

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

= maintenance of stable conditions in the internal body environment

Maintenance of Constant Volume and Composition of Body Fluids

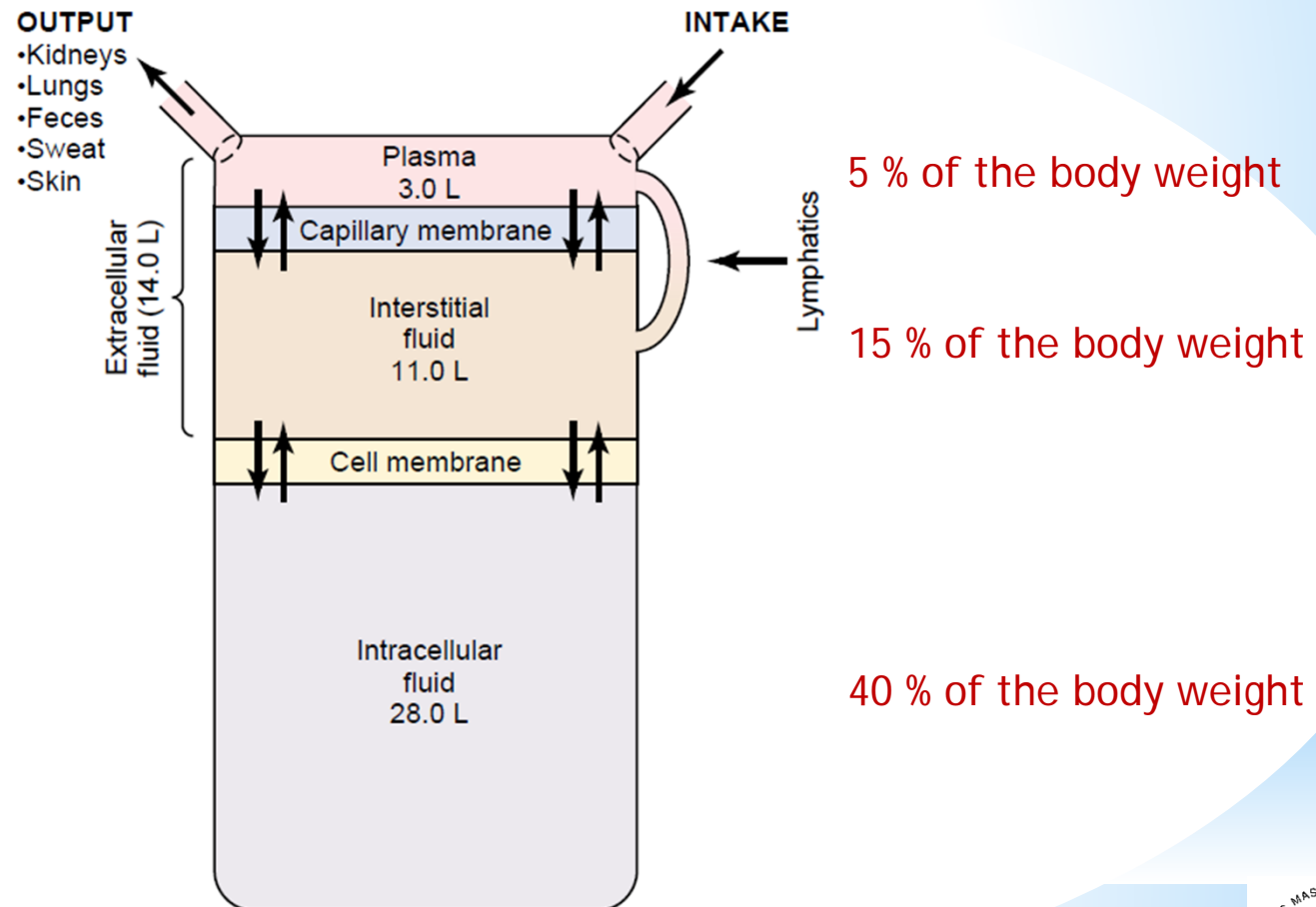
Maintenance of Acid-Base Balance

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

Body Fluids – Types and Volumes

Compartments

60 % of the body weight in total



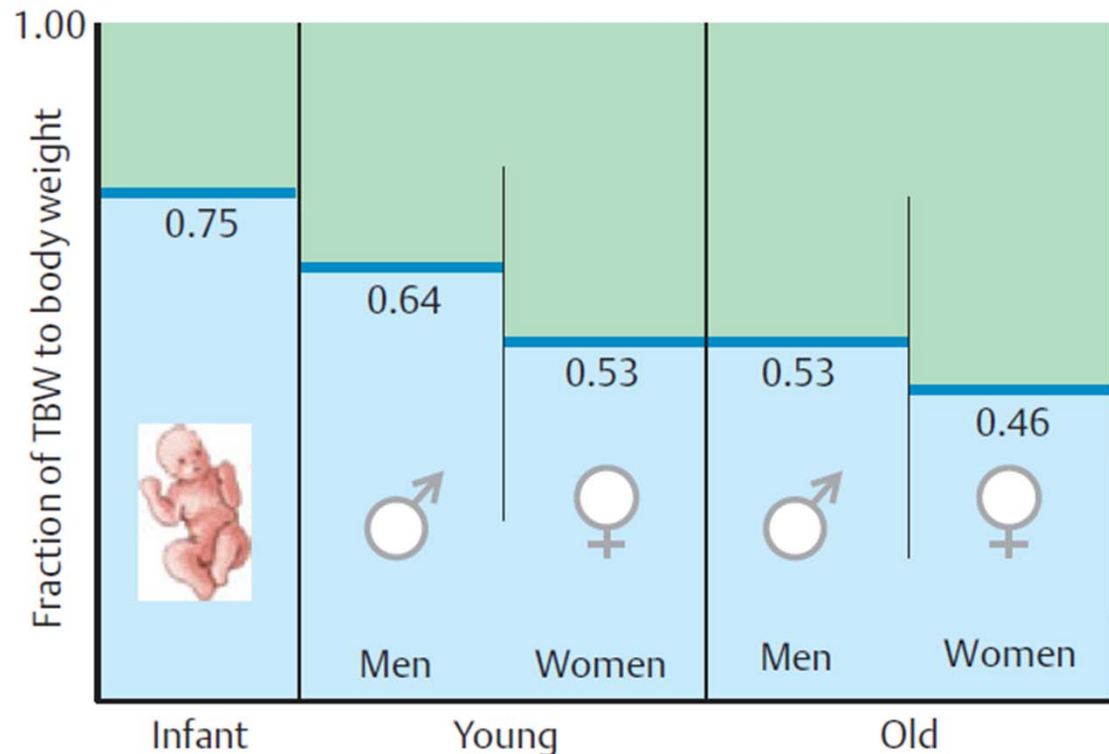
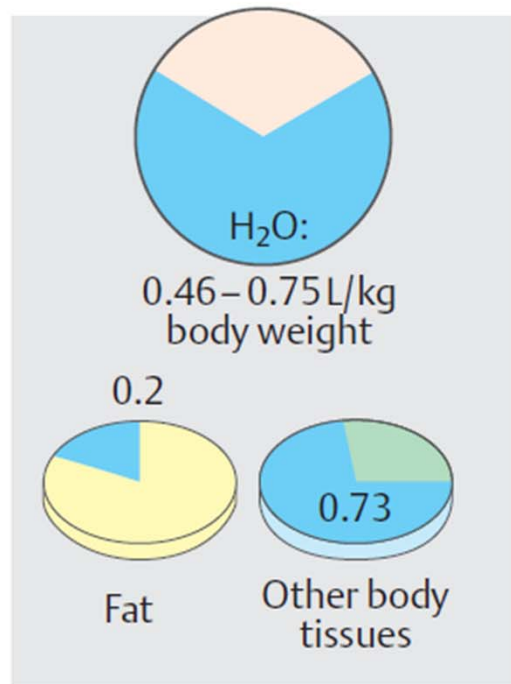
Transcellular fluid (1-2 l) - special type of ECF

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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

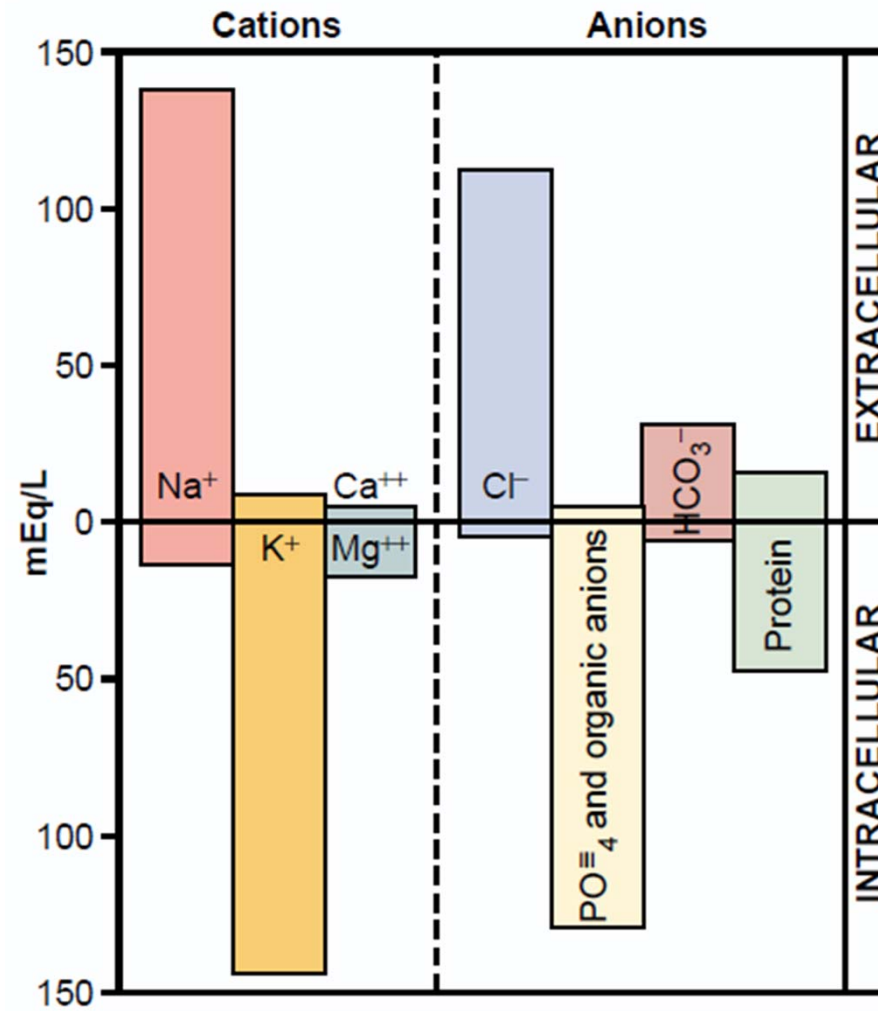
Daily Intake and Output of Water (ml/day)

	Normal	Prolonged, Heavy Exercise
Intake		
Fluids ingested	2100	?
From metabolism	<u>200</u>	<u>200</u>
Total intake	2300	?
Output		
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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Body Fluids – Composition

ECF vs. ICF



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Body Fluids – Composition

plasma vs. ISF

	Plasma (mOsm/L H ₂ O)	Interstitial (mOsm/L H ₂ O)
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 ₂ PO 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 H₂O



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



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



Precise regulation of osmolality of ESF is necessary!

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

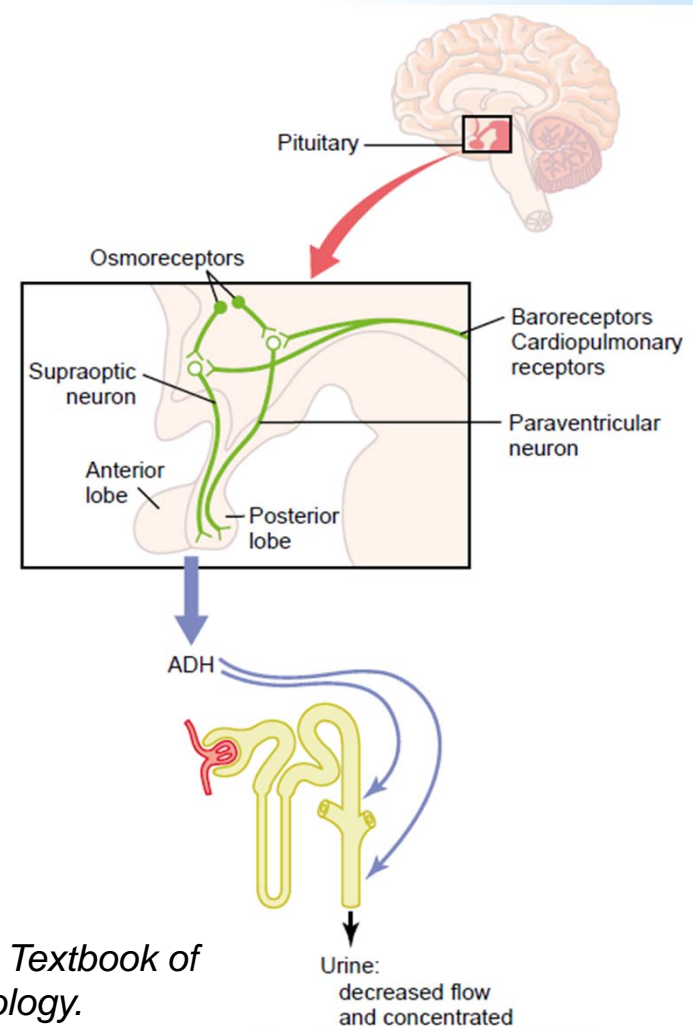
- **aldosteron**
- **natriuretic peptides**

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



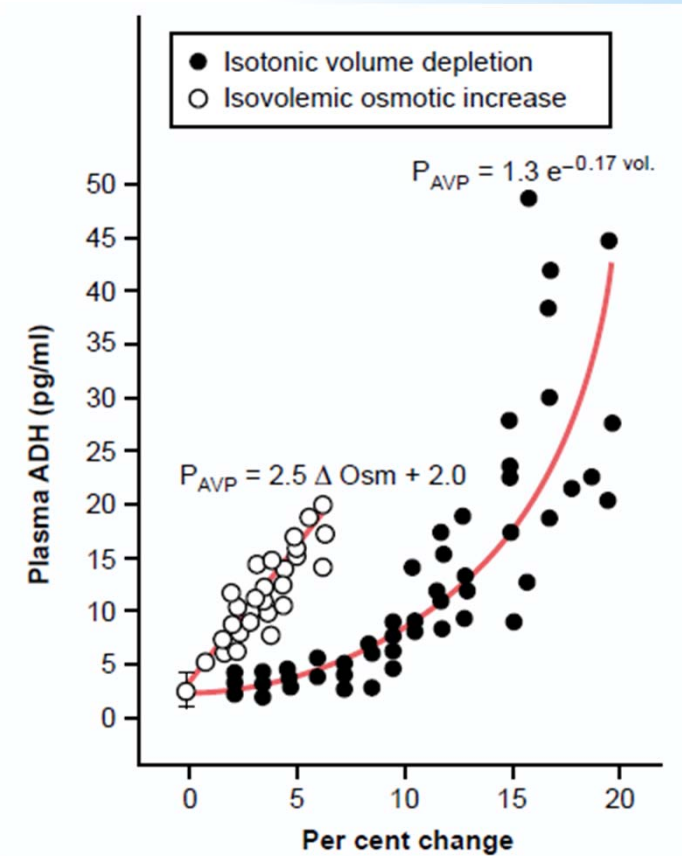
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Humoral Regulation of Body Fluids

Antidiuretic Hormone (*vasopressin*)

- regulation of secretion:

- ↑ - ↑ osmolality
- ↓ volume of ECF
- pain, emotions, stress (surgical), physical exertion; standing
- nausea, vomiting
- angiotensin II
- morphine, 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 \uparrow plasmatic concentration of K^+ and $\downarrow Na^+$ (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 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

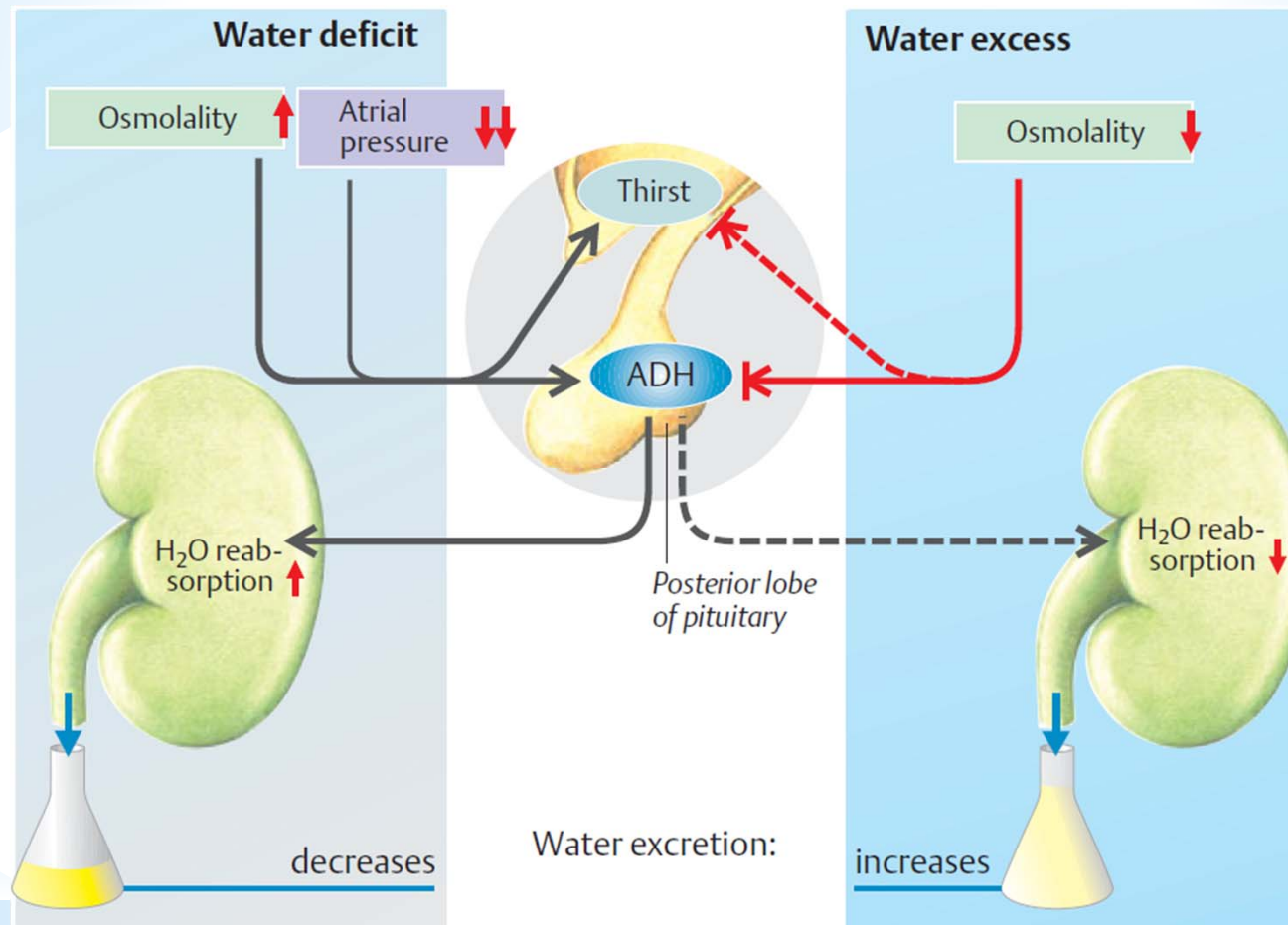
Atrial Natriuretic Peptide

- 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

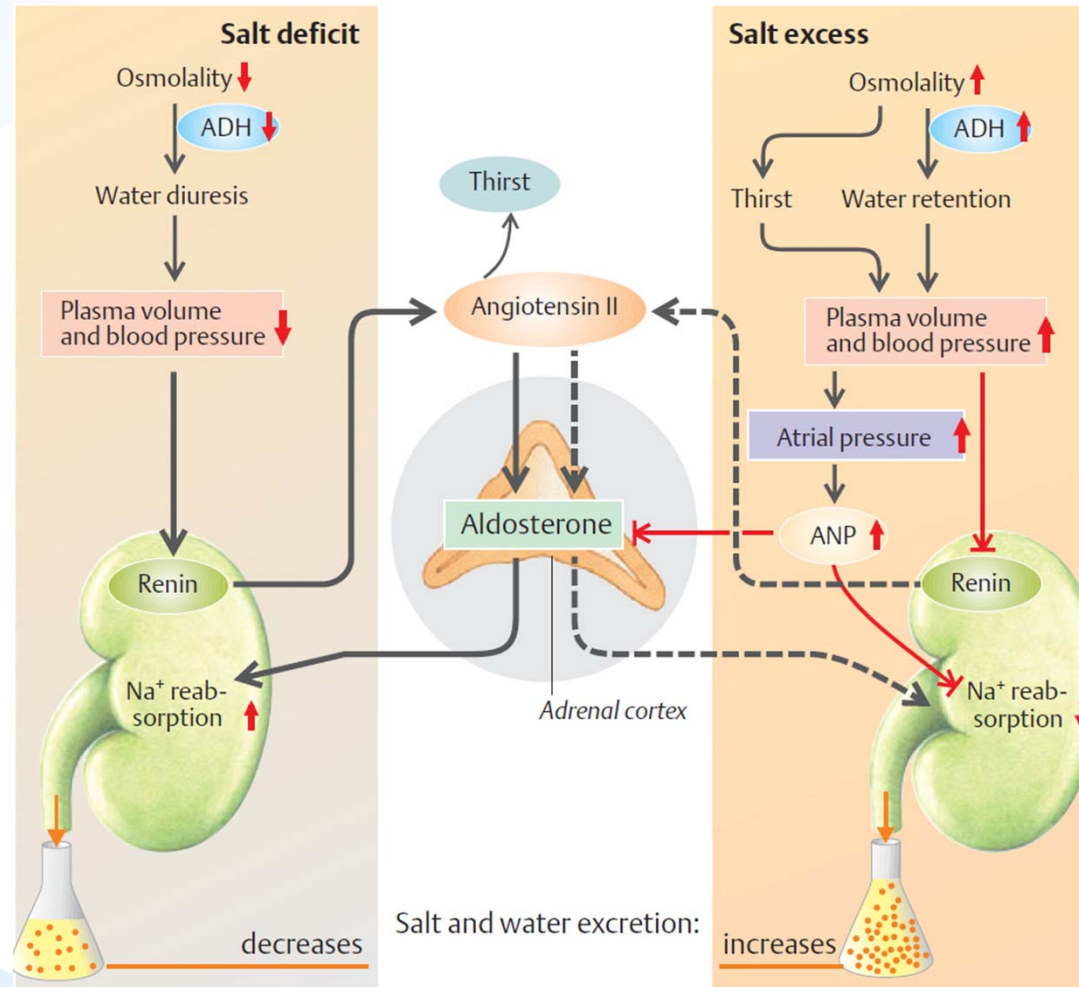
water intoxication



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Humoral Regulation of Body Fluids

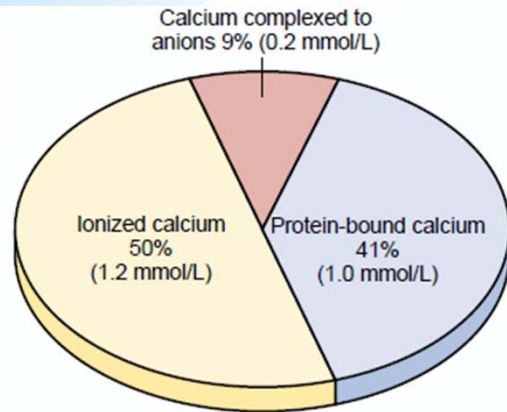
Salt Homeostasis



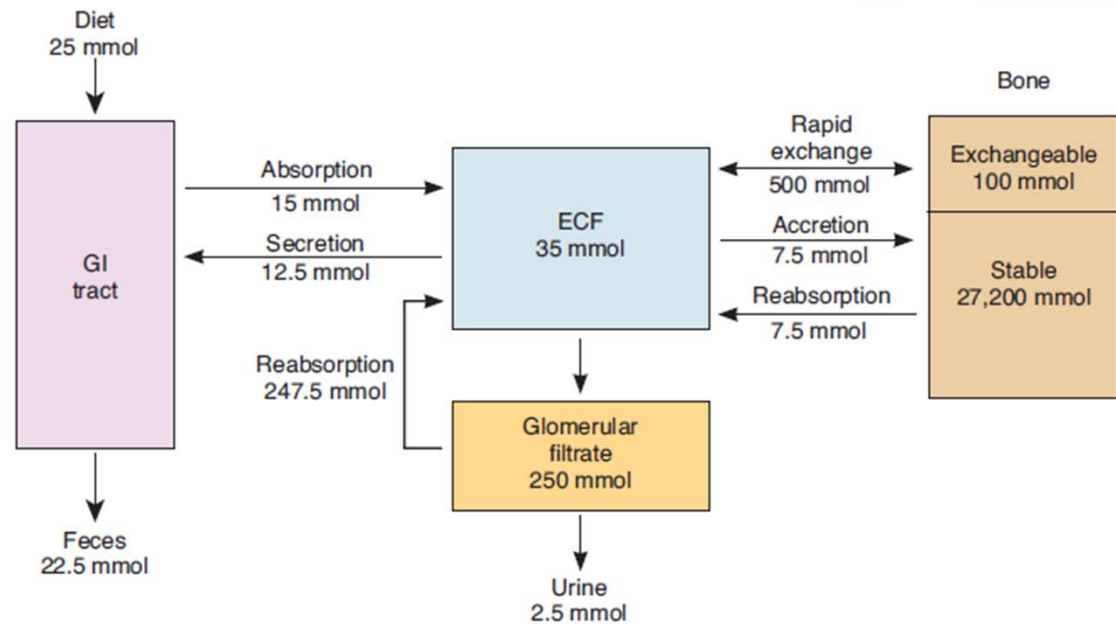
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Humoral Regulation of Body Fluids

Calcium in the Body



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Ganong's Review of Medical Physiology

hypocalcemia
hypercalcemia

Humoral Regulation of Body Fluids

Hormonal Regulation of Calcemia

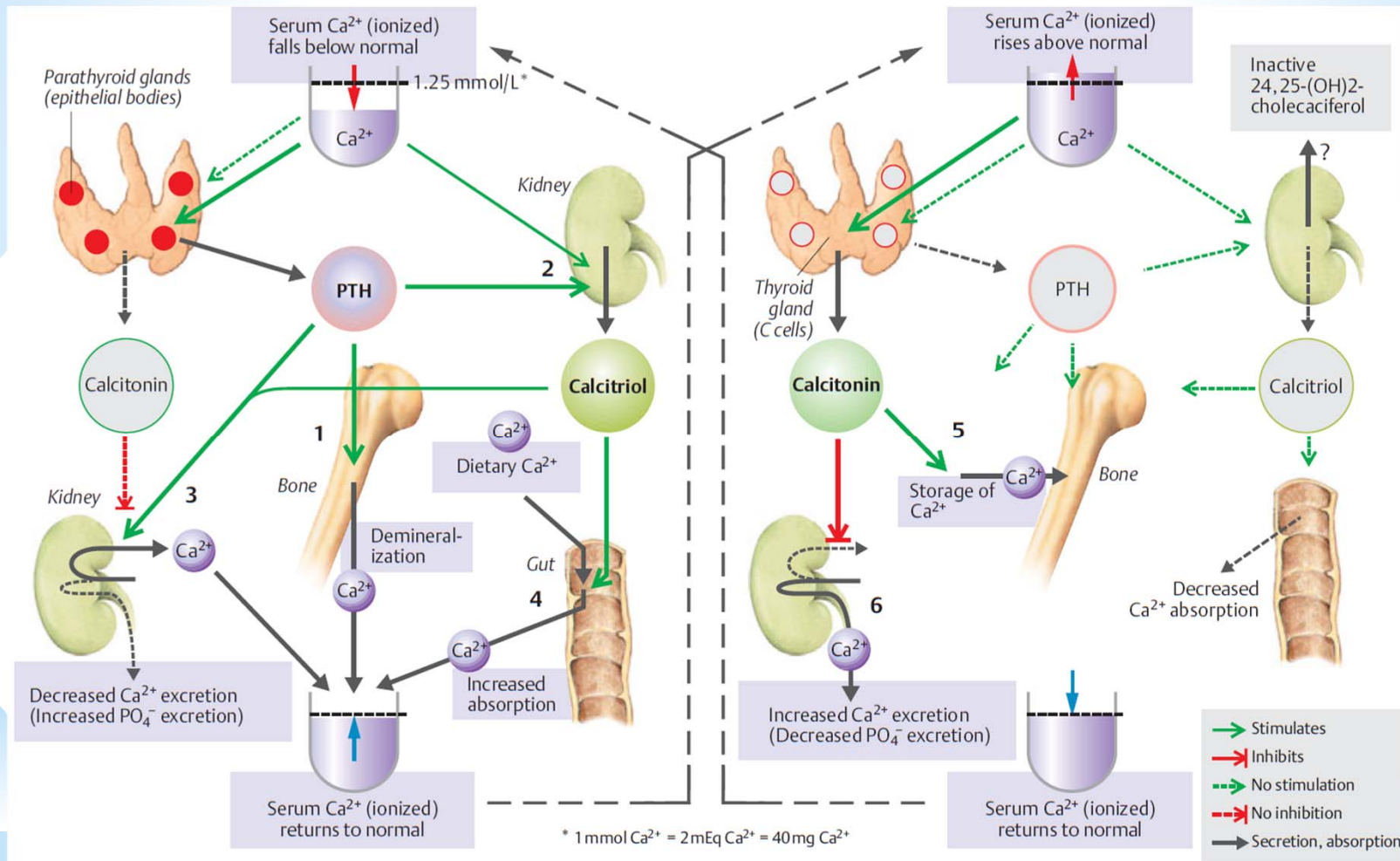
Parathormone

Vitamin D

Calcitonin

Humoral Regulation of Body Fluids

Hormonal Regulation of Calcemia



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Acid-Base Balance

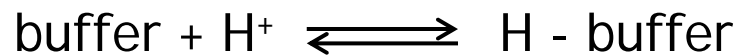
- Regulation by Kidneys -

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⁺:



↑[H⁺] direction to the right favoured till free buffer is available

↓[H⁺] direction to the left favoured, H⁺ released

2) Lungs

- fast regulation (minutes even hours)
- elimination of CO₂ 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

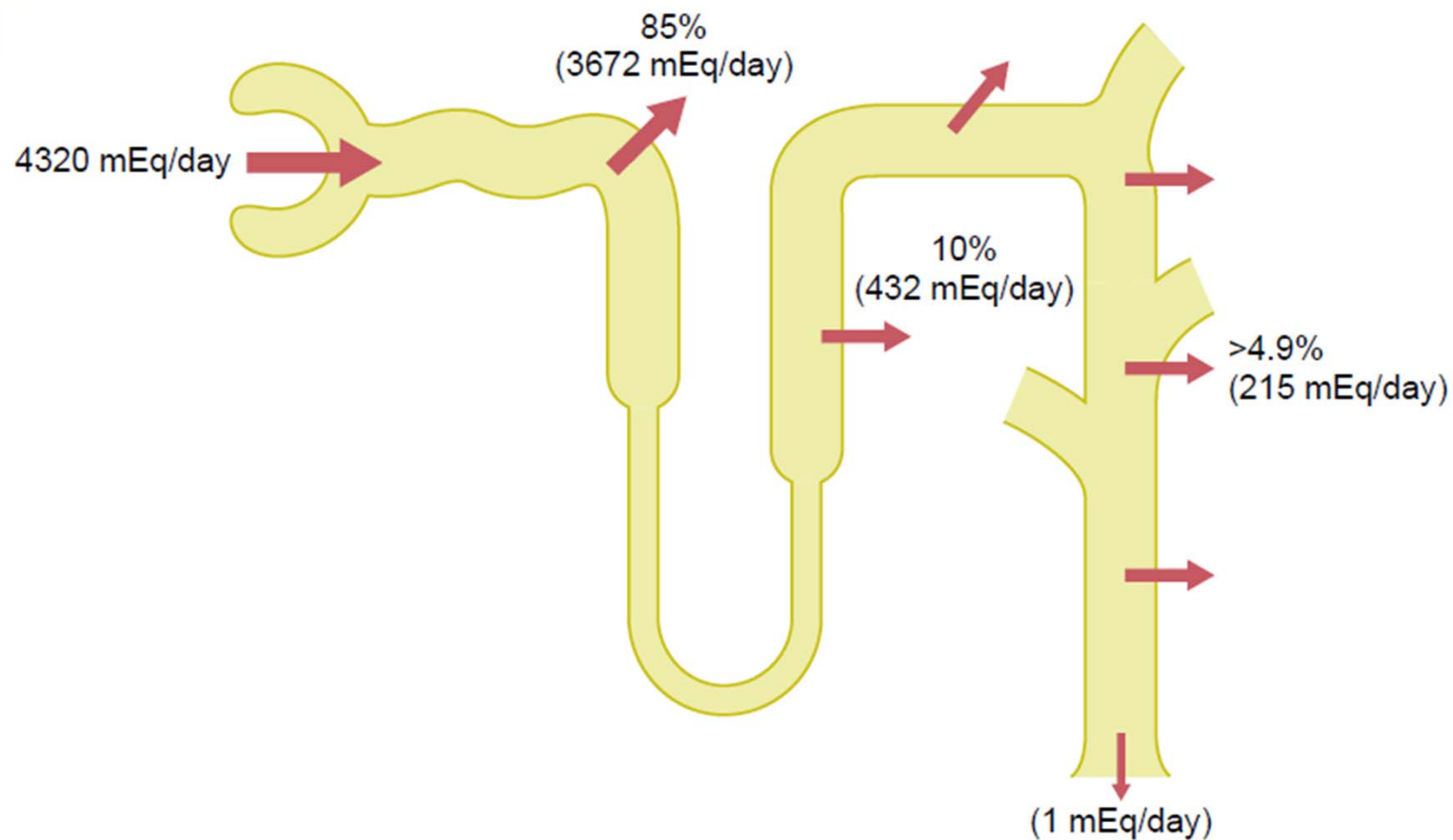
Regulation of Acid-Base Balance by Kidneys

- by excretion of acid or alkalic urine
- a high amount of 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 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^-

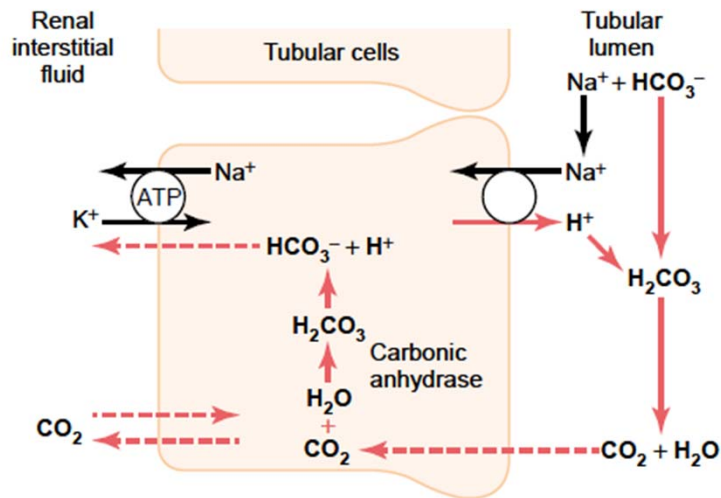


Acid-Base Balance and its Regulation

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:

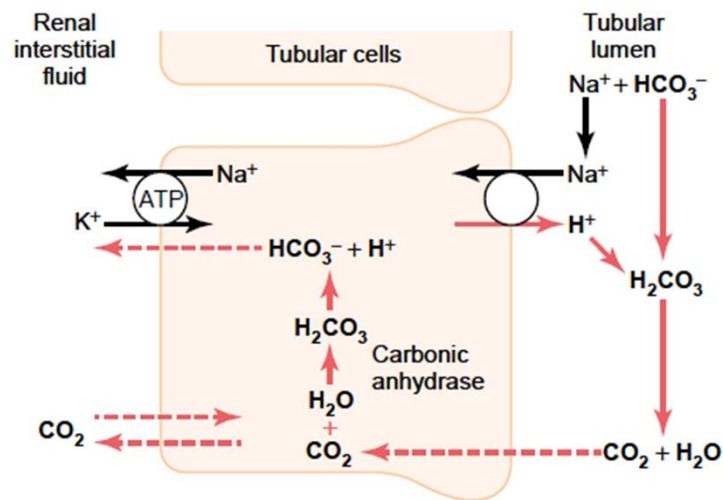
- $Na^+-HCO_3^-$ co-transport (the proximal tubule)
- $Cl^- - HCO_3^-$ exchanger (the end of proximal tubule and the following parts of tubulus except for the thin loop of Henle)

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

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

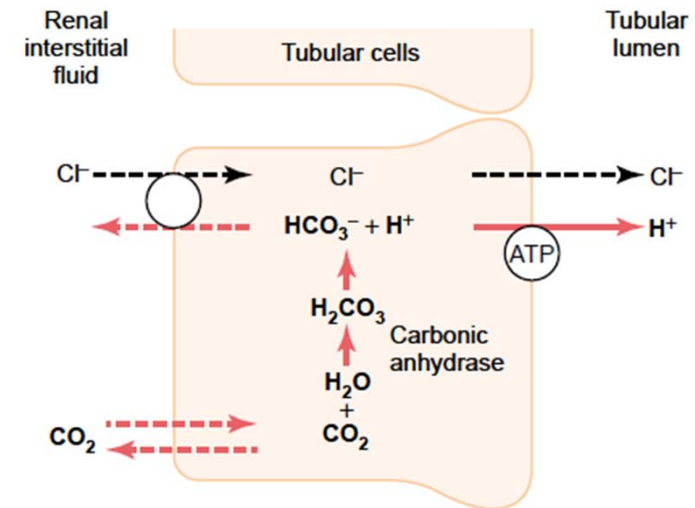
❖ in the proximal tubule, thick loop of Henle and at the beginning of the distal tubule



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)

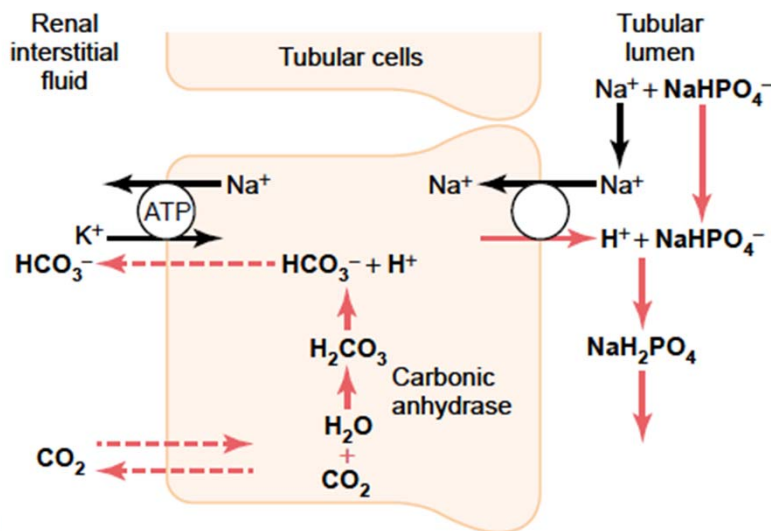
acidification of urine

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

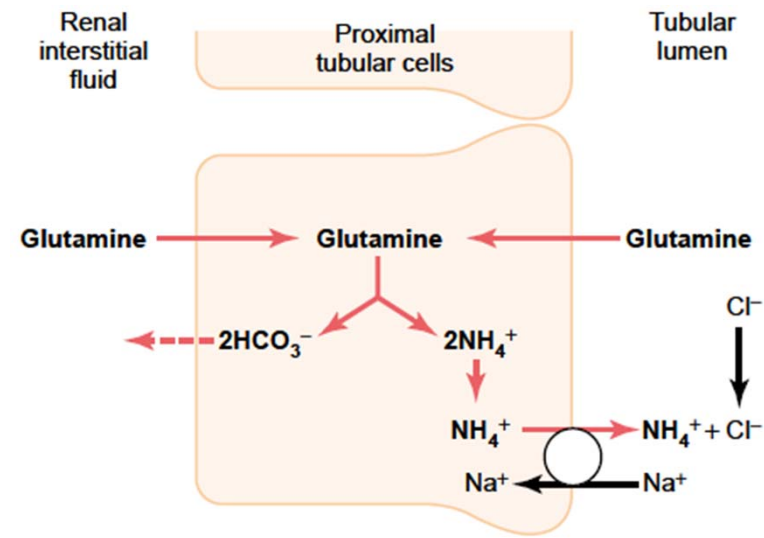
- 1) Secretion of H^+
- 2) Reabsorption of HCO_3^-
- 3) Production of HCO_3^- *de novo*

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



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

❖ Ammonium buffer (NH_3 , NH_4^+)



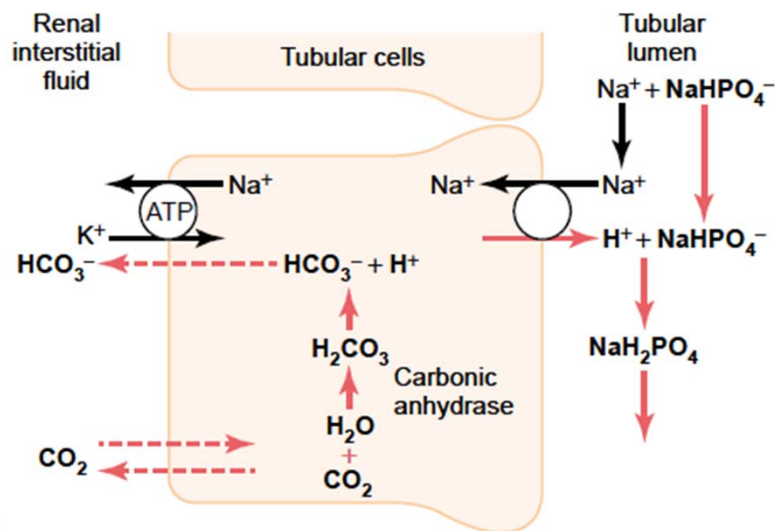
NH_4^+ originates from glutamine - the proximal tubule, thick ascending loop of Henle and distal tubule

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

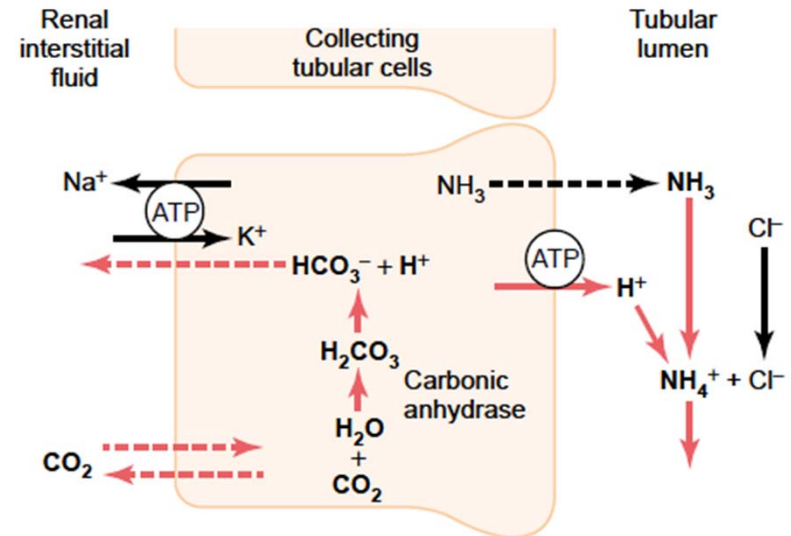
- 1) Secretion of H^+
- 2) Reabsorption of HCO_3^-
- 3) Produkce nového HCO_3^-

❖ 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^+)



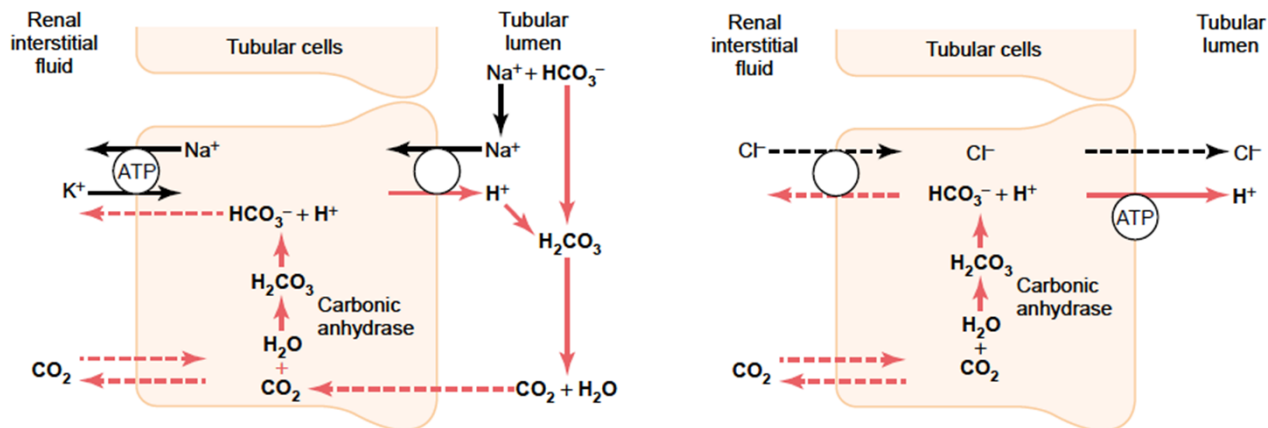
the collecting duct (permeable for NH_3 but far less for NH_4^+ - excreted by urine)
50% of H^+ secretion and HCO_3^- formed *de novo!*

Acid-Base Balance and its Regulation

Regulation of Acid-Base Balance by Kidneys

Regulation of H⁺ secretion

- ↑ - ↑ pCO₂ in ECF (respiratory acidosis; direct stimulation due to ↑ formation of H⁺ in tubular cells)



- ↓ pH in ECF (respiratory or metabolic acidosis)
- ↑ secretion of aldosterone (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 HCO₃⁻ Reabsorption by the Renal Tubules

Increase H⁺ Secretion and HCO₃⁻ Reabsorption

↑ PCO₂

↑ H⁺, ↓ HCO₃⁻

↓ Extracellular fluid volume

↑ Angiotensin II

↑ Aldosterone

Hypokalemia

RAS

Decrease H⁺ Secretion and HCO₃⁻ Reabsorption

↓ PCO₂

↓ H⁺, ↑ HCO₃⁻

↑ Extracellular fluid volume

↓ Angiotensin II

↓ Aldosterone

Hyperkalemia

↑ 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

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

- **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 HCO_3^- + its formation *de novo* (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 H^+ and 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

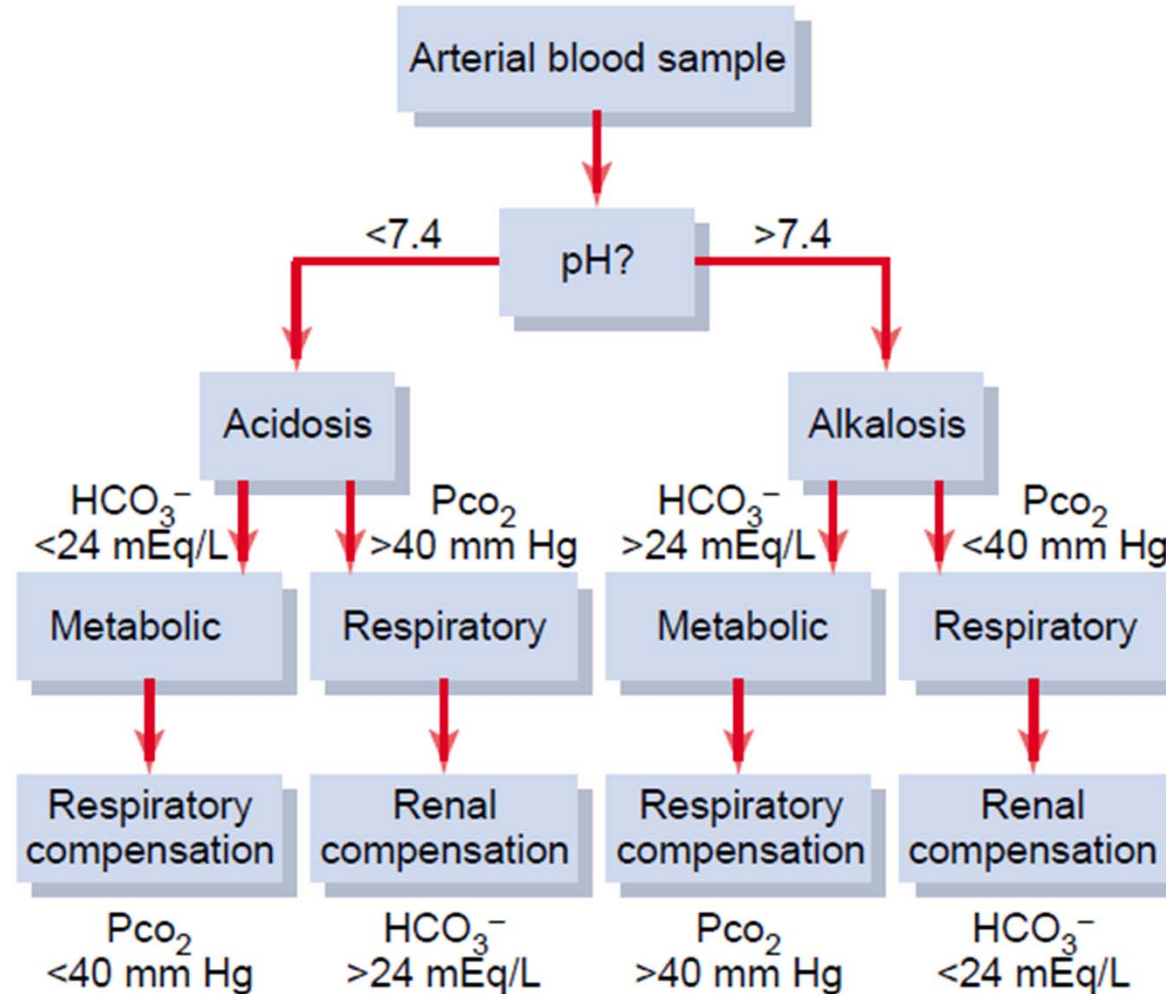
Alkalosis - correction by kidneys

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

- **metabolic alkalosis:** due to $\uparrow \text{HCO}_3^-$
renal correction: $\uparrow \text{HCO}_3^-$ in ECF \rightarrow \uparrow filtered $\text{HCO}_3^- \rightarrow$ incomplete HCO_3^- reabsorption (lack of 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 H^+ and HCO_3^- in tubular cells \rightarrow $\downarrow \text{H}^+$ secretion + $\downarrow \text{HCO}_3^-$ reabsorption \rightarrow pH normalization

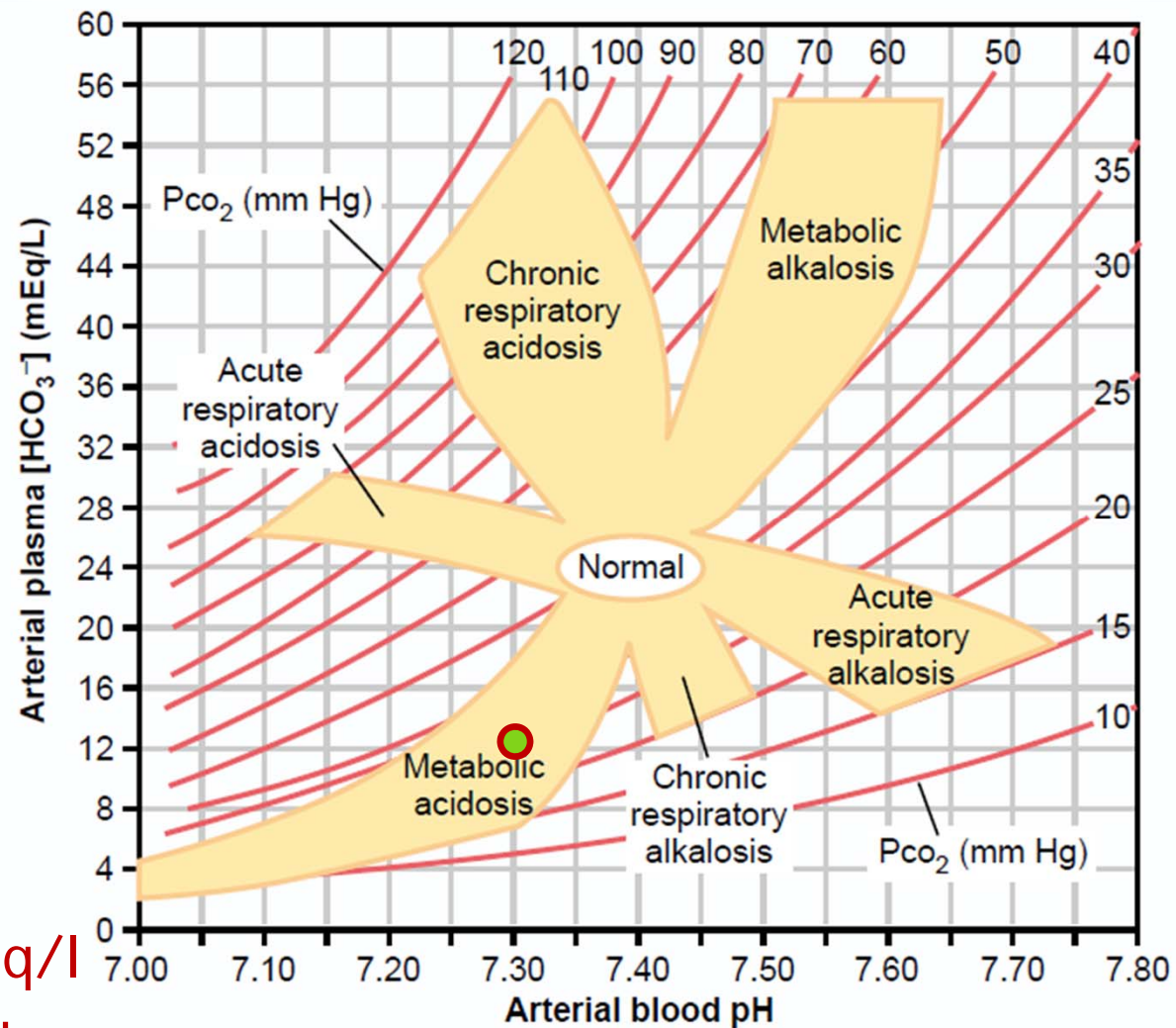
Acid-Base Balance and its Regulation

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

