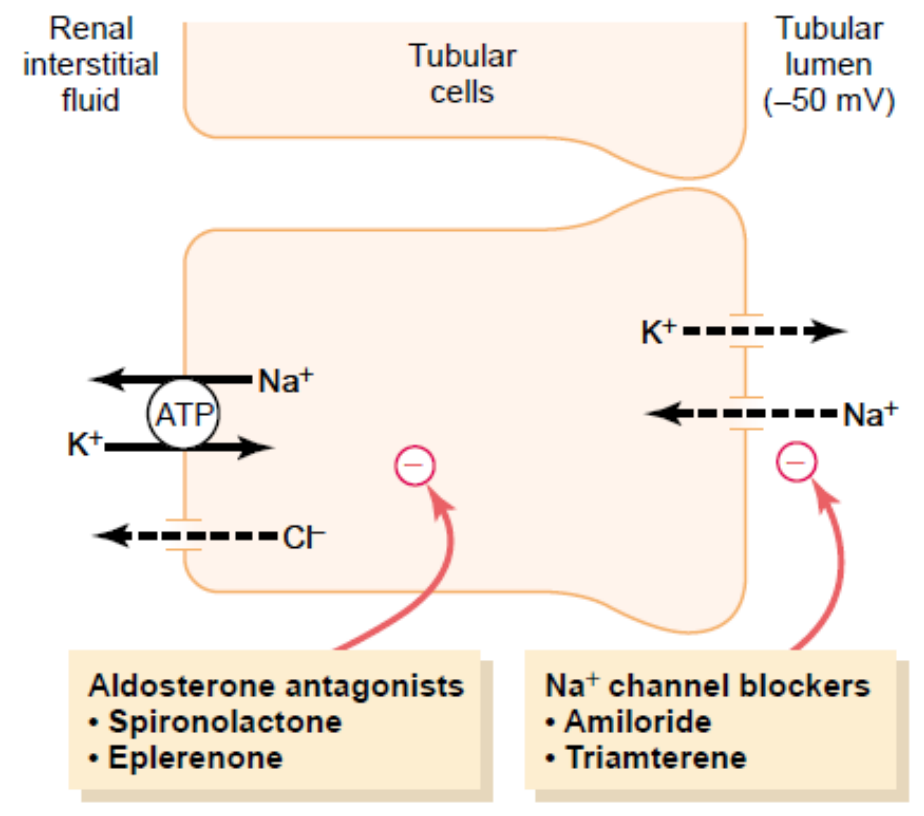
- the most important steroid with the mineralocorticoid effect

- mechanism of action:

  binding to the mineralocorticoid receptor → binding of the hormone-receptor complex to DNA → mRNA → synthesis of proteins:

  - namely Na^+/K^+-ATPase
  - ↑ number of amiloride-inhibited Na^+-channels in the membrane of target cells

Start of the effect even 10 – 30 min after release of the hormone!



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Humoral Regulation of Body Fluids

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  - namely Na^+/K^+-ATPase
  - ↑ number of amiloride-inhibited Na^+-channels in the membrane of target cells
  - ↑ activity of H^+-pump in collecting ducts of the renal cortex
  - ↑ activity of Na^+/H^+-antiport in both distal and proximal parts of nephrons

  Start of the effect even 10 – 30 min after release of the hormone!

Humoral Regulation of Body Fluids

Aldosteron

- the most important steroid with the mineralocorticoid effect

- effects:

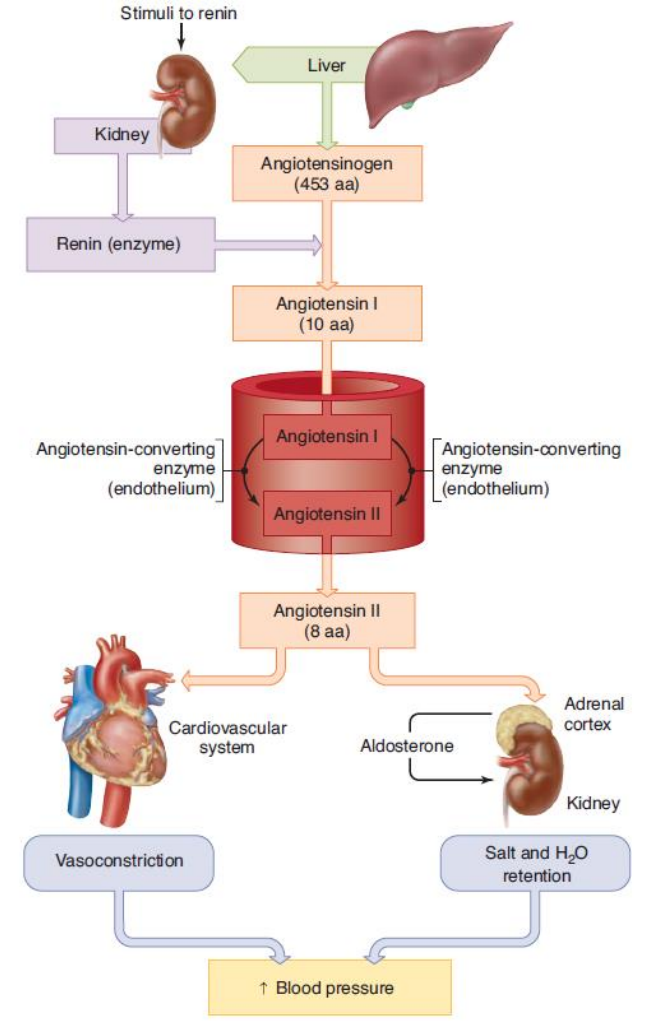
  → ↑ Na^+ reabsorption from urine, sweat, saliva, gastric juice
  → ↑ K^+ urine excretion, ↑ acidity of urine (exchange for Na^+)
  → ↑ K^+ content and ↓ Na^+ content in muscle and brain cells

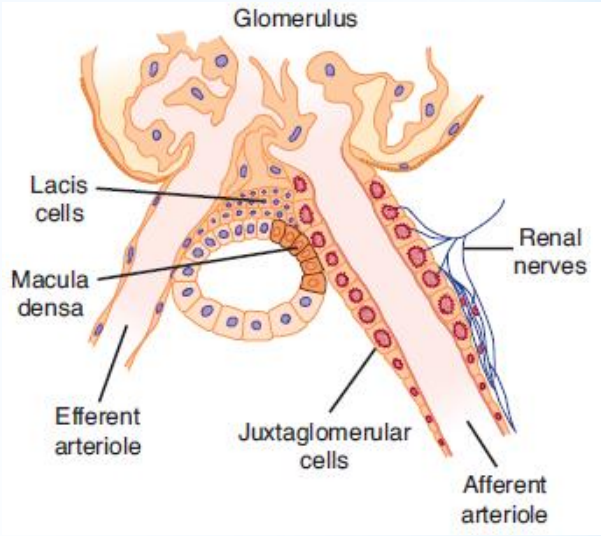
- regulation of its secretion:

  - ACTH from the adenohypophysis (transient effect)
  - direct stimulatory effect of ↑ plasmatic concentration of K^+ (even a small change – even after a meal rich for K^+ - fruit, vegetable) and ↓ Na^+ (only a big change)
  - renin-angiotensine-aldosteron system

Humoral Regulation of Body Fluids

Renin-Angiotensine-Aldosteron System





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Humoral Regulation of Body Fluids

Aldosteron

- the most important steroid with the mineralocorticoid effect

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  - ACTH from the adenohypophysis (a transient effect)
  - direct stimulatory effect of ↑ plasmatic concentration of K^+ (even a small change – even after a meal rich for K^+ - fruit, vegetable) and ↓ Na^+ (only a big change)
  - renin-angiotensine-aldosteron system
  - atrial natriuretic peptide (inhibition of renin secretion, ↓ reactivity of *zona glomerulosa* to angiotensine II)
  - other hormones of adenohypophysis (besides ACTH; 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

→ heavy K^+ depletion
→ hypertension
→ ECF expansion (without edemas, without marked hypernatremia – redundant salts released by the so called escape phenomena)

→ at a prolonged K^+ depletion:
- →renal damage → polyuria (the hypocalemic nephropathy)
- →muscle weekness
- →metabolic alkalosis → ↓ plasmatic concentration of Ca^{2+} → latent or fully developed tetany
- →glucose intolerance

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)
- receptors (ANPR-A – the highest affinity to ANP, ANPR-B – CNP, ANPR-C – all NP)
- short half-life

- secreted by atrial cardiomyocytes, found also in the brain

Humoral Regulation of Body Fluids

Atrial Natriuretic Peptide

- one of natriuretic peptides (BNP – cardiac ventricles, CNP – brain)

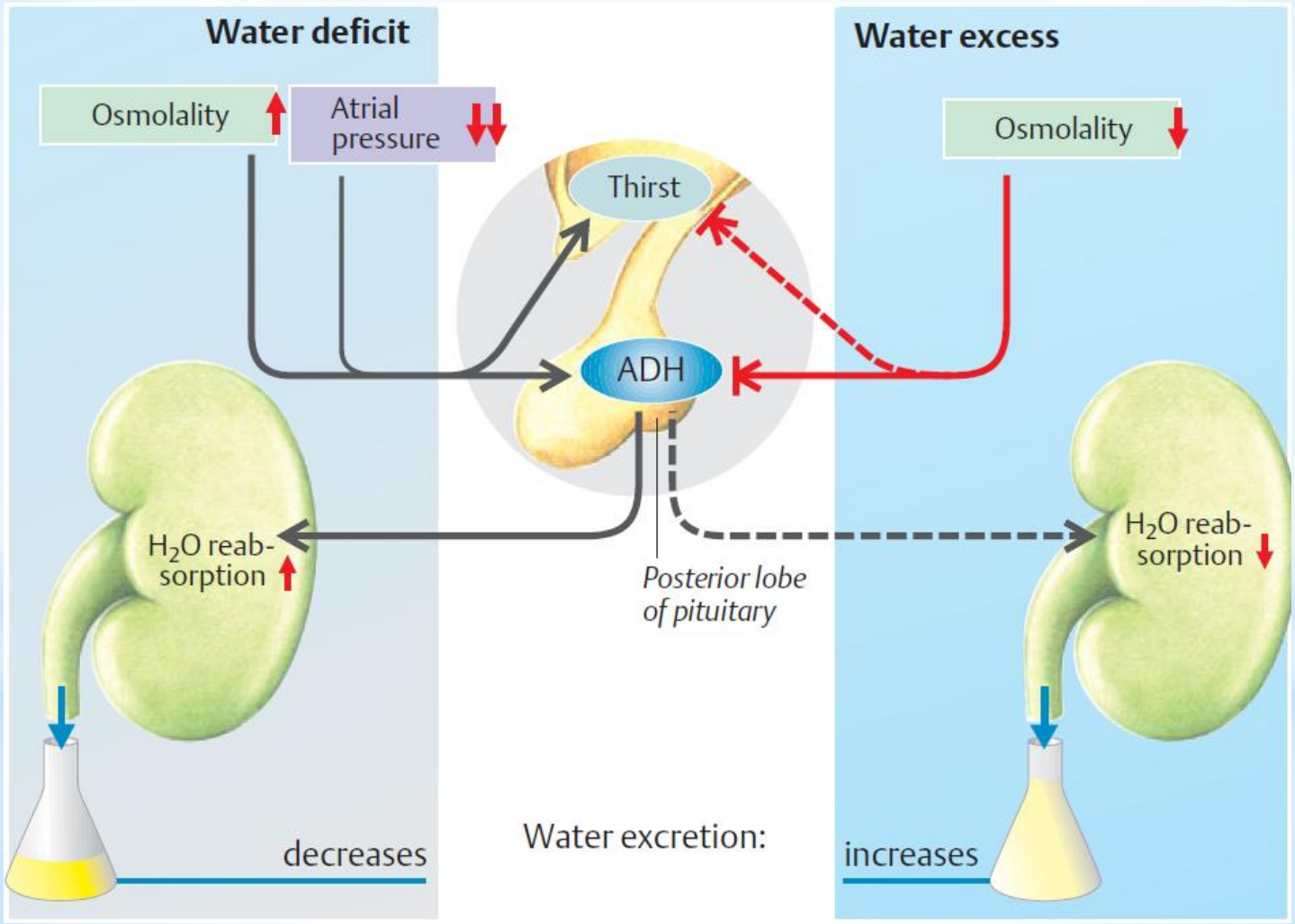
- effects (through ↑ cGMP): → ↓ **BP** (also through the brain stem)
  - → natriuresis (1. ↑ GFR – increased area for the filtration through relaxation of mesangial cells, 2. ↑ Na^+ excretion – decrease tubular Na^+ reabsorption)
  - → ↓ reactivity of vascular smooth muscles for vasocontrictive substances
  - → inhibition of renin secretion, ↓ reactivity of *zona glomerulosa* for stimuli ↑ aldosteron secretion
  - → inhibition of ADH secretion → ↑ water excretion

- regulation of its secretion:
  - ↑ - ↑ ECF volume (atrial cells´ stretch at higher atrial filling)
  - ↓ - ↓ CVP at orthostasis

Humoral Regulation of Body Fluids

Water Homeostasis

water intoxication



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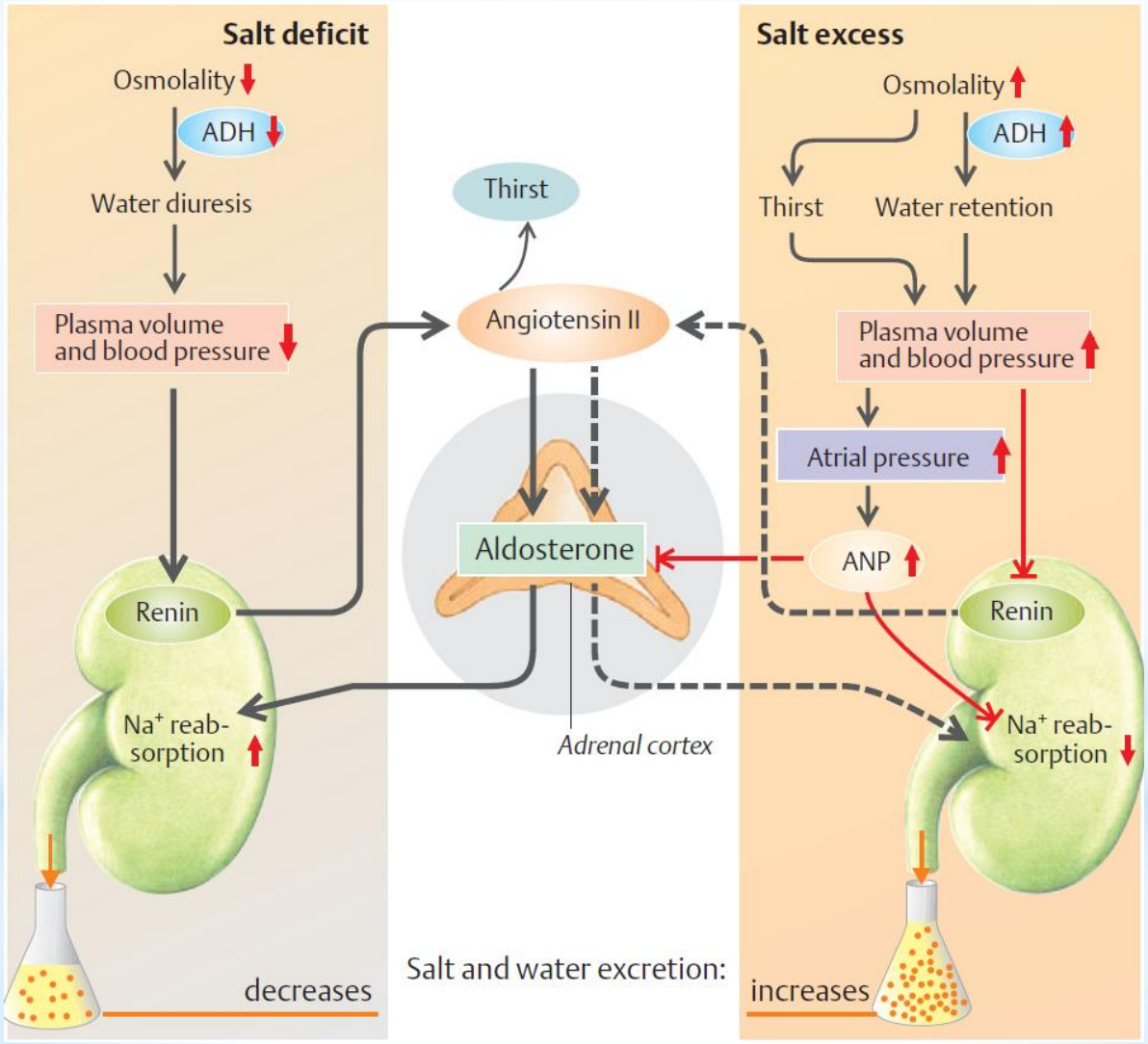
Humoral Regulation of Body Fluids

Salt Homeostasis



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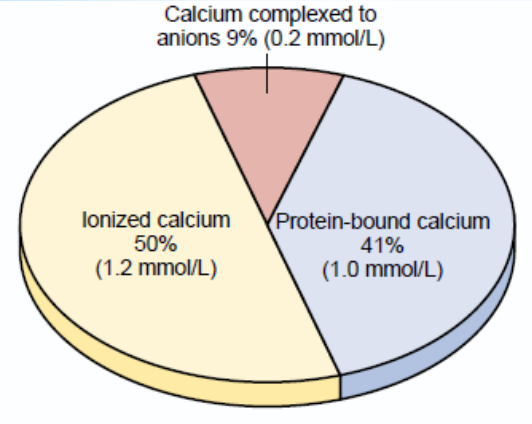
Humoral Regulation of Body Fluids

Calcium in the Body



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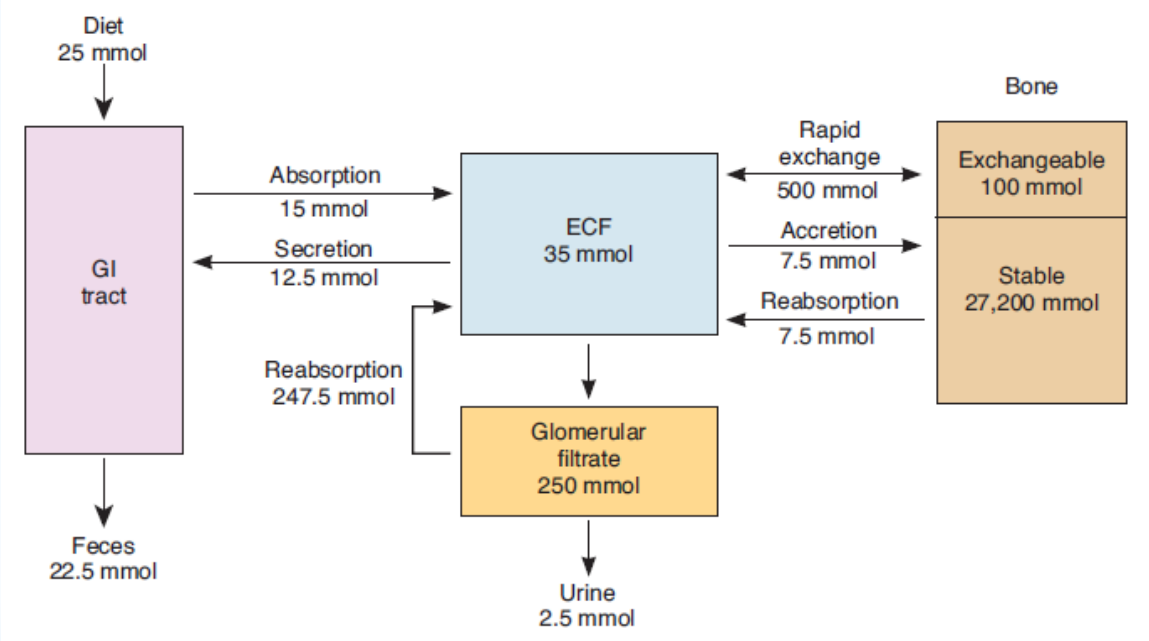

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hypocalcemia

hypercalcemia

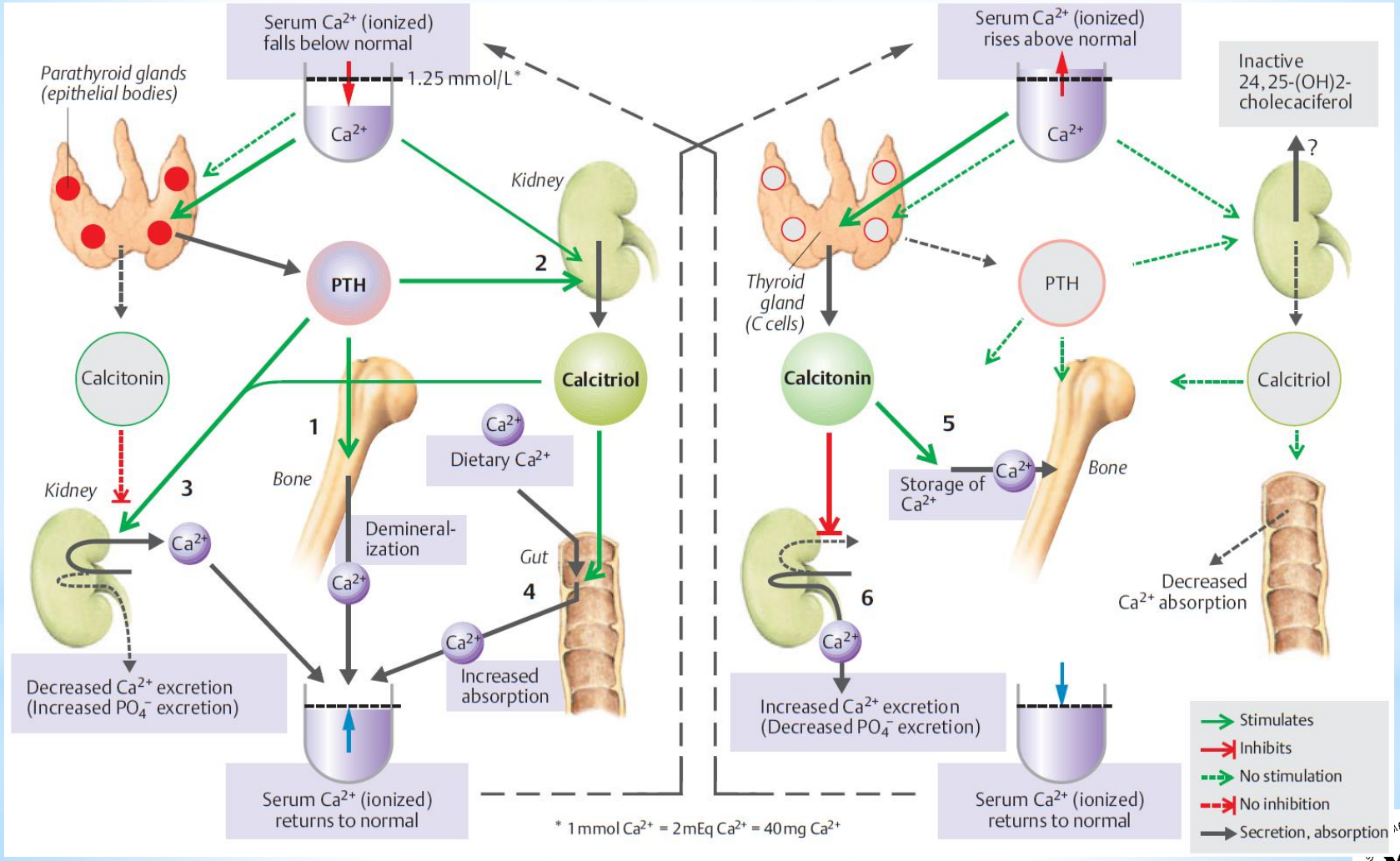
Humoral Regulation of Body Fluids

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 — substance releasing H^+ (*e.g.* $H_2CO_3 \rightarrow H^+ + HCO_3^-$)

base — substance binding H^+ (*e.g.* $HCO_3^- + H^+ \rightarrow H_2CO_3$; proteins)

$[H^+]$

- influences activity of almost all enzymatic systems
- very low compared to the concentration of other ions; $[H^+]$ = 40 nEq/l but for example $[Na^+]$ = 142 mEq/l
- thus, its changes has to be much smaller (3-5 nEg/l) $\Rightarrow$ precise regulation of $[H^+]$ is necessary!

Since $[H^+]$ is a very small number, its negative logarhithm is used:

$$pH = -\log [H^+] = -\log 0.000\,000\,040 = 7.4$$

The value of pH is thus inversely proportional to $[H^+]$.

Change of pH by 1 ~ change of $[H^+]$ 10-times bigger!

Acid-Base Balance and its Regulation

Physiological value of pH:

- arterial blood pH = 7.4
- venous blood pH = 7.35 (CO_2 from tissues)
- ICF pH = 6.0 – 7.4 (according to the cell type)
- urine pH = 4.5 – 8.0

The value of pH 6.8 – 8.0 can be survived for several hours!

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 Buffers

1) Bicarbonate buffer

- the most important buffer system
- weak acid H_2CO_3 and its salt $NaHCO_3$

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^- + Na^+$$

- the most powerful (despite not expected to be so powerful, pK = 6.1)

2) Phosphate buffer

- an important buffer system of the renal tubular fluid and of the intracellular fluid (high concentration + pH nearer to pK = 6.8)
- $H_2PO_4^-$, HPO_4^{2-}

3) Protein buffer

- an important buffer of an important buffer system of (conc. + pK)

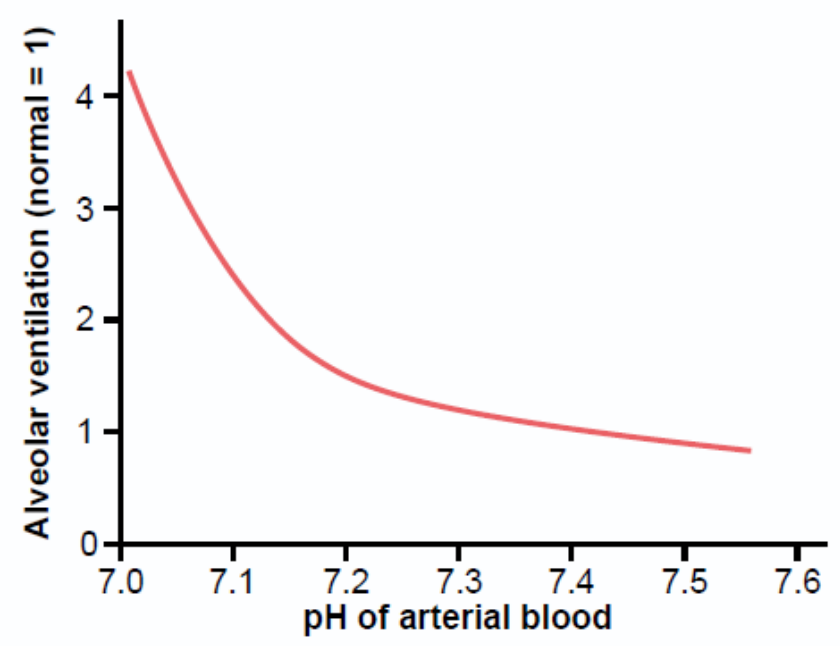
60 – 70% of the buffer capacity of body fluids sites in the cells and is dependent on proteins!

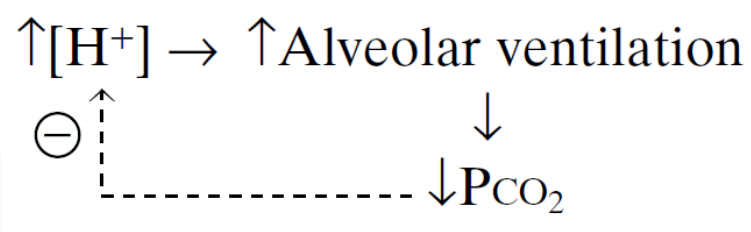
Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Lungs

- by the hyper- or hypoventilation

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





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

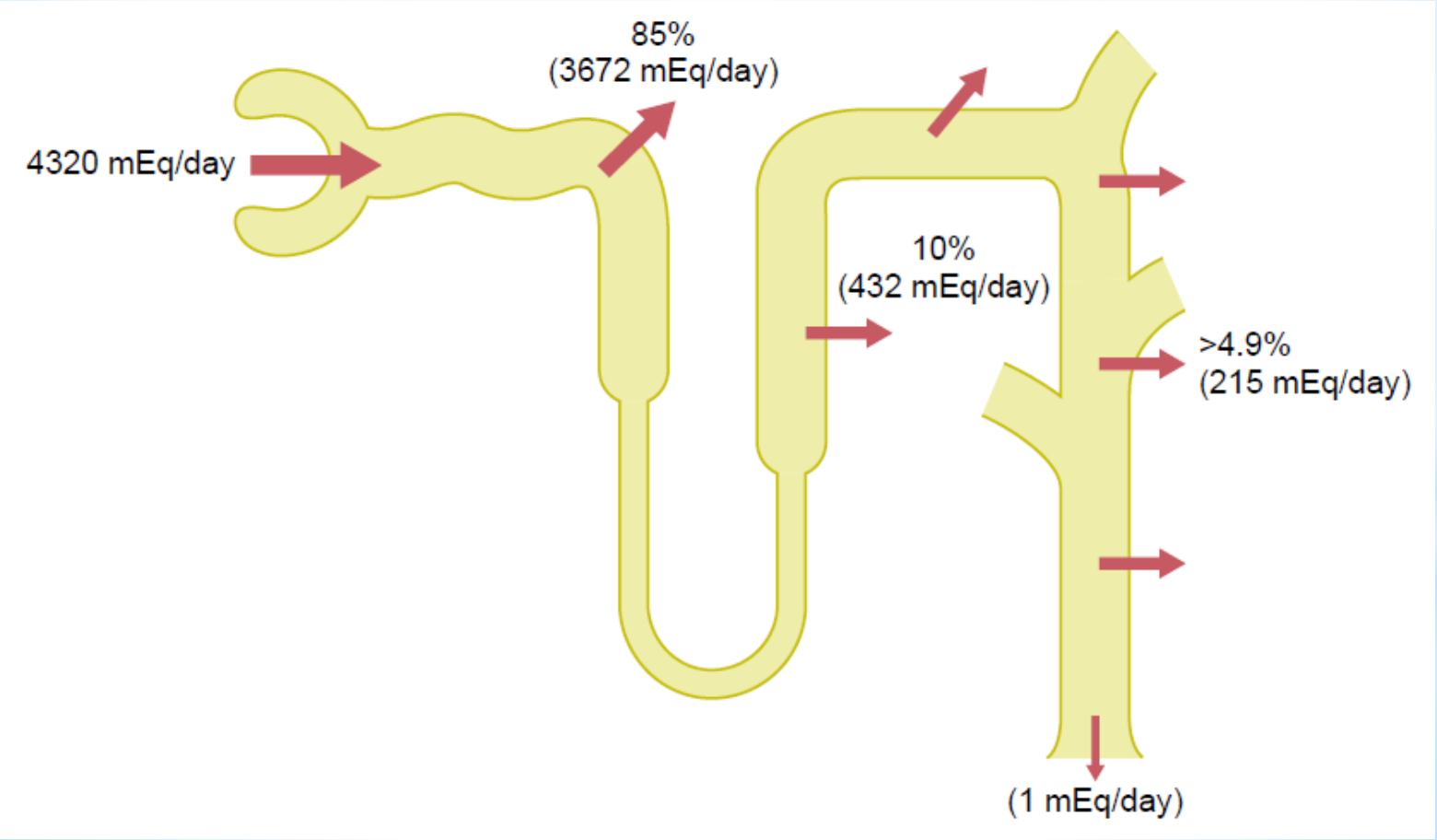
  GFR 180 l/day, $[HCO_3^-]_{plasma}$ 24 mEq/l $\rightarrow$ 4320 mEq HCO_3^- filtered per day – almost all ordinarily reabsorbed
- a high amount of H^+ still secreted in renal tubules

  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

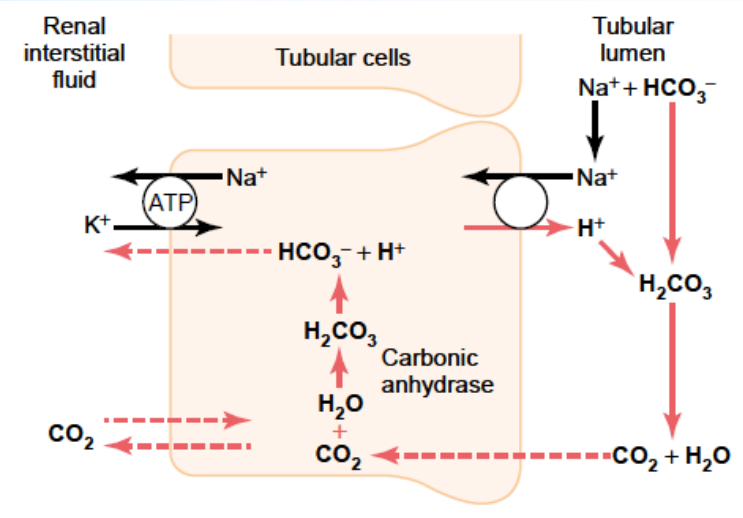
1) Secretion of H^+
2) Reabsorption of HCO_3^-



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:

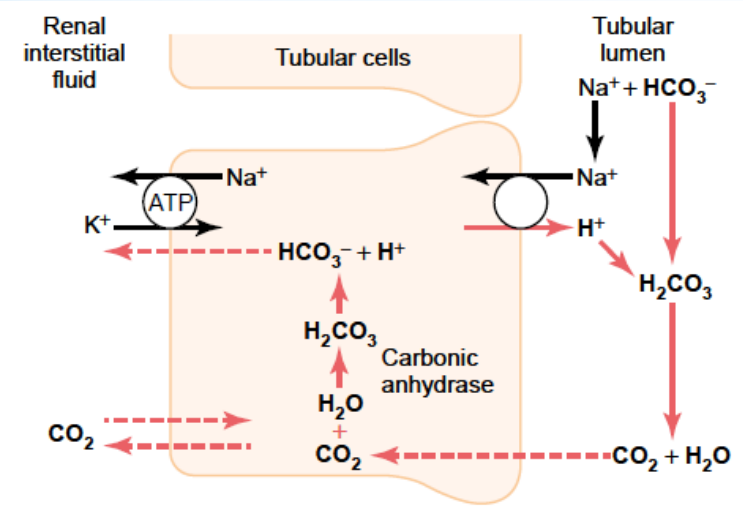
- Na^+-HCO_3^- co-transport
  (the proximal tubule)
- Cl^--HCO_3^- exchanger
  (the end of proximal tubule and the following parts of tubulus except for the thin loop of Henle)

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

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

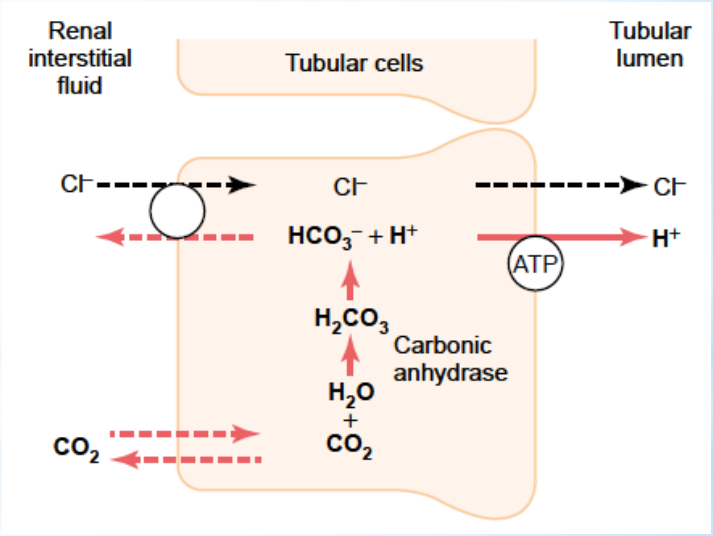
- ❖ in the proximal tubule, thick loop of Henle and at the beginning of the distal tubule



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)

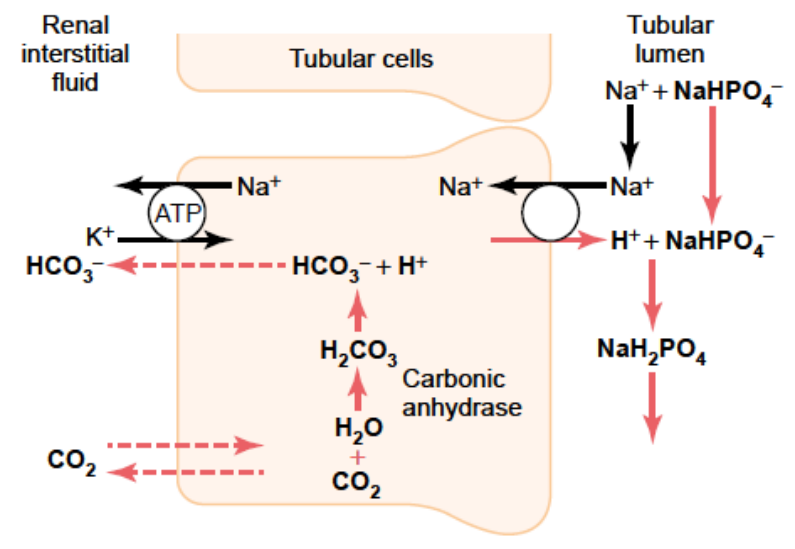
acidification of urine

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

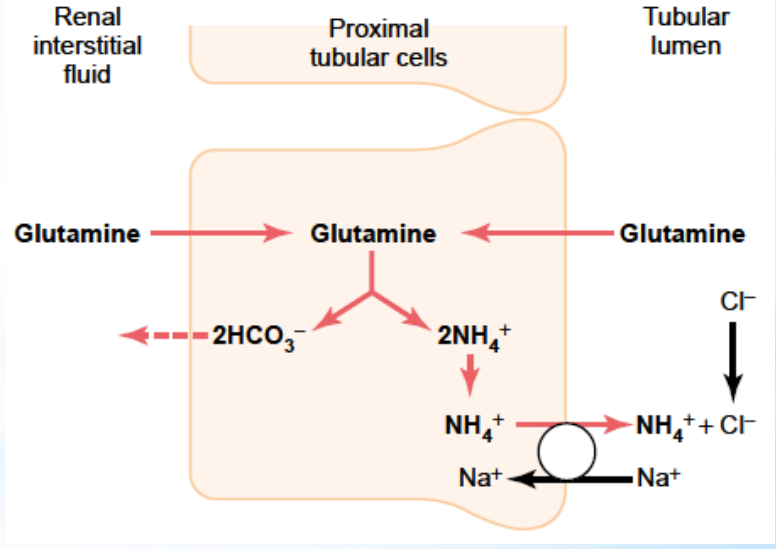
1) Secretion of H^+
2) Reabsorption of HCO_3^-
3) Production of HCO_3^- *de novo*

- 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^+)



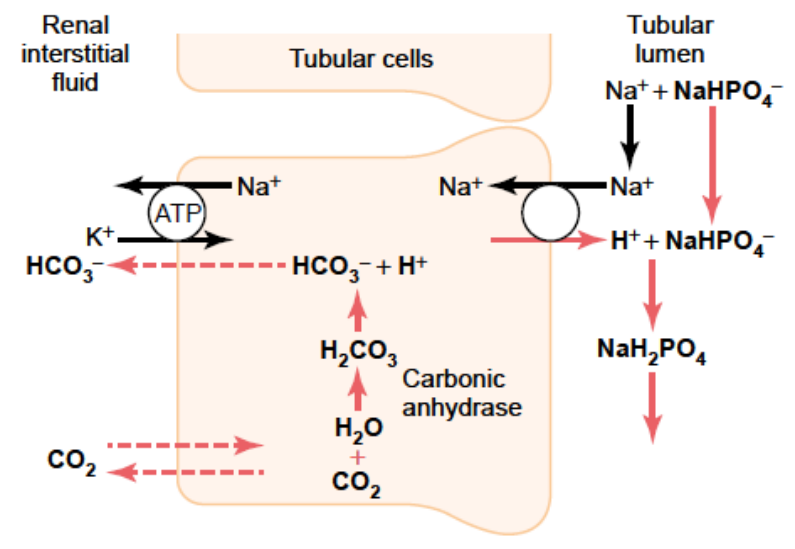
NH_4^+ originates from glutamine – the proximal tubule, thick ascending loop of Henle and distal tubule

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

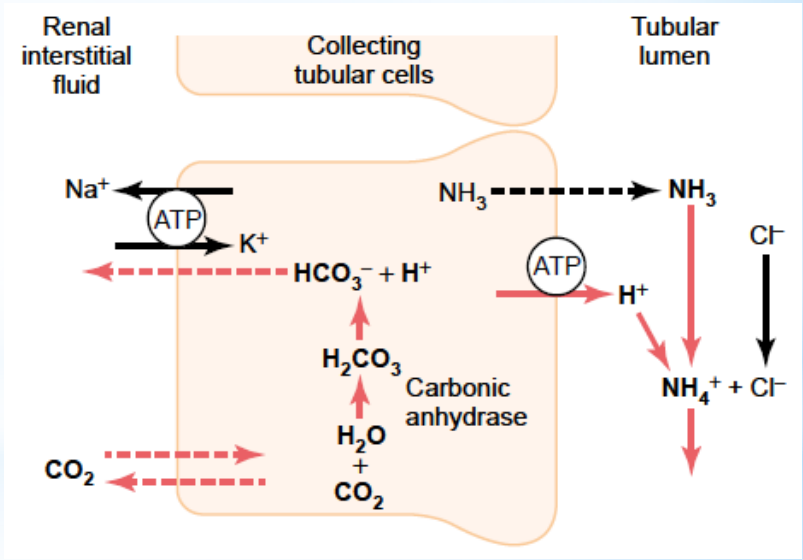
1) Secretion of H^+
2) Reabsorption of HCO_3^-
3) Produkce nového HCO_3^-

- 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

- Ammonium buffer (NH_3, NH_4^+)



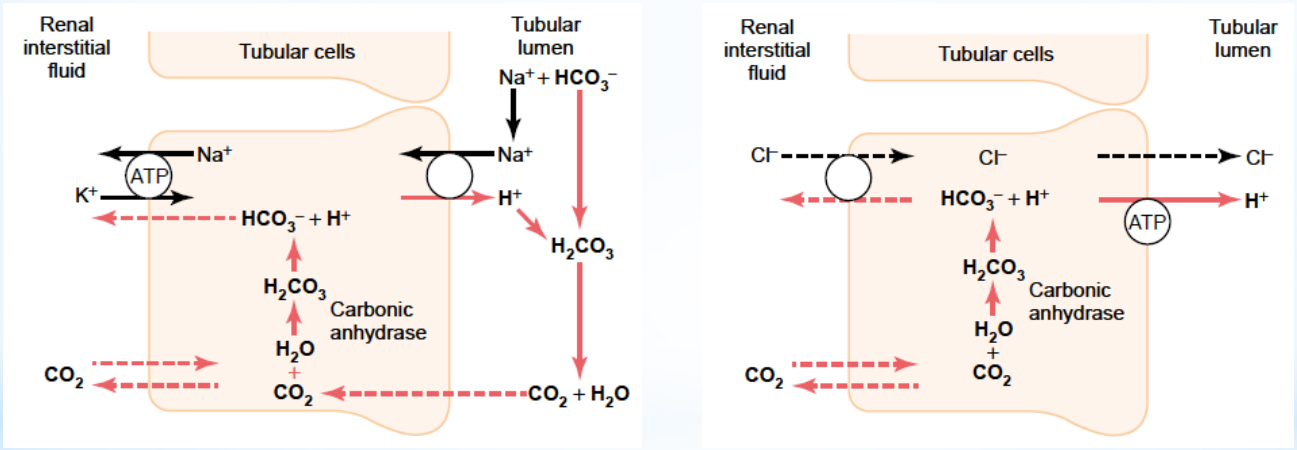
the collecting duct (permeable for NH_3 but far less for NH_4^+ - excreted by urine)
50% of H^+ secretion and HCO_3^- formed *de novo*!

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

Regulation of H^+ 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 active H^+ secretion in intercalated cells of collecting ducts, also through Na^+/H^+ antiport; 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

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

- 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

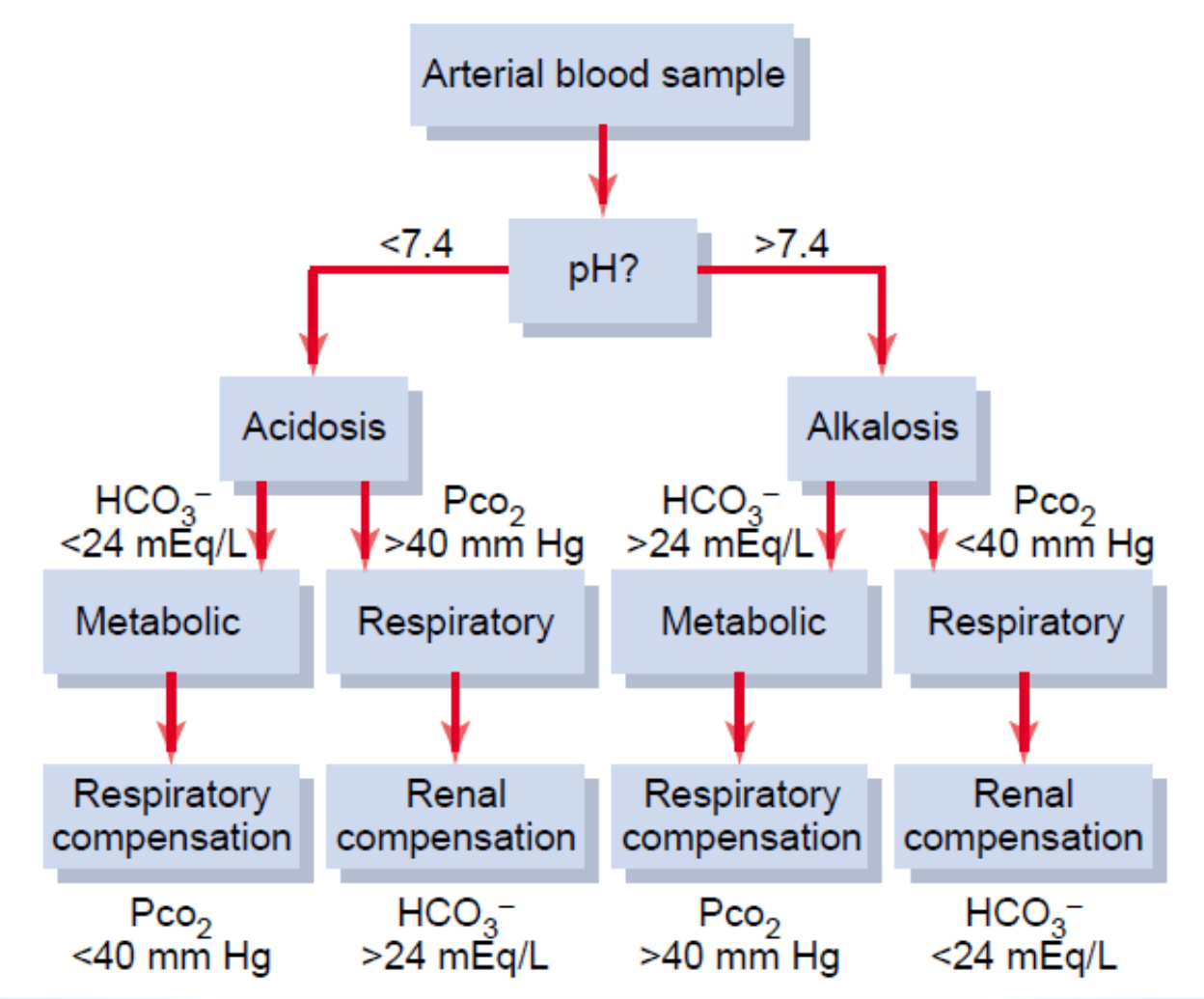
Alkalosis – correction by kidneys

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

- 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

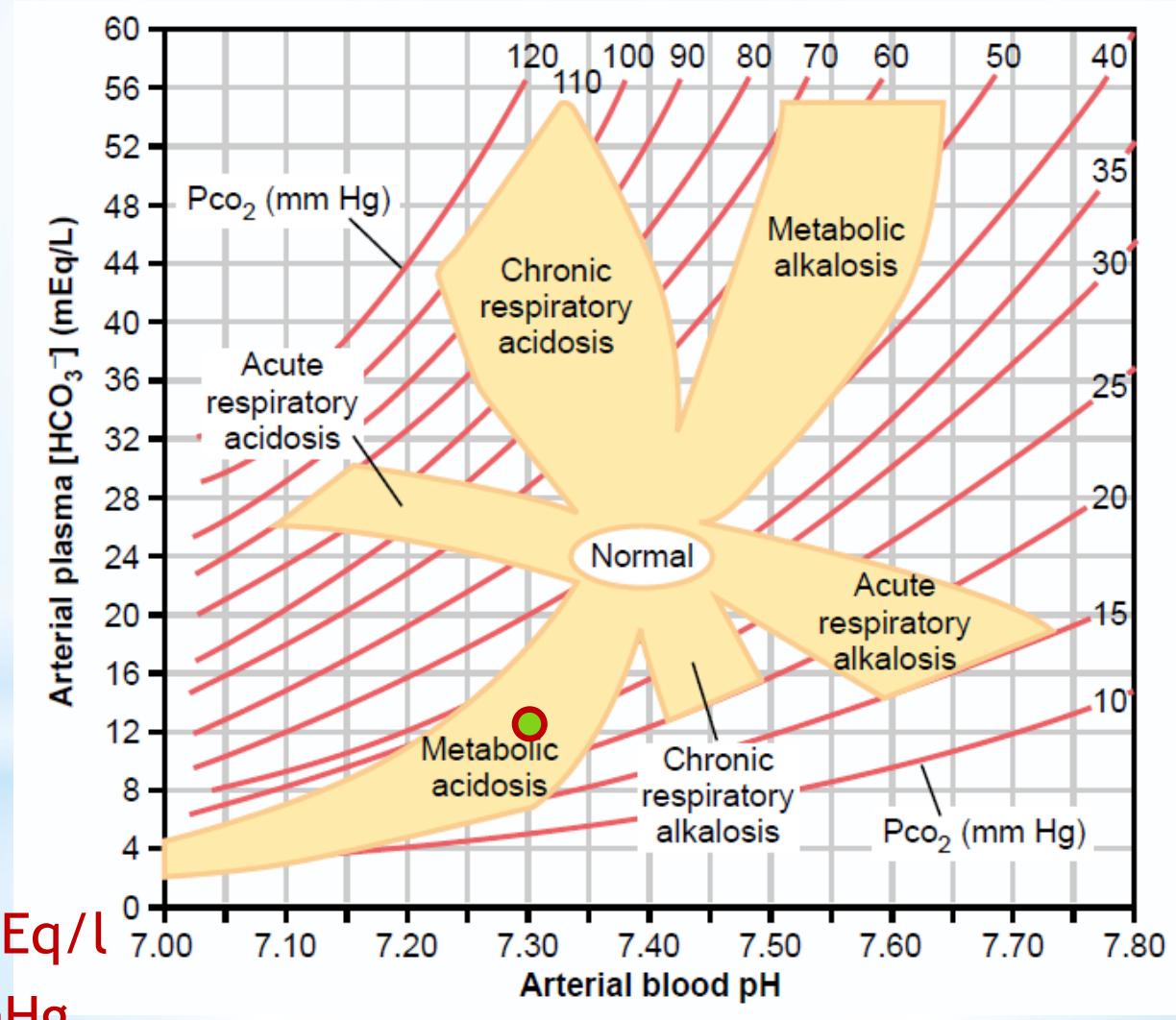
Acid-Base Balance and its Regulation

Diagnostics



Acid-Base Balance and its Regulation

Diagnostics



pH: 7,3

HCO_3^-: 12 mEq/l

P_{CO2}: 25 mmHg