PHYSIOLOGY

FACULTY OF PHARMACEUTICAL SCIENCES
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LECTURE 11, PARTS (1) & (2): FLUID COMPARTMENTS

Objectives

1. Discuss **fluid compartments and fluid homeostasis.**

2. Explore **electrolytes in body fluids.**

(Pages 1024- 1037 of the reference)

FLUID COMPARTMENTS AND FLUID HOMEOSTASIS

- In lean adults, **body fluids constitute between 55% and 60%** of total body mass **in females and males**, respectively.

- **Body fluids are present in two main "compartments"—inside cells and outside cells.** About two-thirds of body fluid is **intracellular fluid (ICF)** or cytosol, the fluid within cells. The other third, called **extracellular fluid (ECF),** is outside cells and includes all other body fluids.

- **About 80% of the ECF is interstitial fluid**, which occupies the microscopic spaces between tissue cells, and **20% of the ECF is plasma, the liquid portion of the blood.**

FLUID COMPARTMENTS AND FLUID HOMEOSTASIS

- **Two general "barriers" separate intracellular fluid, interstitial fluid, and blood plasma:**

1. **The plasma membrane** of individual cells separates intracellular fluid from the surrounding interstitial fluid.
2. **Blood vessel walls** divide the interstitial fluid from blood plasma.

- The term body fluid refers to body water and its dissolved substances.

- The body is in fluid balance when the required amounts of water and solutes are present and are correctly proportioned among the various compartments.
- Water is by far the largest single component of the body.

FLUID COMPARTMENTS AND FLUID HOMEOSTASIS

- The processes of **filtration, reabsorption, diffusion, and osmosis** allow continual exchange of water and solutes among body fluid compartments.
- Because **most solutes in body fluids** are electrolytes, inorganic compounds that dissociate into ions, fluid balance is closely related to electrolyte balance.
- **Because intake of water and electrolytes rarely occurs in exactly the same proportions as their presence in body fluids, the ability of the kidneys to excrete excess water by producing dilute urine, or to excrete excess electrolytes by producing concentrated urine, is of utmost importance in the maintenance of homeostasis.**

SOURCES OF BODY WATER GAIN AND LOSS

- The main sources of body water are **ingested liquids** (تبتلع) **(about 1600 mL)** and **moist foods (about 700 mL)** absorbed from the gastrointestinal (GI) tract, which **total about 2300 mL/day**.

- The other source of water is **metabolic water** that is **produced in the body mainly when electrons are accepted by oxygen during aerobic respiration**.

- Normally, **body fluid volume remains constant because water loss equals water gain. Water loss occurs in four ways.** Each day **the kidneys excrete** about 1500 mL in urine, **the skin evaporates** about 600 mL (400 mL through insensible perspiration— sweat that evaporates before it is perceived as moisture—and 200 mL as sweat), **the lungs exhale** about 300 mL as water vapor, and **the gastrointestinal tract eliminates** about 100 mL in feces. In women of reproductive age, **additional water is lost in menstrual flow**. On average, daily water loss totals about 2500 mL.

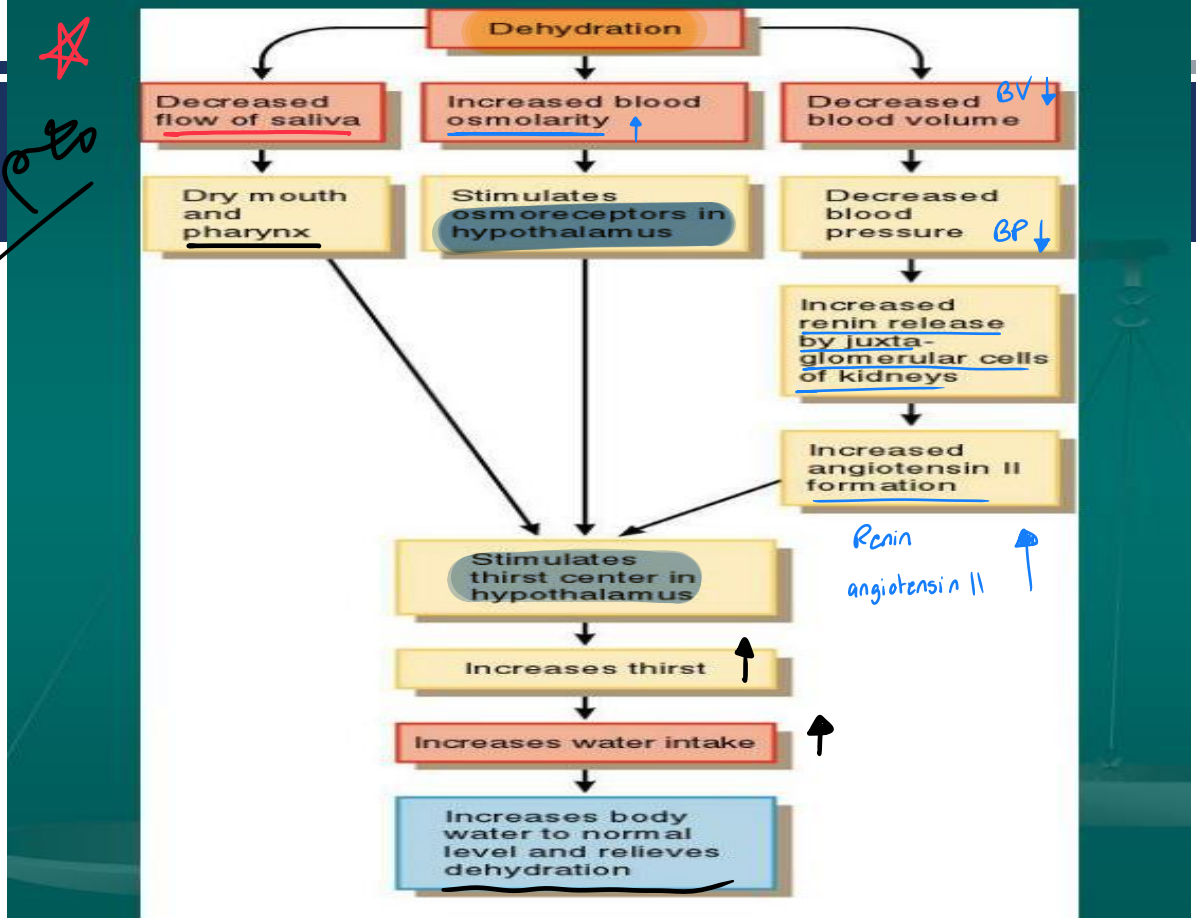
REGULATION OF BODY WATER GAIN

- **An area in the hypothalamus known as the thirst center governs the urge to drink.**

- ✓ When water loss is greater than water gain, dehydration—a decrease in volume and an increase in osmolarity of body fluids— stimulates thirst.

H_2O ↓ electrolyte ↑ dehydration

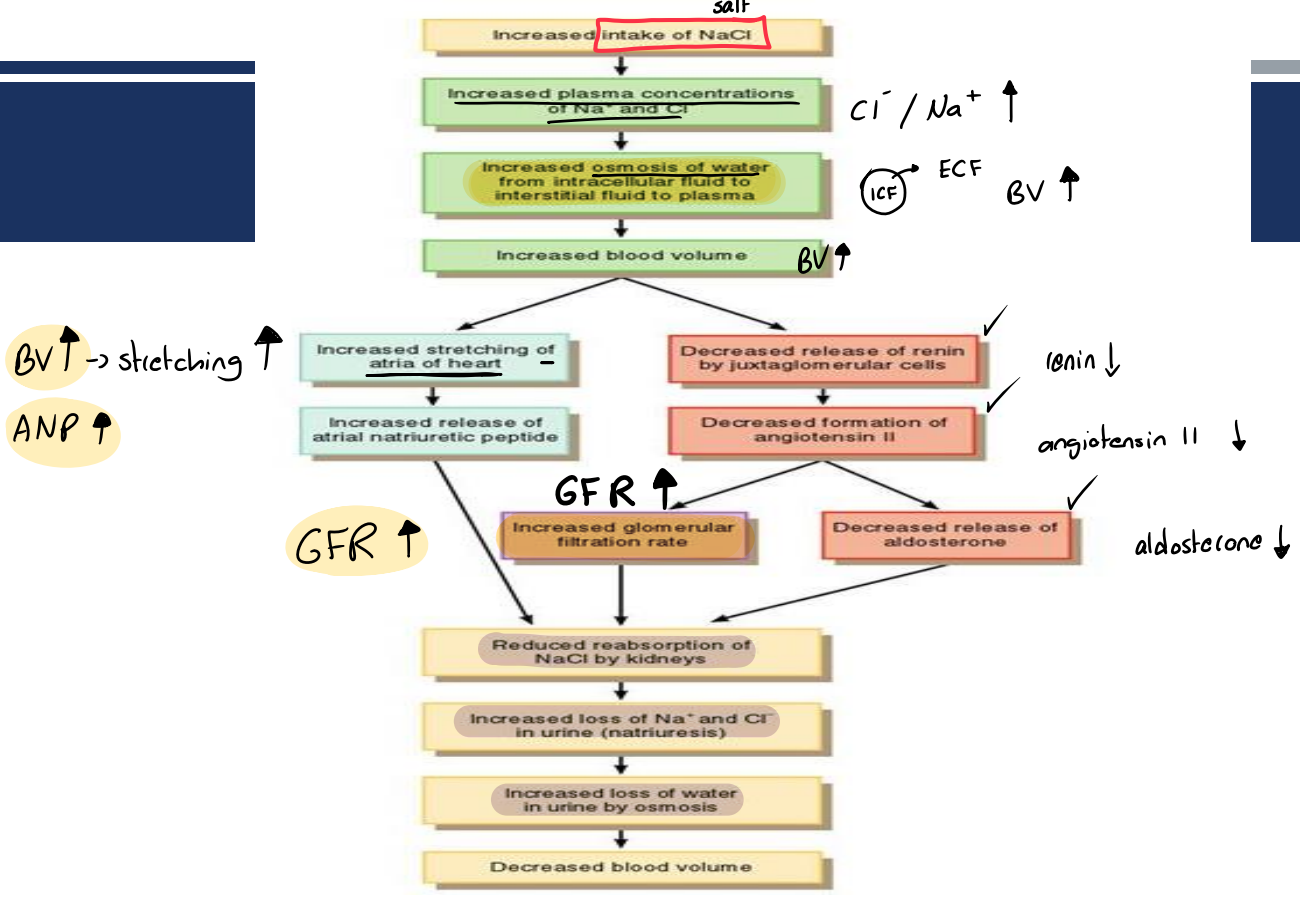
Cl^-/Na^+


Dehydration
Decreased flow of saliva
Increased blood osmolarity
Decreased blood volume
BV ↓
Dry mouth and pharynx
Stimulates osmoreceptors in hypothalamus
Decreased blood pressure
BP ↓
Increased renin release by juxta-glomerular cells of kidneys
Increased angiotensin II formation
Renin
angiotensin II
Stimulates thirst center in hypothalamus
Increases thirst
Increases water intake
Increases body water to normal level and relieves dehydration

REGULATION OF WATER AND SOLUTE LOSS

Even though the loss of water and solutes through sweating and exhalation increases during exercise, elimination of excess body water or solutes occurs mainly by control of their loss in urine.

The extent of urinary salt (NaCl) loss is the main factor that determines body fluid volume. The three most important hormones that regulate the extent of renal sodium and chloride ions reabsorption (and thus how much is lost in the urine) are angiotensin II, aldosterone, and atrial natriuretic peptide (ANP).


salt
Increased intake of NaCl
Increased plasma concentrations of Na+ and Cl-
Cl⁻ / Na⁺ ↑
Increased osmosis of water from intracellular fluid to interstitial fluid to plasma
ICF
ECF
BV ↑
Increased blood volume
BV ↑
BV ↑ -> stretching ↑
ANP ↑
Increased stretching of atria of heart
Increased release of atrial natriuretic peptide
Decreased release of renin by juxtaglomerular cells
renin ↓
Decreased formation of angiotensin II
angiotensin II ↓
GFR ↑
GFR ↑
Increased glomerular filtration rate
Decreased release of aldosterone
aldosterone ↓
Reduced reabsorption of NaCl by kidneys
Increased loss of Na+ and Cl- in urine (natriuresis)
Increased loss of water in urine by osmosis
Decreased blood volume

Summary of Factors That Maintain Body Water Balance

FACTOR	MECHANISM	EFFECT
Thirst center in hypothalamus	Stimulates desire to drink fluids.	Water gain if thirst is quenched.
Angiotensin II	Stimulates secretion of aldosterone.	Reduces loss of water in urine.
Aldosterone	By promoting urinary reabsorption of Na^+ and Cl^-, increases water reabsorption via osmosis.	Reduces loss of water in urine.
Atrial natriuretic peptide (ANP)	Promotes natriuresis, elevated urinary excretion of Na^+ (and Cl^-), accompanied by water.	Increases loss of water in urine.
Antidiuretic hormone (ADH), also known as vasopressin	Promotes insertion of water-channel proteins (aquaporin-2) into the apical membranes of principal cells in the collecting ducts of the kidneys. As a result, the water permeability of these cells increases and more water is reabsorbed.	Reduces loss of water in urine.

ADH

MOVEMENT OF WATER BETWEEN BODY FLUID COMPARTMENTS

- Normally, **cells neither shrink nor swell because intracellular and interstitial fluids have the same osmolarity.** Changes in the osmolarity of interstitial fluid, however, cause fluid imbalances. An increase in the osmolarity of interstitial fluid draws water out of cells, and they shrink slightly. A decrease in the osmolarity of interstitial fluid, by contrast, causes cells to swell.

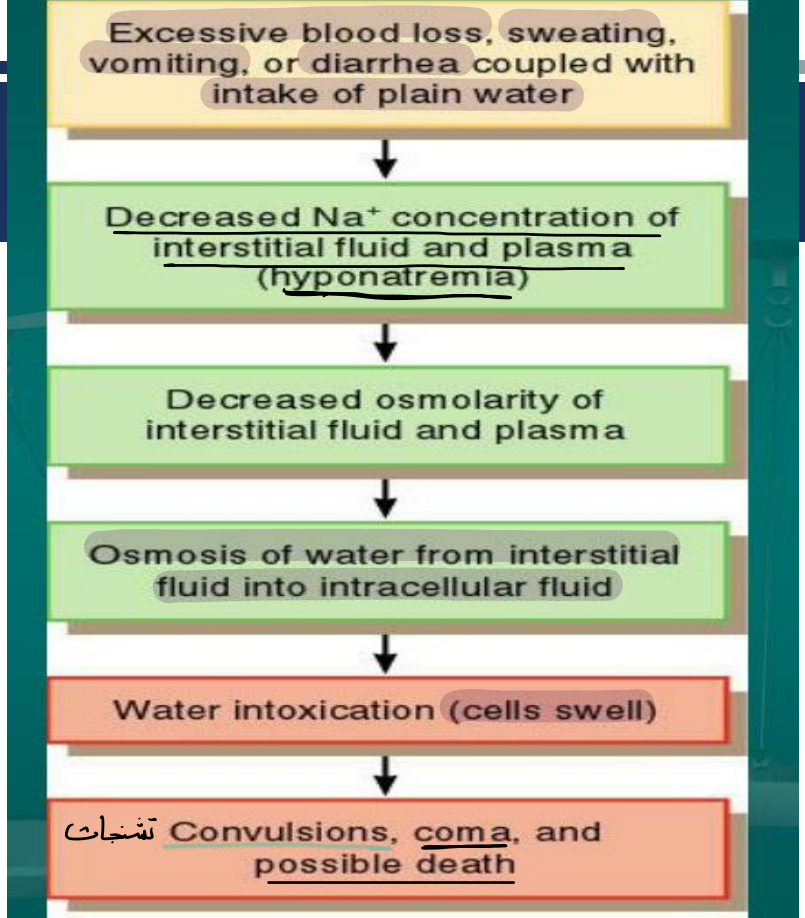
ECF

ECF

- **Water intoxication** is a state in which excessive body water causes cells to swell.

hyponatremia
Na^+ ↓

osmolarity ↓



ELECTROLYTES IN BODY FLUIDS

- **The ions** formed when electrolytes dissolve and dissociate serve four general functions in the body.

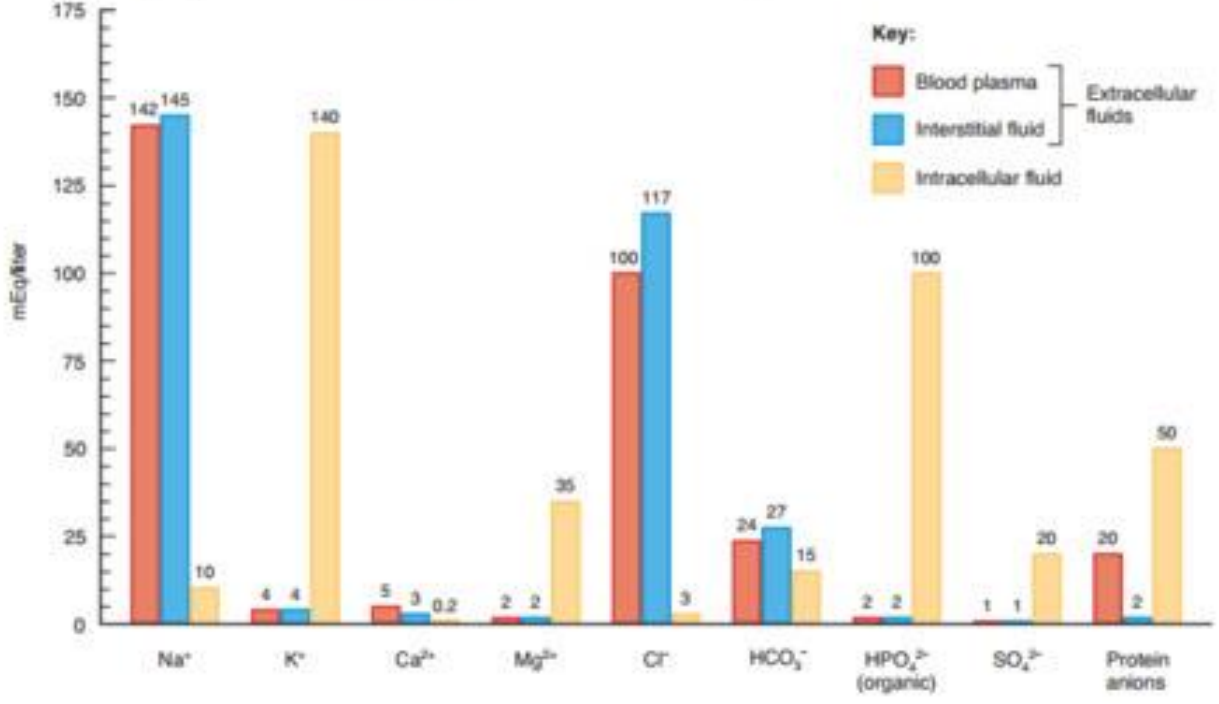
- (1) Because **they are largely confined to particular fluid compartments** and are more numerous than nonelectrolytes, certain ions control the osmosis of water between fluid compartments.
- (2) Ions **help maintain the acid– base balance required for normal cellular activities**.
- (3) Ions **carry electrical current**, which allows production of action potentials and graded potentials.
- (4) Several ions serve as **cofactors needed for optimal activity of enzymes**.

CONCENTRATIONS OF ELECTROLYTES IN BODY FLUIDS

- The **concentration of ions** is typically expressed in units of **milliequivalents per liter (mEq/liter).** These units give the concentration of cations or anions in a given volume of solution.

Figure 27.6 Electrolyte and protein anion concentrations in plasma, interstitial fluid, and intracellular fluid. The height of each column represents milliequivalents per liter (mEq/liter).

The electrolytes present in extracellular fluids are different from those present in intracellular fluid.



SODIUM

- Sodium ions **are the most abundant ions** in extracellular fluid, accounting for 90% of the extracellular cations. **The normal blood plasma sodium ions concentration is 136–148 mEq/liter.**
- Sodium ions plays a **pivotal role in fluid and electrolyte balance** because it accounts for almost half of the osmolarity of extracellular fluid.
- The sodium ions level in the blood is **controlled by aldosterone, antidiuretic hormone (ADH), and atrial natriuretic peptide (ANP).**
- Aldosterone increases renal reabsorption of sodium ions.
- When the blood plasma concentration of sodium ions drops below 135 mEq/liter, a condition called **hyponatremia, ADH release ceases**.
- The lack of ADH in turn permits **greater excretion of water in urine and restoration of the normal sodium ions level in ECF**. **Atrial natriuretic peptide increases sodium ions excretion by the kidneys when the sodium ions level is above normal, a condition called hypernatremia.**

ADH
ANP

CHLORIDE

- Chloride ions are the **most prevalent** **anions in extracellular fluid.**
- **The normal blood plasma chloride ions concentration is 95–105 mEq/liter.**
- **Chloride ions moves relatively easily between the extracellular and intracellular compartments** because most plasma membranes contain many chloride ions leakage channels and antiporters.
- **Processes that increase or decrease renal reabsorption of sodium ions also affect reabsorption of chloride ions.**

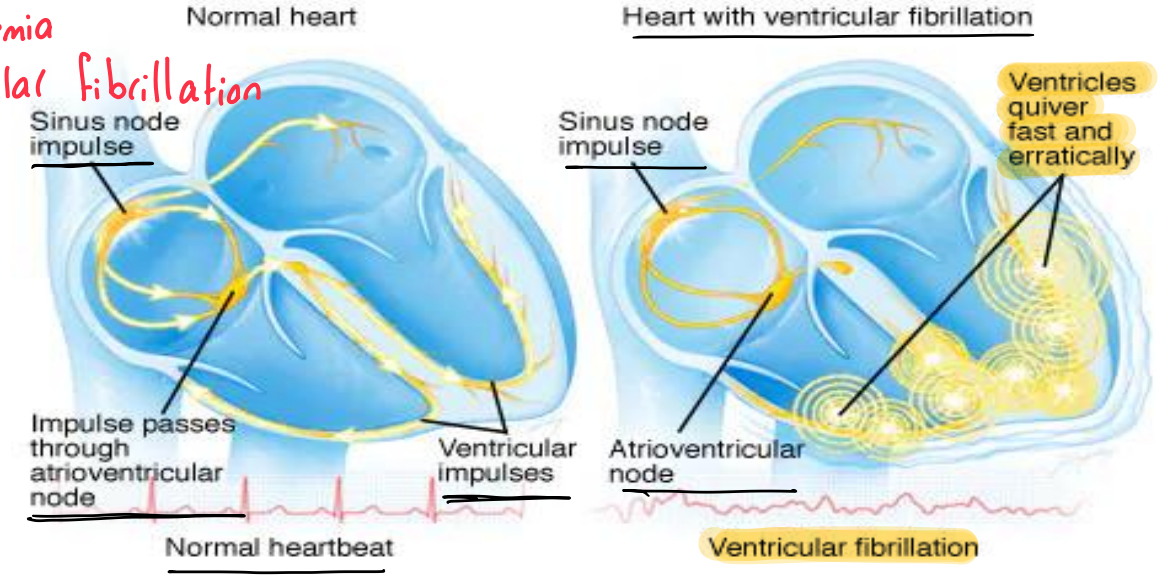
Na^+

POTASSIUM

- Potassium ions are **the most abundant cations in intracellular fluid** (140 mEq/liter).
- Potassium ions plays **a key role in establishing the resting membrane potential** and **in the repolarization phase of action potentials in neurons and muscle fibers**.
- Potassium ions also **helps maintain normal intracellular fluid volume**.
- When potassium ions moves into or out of cells, it often **is exchanged for hydreogen ions and thereby helps regulate the pH of body fluids**.
- It is **controlled mainly by aldosterone.**
- **Because potassium ions is needed during the repolarization phase of action potentials, abnormal potassium ions levels can be lethal. For instance, hyperkalemia (above-normal concentration of K in blood) can cause death due to ventricular fibrillation.**

رجفان

HyperKalemia
-> ventricular fibrillation



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BICARBONATE

- Bicarbonate ions are the **second most prevalent extracellular anions**.
- Normal blood plasma of bicarbonate ions concentration is 22–26 mEq/liter in systemic arterial blood and 23–27 mEq/liter in systemic venous blood.
- **Bicarbonate ions concentration increases as blood flows through systemic capillaries** because the carbon dioxide released by metabolically active cells combines with water to form carbonic acid; the carbonic acid then dissociates into hydrogen ions and bicarbonate ions.
- **As blood flows through pulmonary capillaries, however, the concentration of bicarbonate ions decreases again as carbon dioxide is exhaled**.
- The **kidneys are the main regulators of blood bicarbonate ions concentration**.
- The intercalated cells of the renal tubule can either form bicarbonate ions and release it into the blood when the blood level is low or excrete excess bicarbonate ions in the urine when the level in blood is too high.

CALCIUM

- Because such **a large amount of calcium** is stored in bone, it is **the most abundant mineral in the body**. **About 98% of the calcium in adults is located in the skeleton and teeth**, where it is combined with phosphates to form a crystal lattice of mineral salts.

PO_3^{-4}

- Besides **contributing to the hardness of bones and teeth**, calcium ion plays important roles in **blood clotting, neurotransmitter release, maintenance of muscle tone, and excitability of nervous and muscle tissue**.

CALCIUM

- The most **important regulator of calcium ion concentration** in blood plasma is parathyroid hormone (PTH).
- A **low level of calcium** ion in blood plasma promotes **release of more PTH,** which stimulates **osteoclasts in bone tissue to release calcium (and phosphate) from bone extracellular matrix**. Thus, **PTH increases bone resorption**.
- **Parathyroid hormone** also **enhances reabsorption of calcium ion** from glomerular filtrate through renal tubule cells and back into blood, and **increases production of calcitriol (the form of vitamin D that acts as a hormone),** which in turn **increases calcium ion absorption from food in the gastrointestinal tract**.

PHOSPHATE

- About 85% of the phosphate in adults is present as **calcium phosphate salts, which are structural components of bone and teeth.**
- **Three phosphate ions are important intracellular anions.**
- The same two hormones that govern calcium homeostasis—**parathyroid hormone (PTH) and calcitriol**—also **regulate the level of phosphate ions in blood plasma.**
- **PTH stimulates resorption of** bone extracellular matrix by osteoclasts, which releases both **phosphate and calcium** ions into the bloodstream.
- **In the kidneys, however, PTH inhibits reabsorption of phosphate ions while stimulating reabsorption of calcium ions by renal tubular cells. Thus, PTH increases urinary excretion of phosphate and lowers blood phosphate level.**
- **Calcitriol promotes absorption of both phosphates and calcium from the gastrointestinal tract.**

MAGNESIUM

- In adults, about 54% of the total body magnesium **is part of bone matrix as magnesium salts**. The remaining 46% occurs as magnesium ions in intracellular fluid (45%) and extracellular fluid (1%).
- Magnesium ions is the **second most common intracellular cation** (35 mEq/liter).
- Functionally,
  - Magnesium ion (Mg^{+2}) **is a cofactor for certain enzymes** needed for the metabolism of carbohydrates and proteins and for the sodium–potassium pump.
  - Magnesium ion **is essential for normal neuromuscular activity, synaptic transmission, and myocardial functioning.**
  - In addition, **secretion of parathyroid hormone (PTH) depends on magnesium ion.**
- The kidneys **increase urinary excretion of magnesium ions** in response to hypercalcemia, hypermagnesemia, increases in extracellular fluid volume, decreases in parathyroid hormone, and acidosis. The opposite conditions decrease renal excretion of magnesium ions.

TABLE 27.2

Blood Electrolyte Imbalances

	DEFICIENCY		EXCESS	
ELECTROLYTE*	NAME AND CAUSES	SIGNS AND SYMPTOMS	NAME AND CAUSES	SIGNS AND SYMPTOMS
Sodium (Na^+) 136–148 mEq/liter	**Hyponatremia** (hī-pō-na-TRĒ-mē-a) may be due to decreased sodium intake; increased sodium loss through vomiting, diarrhea, aldosterone deficiency, or taking certain diuretics; and excessive water intake.	Muscular weakness; dizziness, headache, and hypotension; tachycardia and shock; mental confusion, stupor, and coma.	**Hypernatremia** may occur with dehydration, water deprivation, or excessive sodium in diet or intravenous fluids; causes hypertonicity of ECF, which pulls water out of body cells into ECF, causing cellular dehydration.	Intense thirst, hypertension, edema, agitation, and convulsions.
Chloride (Cl^-) 95–105 mEq/liter	**Hypochloremia** (hī-pō-klō-RĒ-mē-a) may be due to excessive vomiting, overhydration, aldosterone deficiency, congestive heart failure, and therapy with certain diuretics such as furosemide (Lasix®).	Muscle spasms, metabolic alkalosis, shallow respirations, hypotension, and tetany.	**Hyperchloremia** may result from dehydration due to water loss or water deprivation; excessive chloride intake; or severe renal failure, hyperaldosteronism, certain types of acidosis, and some drugs.	Lethargy, weakness, metabolic acidosis, and rapid, deep breathing.
Potassium (K^+) 3.5–5.0 mEq/liter	**Hypokalemia** (hī-pō-ka-LĒ-mē-a) may result from excessive loss due to vomiting or diarrhea, decreased potassium intake, hyperaldosteronism, kidney disease, and therapy with some diuretics.	Muscle fatigue, flaccid paralysis, mental confusion, increased urine output, shallow respirations, and changes in electrocardiogram, including flattening of T wave.	**Hyperkalemia** may be due to excessive potassium intake, renal failure, aldosterone deficiency, crushing injuries to body tissues, or transfusion of hemolyzed blood.	Irritability, nausea, vomiting, diarrhea, muscular weakness; can cause death by inducing ventricular fibrillation.
Calcium (Ca^{2+}) Total = 9.0–10.5 mg/dL; ionized = 4.5–5.5 mEq/liter	**Hypocalcemia** (hī-pō-kal-SĒ-mē-a) may be due to increased calcium loss, reduced calcium intake, elevated phosphate levels, or hypoparathyroidism.	Numbness and tingling of fingers; hyperactive reflexes, muscle cramps, tetany, and convulsions; bone fractures; spasms of laryngeal muscles that can cause death by asphyxiation.	**Hypercalcemia** may result from hyperparathyroidism, some cancers, excessive intake of vitamin D, and Paget's disease of bone.	Lethargy, weakness, anorexia, nausea, vomiting, polyuria, itching, bone pain, depression, confusion, paresthesia, stupor, and coma.
Phosphate (HPO_4^{2-}) 1.7–2.6 mEq/liter	**Hypophosphatemia** (hī-pō-fos'-fa-TĒ-mē-a) may occur through increased urinary losses, decreased intestinal absorption, or increased utilization.	Confusion, seizures, coma, chest and muscle pain, numbness and tingling of fingers, decreased coordination, memory loss, and lethargy.	**Hyperphosphatemia** occurs when kidneys fail to excrete excess phosphate, as in renal failure; can also result from increased intake of phosphates or destruction of body cells, which releases phosphates into blood.	Anorexia, nausea, vomiting, muscular weakness, hyperactive reflexes, tetany, and tachycardia.
Magnesium (Mg^{2+}) 1.3–2.1 mEq/liter	**Hypomagnesemia** (hī'-pō-mag'-ne-SĒ-mē-a) may be due to inadequate intake or excessive loss in urine or feces; also occurs in alcoholism, malnutrition, diabetes mellitus, and diuretic therapy.	Weakness, irritability, tetany, delirium, convulsions, confusion, anorexia, nausea, vomiting, paresthesia, and cardiac arrhythmias.	**Hypermagnesemia** occurs in renal failure or due to increased intake of Mg^{2+}, such as Mg^{2+}-containing antacids; also occurs in aldosterone deficiency and hypothyroidism.	Hypotension, muscular weakness or paralysis, nausea, vomiting, and altered mental functioning.

*Values are normal ranges of blood plasma levels in adults.

Please, return back to this table (Table 27.2).

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ACID–BASE BALANCE

- **Various ions** play different roles that **help maintain homeostasis**.
- A major homeostatic challenge is keeping the hydrogen ions concentration (pH) of body fluids at an appropriate level.
- This task—**the maintenance of acid–base balance**—**is of critical importance to normal cellular function**. For example, the three-dimensional shape of all **body proteins**, which enables them to perform specific functions, is very **sensitive to pH changes**.
- Because metabolic reactions often produce a huge excess of hydrogen ions , the lack of any mechanism for the disposal of hydrogen ions would cause hydrogen ions in body fluids to rise quickly to a lethal level.
- **Homeostasis of hydrogen ions concentration within a narrow range is thus essential to survival**.

ACID–BASE BALANCE

- **The removal of hydrogen ions from body fluids and its subsequent elimination from the body depend on the following three major mechanisms:**

1. **Buffer systems**. Buffers act quickly to temporarily bind hydrogen ions, removing the highly reactive, excess hydrogen ions from solution. Buffers thus raise pH of body fluids but do not remove hydrogen ions from the body.
2. **Exhalation of carbon dioxide**. By increasing the rate and depth of breathing, more carbon dioxide can be exhaled. Within minutes this reduces the level of carbonic acid in blood, which raises the blood pH (reduces blood hydrogen ions level).
3. **Kidney excretion of hydrogen ions**. The slowest mechanism, but the only way to eliminate acids other than carbonic acid, is through their excretion in urine.

THE ACTIONS OF BUFFER SYSTEMS

- **Most buffer systems** in the body consist of a weak acid and the salt of that acid, which functions as a weak base.
- **Buffers prevent rapid, drastic changes in the pH of body fluids** by **converting strong acids and bases into weak acids and weak bases within fractions of a second**.
- **Strong acids lower pH more than weak acids** because strong acids release hydrogen ions more readily and thus contribute more free hydrogen ions. Similarly, **strong bases raise pH more than weak ones**.

PROTEIN BUFFER SYSTEM

- **It is the most abundant buffer in intracellular fluid (ICF) and blood plasma.**
- For example, the **protein hemoglobin** is an especially good buffer within red blood cells, and **albumin** is the main protein buffer in blood plasma.
- **Proteins are composed of amino acids**, organic molecules that contain at least **one carboxyl group** (–COOH) and at least **one amino group** (–NH2); **these groups are the functional components of the protein buffer system**.
- **The free carboxyl group at one end of a protein acts like an acid by releasing hydrogen ions when pH rises. The hydrogen ions is then able to react with any excess OH- in the solution to form water.**
- **The free amino group at the other end of a protein can act as a base by combining with hydrogen ions when pH falls.**
- **So, proteins can buffer both acids and bases.**

PROTEIN BUFFER SYSTEM

- **The protein hemoglobin is an important buffer of hydrogen ion in red blood cells**. As blood flows through the systemic capillaries, carbon dioxide (CO_2) passes from tissue cells into red blood cells, where it combines with water (H_2O) to form carbonic acid (H_2CO_3). Once formed, H_2CO_3 dissociates into hydrogen ion and HCO_3-. At the same time that CO_2 is entering red blood cells, oxyhemoglobin ($Hb–O_2$) is giving up its oxygen to tissue cells. Reduced hemoglobin (deoxyhemoglobin) picks up most of the hydrogen ion. For this reason, reduced hemoglobin usually is written as Hb–H. The following reactions summarize these relationships:

acids hates themselves

$$H_2O + CO_2 \rightarrow H_2CO_3$$

Water + Carbon dioxide (entering RBCs) → Carbonic acid

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

Carbonic acid → Hydrogen ion + Bicarbonate ion

$$Hb–O_2 + H^+ \rightarrow Hb–H + O_2$$

Oxyhemoglobin (in RBCs) + Hydrogen ion (from carbonic acid) → Reduced hemoglobin + Oxygen (released to tissue cells)

Red blood cells

CARBONIC ACID–BICARBONATE BUFFER SYSTEM

- The carbonic acid–bicarbonate buffer system **is based on the bicarbonate ion (HCO_3^-)**, which can act as a weak base, and **carbonic acid (H_2CO_3)**, which can act as a weak acid. As you have already learned, **HCO3- is a significant anion in both intracellular and extracellular fluids.**

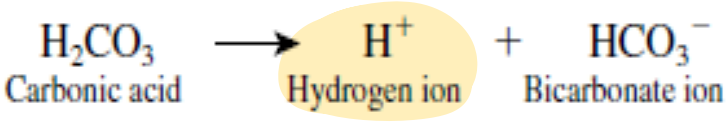
HCO_3^- reabsorbed

- **Because the kidneys also synthesize new HCO3- and reabsorb filtered HCO3-, this important buffer is not lost in the urine**. If there is an excess of hydrogen ion, the HCO3- can function as a weak base and remove the excess hydrogen ion as follows:

$$\underset{\text{Hydrogen ion}}{H^+} + \underset{\text{Bicarbonate ion (weak base)}}{HCO_3^-} \longrightarrow \underset{\text{Carbonic acid}}{H_2CO_3}$$

CARBONIC ACID–BICARBONATE BUFFER SYSTEM

- ✓ **Then, H_2CO_3 dissociates into water and carbon dioxide, and the CO_2 is exhaled from the lungs.** Conversely, if there is a shortage of hydrogen ion, the H_2CO_3 can function as a weak acid and provide hydrogen ion as follows:



- ✓ **Because CO_2 and H_2O combine to form H_2CO_3, this buffer system cannot protect against pH changes due to respiratory problems in which there is an excess or shortage of CO_2.**

PHOSPHATE BUFFER SYSTEM

- ✓ The components of the phosphate buffer system are the ions dihydrogen phosphate and monohydrogen phosphate.

the one for the carbonic acid–bicarbonate buffer system. The components of the phosphate buffer system are the ions *dihydrogen phosphate* ($H_2PO_4^-$) and *monohydrogen phosphate* (HPO_4^{2-}). Recall that phosphates are major anions in intracellular fluid and minor ones in extracellular fluids (see Figure 27.6). The dihydrogen phosphate ion acts as a weak acid and is capable of buffering strong bases such as OH^-, as follows:

$$\underset{\substack{\text{Hydroxide ion}\\\text{(strong base)}}}{OH^-} + \underset{\substack{\text{Dihydrogen}\\\text{phosphate}\\\text{(weak acid)}}}{H_2PO_4^-} \longrightarrow \underset{\text{Water}}{H_2O} + \underset{\substack{\text{Monohydrogen}\\\text{phosphate}\\\text{(weak base)}}}{HPO_4^{2-}}$$

PHOSPHATE BUFFER SYSTEM

The monohydrogen phosphate ion is capable of buffering the H^+ released by a strong acid such as hydrochloric acid (HCl) by acting as a weak base:

$$\underset{\text{Hydrogen ion (strong acid)}}{H^+} + \underset{\text{Monohydrogen phosphate (weak base)}}{HPO_4^{2-}} \longrightarrow \underset{\text{Dihydrogen phosphate (weak acid)}}{H_2PO_4^-}$$

- ✓ **Because the concentration of phosphates is highest in intracellular fluid, the phosphate buffer system is an important regulator of pH in the cytosol. It also acts to a smaller degree in extracellular fluids and buffers acids in urine.**

EXHALATION OF CARBON DIOXIDE

- ✓ The simple act of breathing also plays an important role in maintaining the pH of body fluids. An increase in the carbon dioxide (CO_2) concentration in body fluids increases hydrogen ion concentration and thus lowers the pH (makes body fluids more acidic).

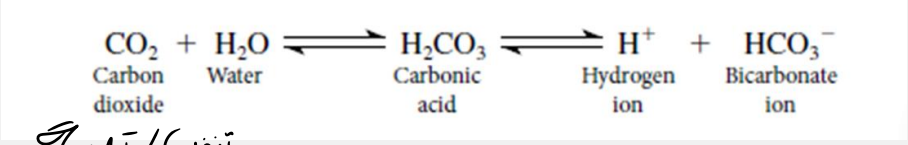
- ✓ Conversely, a decrease in the CO_2 concentration of body fluids raises the pH (makes body fluids more alkaline). This chemical interaction is illustrated by the following reversible reactions:

short term long term

$$\underset{\text{Carbon dioxide}}{CO_2} + \underset{\text{Water}}{H_2O} \rightleftharpoons \underset{\text{Carbonic acid}}{H_2CO_3} \rightleftharpoons \underset{\text{Hydrogen ion}}{H^+} + \underset{\text{Bicarbonate ion}}{HCO_3^-}$$

lungs renal

EXHALATION OF CARBON DIOXIDE



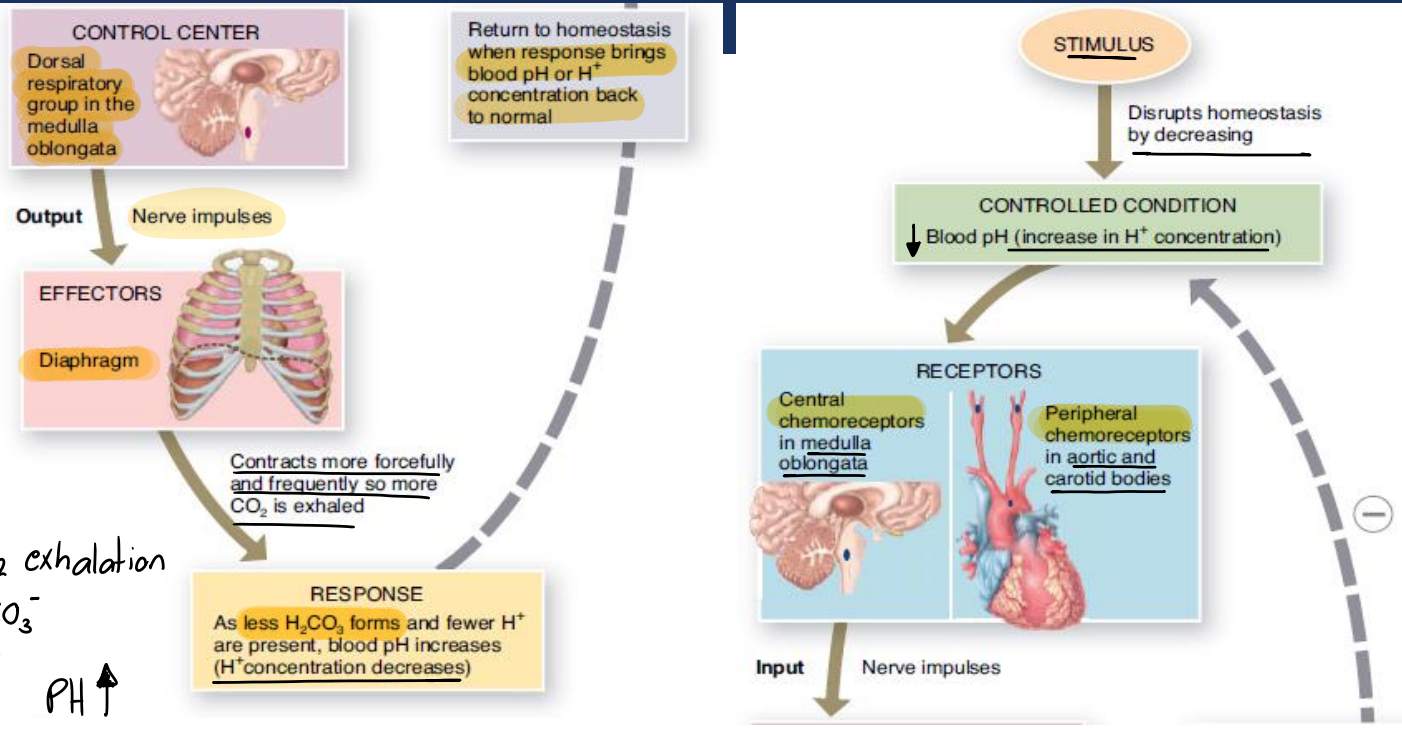
تنفس / تهوية

- ✓ With increased ventilation, more CO_2 is exhaled. When CO_2 levels decrease, the reaction is driven to the left (blue arrows), hydrogen ion concentration falls, and blood pH increases.

- ✓ If ventilation is slower than normal, less carbon dioxide is exhaled. When CO_2 levels increase, the reaction is driven to the right (red arrows), the hydrogen ion concentration increases, and blood pH decreases.

Figure 27.7 Negative feedback regulation of blood pH by the respiratory system.

Exhalation of carbon dioxide lowers the H^+ concentration of blood.



↑ CO_2 exhalation
↓ HCO_3^-
↓ H^+
pH ↑

Acid–Base Balance

TABLE 27.3

Mechanisms That Maintain pH of Body Fluids

MECHANISM	COMMENTS
Buffer systems	Most consist of a weak acid and its salt, which functions as a weak base. They prevent drastic changes in body fluid pH.
Proteins	The most abundant buffers in body cells and blood. Hemoglobin inside red blood cells is a good buffer.
Carbonic acid–bicarbonate	Important regulator of blood pH. The most abundant buffers in extracellular fluid (ECF).
Phosphates	Important buffers in intracellular fluid and urine.
Exhalation of CO_2	With increased exhalation of CO_2, pH rises (fewer H^+). With decreased exhalation of CO_2, pH falls (more H^+).
Kidneys	Renal tubules secrete H^+ into urine and reabsorb HCO_3^- so it is not lost in urine.

ICF

ECF

ICF

CO_2 ↓

↑ CO_2 exhaled → HCO_3^- ↓

pH ↑ ← ↓ H^+ ↲

H^+ secreted

HCO_3^- reabsorbed] Kidneys

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ACID–BASE IMBALANCES

- **The normal pH range of systemic arterial blood is between 7.35 and 7.45.**
- **Acidosis (or acidemia)** is a condition in which **blood pH is below 7.35**.
- **alkalosis (or alkalemia)** is a condition in which **blood pH is higher than 7.45**.

CNS

- **The major physiological effect of acidosis** is depression of the central nervous system through depression of synaptic transmission. If the systemic arterial blood pH falls below 7, depression of the nervous system is so severe that the individual becomes disoriented, then comatose, and may die. Patients with severe acidosis usually die while in a coma.

CNS / PNS

- **The major physiological effect of alkalosis,** by contrast, is overexcitability in both the central nervous system and peripheral nerves. Neurons conduct impulses repetitively, even when not stimulated by normal stimuli; the results are nervousness, muscle spasms, and even convulsions and death.

ACID–BASE IMBALANCES

- ✓ **Change in blood pH that leads to acidosis or alkalosis may be countered by compensation, the physiological response to an acid–base imbalance that acts to normalize arterial blood pH. Compensation may be either complete, if pH indeed is brought within the normal range, or partial, if systemic arterial blood pH is still lower than 7.35 or higher than 7.45.**

ACID–BASE IMBALANCES: RESPIRATORY ACIDOSIS

- **Inadequate exhalation of CO_2 causes the blood pH to drop.**
- Such conditions include pulmonary edema, injury to the respiratory center of the medulla oblongata, airway obstruction, or disorders of the muscles involved in breathing.
- If the respiratory problem is not too severe, the kidneys can help raise the blood pH into the normal range by increasing excretion of hydrogen ion and reabsorption of HCO_3^- (renal compensation).
- The goal in treatment of respiratory acidosis is to increase the exhalation of CO_2, as, for instance, by providing ventilation therapy. In addition, intravenous administration of HCO_3^- may be helpful.

ACID–BASE IMBALANCES: RESPIRATORY ALKALOSIS

- **The cause is the increase of pH (hyperventilation).** مرتفعات
- Such conditions include oxygen deficiency due to high altitude or pulmonary disease, cerebrovascular accident (stroke), or severe anxiety.
- Again, renal compensation may bring blood pH into the normal range if the kidneys are able to decrease excretion of hydrogen ion and reabsorption of HCO_3^-.

  H^+ excretion ↓ HCO_3^- reabsorption ↓
- Treatment of respiratory alkalosis is aimed at increasing the level of CO_2 in the body. One simple treatment is to have the person inhale and exhale into a paper bag for a short period; as a result, the person inhales air containing a higher-than-normal concentration of CO_2.

ACID–BASE IMBALANCES: METABOLIC ACIDOSIS

- **The causes the blood pH to decrease.**
- Three situations may lower the blood level of HCO_3^-:

(1) actual loss of HCO_3^-, such as may occur with severe diarrhea or renal dysfunction.

(2) accumulation of an acid other than carbonic acid, as may occur in ketosis.

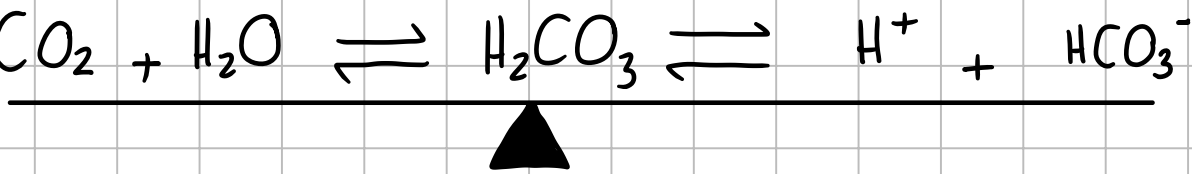
(3) failure of the kidneys to excrete hydrogen ions from metabolism of dietary proteins.

- If the problem is not too severe, hyperventilation can help bring blood pH into the normal range (respiratory compensation).
- Treatment of metabolic acidosis consists of administering intravenous solutions of sodium bicarbonate and correcting the cause of the acidosis.

ACID–BASE IMBALANCES: METABOLIC ALKALOSIS

- **A nonrespiratory loss of acid** or **excessive intake of alkaline drugs** causes the blood pH to increase above 7.45. **Excessive vomiting of gastric contents,** which results in a substantial loss of hydrochloric acid, is probably the most **frequent cause of metabolic alkalosis**.

- Respiratory compensation through hypoventilation may bring blood pH into the normal range. Treatment of metabolic alkalosis consists of giving fluid solutions to correct chloride ions, potassium ions, and other electrolyte deficiencies plus correcting the cause of alkalosis.



seesaw

respiratory

- respiratory acidosis

$Co_2 \uparrow \rightarrow HCO_3^- \uparrow \rightarrow PH \downarrow$

(decresed exhalation)

metabolic

- metabolic acidosis

$PH \downarrow \quad HCO_3^- \downarrow$

respiratory alkalosis

$PH \uparrow$ hyperventilation

$Co \downarrow$ increased Co_2

$HCO_3 \downarrow$ exhalation

$H^+ \downarrow$

metabolic alkalosis

$PH \uparrow \quad HCO_3^- \uparrow$

- excessive vomiting of gastric contents

(respiratory compensation)

hypoventilation

respiratory — $CO_2 \uparrow$ pH $\downarrow$ = respiratory acidosis

opposite — $CO_2 \downarrow$ pH $\uparrow$ = respiratory alkalosis

metabolic — $HCO_3^- \downarrow$ pH $\downarrow$ = metabolic acidosis

equal — $HCO_3^- \uparrow$ pH $\uparrow$ = metabolic alkalosis

hyperKalemia : ventricular fibrillation