„NON SIBI, SED OMNIBUS"

МЕДИЦИНСКИ УНИВЕРСИТЕТ ПЛЕВЕН

MEDICAL UNIVERSITY - PLEVEN
FACULTY OF MEDICINE
Physiology

Lecture № 4

The body fluid compartments: extracellular and intracellular fluids. Regulation of the fluid volume and osmolarity – renal and hormonal control. Acid-base regulation

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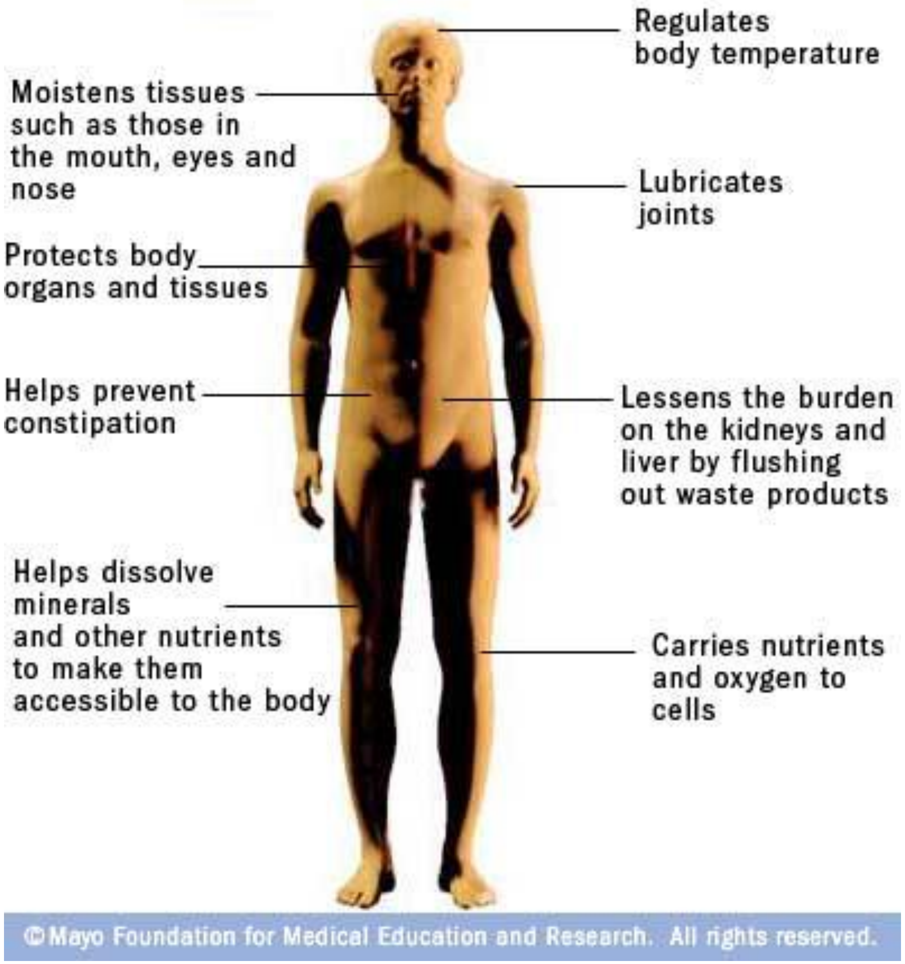
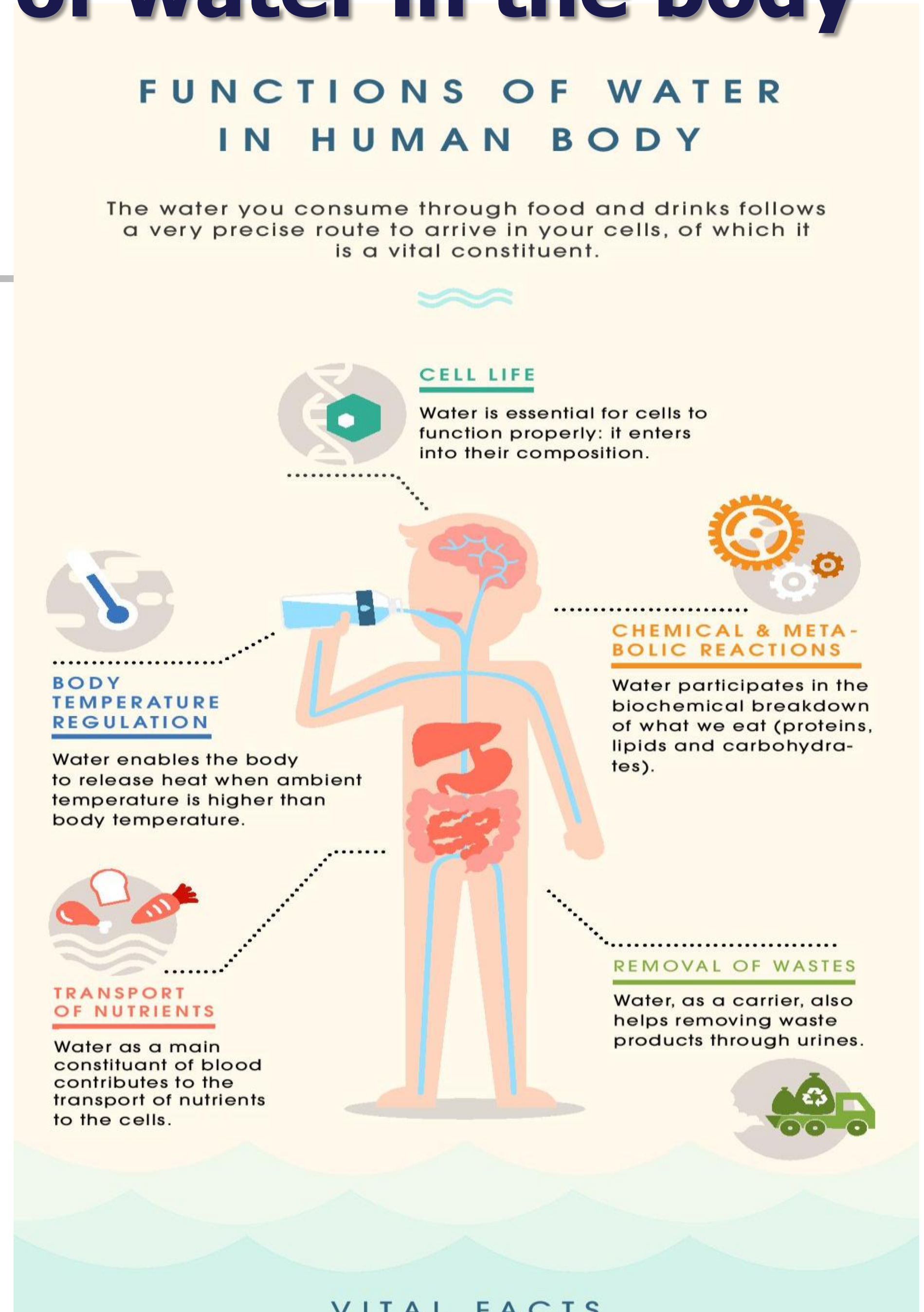
Body Water - Importance/Significance Functions

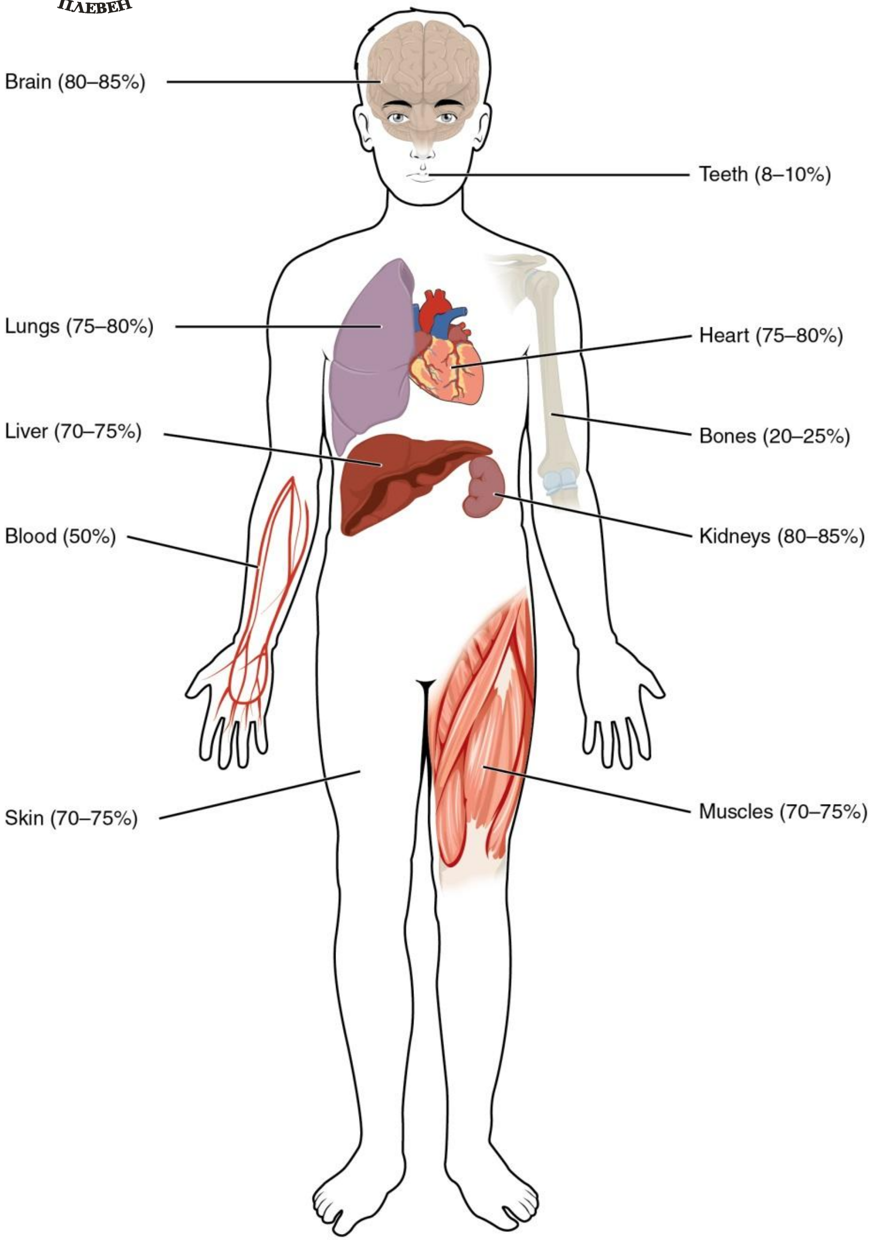
- **Solvent**
- Needed for all chemical reactions in the body
- Intracellular medium - Major component in every cell – shape and size of cells
- Containing medium for electrolytes and all other ions
- Has high heat conductivity
- Electrical conductor – muscle and neuron
- High surface tension – capillary forces of attraction
- Water deprivation leads to DEATH
- Hydrolysis
  - ATP + H_2O = Energy + ADP + Inorganic Phosphate
  - Digestion

Functions of water in the body





Body Water Content



- 75% of body mass in newborns (65% infants)
- about av. 60 % in adult men and women
- 45 % in old age
- brain and kidneys have the highest proportions of water, which composes 80–85% of their masses
- teeth have the lowest proportion of water, at 8–10 %

Total Body Water Depends on:

- Age
- Sex
- Degree of obesity

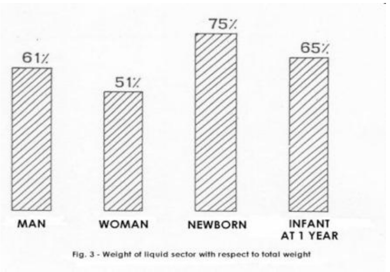


Fig. 3 - Weight of liquid sector with respect to total weight

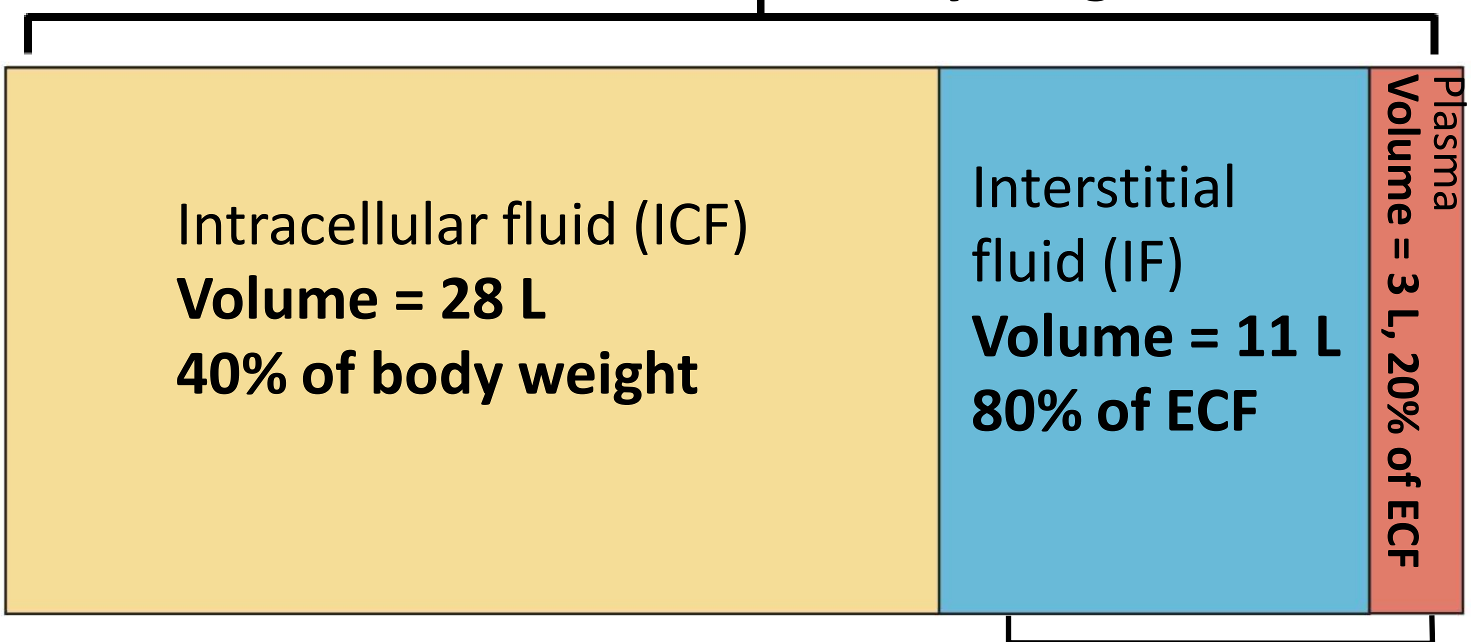
- **With Increasing Age**
  - Percentage of total weight that is water decreases; More in children
  - Aging – gradual decrease of body water
  - Fat – decreases percentage of water in body

- **Women – More body fat than men**
  - Contain slightly less water than men in proportion to their weight
    - Male (60%) 54 – 70%
    - Female (50%) 45 – 60%

The Major Fluid Compartments of the Body

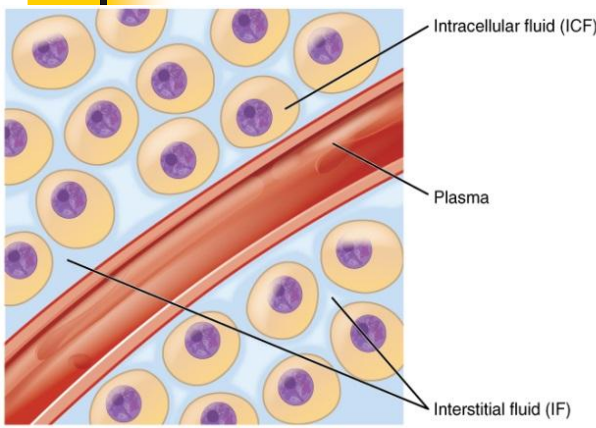
Average 70 kg adult man – 42 L

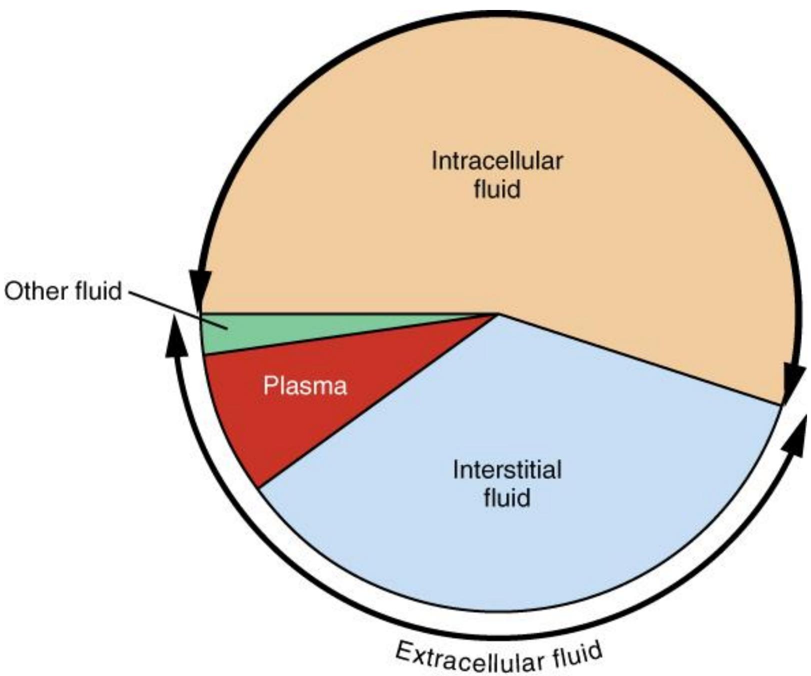
The 60 - 40 - 20 Rule:

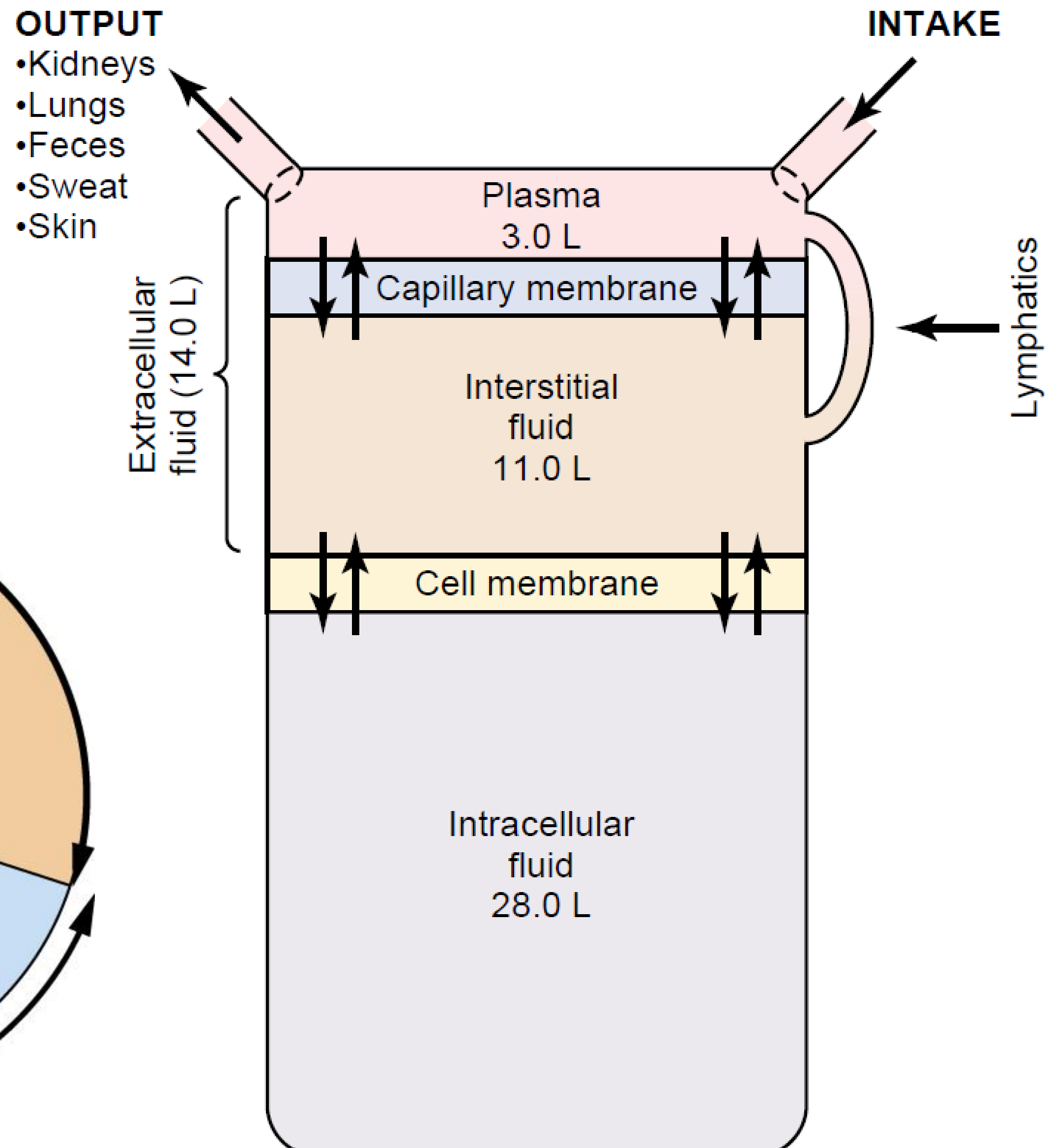


60% of b. w. - total body water (**TBW**)
40% of b. w. - intracellular fluids (**ICF**)
20% of b. w. - extracellular fluid (**ECF**)

Body Fluid Distribution







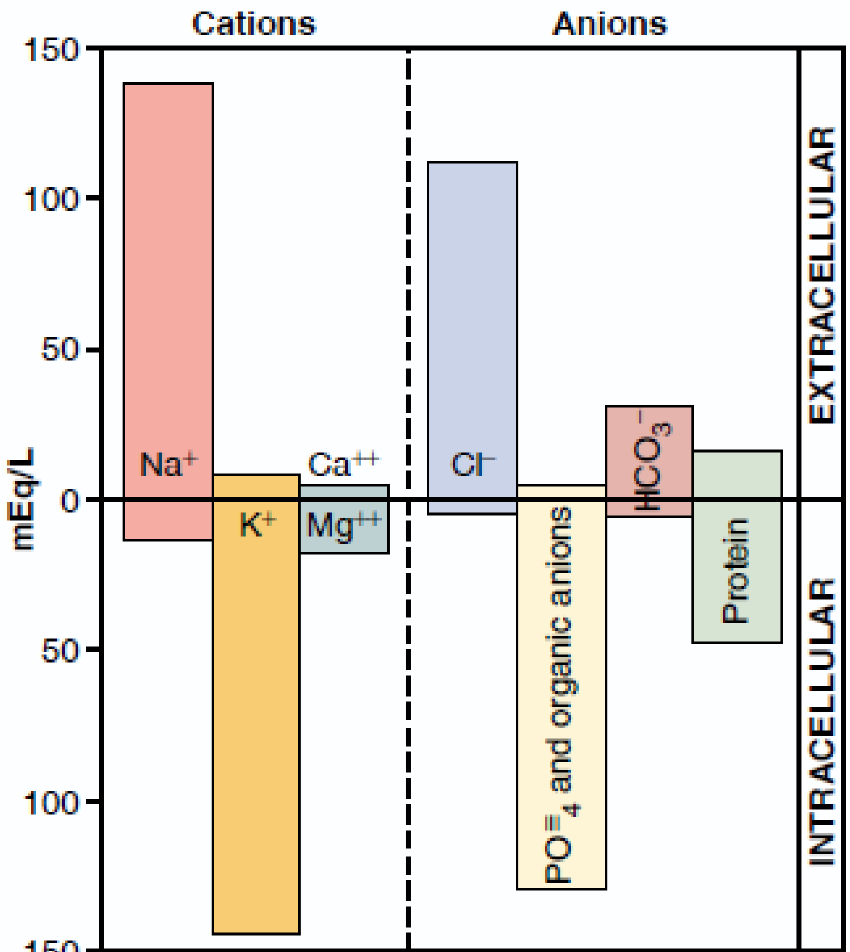
Intracellular Fluid (ICF)

- Comprises 2/3 of the total body water (28 L out of 42)
- ICF is about 40% of the body weight
- The ICF is primarily a solution of
  - low Na^+ and Cl^-
  - **major cations are K^+ and magnesium**
  - **major anions are proteins and organic HPO_4^{2-}** (ATP, ADP, and AMP)
- The cell membranes and cellular metabolism control the constituents of the ICF
- ICF **is not homogeneous**. It represents a conglomeration of fluids from all the different cells
- Unevenly distributed in the different cells and organs

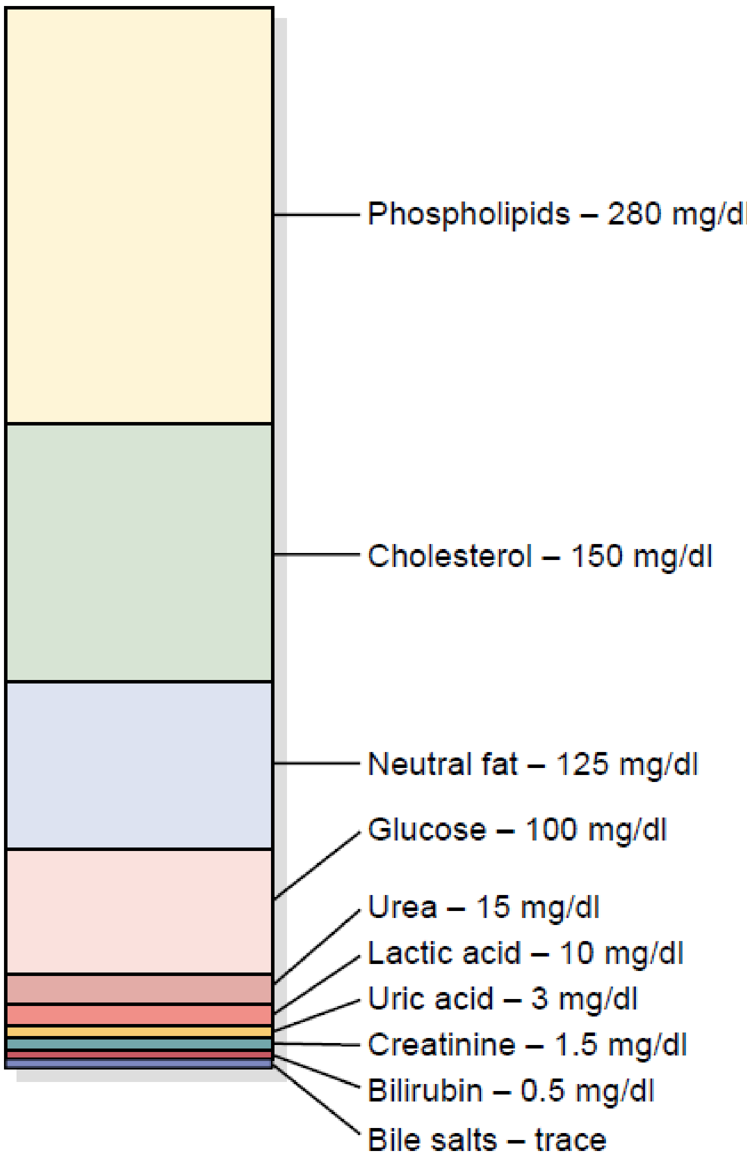
Extracellular Fluid (ECF)

- is about 1/3 of of the total body water, 20% of b. w. (14 l)
- The ECF is primarily a NaCl and $NaHCO_3$ solution
  - **Major cation: Na^+ Major anion: Cl^-**
- All similar
- Primarily transport function
- The ECF is further subdivided into three subcompartments:
  - **Interstitial Fluid (ISF)** surrounds the cells, but does not circulate. It comprises about 3/4 of the ECF (1/4 of TBW, 11 l)
  - **Plasma** circulates as the extracellular component of blood. It makes up about 1/4 of the ECF (1/12 of TBW, 3 l)
  - **Transcellular fluid** is a set of fluids that are outside of the normal compartments - CSF, humors of the eye, synovial fluid, serous fluid, and gastrointestinal secretions, etc.

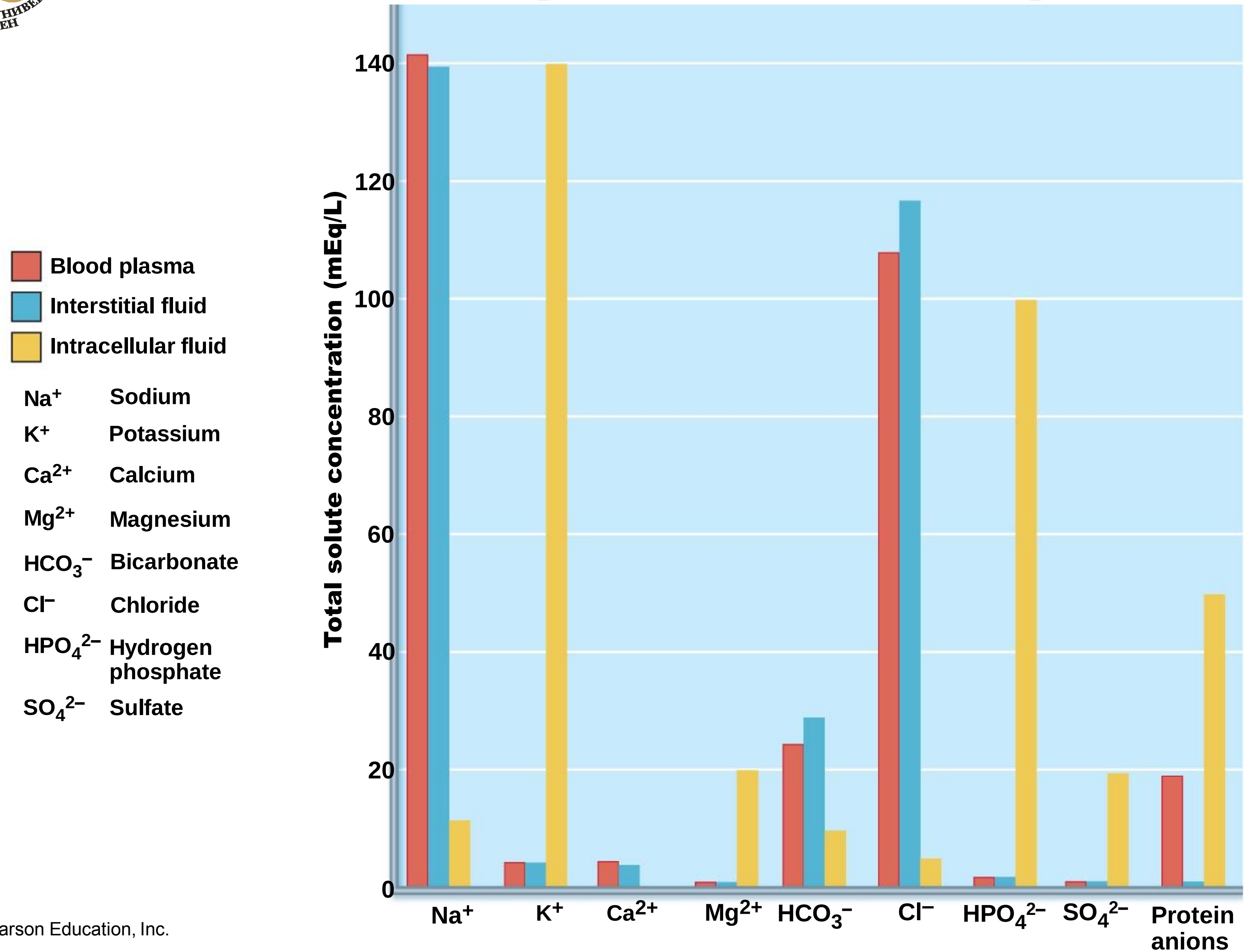
Constituents of ICF and ECF



Nonelectrolytes of the plasma.



Composition of Body Fluids



Na^+	Sodium
K^+	Potassium
Ca^{2+}	Calcium
Mg^{2+}	Magnesium
HCO_3^-	Bicarbonate
Cl^-	Chloride
HPO_4^{2-}	Hydrogen phosphate
SO_4^{2-}	Sulfate

Osmolar Substances in ECF and ICF

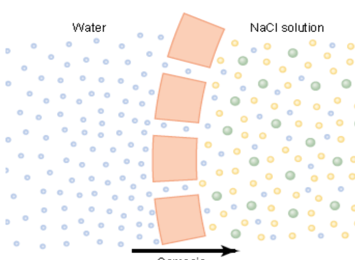
Osmolar Substances in Extracellular and Intracellular Fluids

	Plasma (mOsm/L H_2O)	Interstitial (mOsm/L H_2O)	Intracellular (mOsm/L H_2O)
Na^+	142	139	14
K^+	4.2	4.0	140
Ca^{++}	1.3	1.2	0
Mg^+	0.8	0.7	20
Cl^-	108	108	4
HCO_3^-	24	28.3	10
HPO_4^-, $H_2PO_4^-$	2	2	11
SO_4^-	0.5	0.5	1
Phosphocreatine			45
Carnosine			14
Amino acids	2	2	8
Creatine	0.2	0.2	9
Lactate	1.2	1.2	1.5
Adenosine triphosphate			5
Hexose monophosphate			3.7
Glucose	5.6	5.6	
Protein	1.2	0.2	4
Urea	4	4	4
Others	4.8	3.9	10
Total mOsm/L	301.8	300.8	301.2
Corrected osmolar activity (mOsm/L)	282.0	281.0	281.0
Total osmotic pressure at 37°C (mm Hg)	5443	5423	5423

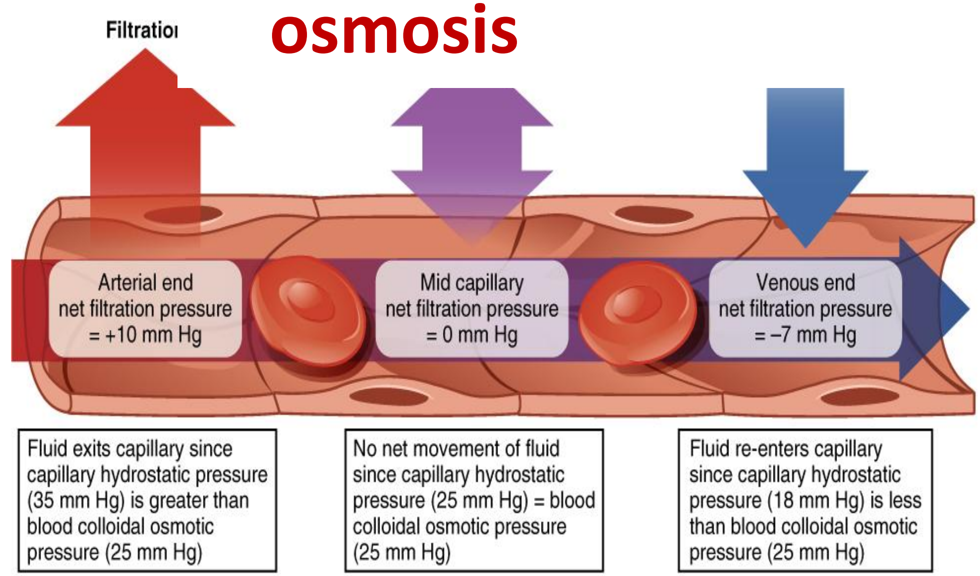
The high levels of potassium and low levels of sodium in the ICF are maintained by sodium-potassium pumps in the cell membranes

Osmosis

- Osmosis is the diffusion of water from regions of higher concentration to regions of lower concentration, along an osmotic gradient across a semi-permeable membrane until osmolarities of the two become equal
- As a result, **water will move** into and out of cells and tissues, **depending on the relative concentrations of the water and solutes**



- Water moves through semi-permeable membranes of cells and from one compartment of the body to another by **osmosis**



Osmotic Equilibrium

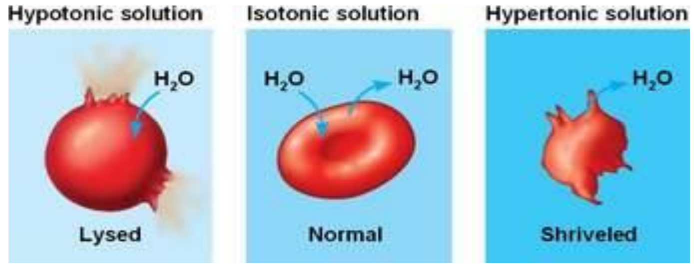
- **Osmolality** - concentration expressed as osmoles per kg of water
- **Osmolarity** - concentration expressed as osmoles per liter of solution

Osmole - number of osmotically active particles in a solution rather than the molar concentration

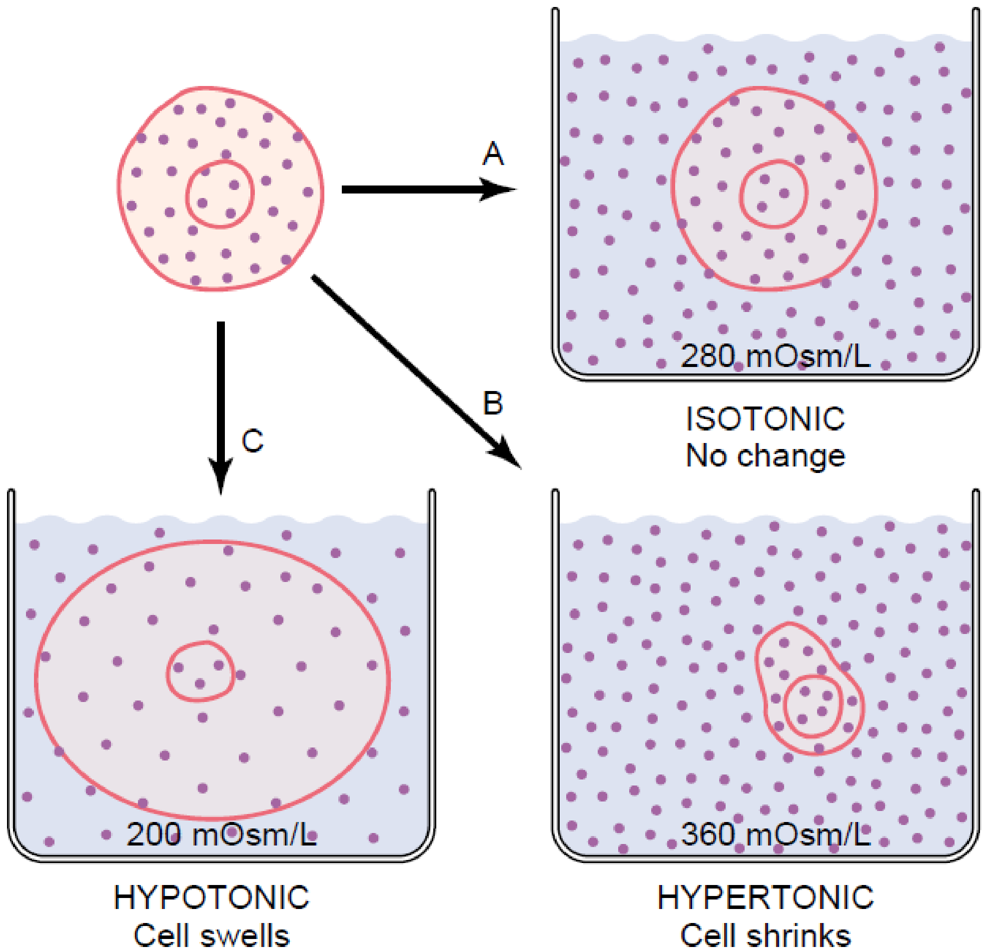
- TBW - final distribution determined by osmotic and hydrostatic forces
- Osmosis
- Osmotic pressure – pressure required to prevent osmosis
- Osmolality of blood plasma - 290 mOsm/kg
- **Isotonicity, hypotonicity, hypertonicity**

  Isotonic solutions - 0.9% NaCl, 5% Glucose

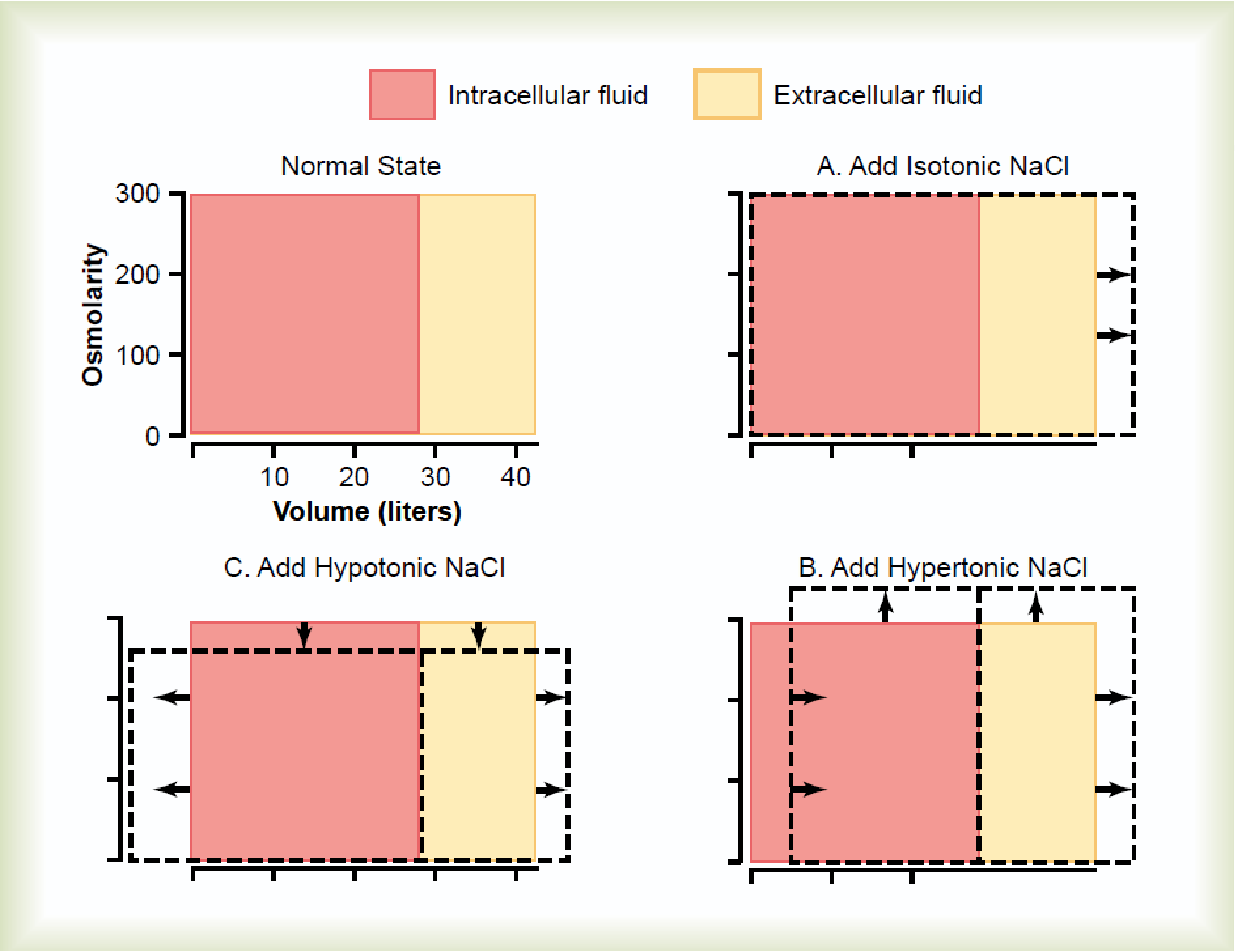
Tonicity



Effects of isotonic (*A*), hypertonic (*B*), and hypotonic (*C*) solutions on cell volume.



Dynamics of Body Fluids



Effect of adding isotonic, hypertonic, and hypotonic solutions to the extracellular fluid after osmotic equilibrium

Water Balance

Water intake = water output

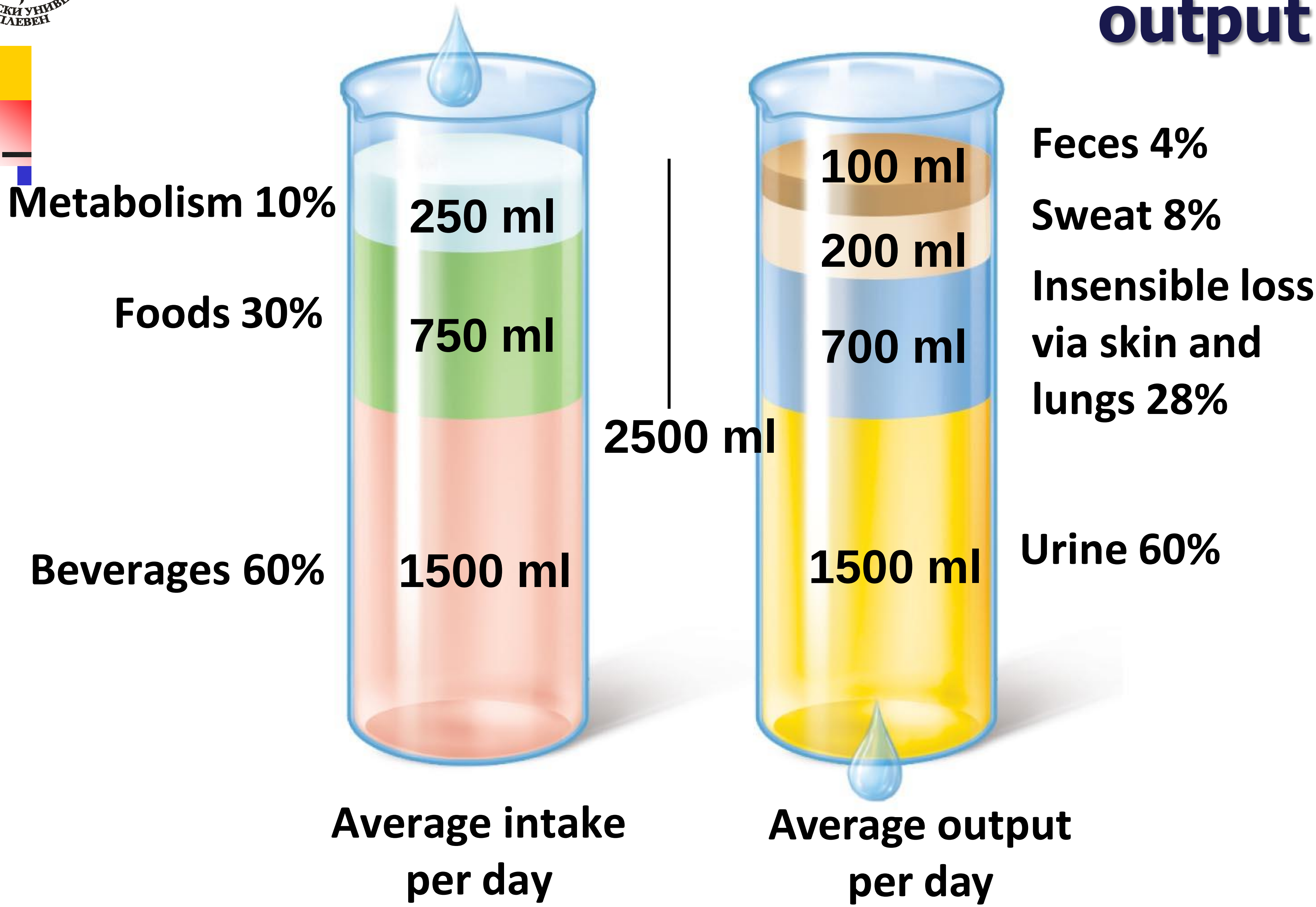
- **Daily Intake of Water**
- Water Sources:
  - a) Water drinking
  - b) Water contained in food both 2300 ml
  - c) Metabolism to CO_2 and H_2O – 200 ml
- *Net Intake = 2500 ml*

- **Daily Output of Water (Water loss)**
- Insensible (skin) – 350 ml
- Insensible (lungs) – 450 ml
- Sweat – 100 ml
- Feces – 100 ml
- Urine – 1500 ml (0.5)
- *Net Output = 2500 ml*

- Determined by social considerations rather than physiological needs
- Thirst safeguards fluid intake

- **Increased Water loss**
- Exercise (3300 ml/day)
- Hot weather (6600 ml/day)
- Pathological (4 - 8 L/day)

Major sources of water intake and output

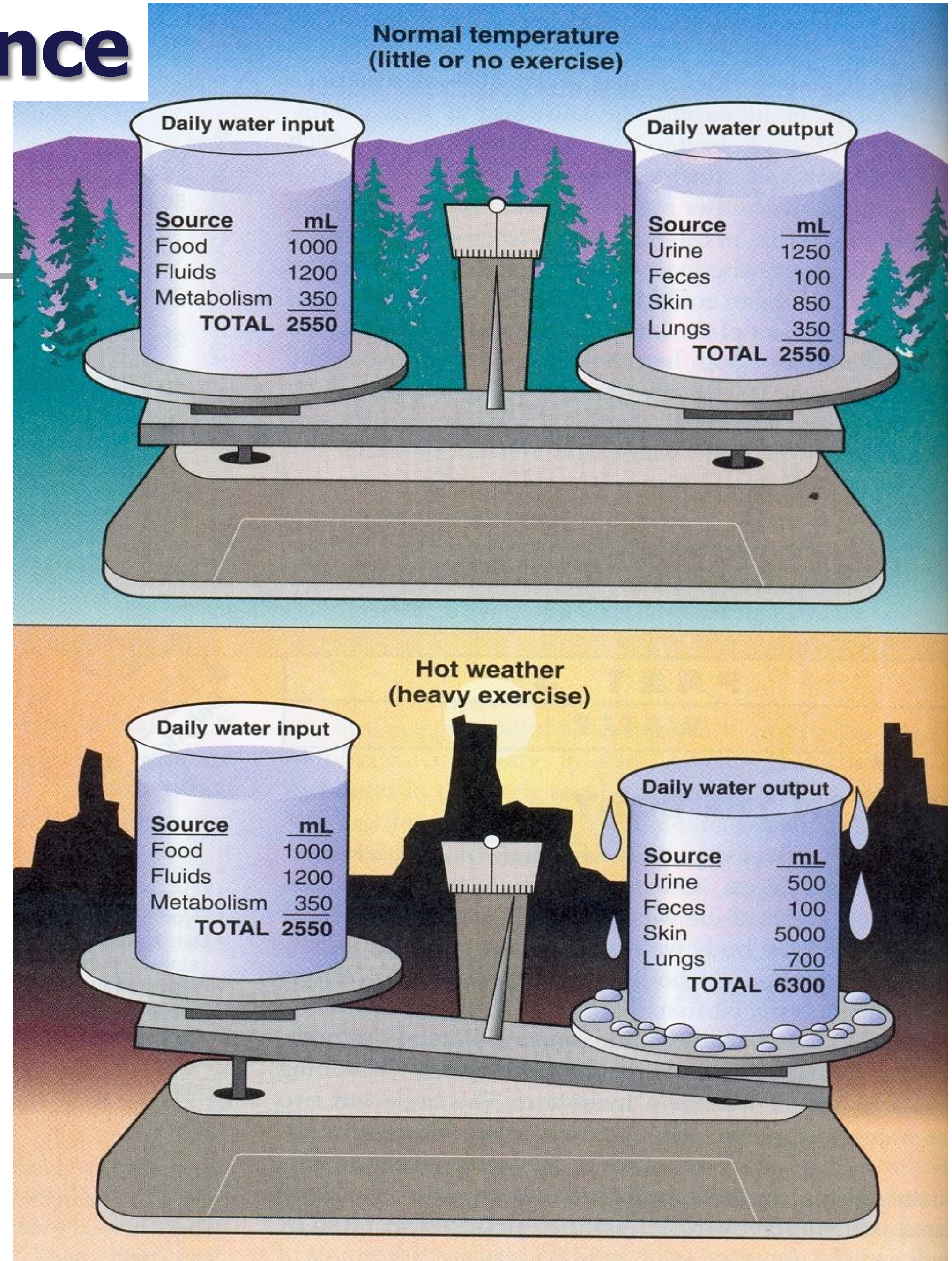


Water Balance

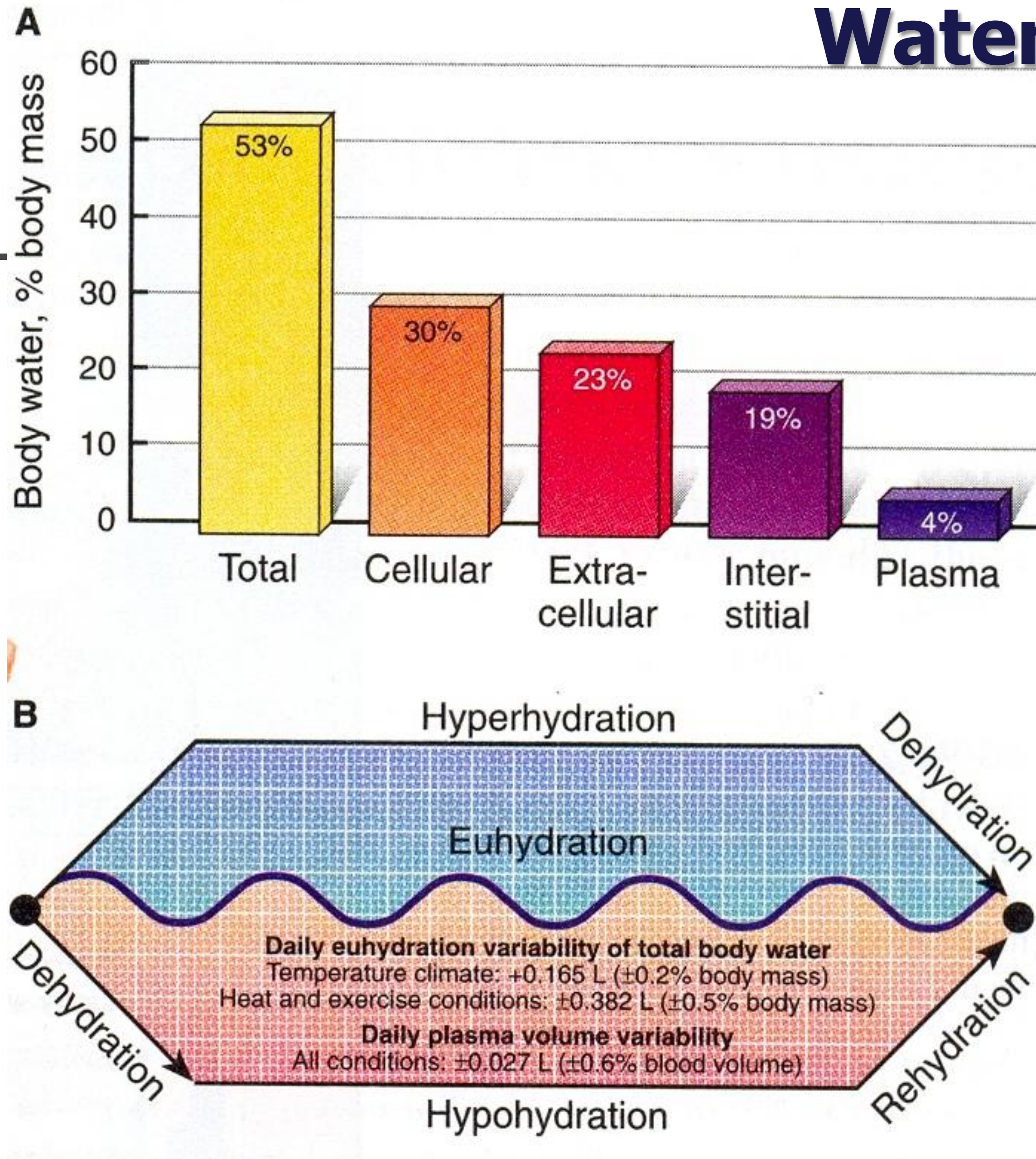
- In health total body water is kept reasonably constant in spite of wide fluctuations in daily intake

Daily intake = Daily output

- (20 ºC, No exercise)

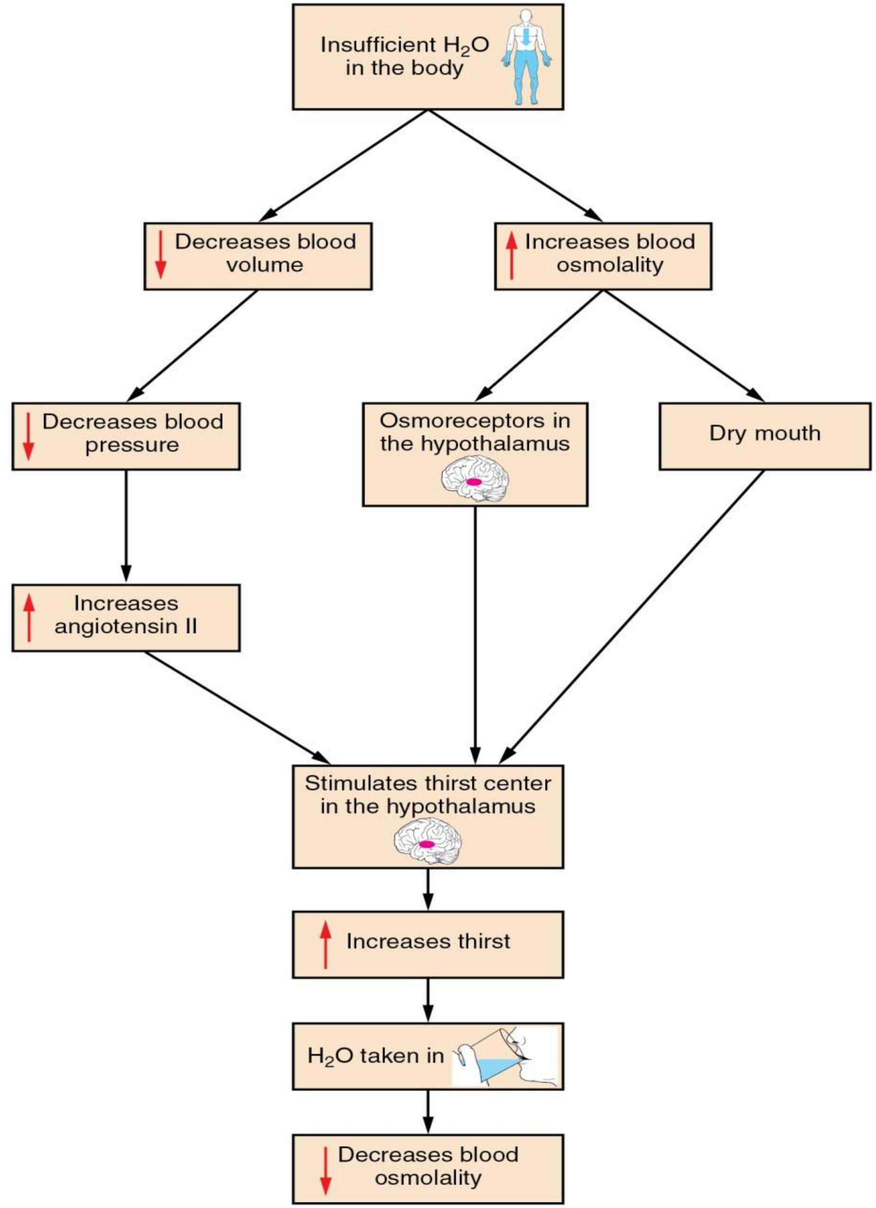


Water Balance



Maintenance of Body fluid Osmolality

- Osmolality maintained at ~ 280 – 300 mOsm
- Rise in osmolality →
  - Stimulates thirst
  - ADH release
- Decrease in osmolality →
  - Thirst inhibition
  - – ADH inhibition



Water Imbalance

- **Positive water balance**
- *Increased water intake than water loss*
- **CAUSES**
- Infants
- Growing children
- Athletes
- Pregnancy

- **Negative water balance**
- *Decreased water intake than water loss*
- **CAUSES**
- Fatty meal
- Diuretics use
- Dehydration - Thirst

Water Depletion/dehydration

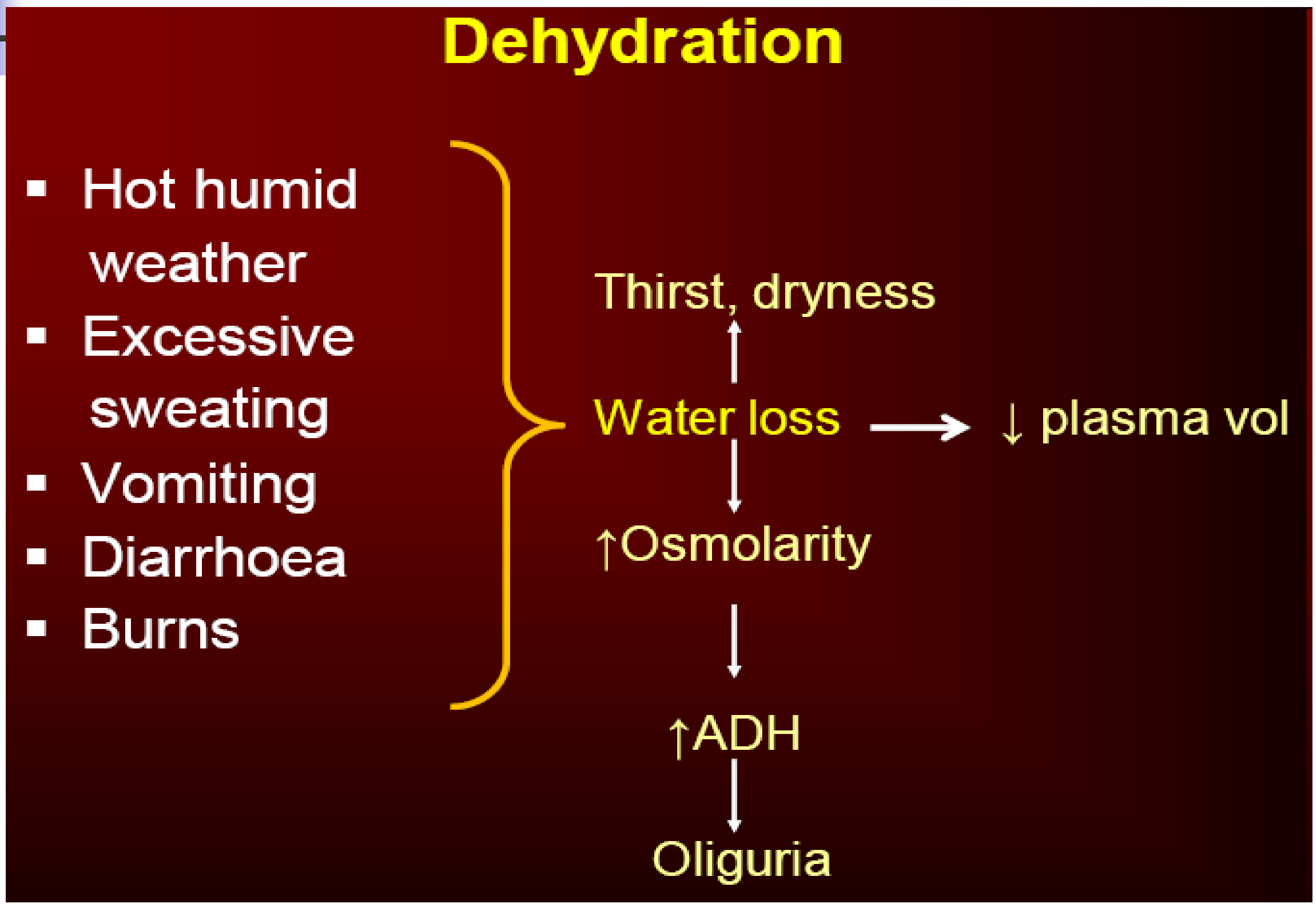
Causes

- Low intake
- Poor absorption
- Increased loss
  - Diarrhea
  - Vomiting
  - Cholera

Clinical features

- Thirst
- Dryness of mouth
- Dry loose skin
- Oliguria
- Sunken eyes
- Hypotention
- Delerium
- Haemoconcentration

Water Depletion/Dehydration



Water Excess (water toxicity)

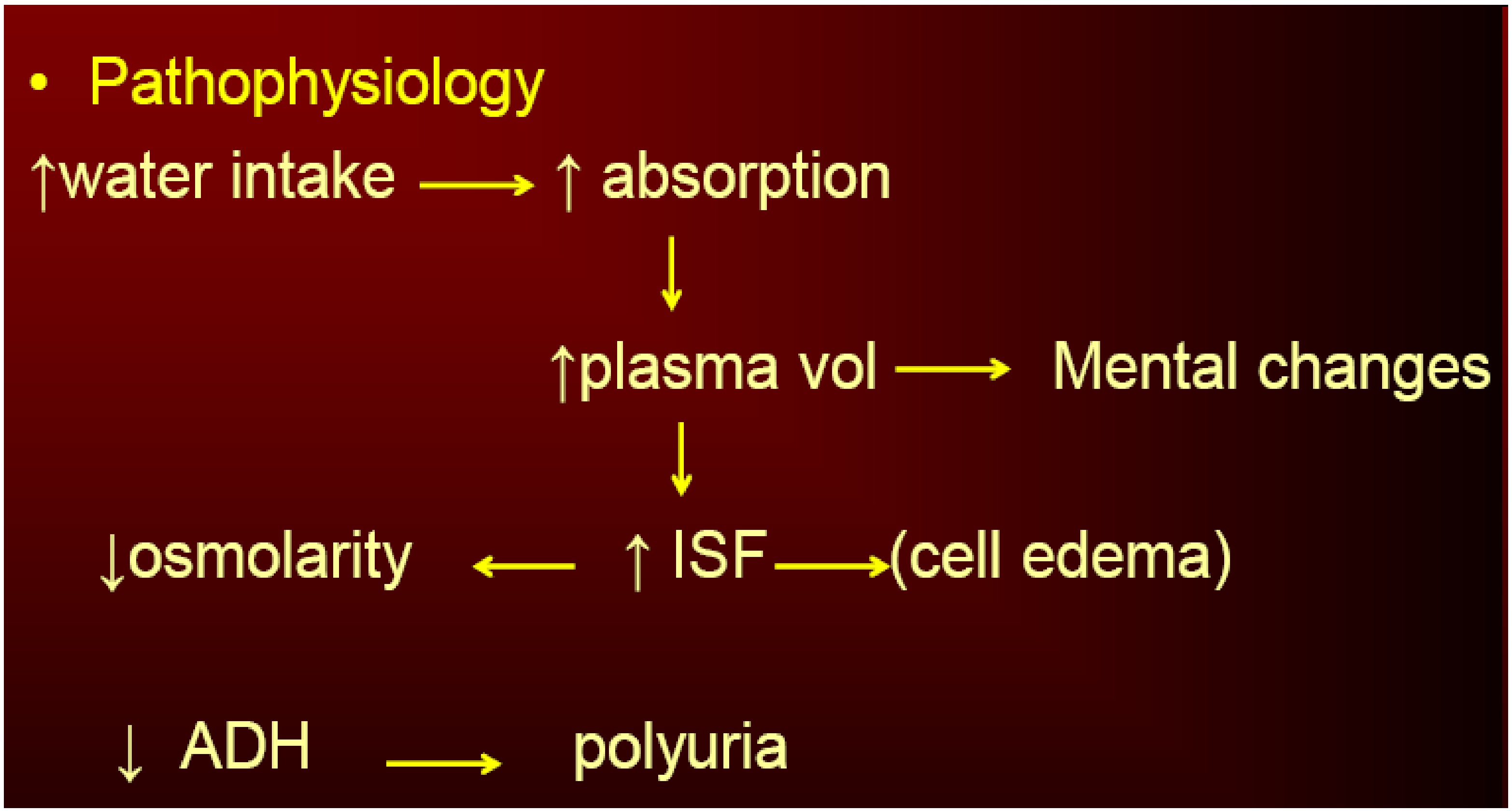
CAUSES

- Excessive intake
- Renal retention/dysfunctional nephrosis
- Nephrotic syndrome
- Liver damage - hypoproteinemia
- Raised ADH
- Drugs e.g. narcotics
- Hypothyroidism

CLINICAL FEATURES

- Headache
- Nausea/vomiting
- Cramps
- Raised BP
- Polyuria
- Cardiac overload
- Haemodilution

Water Excess (water toxicity)



Edema: Accumulation of excessive fluid in body tissues

- **Types**
- Intracellular
- Extracellular (more common)

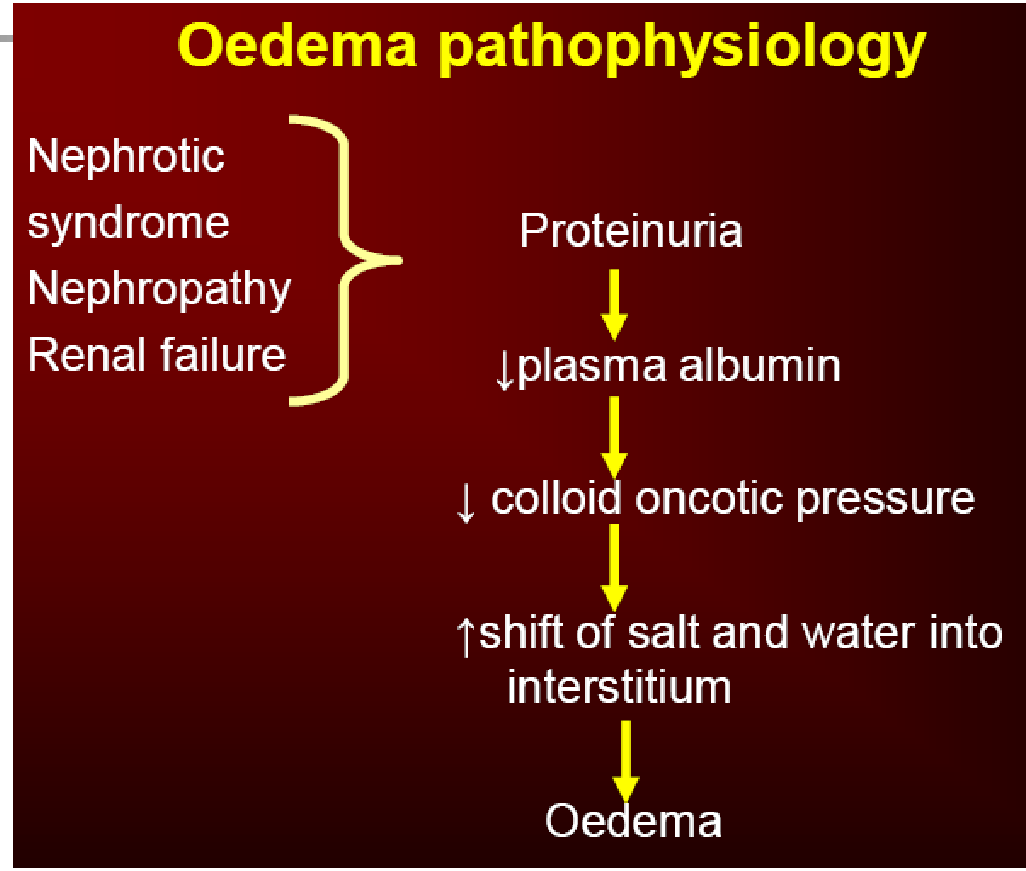
Intracellular edema

- **Causes**
- Depression of metabolic systems of tissues (cells)
- Lack of adequate nutrition
- Na+-K+ ATPase pump failure
- Inflammed tissues

Extracellular edema

- **•Pathophysiology**
- Abnormal fluid leakage from blood capillaries
- Failure of lymphatic drainage system
- **•Causes**
- Increased capillary pressure
- Decreased plasma proteins
- Increased capillary permeability
- Lymphatic blockage

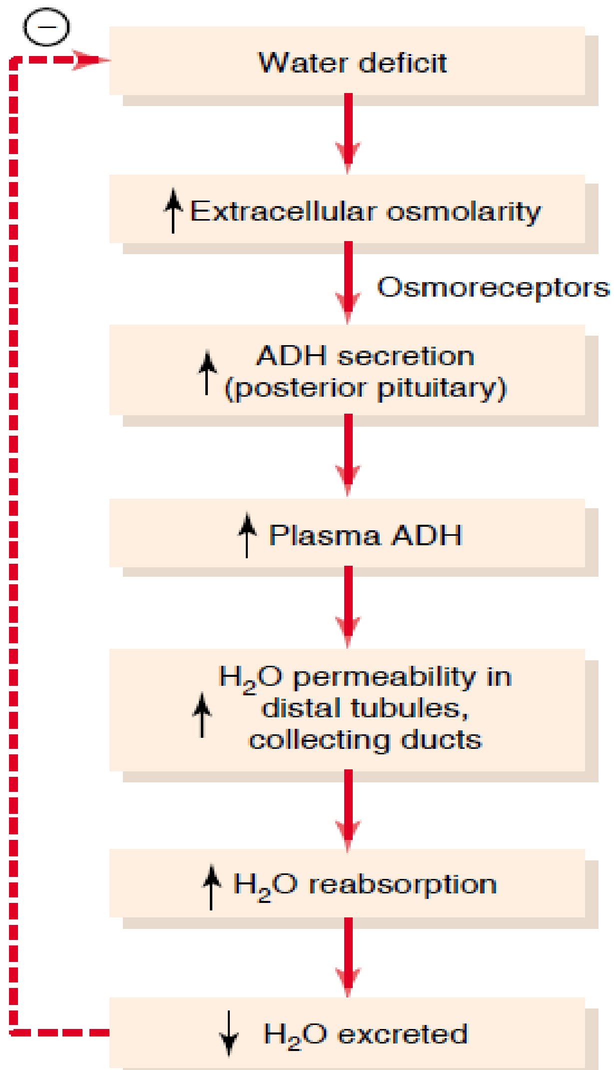
Edema



Oedema pathophysiology
Nephrotic syndrome
Nephropathy
Renal failure
Proteinuria
↓plasma albumin
↓ colloid oncotic pressure
↑shift of salt and water into interstitium
Oedema

Osmoreceptor - ADH Feedback System

Osmolarity increases above normal (plasma sodium concentration)



in the anterior HT near the supraoptic nuclei shrink – send signals to nerve cells in the supraoptic nuclei

Regulation of ADH Secretion

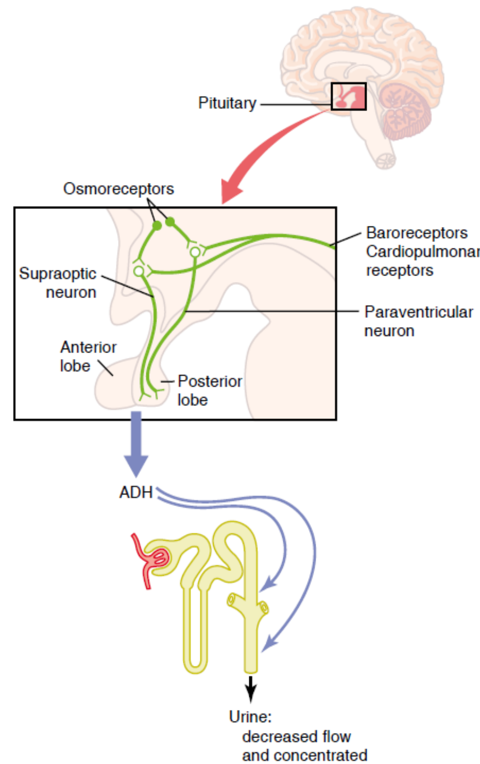
Regulation of ADH Secretion

Increase ADH	Decrease ADH
↑ Plasma osmolarity	↓ Plasma osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
Nausea	
Hypoxia	
Drugs:	Drugs:
Morphine	Alcohol
Nicotine	Clonidine (antihypertensive drug)
Cyclophosphamide	Haloperidol (dopamine blocker)

Control of thirst

Control of Thirst

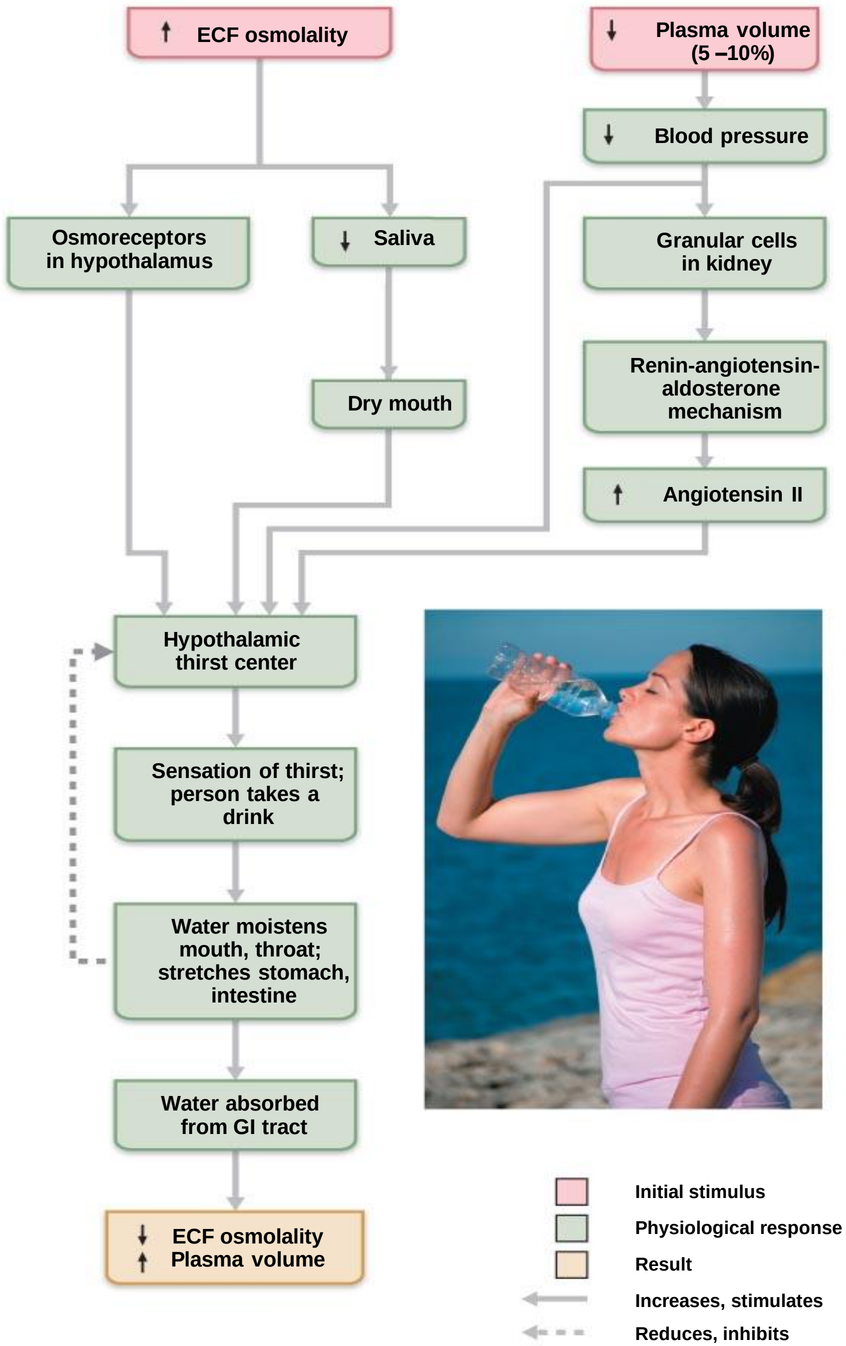
Increase Thirst	Decrease Thirst
↑ Osmolarity	↓ Osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
↑ Angiotensin	↓ Angiotensin II
Dryness of mouth	Gastric distention



Thirst – conscious desire for water

Thirst center: anteroventral region of the third ventricle – AV3V, and area in the preoptic nucleus - stimulate thirst

Figure 26.5 The thirst mechanism for regulating water intake.



Electrolyte balance

- Electrolytes are salts, acids, bases, some proteins
- **Electrolyte balance** usually refers only to salt balance
- Salts control fluid movements; provide minerals for excitability, secretory activity, membrane permeability
- Salts enter body by ingestion and metabolism; lost via perspiration, feces, urine, vomit

Sodium

- the major cation of the extracellular fluid
- responsible for one-half of the osmotic pressure gradient
- sodium salts contribute 280 mOsm of total 290 mOsm ECF solute concentration
- **Controls ECF volume and water distribution**
- People eating a typical Western diet, which is very high in NaCl, routinely take in 130 to 160 mmol/day of sodium, but humans require only 1 to 2 mmol/day
- This excess sodium – the major factor in hypertension
- Excretion of sodium is accomplished primarily by the kidneys
- Sodium is freely filtered through the glomerular capillaries of the kidneys, much of the filtered sodium is reabsorbed in the proximal convoluted tubule, some remains in the filtrate and urine, and is normally excreted

Table 26.2 Sodium Concentration and Sodium Content

Table 26.2 Sodium Concentration and Sodium Content

	ECF Na^+ CONCENTRATION	BODY Na^+ CONTENT
Homeostatic Importance	ECF osmolality	Blood volume and blood pressure
Sensors	Osmoreceptors	Baroreceptors
Regulation	ADH and thirst mechanisms	Renin-angiotensin-aldosterone and ANP hormone mechanisms*

*ADH and thirst are also required to maintain blood volume and for long-term control of blood pressure.

- ↓ filtrate NaCl concentration
- ↓ stretch (due to ↓ blood pressure) of granular cells

Figure 26.8 Mechanisms and consequences of aldosterone release.

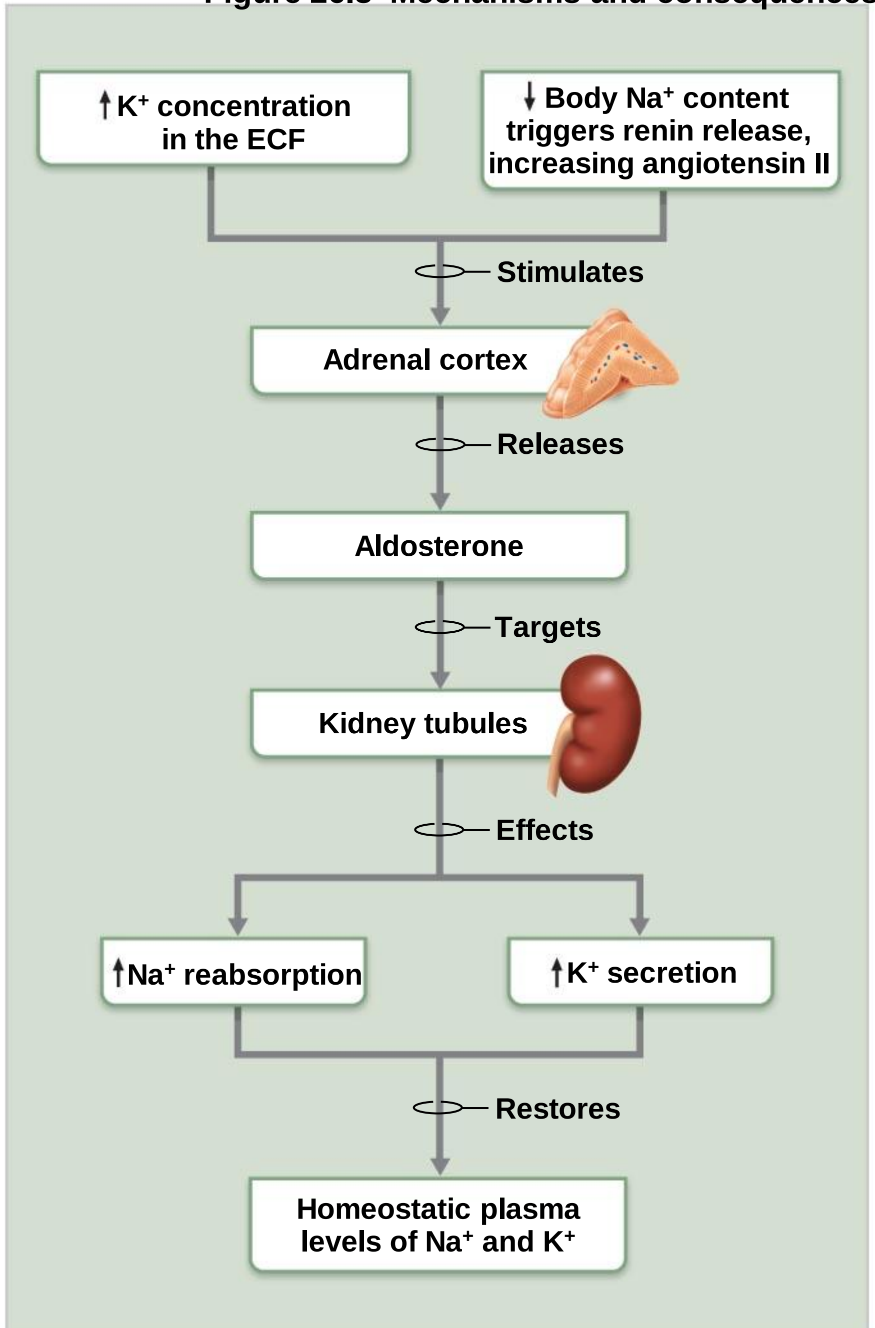
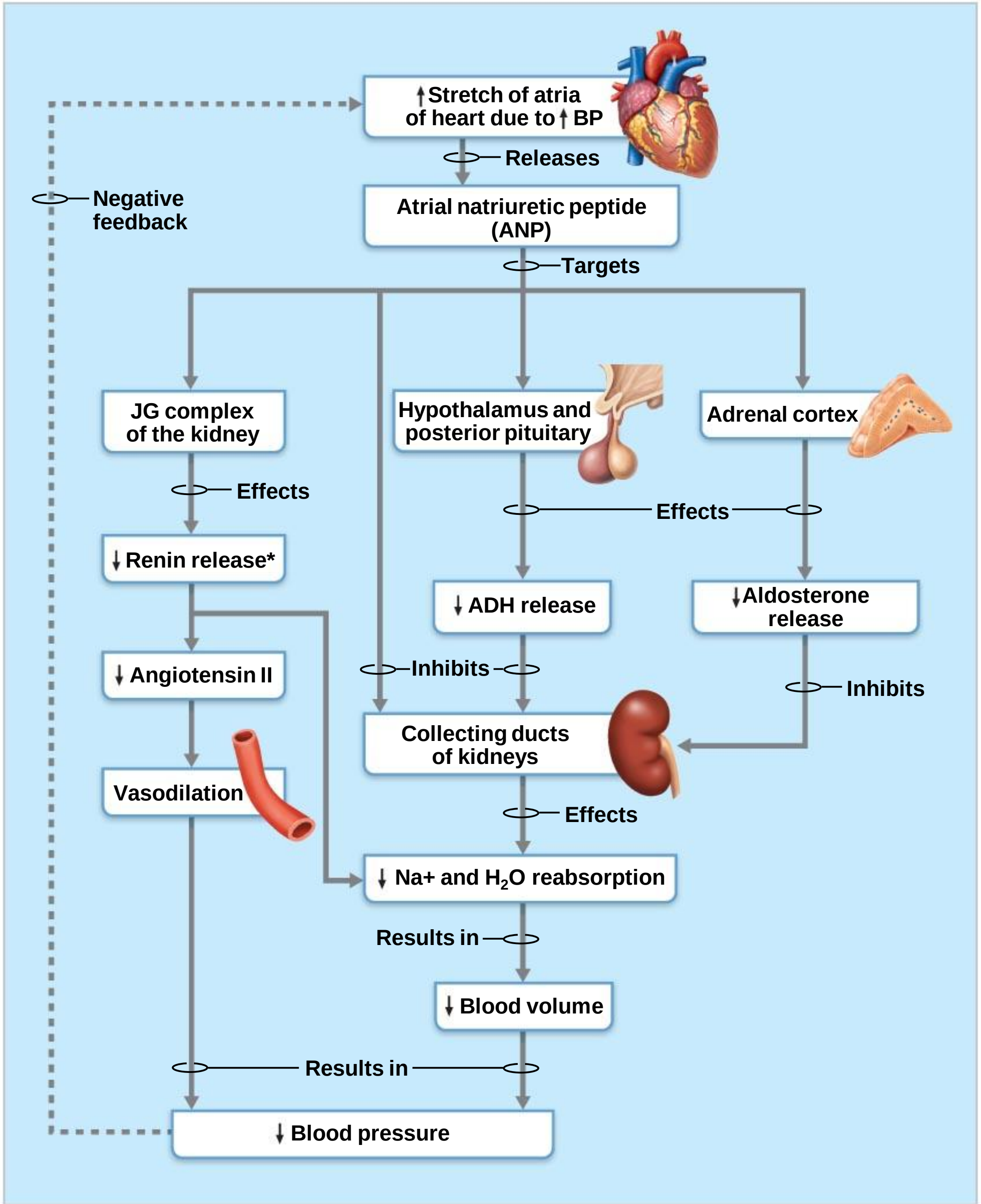


Figure 26.9 Mechanisms and consequences of ANP release.



Influence of other Hormones

- Female sex hormones
  - **Estrogens**: ↑ NaCl reabsorption (like aldosterone)
    - → H_2O retention during menstrual cycles and pregnancy
  - **Progesterone**: ↓ Na^+ reabsorption (blocks aldosterone)
    - Promotes Na^+ and H_2O loss
- Glucocorticoids: ↑ Na^+ reabsorption and promote edema

Abnormalities of Body Fluid Volume Regulation: Hyponatremia and Hypernatremia

Abnormalities of Body Fluid Volume Regulation: Hyponatremia and Hypernatremia

Abnormality	Cause	Plasma Na^+ Concentration	Extracellular Fluid Volume	Intracellular Fluid Volume
Hypo-osmotic dehydration	Adrenal insufficiency; overuse of diuretics	↓	↓	↑
Hypo-osmotic overhydration	Excess ADH; bronchogenic tumor	↓	↑	↑
Hyper-osmotic dehydration	Diabetes insipidus; excessive sweating	↑	↓	↓
Hyper-osmotic overhydration	Cushing's disease; primary aldosteronism	↑	↑	↓

ADH, antidiuretic hormone.

Na+ = 142 mEq/L
Hypo-osmotic = hyponatremia
Hyper-osmotic = hypernatremia

Causes of **hyponatremia** – excess water or loss of sodium
Causes of **hypernatremia** – water loss or excess of sodium

Potassium

- the major intracellular cation
- helps establish the resting membrane potential in neurons and muscle fibers after membrane depolarization and action potentials
- has very little effect on osmotic pressure
- Potassium is excreted, both actively and passively, through the renal tubules, especially the distal convoluted tubule and collecting ducts
- Potassium participates in the exchange with sodium in the renal tubules under the influence of aldosterone, which also relies on basolateral sodium-potassium pumps

❑ **Hyperkalemia** - too much K^+; **Hypokalemia** - too little K^+

❑ Both disrupt electrical conduction in heart →Sudden death

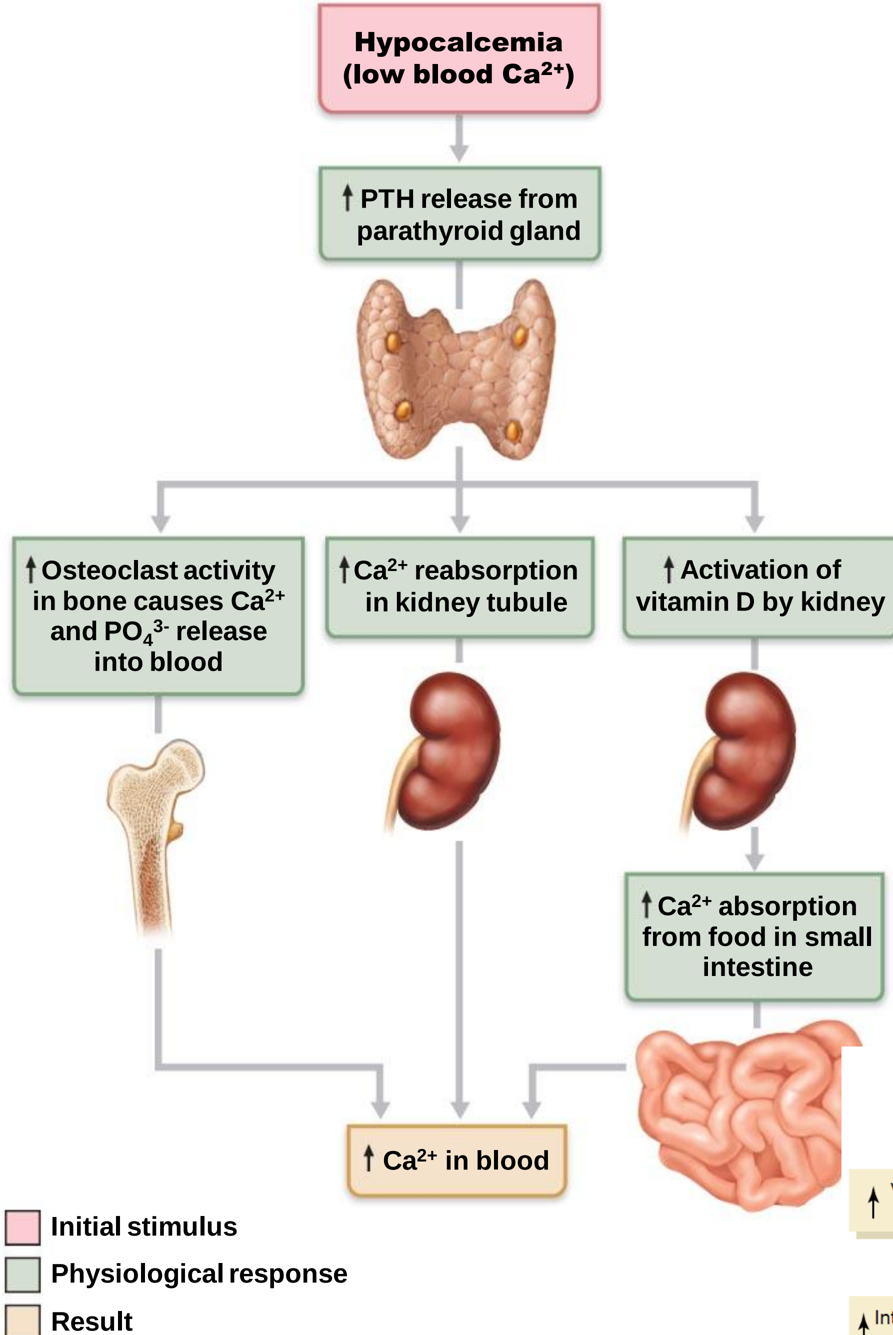
Chloride

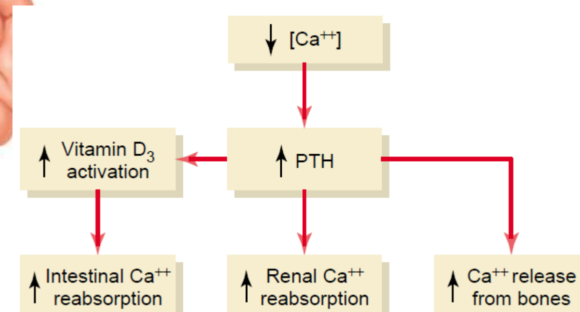
- extracellular anion
- A major contributor to the osmotic pressure gradient between the ICF and ECF
- plays an important role in maintaining proper hydration
- The paths of secretion and reabsorption of chloride ions in the renal system follow the paths of sodium ions
- **Hypochloremia** - defective renal tubular absorption Vomiting, diarrhea, and metabolic acidosis can also lead to hypochloremia
- **Hyperchloremia**, or higher-than-normal blood chloride levels, can occur due to dehydration, excessive intake of dietary salt (NaCl) or swallowing of sea water, aspirin intoxication, congestive heart failure, and the hereditary, chronic lung disease, cystic fibrosis

Calcium ions - Ca^{2+}

- bound up in bone
- one-half of blood calcium is bound to proteins, leaving the rest in its ionized form
- Calcium ions are necessary for:
- muscle contraction,
- enzyme activity,
- blood coagulation
- helps to stabilize cell membranes
- is essential for the release of neurotransmitters from neurons and of hormones from endocrine glands
- Reabsorbed with the help of activated vitamin D
- **Hypocalcemia**, seen in hypoparathyroidism -↑ excitability and muscle tetany
- **Hypercalcemia** - inhibits neurons and muscle cells, may cause heart arrhythmias

Figure 16.13 Effects of parathyroid hormone on bone, the kidneys, and the intestine.





Regulation of Acid-base Balance

- Homeostasis
- Hydrogen ion (H+) balance
- a balance between the intake or production of H+ and the net removal of H+ from the body
- Definition $$pH = \log \frac{1}{[H^+]} = -\log [H^+]$$

$$CO_2 + H_2O \underset{\longrightarrow}{\xleftarrow{\text{carbonic anhydrase}}} H_2CO_3 \qquad H_2CO_3 \rightleftarrows H^+ + HCO_3^-$$

- Most H^+ produced by metabolism – **volatile and nonvolatile acids**
  - Phosphorus-containing protein breakdown releases *phosphoric acid* into ECF
  - *Lactic acid* from anaerobic metabolism of glucose
  - *Fatty acids* and *ketone bodies* from fat metabolism
  - H^+ liberated when CO_2 converted to HCO_3^- in blood

pH and H+ Concentration of Body Fluids

pH and H^+ Concentration of Body Fluids

	H^+ Concentration (mEq/L)	pH
Extracellular fluid		
Arterial blood	4.0×10^{-5}	7.40
Venous blood	4.5×10^{-5}	7.35
Interstitial fluid	4.5×10^{-5}	7.35
Intracellular fluid	1×10^{-3} to 4×10^{-5}	6.0 to 7.4
Urine	3×10^{-2} to 1×10^{-5}	4.5 to 8.0
Gastric HCl	160	0.8

$$CO_2 + H_2O \underset{}{\overset{\text{carbonic anhydrase}}{\rightleftarrows}} H_2CO_3$$

$$H_2CO_3 \rightleftarrows H^+ + HCO_3^-$$

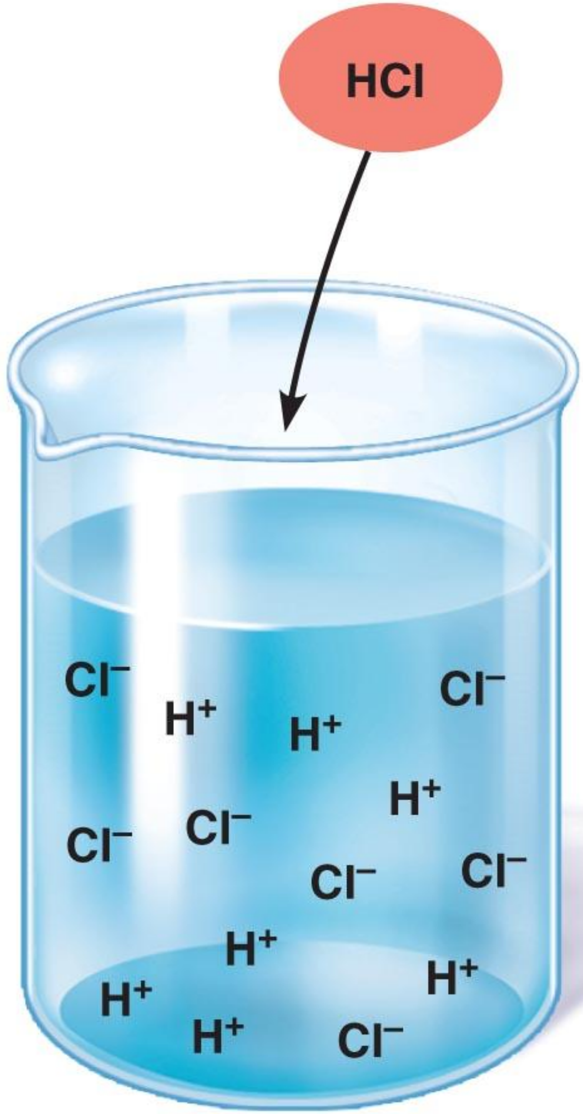
- **Alkalosis** or alkalemia: arterial pH >7.45
- **Acidosis** or acidemia: arterial pH <7.35

The lower limit of arterial blood pH at which a person can live more than a few hours is about 6.8, and the upper limit is about 8.0

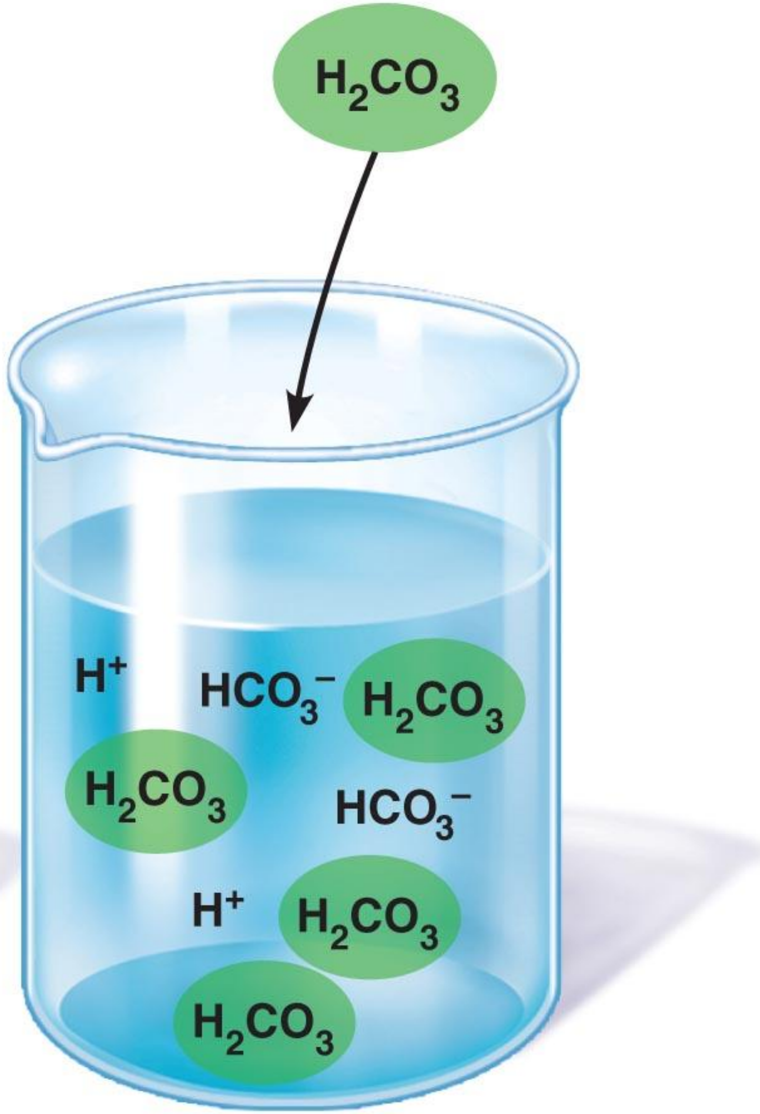
Acids and Bases: Definitions and Meanings

- Molecules containing hydrogen atoms that **can release hydrogen ions** in solutions are referred to as acids – HCl, H_2CO_3
- A base is an ion or a molecule that **can accept an H+**
- base and alkali - used synonymously
- An *alkali is a molecule* formed by the combination of one or more of the alkaline metals
- *Alkalosis* refers to excess removal of H+ from the body fluids, in contrast to the excess addition of H+, which is referred to as *acidosis*
- **Strong and Weak Acids and Bases**

Figure 26.11 Dissociation of strong and weak acids in water.



(a) **A strong acid such as HCl dissociates completely into its ions.**



(b) **A weak acid such as H_2CO_3 does not dissociate completely.**

Defenses Against Changes in [H+]: Buffers, Lungs, and Kidneys

- (1) the ***chemical acid-base buffer systems*** of the body fluids, which immediately combine with acid or base to prevent excessive changes in H+ concentration;
  - React within a fraction of a second to minimize the changes; they do not eliminate H+ from or add them to the body
- (2) the ***respiratory center,*** which regulates the removal of CO_2 (and, therefore, H_2CO_3) from the extracellular fluid; and
  - acts within a few minutes
- (3) the ***kidneys*** can eliminate the excess acid or base from the body
  - over a period of hours to several days, they are by far the most powerful of the acid-base regulatory systems

Buffer systems

4 buffers in the blood

A buffer is any substance that can reversibly bind H+

- **Bicarbonate buffer system**: *a weak acid* and *bicarbonate salt*

H_2CO_3 acid and $NaHCO_3$ base (1:20)

$$HCl + NaHCO_3 \rightarrow NaCl + H_2CO_3$$

$$\uparrow H^+ + HCO_3^- \longrightarrow H_2CO_3 \longrightarrow CO_2 + H_2O$$

$$NaOH + H_2CO_3 \longrightarrow NaHCO_3 + H_2O$$

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + \underbrace{HCO_3^-}_{+\ Na^+}$$

- **Phosphate buffer system:**

NaH_2PO_4 20%, primary, acid

and Na_2HPO_4 80%, secondary, base

$H_2PO_4^-$ and $HPO_4^=$

base $HPO_4^=$

$$HCl + Na_2HPO_4 \longrightarrow NaH_2PO_4 + NaCl$$

$$NaOH + NaH_2PO_4 \longrightarrow Na_2HPO_4 + H_2O$$

$$H^+ + Hb \rightleftharpoons HHb$$

Protein Na+protein /H+protein

Hb K+Hb /H+Hb

"Buffer Power"

- Is determined by the amount and relative concentrations of the buffer components
- **Bicarbonate buffer system** is the most important extracellular buffer
- the phosphate buffer system – intracellular and *is especially important in the tubular fluids of the kidneys*
- Proteins - within the cells
- Approximately 60 to 70 % of the total chemical buffering of the body fluids is inside the cells, and most of this results from the intracellular proteins

Respiratory Regulation of Acid-Base Balance

- An increase in ventilation eliminates CO_2 from extracellular fluid, which reduces the H+ concentration
- Decreased ventilation increases CO_2, thus also increasing H+ concentration in the extracellular fluid

Respiratory Regulation of Acid-Base Balance

- **Hypercapnia** activates medullary chemoreceptors
  - → Increased respiratory rate and depth
- Rising plasma H^+ activates peripheral chemoreceptors
  - → Increased respiratory rate and depth
  - More CO_2 is removed from the blood
  - H^+ concentration is reduced
- Alkalosis depresses respiratory center
  - Respiratory rate and depth decrease
  - H^+ concentration increases
- Respiratory system impairment causes acid-base imbalances
  - **Hypoventilation** → **respiratory acidosis**
  - **Hyperventilation** → **respiratory alkalosis**

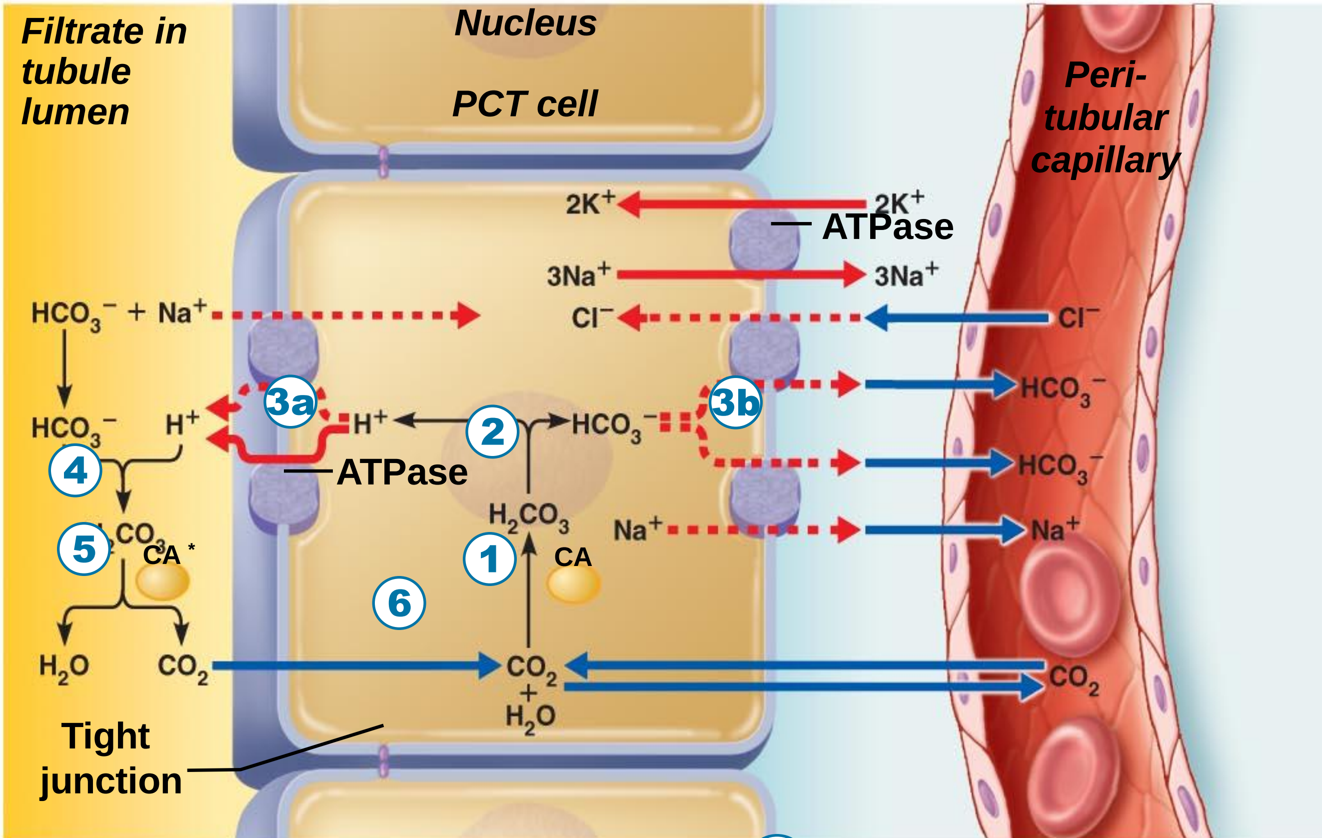
Renal control of ABB

- the kidneys regulate extracellular fluid [H+] through three fundamental mechanisms:
- (1) secretion of H+,
- (2) reabsorption of filtered HCO_3^-, and
- (3) production of new HCO_3^-
  - Excreting HCO_3^-
- Generating or reabsorbing one HCO_3^- same as losing one H^+
- Excreting one HCO_3^- same as gaining one H^+
- H^+ secretion occurs in PCT and collecting duct type A intercalated cells:
  - The H^+ comes from H_2CO_3 produced in reactions catalyzed by carbonic anhydrase inside cells; As H^+ secreted, Na^+ reabsorbed

Figure 26.12 Reabsorption of filtered HCO_3^- is coupled to H^+ secretion.

1 CO_2 combines with water within the tubule cell, forming H_2CO_3.

2 H_2CO_3 is quickly split, forming H^+ and bicarbonate ion (HCO_3^-).



3a H^+ is secreted into the filtrate.

3b For each H^+ secreted, a HCO_3^- enters the peritubular capillary blood either via symport with Na^+ or via antiport with Cl^-.

4 Secreted H^+ combines with HCO_3^- in the filtrate, forming carbonic acid (H_2CO_3). HCO_3^- disappears from the filtrate at the same rate that HCO_3^- (formed within the tubule cell) enters the peritubular capillary blood.

5 The H_2CO_3 formed in the filtrate dissociates to release CO_2 and H_2O.

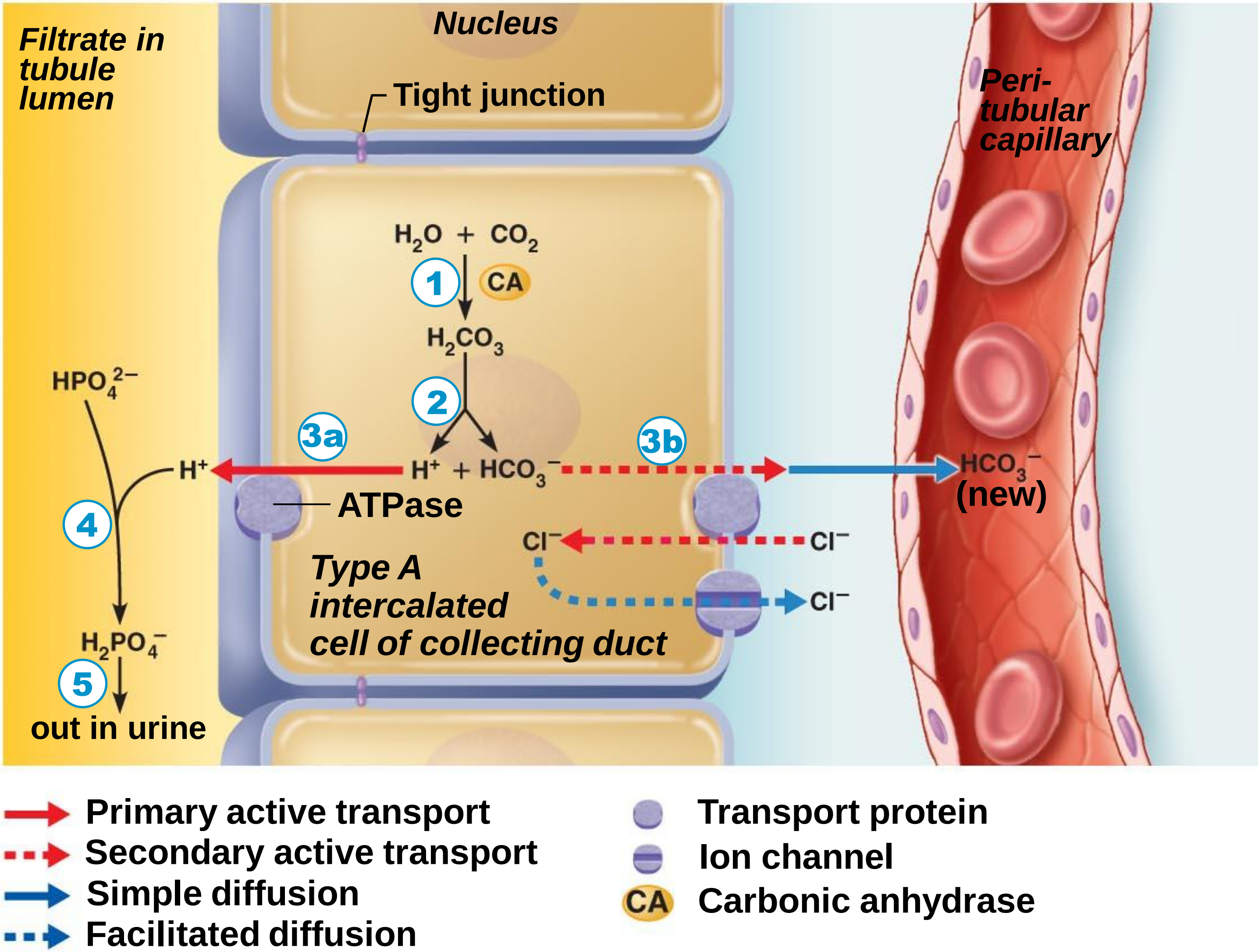
6 CO_2 diffuses into the tubule cell, where it triggers further H^+ secretion.

Figure 26.13 New HCO_3^- is generated via buffering of secreted H^+ by HPO_4^{2-} (monohydrogen phosphate).

1 CO_2 combines with water within the type A intercalated cell, forming H_2CO_3.

2 H_2CO_3 is quickly split, forming H^+ and bicarbonate ion (HCO_3^-).

3a H^+ is secreted into the filtrate by a H^+ ATPase pump.

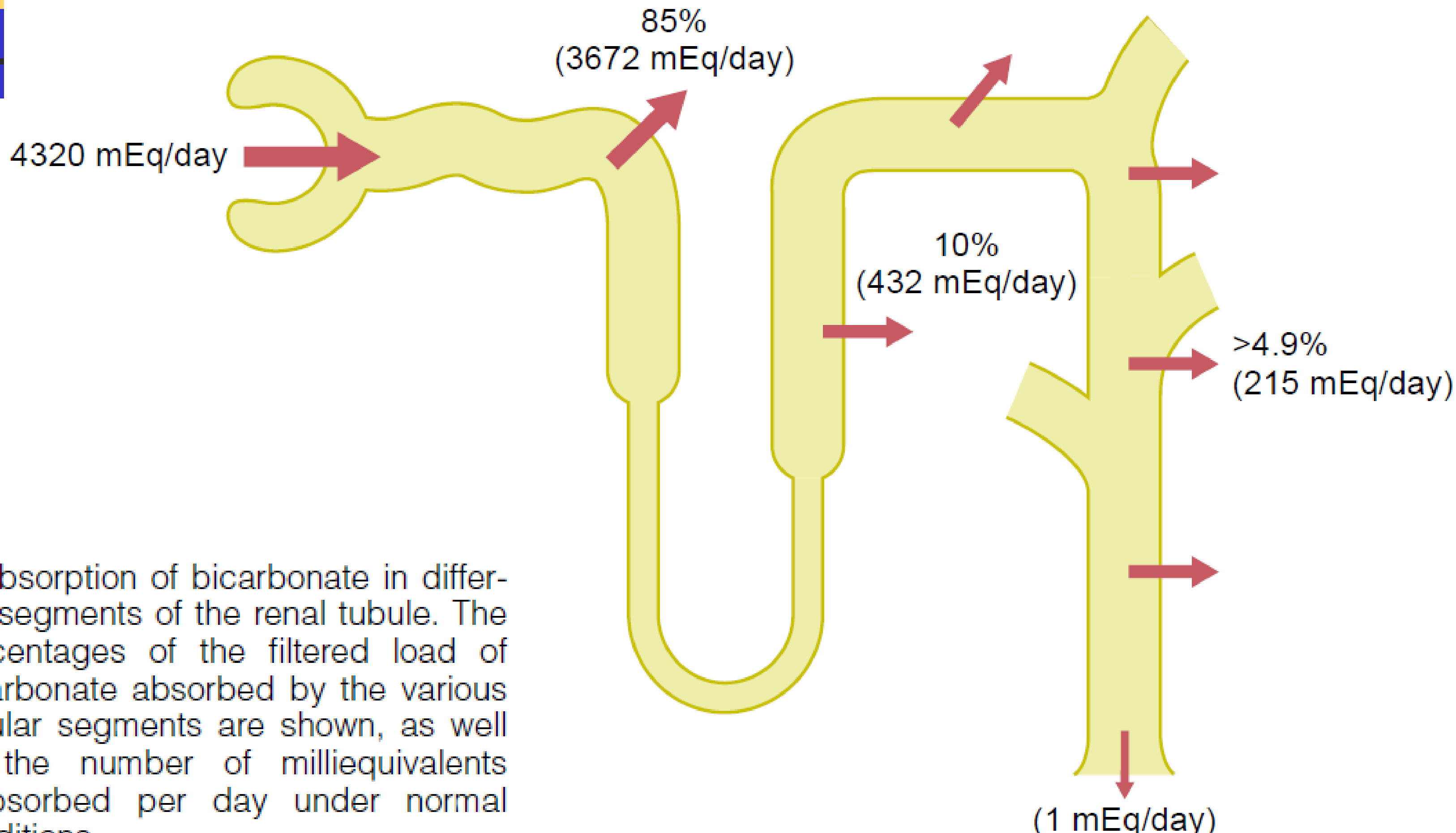


3b For each H^+ secreted, a HCO_3^- enters the peritubular capillary blood via an antiport carrier in a HCO_3^--Cl^- exchange process.

4 Secreted H^+ combines with HPO_4^{2-} in the tubular filtrate, Forming $H_2PO_4^-$.

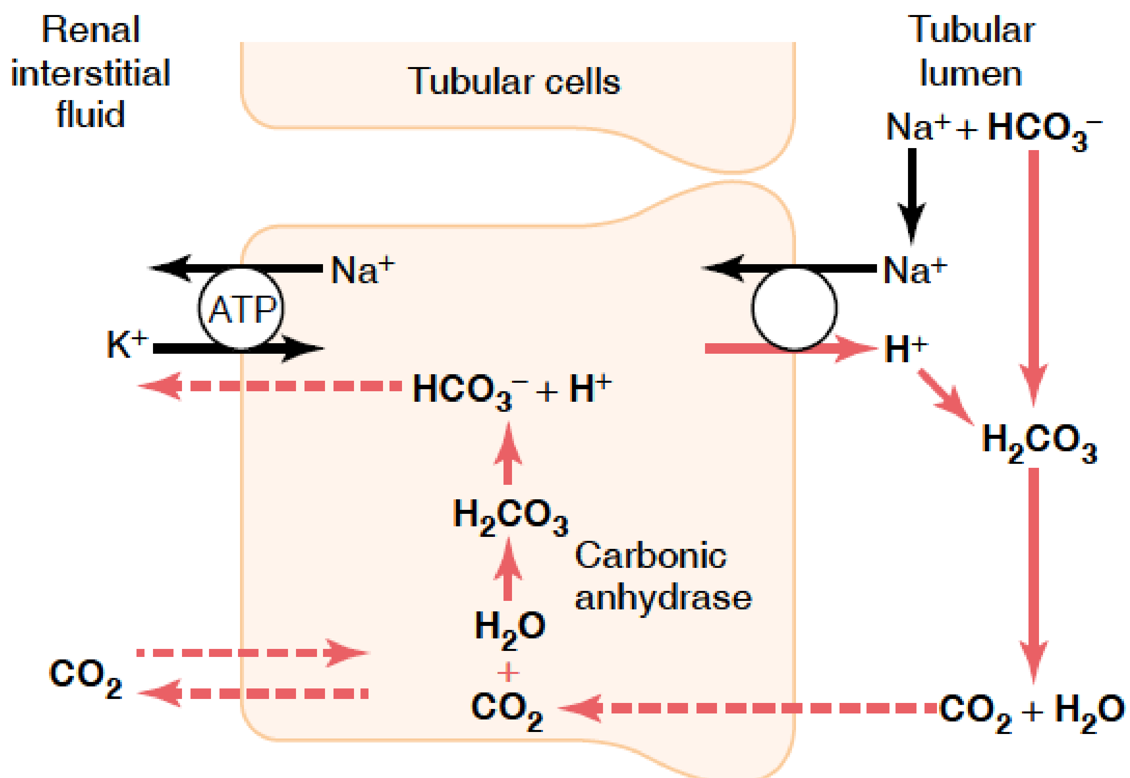
5 The $H_2PO_4^-$ is excreted in the urine.

Bicarbonate reabsorption

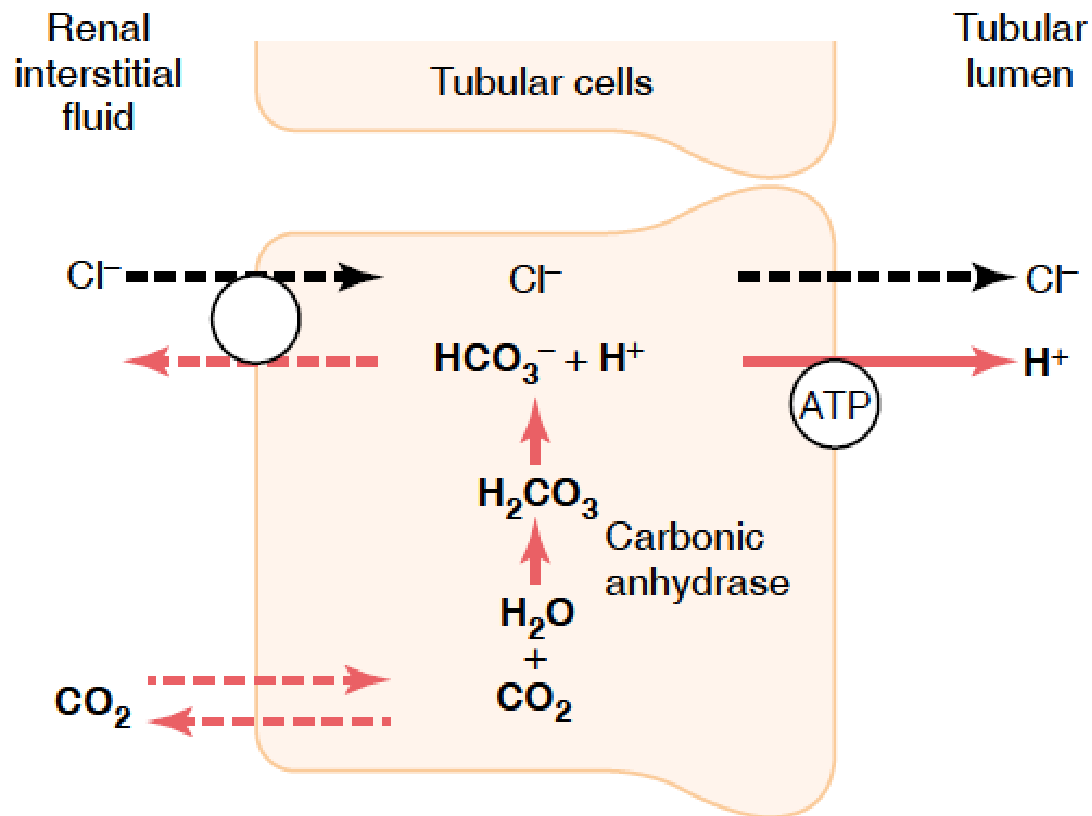


Reabsorption of bicarbonate in different segments of the renal tubule. The percentages of the filtered load of bicarbonate absorbed by the various tubular segments are shown, as well as the number of milliequivalents reabsorbed per day under normal conditions.

Renal control of ABB

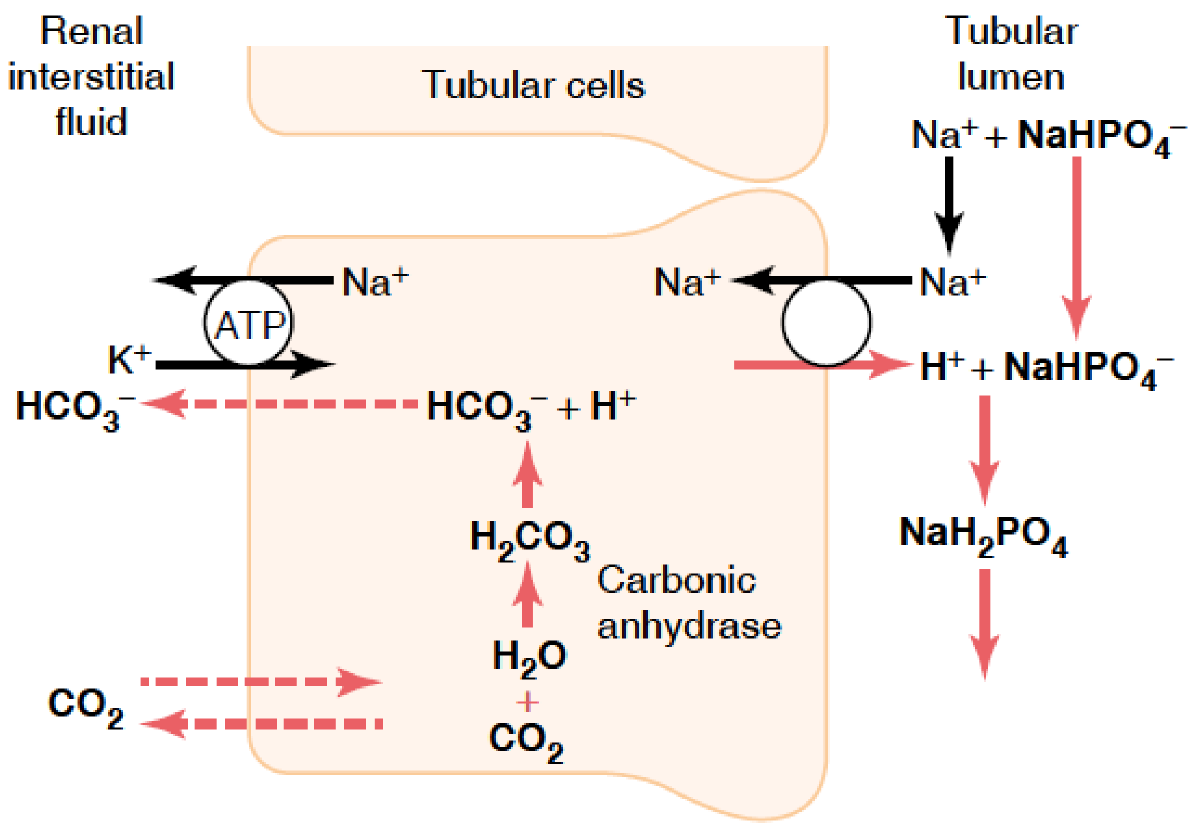


Cellular mechanisms for (1) active secretion of hydrogen ions into the renal tubule; (2) tubular reabsorption of bicarbonate ions by combination with hydrogen ions to form carbonic acid, which dissociates to form carbon dioxide and water; and (3) sodium ion reabsorption in exchange for hydrogen ions secreted. This pattern of hydrogen ion secretion occurs in the proximal tubule, the thick ascending segment of the loop of Henle, and the early distal tubule.



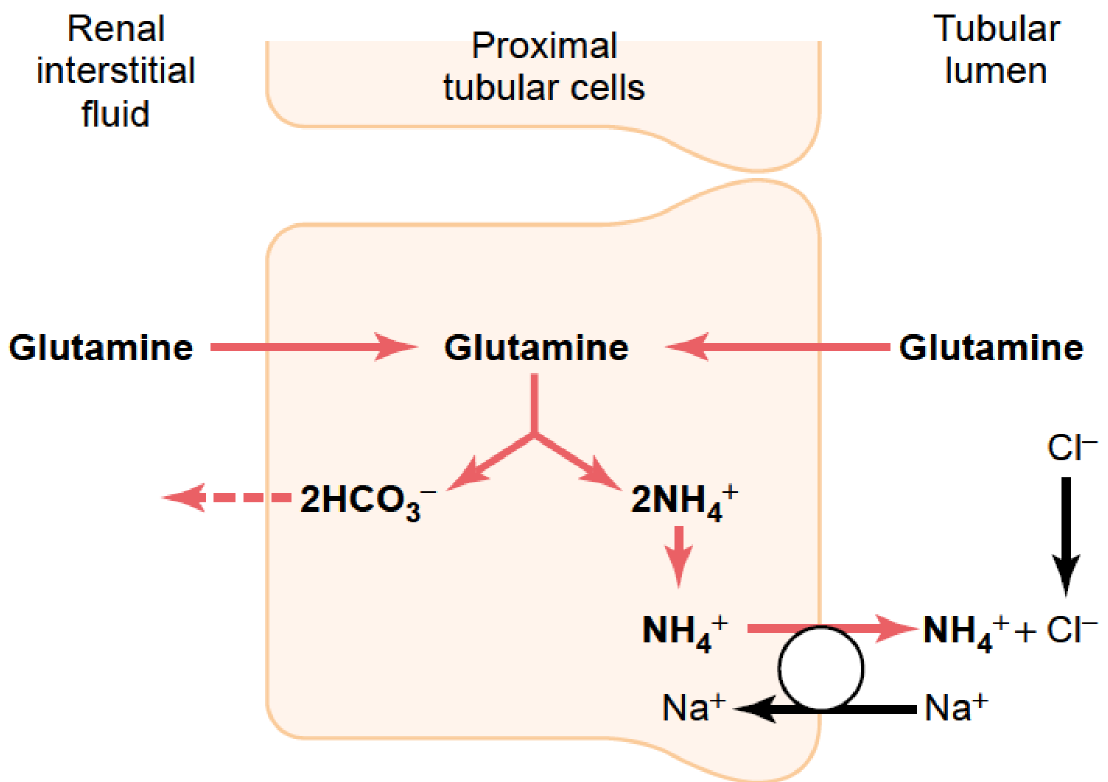
Primary active secretion of hydrogen ions through the luminal membrane of the intercalated epithelial cells of the late distal and collecting tubules. Note that one bicarbonate ion is absorbed for each hydrogen ion secreted, and a chloride ion is passively secreted along with the hydrogen ion.

Phosphate Buffer System

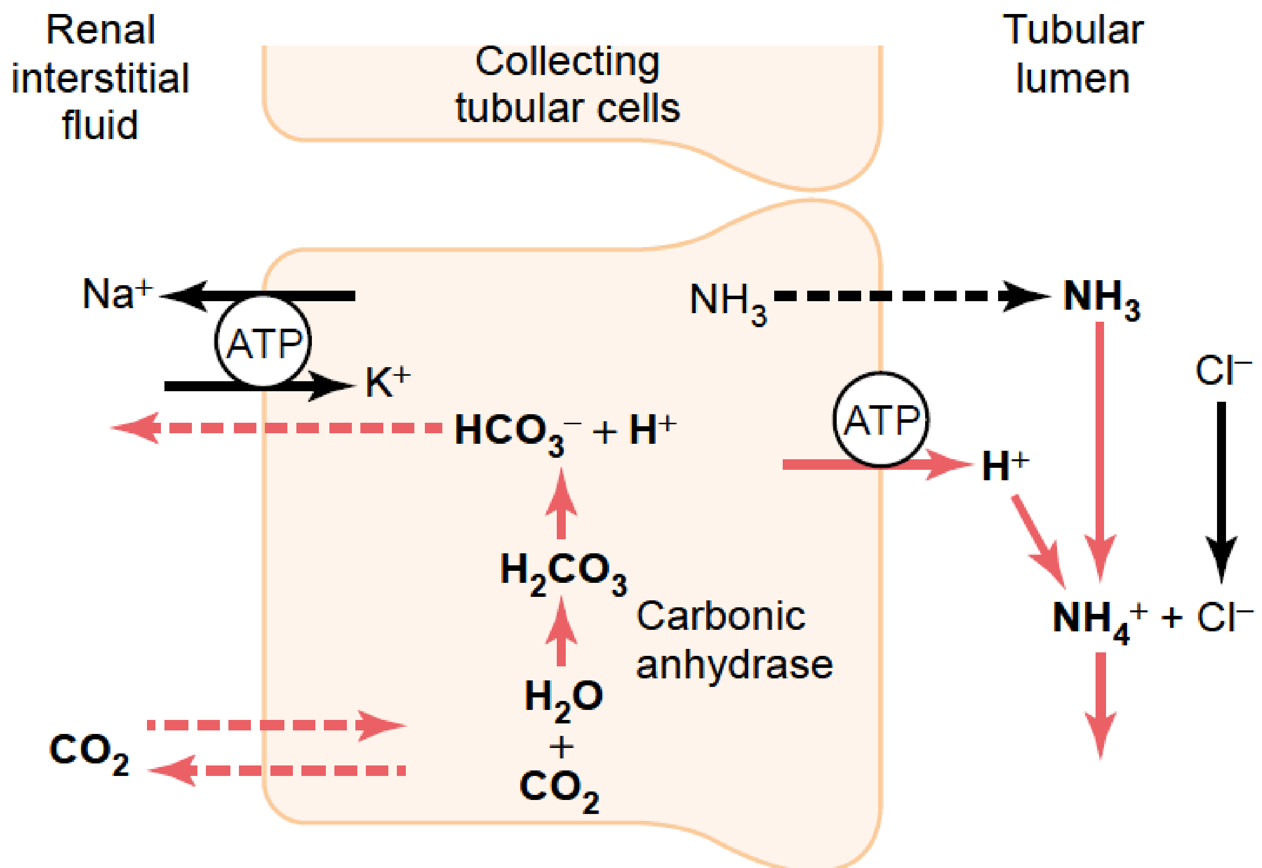


Buffering of secreted hydrogen ions by filtered phosphate ($NaHPO_4^-$). Note that a new bicarbonate ion is returned to the blood for each $NaHPO_4^-$ that reacts with a secreted hydrogen ion.

Ammonia Buffer System



Production and secretion of ammonium ion (NH_4^+) by proximal tubular cells. Glutamine is metabolized in the cell, yielding NH_4^+ and bicarbonate. The NH_4^+ is secreted into the lumen by a sodium-NH_4^+ pump. For each glutamine molecule metabolized, two NH_4^+ are produced and secreted and two HCO_3^- are returned to the blood.



Buffering of hydrogen ion secretion by ammonia (NH_3) in the collecting tubules. Ammonia diffuses into the tubular lumen, where it reacts with secreted hydrogen ions to form NH_4^+, which is then excreted. For each NH_4^+ excreted, a new HCO_3^- is formed in the tubular cells and returned to the blood.

Characteristics of Primary Acid-Base Disturbances

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
Respiratory acidosis	↓	↑	↑↑	↑
Respiratory alkalosis	↑	↓	↓↓	↓
Metabolic acidosis	↓	↑	↓	↓↓
Metabolic alkalosis	↑	↓	↑	↑↑

Metabolic Acidosis Associated with Normal or Increased Plasma Anion Gap

Increased Anion Gap (Normochloremia)	Normal Anion Gap (Hyperchloremia)
Diabetes mellitus (ketoacidosis)	Diarrhea
Lactic acidosis	Renal tubular acidosis
Chronic renal failure	Carbonic anhydrase inhibitors
Aspirin (acetylsalicylic acid) poisoning	Addison's disease
Methanol poisoning	
Ethylene glycol poisoning	
Starvation	

Metabolic Acidosis and Alkalosis

- **Metabolic acidosis** – low blood pH and HCO_3^-
  - Causes
    - Ingestion of too much alcohol ($\rightarrow$ acetic acid)
    - Excessive loss of HCO_3^- (e.g., persistent diarrhea)
    - Accumulation of lactic acid (exercise or shock), ketosis in diabetic crisis, starvation, and kidney failure
- **Metabolic alkalosis** much less common than metabolic acidosis
  - Indicated by rising blood pH and HCO_3^-
  - Causes include vomiting of acid contents of stomach or by intake of excess base (e.g., antacids)

Normal values of acid base parameters in arterial blood

Parameter	Normal range
pH	7.35 - 7.45
p_aCO_2	35 - 45 mmHg
Actual bicarbonate	22 - 26 mmol/l
Standard bicarbonate	20 - 28 mmol/l
Base excess (BE) /deficit	- 2.5 to + 2.5 mmol/l
Buffer base	about 48 mmol/l

The values for bicarbonate and BE have to be measured under standardized conditions in order to be of value for the distinction between disturbances of respiratory or metabolic origin. These conditions are at pH 7.4, p_aCO_2 = 40 mmHg and 37 °C. Under these conditions the bicarbonate is referred to as standard bicarbonate and is a parameter which reflects metabolic changes in acid-base balance.

Astrup formula

- Deficit ml (Mmol/l) = 0,3 x body weight (kg) x base excess (BE)