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

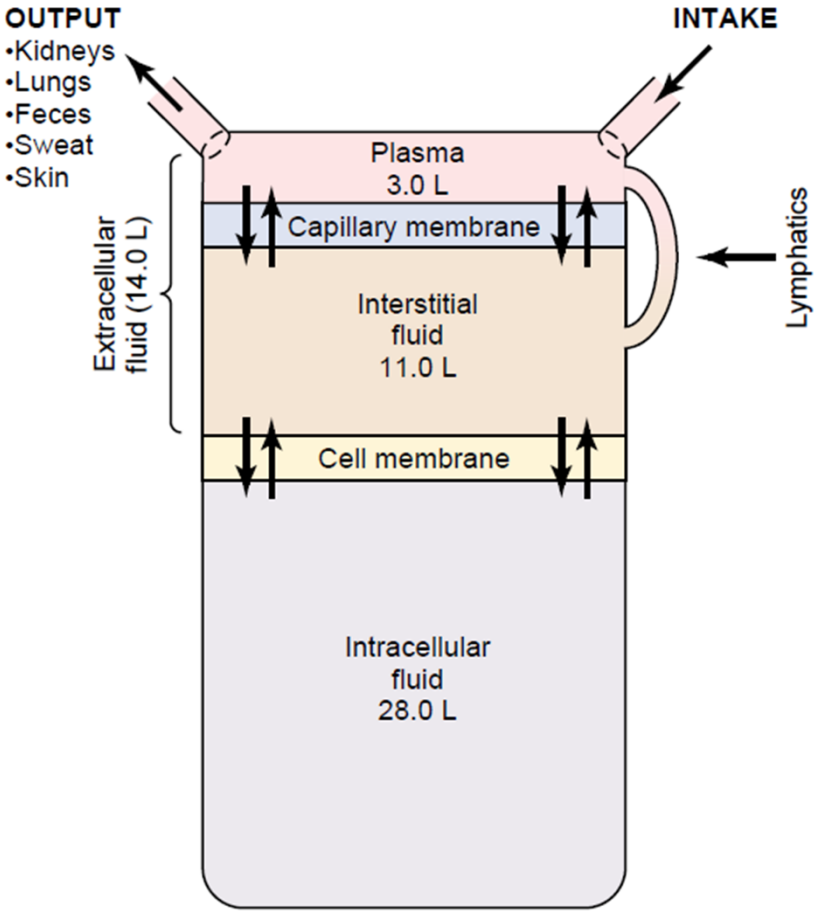
Maintainance of Acid-Base Balance

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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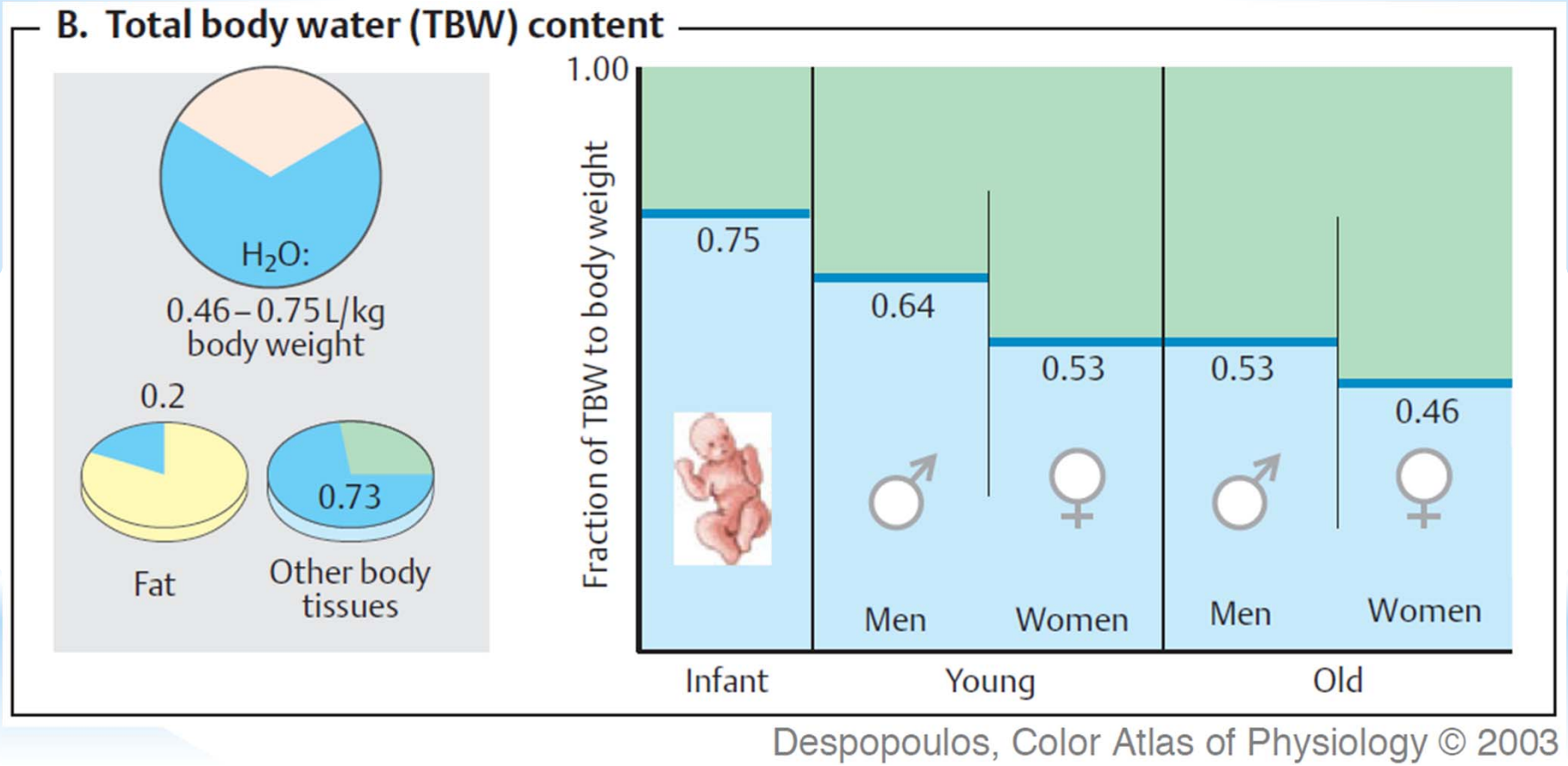
Body Fluids – Types and Volumes

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

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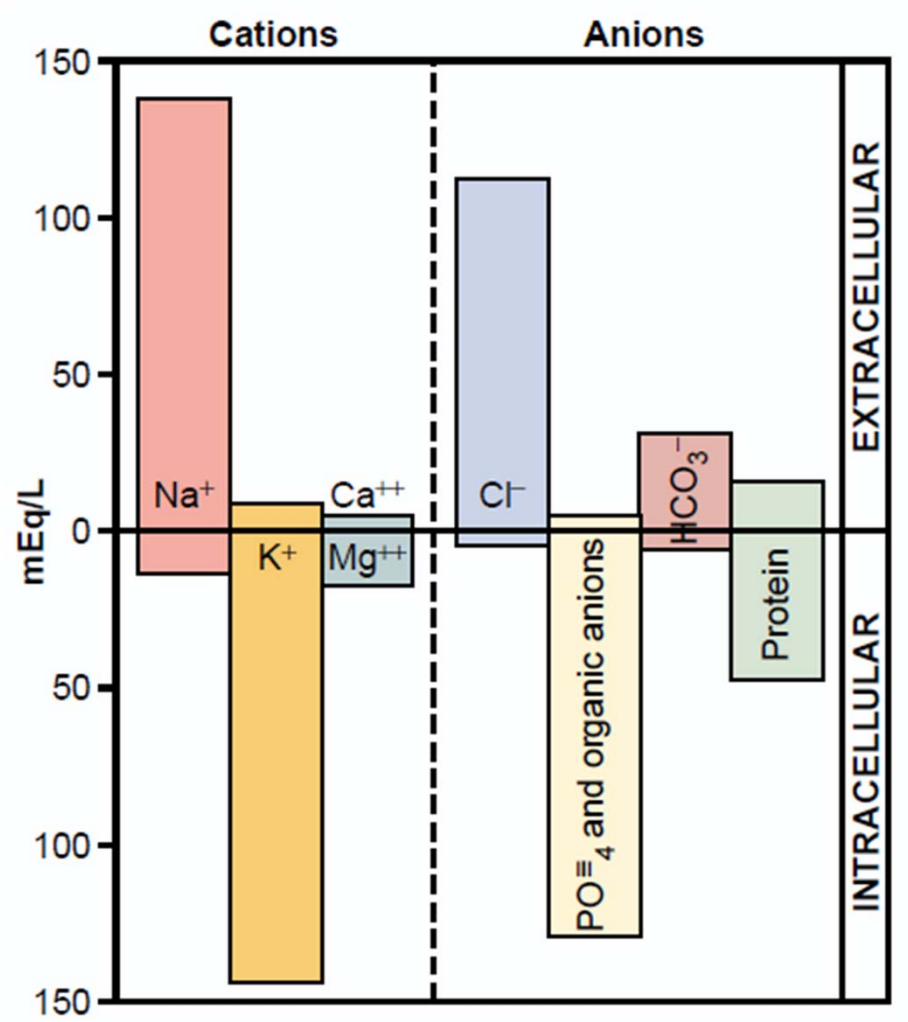
Body Fluids – Composition

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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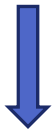
Body Fluids – Composition

osmolality 285 mosm/kg H_2O

↑ ↑ NaCl intake, loss of water → 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

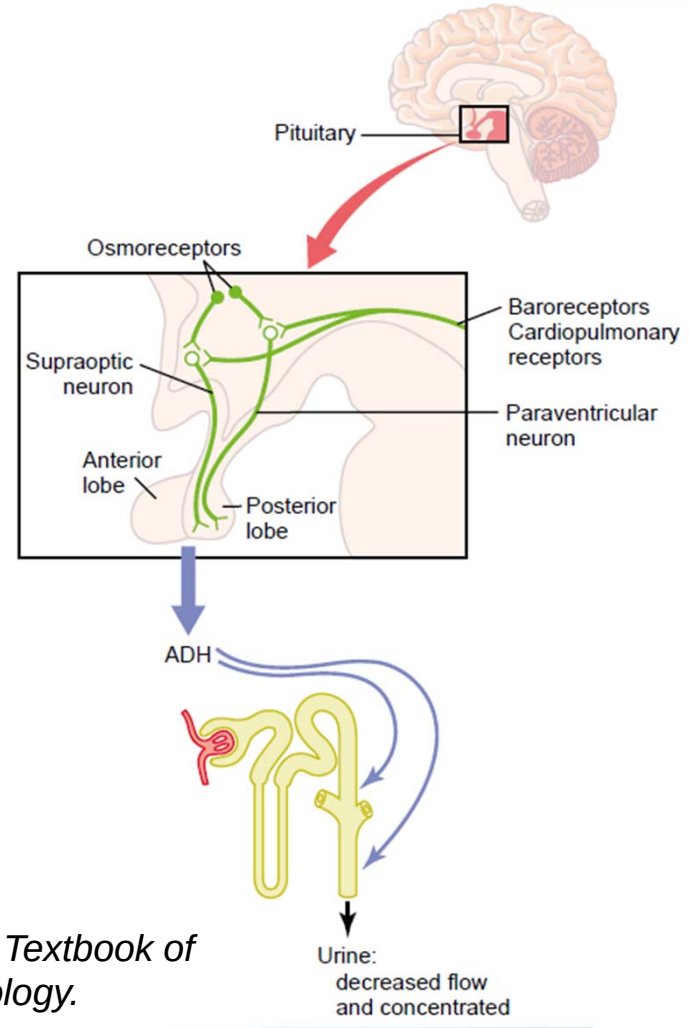
(vasopressin)

- 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

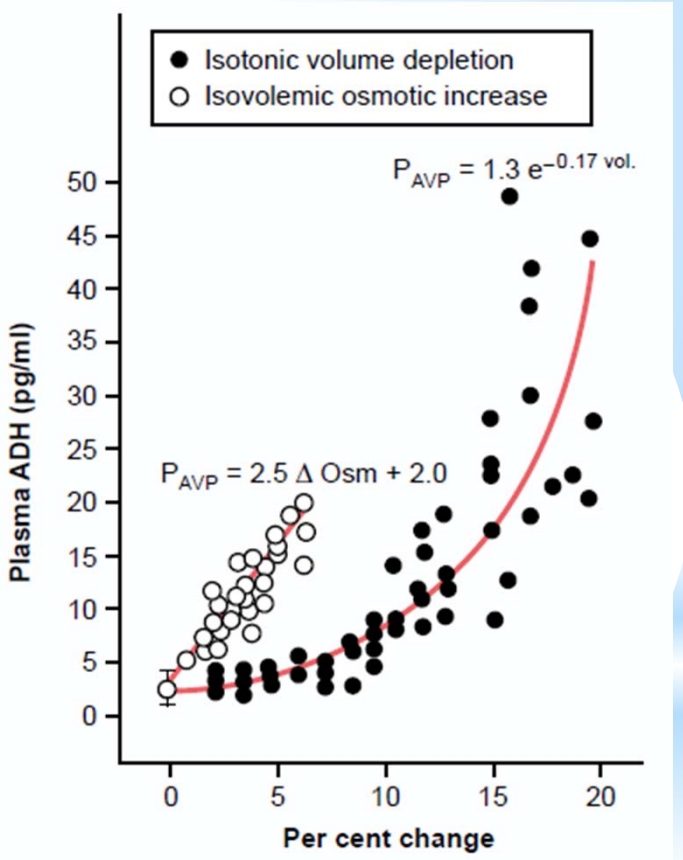
Antidiuretic Hormone

(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)

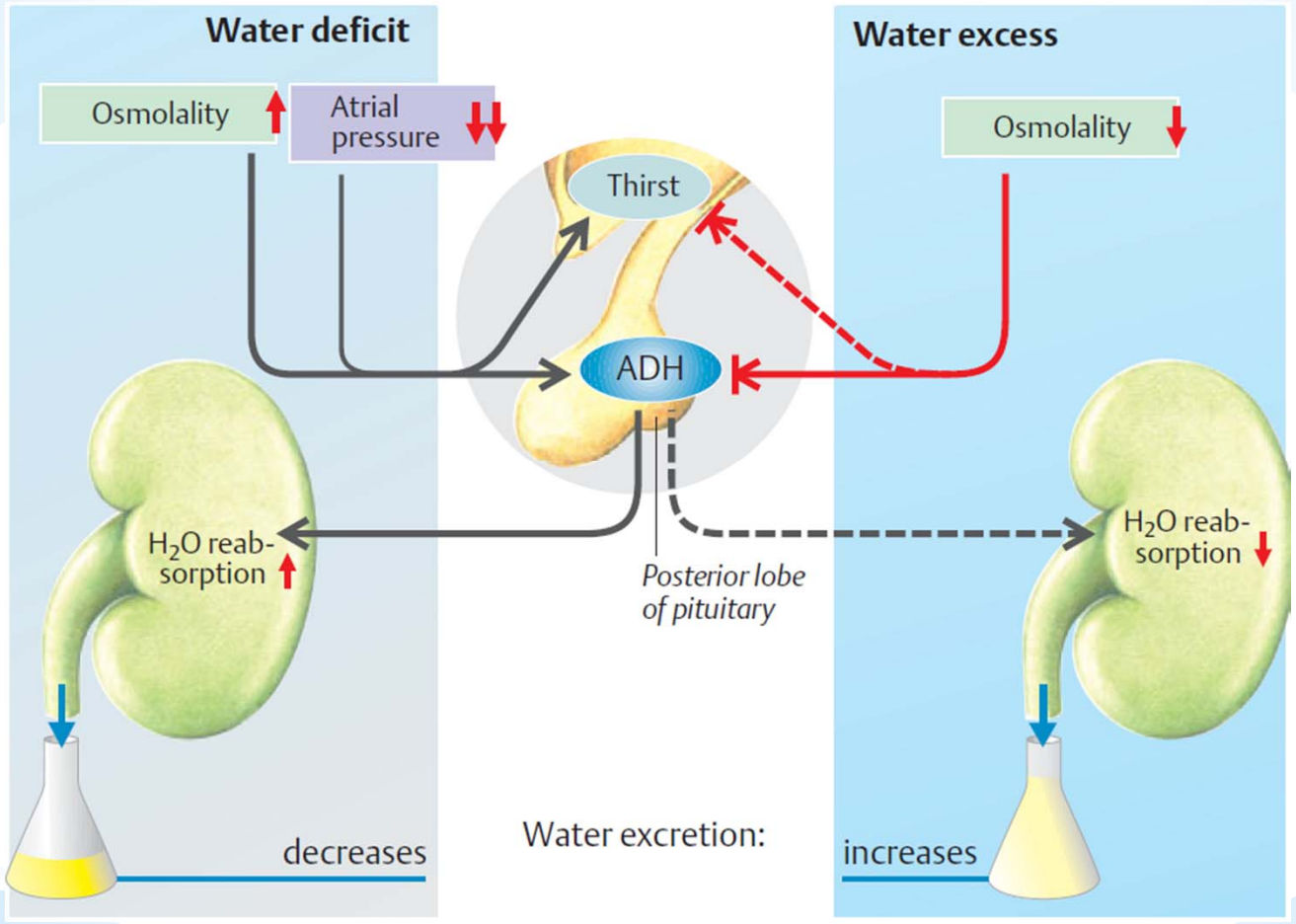
- effects (through ↑ cGMP): → ↓ **BP** (also through the brain stem)
  - → natriuresis
  - → ↓ reactivity of vascular smooth muscles for vasocontrictive substances
  - → inhibition of renin secretion, ↓ reactivity of *zona glomerulosa* for stimuli ↑ aldosteron secretion
  - → inhibition of ADH secretion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

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

Humoral Regulation of Body Fluids

Water Homeostasis

water intoxication



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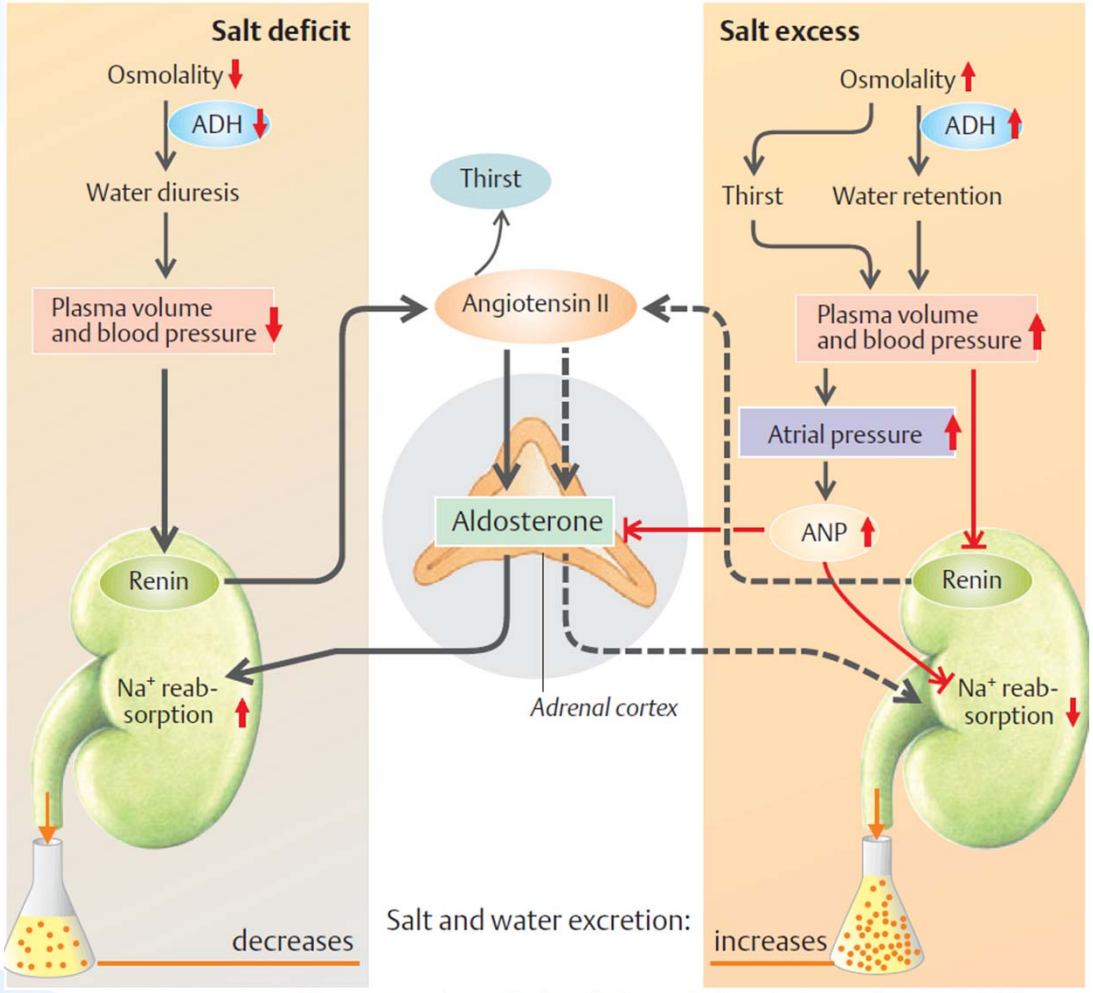
Humoral Regulation of Body Fluids

Salt Homeostasis



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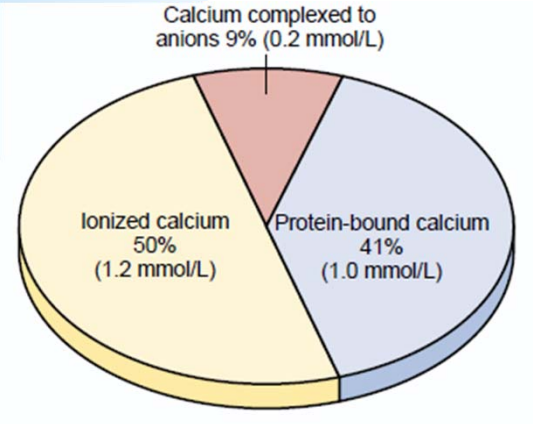
Humoral Regulation of Body Fluids

Calcium in the Body



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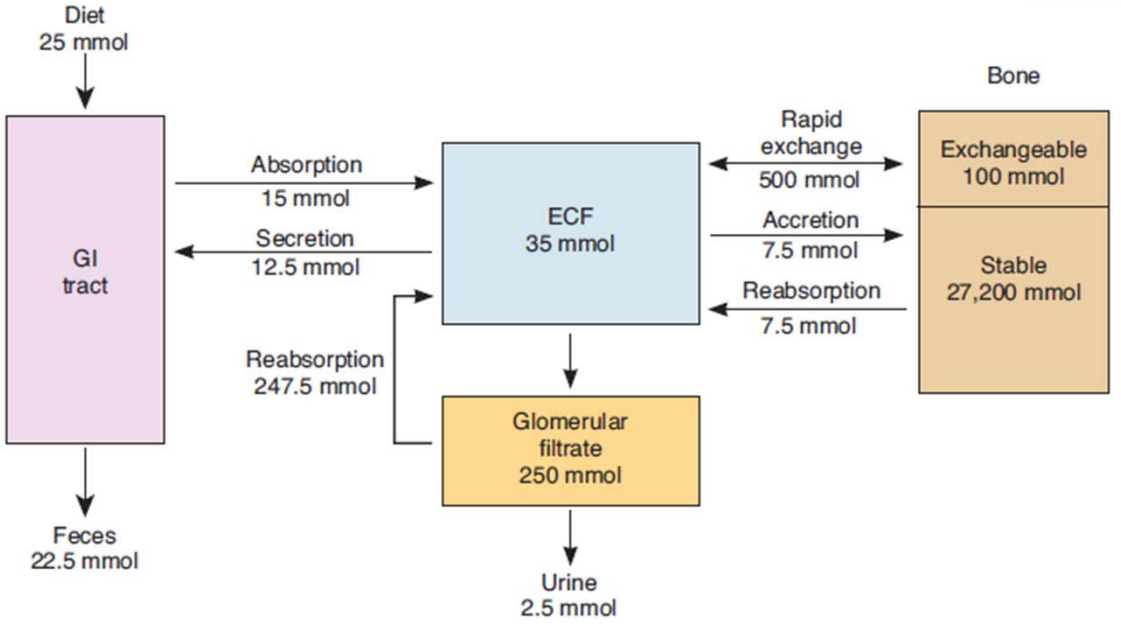


Ganong´s Review of Medical Physiology

hypocalcemia

hypercalcemia

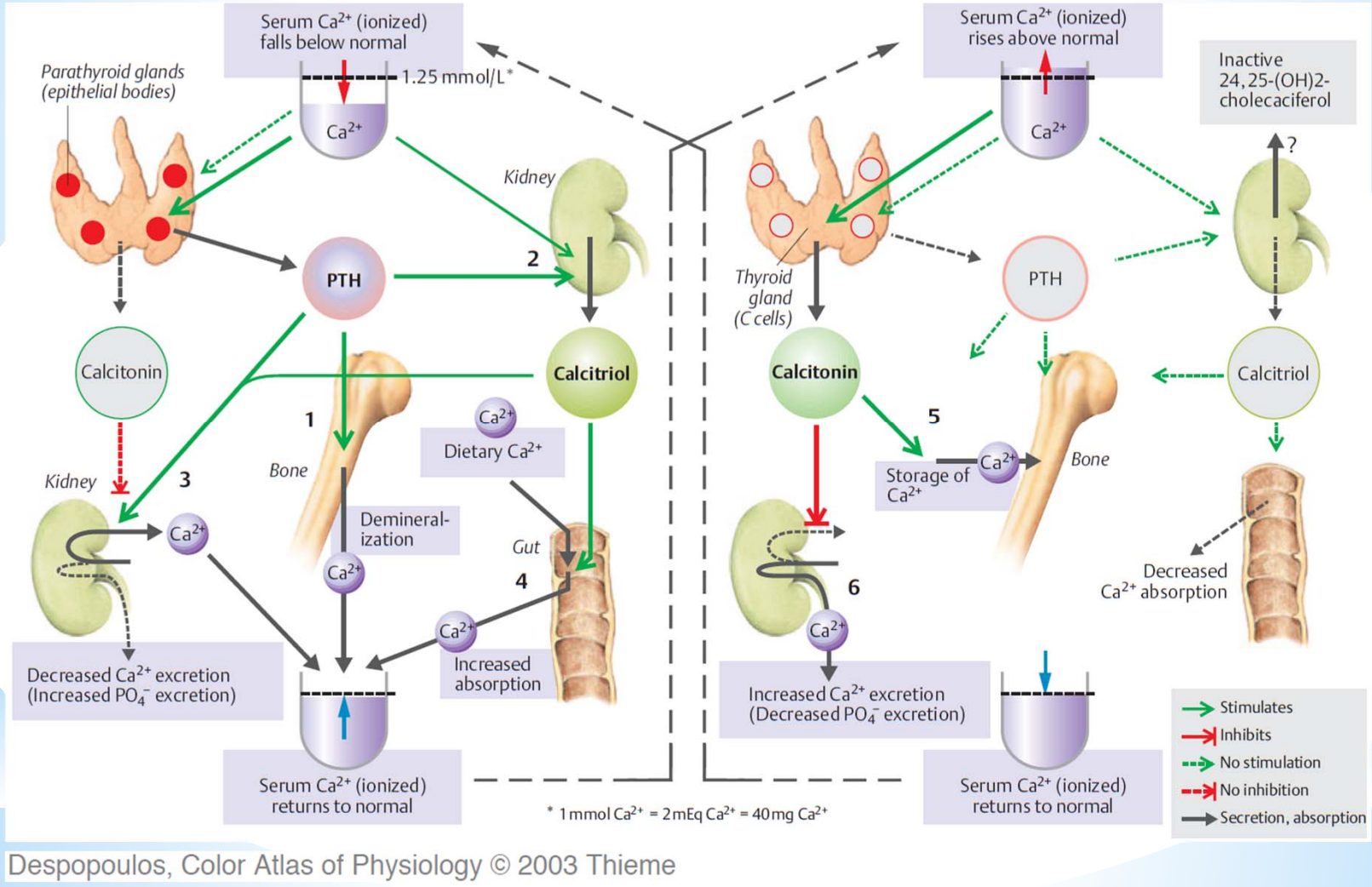
Humoral Regulation of Body Fluids

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

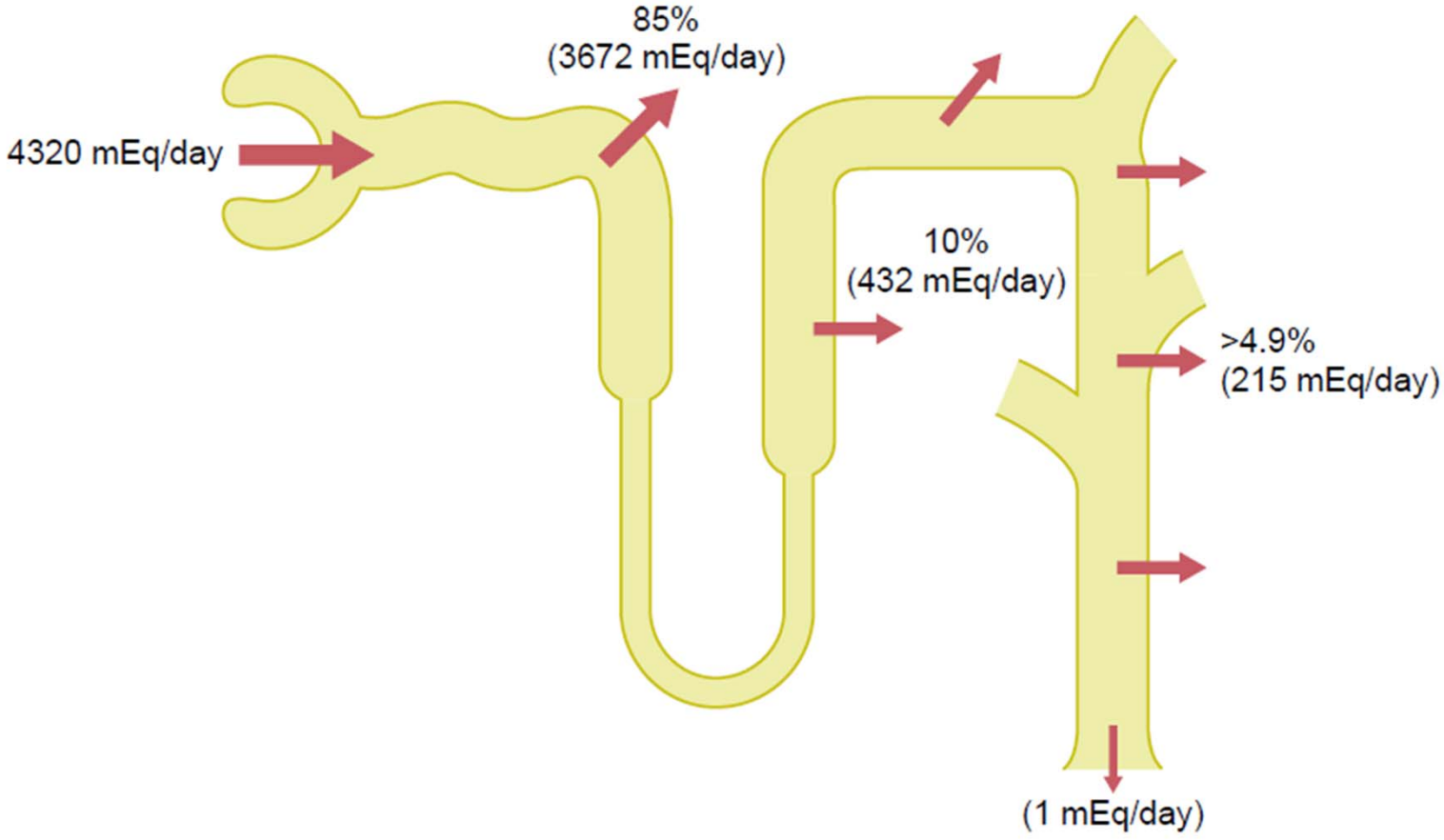
  GFR 180 l/day, $[HCO_3^-]_{plasma}$ 24 mEq/l $\rightarrow$ 4320 mEq HCO_3^- filtered per day – almost all ordinarily reabsorbed
- a high amount of H^+ still secreted in renal tubules

  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

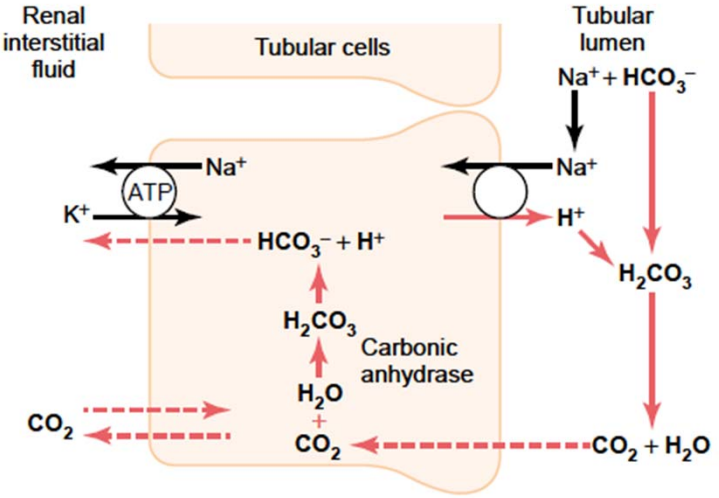
1) Secretion of H^+
2) Reabsorption of HCO_3^-



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:

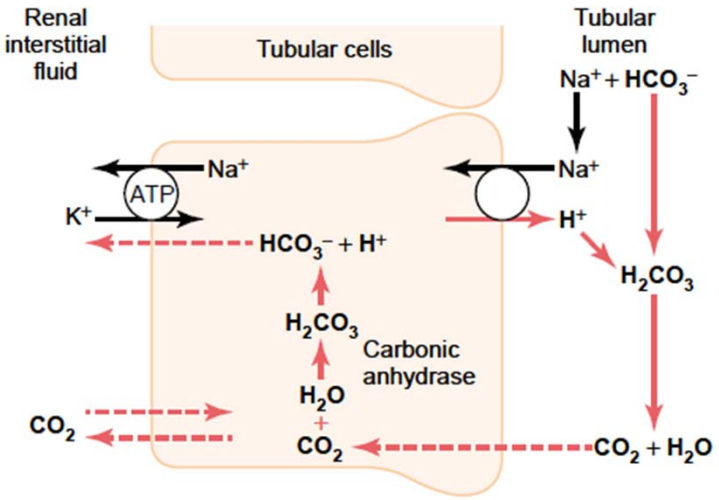
- Na^+-HCO_3^- co-transport
  (the proximal tubule)
- Cl^--HCO_3^- exchanger
  (the end of proximal tubule and the following parts of tubulus except for the thin loop of Henle)

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

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

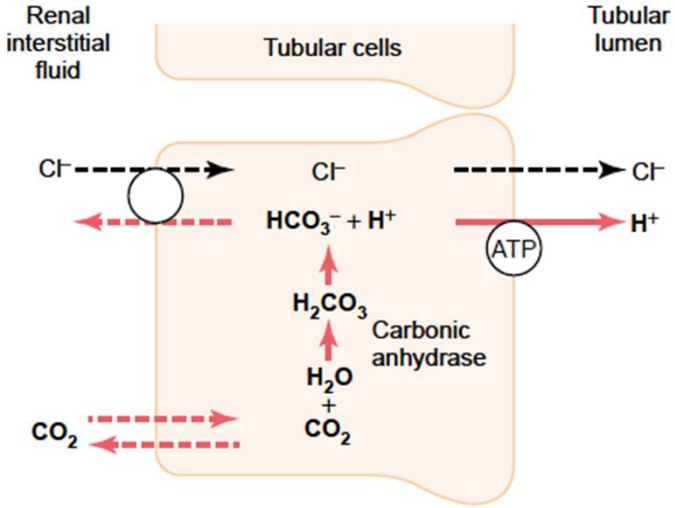
- in the proximal tubule, thick loop of Henle and at the beginning of the distal tubule



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)

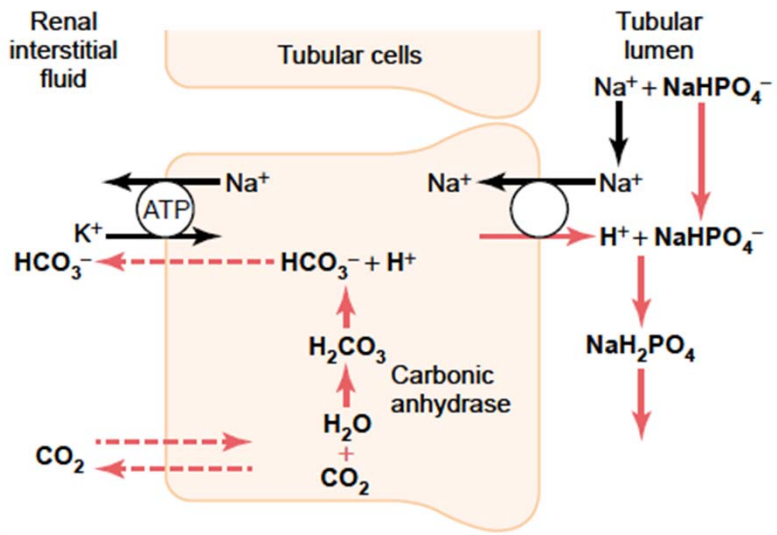
acidification of urine

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

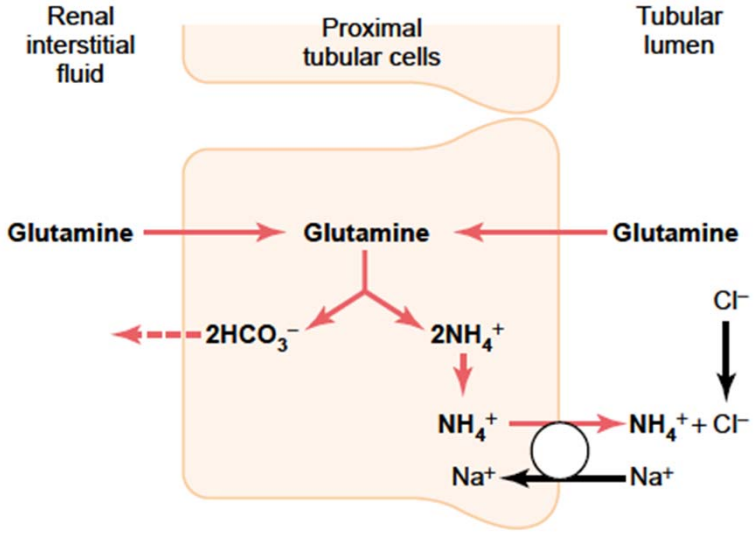
1) Secretion of H^+
2) Reabsorption of HCO_3^-
3) Production of HCO_3^- *de novo*

❖ 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^+)



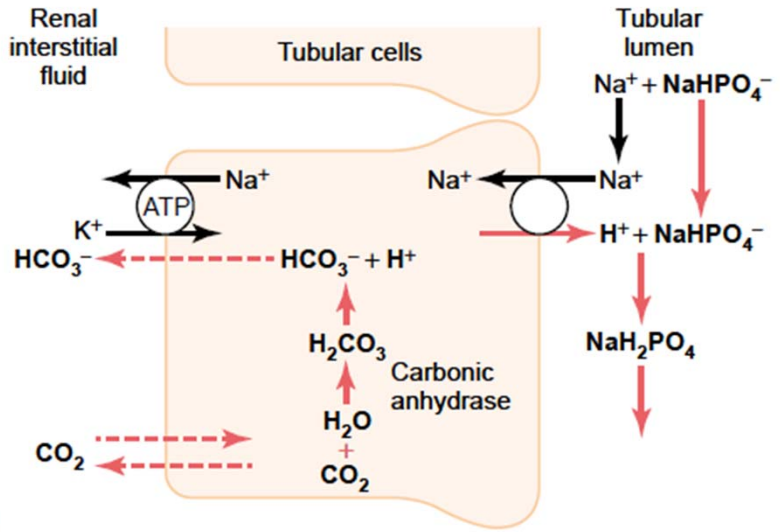
NH_4^+ originates from glutamine – the proximal tubule, thick ascending loop of Henle and distal tubule

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

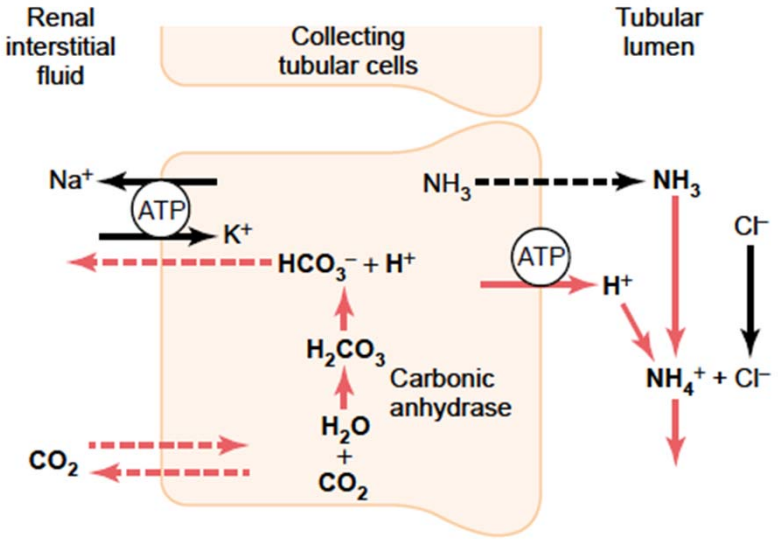
1) Secretion of H^+
2) Reabsorption of HCO_3^-
3) Produkce nového HCO_3^-

❖ 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

❖ Ammonium buffer (NH_3, NH_4^+)



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

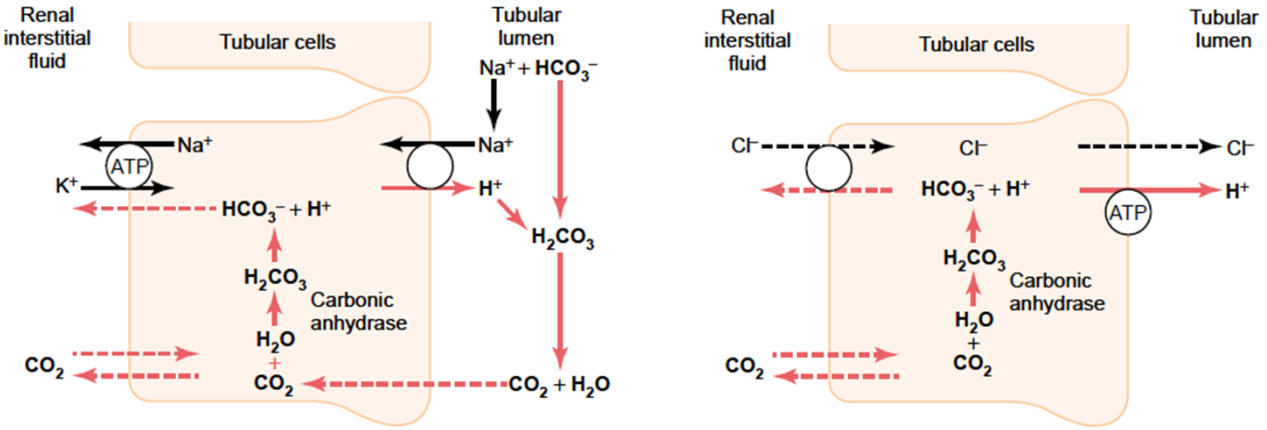
50% of H^+ secretion and HCO_3^- formed *de novo*!

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 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 $\uparrow HCO_3^-$

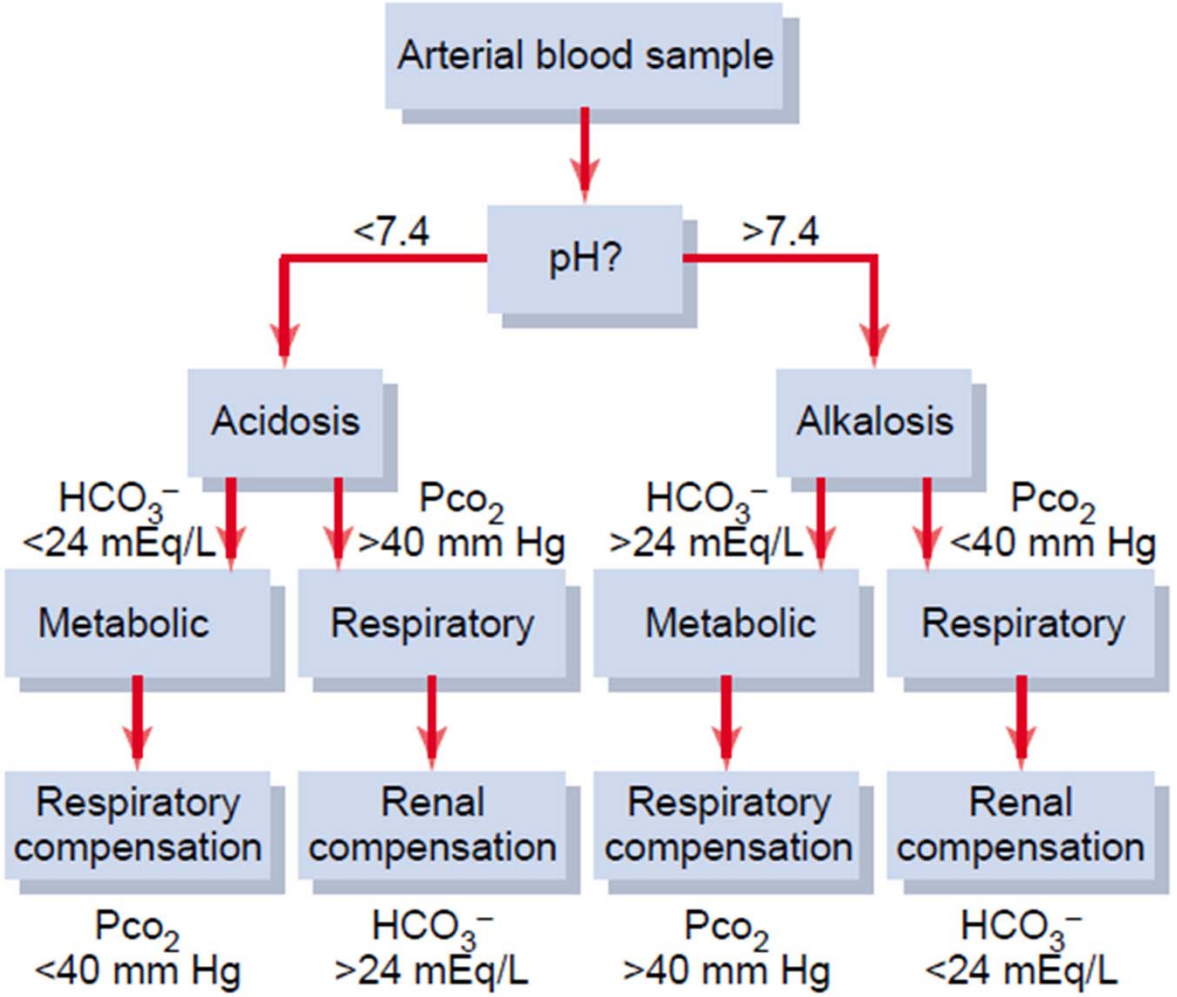
  renal correction: $\uparrow HCO_3^-$ in ECF $\rightarrow \uparrow$ filtered $HCO_3^- \rightarrow$ incomplete HCO_3^- reabsorption (lack of H+) $\rightarrow \uparrow HCO_3^-$ excretion by urine $\rightarrow$ pH normalization

- 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

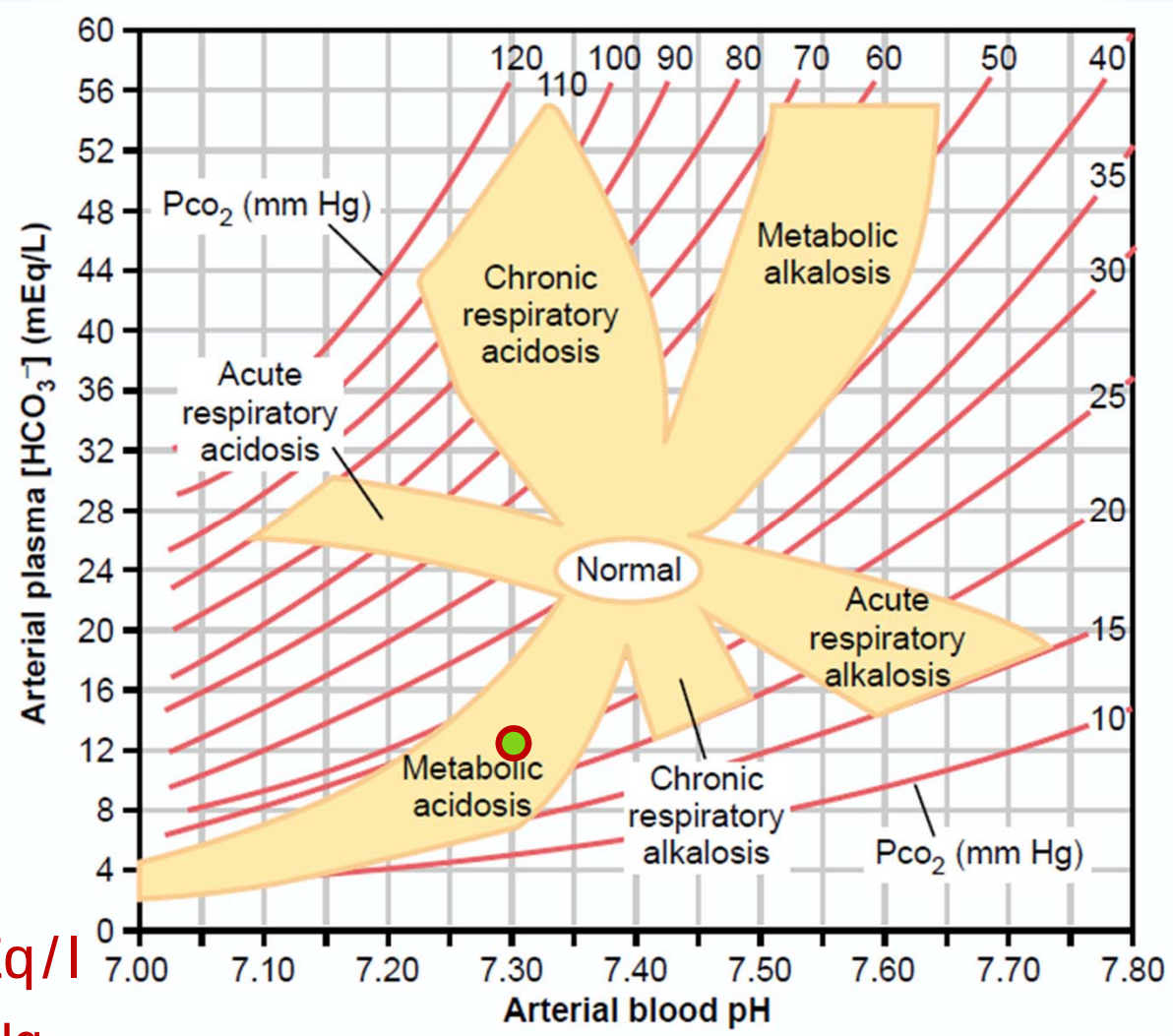
Acid-Base Balance and its Regulation

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