



## Electrolytes and Minerals (Trace Elements) Metabolism

**Minerals** are inorganic substances mined from the earth. They are not of plant or animal origin. They exist naturally on and in the earth and many are critical parts of human tissue and are termed “essential” nutrients.

Of the 92 naturally occurring elements, the 14 minerals that have been shown by research to be **essential** to human health are:

**calcium, chromium, copper, fluorine, iodine, iron, magnesium, manganese, molybdenum, phosphorus, potassium, selenium, sodium and zinc.**

➤ **Essential Macro Minerals**

are those needed in significant quantities (such as calcium) – usually measured in **milligrams**.

➤ **Essential Trace Minerals**

are those needed in minute quantities (such as selenium) – usually measured in **micrograms** (one microgram [ $\mu\text{cg}$ ] equals 1/1,000th of a milligram [ $\text{mg}$ ]).

We have less than 100 years of knowledge on role of elements in the human body. It is estimated that 98% of the body mass of man is made up of nine nonmetallic elements.

The four main electrolytes namely **sodium, magnesium, potassium, and calcium** constitute about 1.98 %, while the rest 0.02% or 8.6 g of an average human adults is made up of **10 typical trace elements**. However, this tiny fraction exerts a tremendous influence on all body functions.

***Minerals are required for a variety of physiological functions, their functions are:***

1. Maintenance of osmotic pressure of cell
2. Transport of oxygen
3. Growth and maintenance of tissues and bones
4. Working of nervous system
5. Muscle contraction
6. Maintenance of electrolytic balance
7. Acid-base balance



The major elements that compose the human body and their relative amounts are as follows:

***Mineral content of human Percent Approximate amount Element body (in gm) in 70 Kg adult. usually measured in micrograms (one microgram [ $\mu\text{g}$ ] equals 1/1,000th of a milligram [mg]).***

Ca<sup>++</sup> 1.50 1050

P 1.00 700

K<sup>+</sup> 0.35 245

Na<sup>+</sup> 0.15 105

Cl<sup>-</sup> 0.15 105

Mg<sup>++</sup> 0.05 035

Fe<sup>++</sup> 0.004 003

Zn<sup>++</sup> 0.0033 02

### **Classification of Minerals according to the important for human body**

#### ➤ **Quantity Elements (Electrolytes)**

Na (Sodium), Mg (Magnesium), K (Potassium), Ca (Calcium), P (Phosphorus), S (Sulfur), Cl (Chlorine).

#### ➤ **Essential Trace Elements**

Mn (Manganese), Fe (Iron), Co (Cobalt), Ni (Nickel), Cu (Copper), Zn (Zinc), Mo (Molybdenum), Se (Selenium), I (Iodine).

#### ➤ **Function suggested from active handling humans, but no specific identified biochemical functions.**

Li (Lithium), V (Vanadium), Cr (Chromium), B (Boron), F (Fluorine), Si (Silicon), As (Arsenic).

### **Electrolytes (Na, K, Mg, Ca, Cl)**

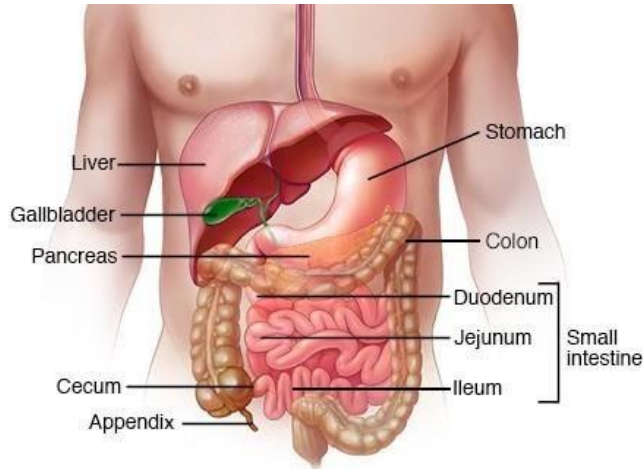
#### **Sodium (Na<sup>+</sup>):**

- ❖ Sodium is a major cation and contributor to the osmolality of the **extracellular** fluid of the body, which is **one-third** of the body water in adults.



## Minerals and Trace Elements Metabolism

- ❖ The sodium content of **natural food** varies between 0.1 and 3.3 mmol/100 g. In contrast, **processed foods** have a sodium content of 11–48 mmol/100 g, partly **sodium nitrate** is used as a **preservative**.
- ❖ Sodium is concentrated in the **extracellular fluid**, giving **osmolarity** and charge moves from the extracellular fluid into cells there is a change in charge and concentration.



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### Sodium content of the body

A male adult weighing 65–70 kg has a total body sodium content of 4 mol (100 g):

- 500 mmol (11.5 g) in intercellular fluid (concentration 2 mmol/l)
- 1500 mmol (34.5 g) in bone
- 2000 mmol (46 g) in extracellular fluid (concentration 130–145 mmol/l)
- daily dietary intake is 50–200 mmol (1.15–4.6 g).

## Absorption and Availability of Sodium

- ✚ Intestinal sodium absorption is very efficient in both the **small intestine** and **colon**.
- ✚ Sodium is absorbed by a variety of processes. In the proximal intestine sodium is absorbed, in part by a solute dependent cotransport system, and is involved in nutrient absorption. In the more distal intestine and colon,
- ✚ sodium absorption is by a **sodium/hydrogen interchange**; in the colon this process is coupled to **chloride/bicarbonate** exchange.
- ✚ In the distal intestine and colon, the process is electroneutral and involves protein carriers.
- ✚ In the distal colon active sodium transport occurs against an electrochemical gradient. Water absorption is a **passive process** that requires **active transport** of sodium and chloride.

The optimum absorption of water occurs when the concentration of glucose in the intestinal lumen is around 110 mmol/l. This finding has been of great importance in the development of oral replacement solutions (ORS).



## Sodium Regulation

- Sodium is **found** in significant amounts in **bone**, but this pool is not readily available at times of rapid loss of sodium.
- The extracellular fluid sodium content is regulated in parallel with the extracellular fluid volume control.

When the extracellular fluid or blood volume falls

1. Neural sympathetic activity increases
2. The response comprises vasoconstriction.
3. A redistribution of renal blood flow
4. Reduced glomerular filtration.
5. Increased sodium and water retention.
6. In addition, there are increases in renin production, circulating angiotensin II, noradrenaline, adrenaline, ACTH and ADH.

## Sodium Excretion

- Sodium is filtered from the plasma in the **kidneys**.
- The reabsorption of sodium occurring as an osmotic phenomenon in the proximal tubule, loop of Henle and distal tubule.
- Distal tubular absorption is very important and is under the control of atrial natriuretic factor.
- Renal sodium excretion is also **controlled by angiotensin II, prostaglandins** and the kallikrein–kinin system.

## Sodium Depletion

- Sodium is lost largely via the **urine**, with only minimal loss occurring via the **feces** or **skin**, unless there are abnormal situations such as **diarrhea** or **excessive sweating**.
- A reduced body sodium pool results in reduced extracellular fluid volume. Increased sodium loss in urine can occur in diseases, e.g., **diabetes mellitus** and **Addison's disease** (adrenal cortical insufficiency), following excessive



doses of **diuretic drugs**, and in cases of **renal tubular damage**, as in **chronic renal failure**.

Healthy kidneys maintain a consistent level of sodium in the body by adjusting the amount excreted in the urine. When sodium consumption and loss are not in balance, the total amount of sodium in the body is affected. The concentration of sodium in the blood may be:

### **Hypernatremia**

The body contains too little water for the amount of sodium. The sodium level in the blood becomes abnormally **high** when water loss exceeds sodium loss. Usually, hypernatremia results from **dehydration**. For example, people may lose body fluids and become dehydrated due to:

1. Drinking too little.
2. Vomiting.
3. Having diarrhea.
4. Using diuretics.
5. Sweating excessively.
6. Insufficient water intake usually plays an important role.

People with **diabetes mellitus** and **high blood sugar** levels may urinate excessive amounts, causing dehydration. Dehydration can also be caused by **kidney disorders** and by **diabetes insipidus**, which also causes people to urinate excessive amounts although without high blood sugar levels, and is due to inadequate or ineffective vasopressin secretion or action.

### **Potassium(k<sup>+</sup>):**

- In **natural** and **processed foods**, the potassium content varies from 2.8 to 10 mmol/kg.
- Dietary potassium tends to be derived from fresh vegetables and meat.
- An adult male weight approximately 70 kg contains 2800–3500 mmol (110–137 g), of which 95% is **intracellular** (150 mmol/l).
- Cellular potassium concentrations are affected by **pH, aldosterone, insulin and the adrenergic nervous system**.



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- The plasma concentration of 3.5–4.5 mmol/l is dependent on **intake, excretion**, and **the balance between extracellular and intracellular** compartments.
- There is a direct, reciprocal relationship between plasma potassium and aldosterone production. Control is mainly through urinary loss, with some additional colonic loss.
- **Insulin excretion** is **increased** when the **plasma potassium increases**, possibly provoking cellular uptake of potassium.

### Transport and Absorption of Potassium:

- The transport of potassium into cells is under the control of the Na/K-ATPase enzyme, and allows transport of potassium against a concentration gradient.
- The ratio of extracellular to intracellular potassium concentration is important in the membrane potential difference in neuron and muscle cells (Na<sup>+</sup>/K<sup>+</sup>-ATPase exchange pump system).

Over 90% of dietary potassium is absorbed in the **proximal small intestine**.

In the **small intestine potassium absorption is passive**, but in the **colon**, it is an **active** process. In the sigmoid colon absorption is mediated by a K<sup>+</sup>/H<sup>+</sup> mechanism. Body stores of potassium most of the potassium is intracellular, i.e., in the cell fluid compartment.

Potassium is **necessary for the normal functioning of cells, nerves, and muscles**. The body must maintain the potassium level in blood within a narrow range. A blood potassium level that is

### Hyperkalemia

The level of **potassium in blood is too high**. A high potassium level has many causes, including **kidney disorders, drugs that affect kidney function, and consumption of too much supplemental potassium**.

Usually, hyperkalemia must be severe before it causes **symptoms**, mainly **abnormal heart rhythms**. Doctors usually detect hyperkalemia when blood tests or electrocardiography is done for other reasons.



### Causes:

Usually, hyperkalemia results from several simultaneous problems, including the following:

1. **Kidney disorders** that prevent the kidneys from excreting enough potassium
2. **Drugs** that prevent the kidneys from excreting normal amounts of potassium (a common cause of mild hyperkalemia)
3. **A diet high in potassium**
4. **Treatments that contain potassium**
5. **Addison disease** can also cause hyperkalemia.

### Hypokalemia

The level of **potassium in blood is too low**. A low potassium level can make **muscles feel weak, cramp, twitch, or even become paralyzed, and abnormal heart rhythms** may develop.

### Causes

Typically, the potassium level becomes low because too much is lost from the **digestive tract** due to **vomiting, diarrhea, or excessive laxative use**. Sometimes too much potassium is **excreted in urine**, usually because of **drugs** that cause the kidneys to **excrete excess sodium, water, and potassium (diuretics)**. In many **adrenal disorders**, such as **Cushing syndrome**, the adrenal glands produce too much aldosterone, a hormone that causes the kidneys to excrete large amounts of potassium.

### Calcium ( $\text{Ca}^{++}$ ):

- Is one of the body's electrolytes, which are minerals that carry an electric charge when dissolved in body fluids such as blood (**but most of the body's calcium is uncharged**).
- About 99% of the body's **calcium is stored in the bones**, but cells (particularly muscle cells) and blood also contain calcium.



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- About 40% of the calcium in blood is attached (bound) to proteins in blood, mainly albumin. Protein-bound calcium acts as a reserve source of calcium for the cells but has no active function in the body. Only unbound calcium affects the body's functions. Calcium is **essential** for the following:
1. Formation of bone and teeth
  2. Muscle contraction
  3. Normal functioning of many enzymes
  4. Blood clotting
  5. Normal heart rhythm

### Calcium Absorption and Balance

- Calcium absorption is largely from the **jejunum** but may also occur in the **ileum and colon**. The predominant absorptive process is by **active transport** and there is also some **simple passive diffusion in the ileum**.
- Phytate (Phytic acid) binds calcium to form insoluble salts within the intestinal lumen, and reduces calcium absorption.
- Approximately 60% of the total plasma calcium is filtered in the kidney glomeruli, and in health 97% of this calcium is reabsorbed.
- Several hormones are involved, including PTH, with increased absorption of calcium and decreased tubular absorption of phosphate.

**The level of calcium in blood is regulated primarily by two hormones:**

- Parathyroid hormone
- Calcitonin

Too much calcium in the blood is called hypercalcemia. Too little calcium in the blood is called hypocalcemia.

### Hypercalcemia

At first, people have **digestive problems**, **feel thirsty**, and may **urate a lot**, but if **severe hypercalcemia** leads to **confusion** and eventually **coma**. If not recognized and treated, the disorder can be life threatening.





**Causes:** Causes of hypercalcemia include the following:

1. **Hyperparathyroidism:** One or more of the four parathyroid glands secrete too much parathyroid hormone, which helps control the amount of calcium in blood.
2. **Too much calcium intake:** Occasionally, hypercalcemia develops in people with **peptic ulcers** if they drink a lot of milk and take calcium-containing antacids for relief. The resulting disorder is called the **milk-alkali syndrome**.
3. **Too much vitamin D intake:** If people take very high daily doses of vitamin D over several months, the amount of calcium absorbed from the digestive tract increases substantially.
4. **Cancer:** cells in kidney, lung, and ovary cancers may secrete large amounts of a protein that, like parathyroid hormone, increases the calcium level in blood. Calcium released into the blood when cancer spreads (metastasizes) to bone and destroys bone cells. Such bone destruction occurs most commonly with prostate, breast, and lung cancers. Multiple myeloma (a cancer involving bone marrow) can also lead to the destruction of bone and result in hypercalcemia. Other cancers can increase the calcium level in blood by means not yet fully understood.
5. **Bone disorders:** If bone is broken down (resorbed) or destroyed, calcium is released into the blood, sometimes causing hypercalcemia. In **Paget disease**, bone is broken down, but the calcium level in blood is usually normal. Severe hyperthyroidism can also cause hypercalcemia by increasing resorption of bone tissue.

## Hypocalcemia

The calcium level in blood is too low.

A low calcium level may result from a problem with the

**parathyroid glands**, as well as **from diet, kidney disorders, or certain drugs**. As hypocalcemia progresses, **muscle cramps** are common, and people may become **confused, depressed, and forgetful and have tingling in their lips, fingers, and feet as well as stiff, achy muscles**.

Usually, the disorder is detected by routine blood tests. **Calcium and vitamin D supplements may be used to treat hypocalcemia**.



Thus, hypocalcemia causes problems only when the level of unbound calcium is low. Unbound calcium has an electrical (ionic) charge, so it is also called ionized calcium.

### Magnesium ( $Mg^{++}$ ):

- One of the body's electrolytes, which are minerals that carry an electric charge when dissolved in body fluids such as blood, but the majority of magnesium in the body is **uncharged and bound to proteins** or **stored in bone**.
- **Bone** contains about **half** of the body's magnesium.
- Blood contains very little.
- Magnesium is necessary for the formation of bone and teeth and for normal nerve and muscle function.
- Many enzymes in the body depend on magnesium to function normally.
- Magnesium is also related to the **metabolism of calcium and the metabolism of potassium**.
- The level of magnesium in the blood depends largely on how the body obtains magnesium from foods and **excretes** it in **urine and stool** and less so on the total body stores of magnesium. The level of magnesium in the blood can become.

### Hypermagnesemia

The level of magnesium in blood is too high. Hypermagnesemia is uncommon. It usually develops only when people with **kidney failure** are given **magnesium salts** or **take drugs that contain magnesium** (such as some antacids or laxatives). Hypermagnesemia may cause

1. Muscle weakness
2. Low blood pressure -Impaired breathing
3. When hypermagnesemia is severe, the heart can stop beating.

### Hypomagnesemia

The level of magnesium in blood is too low.



## **Causes**

Usually, the magnesium level becomes low because people consume less (most often, because of **starvation**) or because **the intestine cannot absorb nutrients normally (called malabsorption)**. But sometimes hypomagnesemia develops because the kidneys or intestine excrete too much magnesium.

## **Hypomagnesemia may also result from the following:**

1. **Consuming large amounts of alcohol (common)**, which reduces consumption of food (and thus magnesium) and increases excretion of magnesium.
2. **Protracted diarrhea** (common), which increases magnesium excretion.
3. **High levels of aldosterone, vasopressin (antidiuretic hormone), or thyroid hormones**, which increase magnesium excretion.
4. **Drugs** that increase magnesium excretion, including diuretics, the antifungal drug amphotericin B, and the chemotherapy drug cisplatin.
5. **Breastfeeding**, which increases requirements for magnesium.

## **Chloride (Cl<sup>-</sup>)**

- Chloride concentration in plasma is 96-106 mEq/L and in Cerebrospinal fluid (CSF), it is about 125 mEq/L.
- Chloride concentration in CSF is higher than any other body fluids. Since CSF protein content is low.
- Renal threshold for Cl<sup>-</sup> is about 110 mEq/L. Daily excretion of Cl<sup>-</sup> is about 5-8 gm/day.

Intake, output and metabolism of sodium and chloride run in parallel. The homeostasis of Na<sup>+</sup>, K<sup>+</sup> and Cl<sup>-</sup> are inter- related. Chloride is **important in the formation of hydrochloric acid in gastric juice**.

## **Hyperchloremia is seen in:**

1. Dehydration
2. Cushing's syndrome. Mineralocorticoids cause increased reabsorption from kidney tubules.



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3. Severe diarrhea leads to loss of bicarbonate and compensatory retention of chloride.
4. Renal tubular acidosis.

### Hypochloremia Causes

1. Excessive vomiting. HCl is lost, so plasma  $\text{Cl}^-$  is lowered. There will be compensatory increase in plasma bicarbonate. This is called hypochloremia alkalosis.
2. Excessive sweating.
3. In Addison's disease, aldosterone is diminished, renal tubular reabsorption of  $\text{Cl}^-$  is decreased, and more  $\text{Cl}^-$  is excreted.

### Manganese (Mn):

Manganese content of foods varies greatly

- ✚ The highest concentrations in nuts, grains, and cereals
- ✚ The lowest in dairy products, meat, poultry, fish, and seafood.
- ✚ Relatively high concentrations of manganese were found in soluble (“instant”) coffee and tea and account for 10% of the total daily intake.

The total body content average human adult has about 15 mg of manganese, typically seen in nucleic acid.

**Daily requirement** is about 2-5 mg/day.

Manganese **acts as an activator of enzyme** and as a component of metalloenzymes.

They have a role to play in **oxidative phosphorylation, fatty acids and cholesterol metabolism, mucopolysaccharide metabolism, and urea cycle.**

### Zinc (Zn):

- ✚ The metal zinc is an omnipotent metal that has **amphoteric nature**. Hence, it is ionized either in acidic or alkaline forms.
- ✚ Content of zinc is 2-3 ng in an average adult.
- ✚ About **99% is intracellular** while the rest is in plasma.
- ✚ The average **daily requirement** is 15-20 mg/day.



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- ✚ Phytase decreases fibers, phosphates, calcium, and copper competes with zinc for absorption from small intestine.
- ✚ About 2-5 mg/day is excreted via **pancreas and intestine**. The other mode of excretion is via proximal tubule and sweat glands.

### Fluorine (F):

Fluorine is a lightest element.

#### Important of Fluorine

1. Fluorine plays an important role in the hard tissues of the body such as bone and teeth.
2. It helps in producing denser bones and fluoride has been suggested as a therapeutic agent in the treatment of osteoporosis.
3. It is thought that fluoride, in conjunction with calcium, stimulates osteoblastic activity.

### Copper (Cu<sup>++</sup>):

- Copper plays a very important role in our metabolism largely because it allows many critical enzymes to function properly.
- **Acidic conditions** promote the solubility which incorporates copper ions either in cupric form or cuprous form into the food chain.

- Mainly copper is available in the

liver, shellfish, dried fruit, milk and milk products, sunflower seeds, sesame seeds, tahini, and sun-dried tomatoes.

- The average adult human of 70 kg weight contains about 100 mg.
- The **daily requirement** is about **2-5 mg** of which 50% is absorbed from the gastrointestinal tract (GIT).



## Iron (Fe):

Iron is an essential constituent of **hemoglobin** and **certain enzymes** such as **cytochrome oxidase, catalase, and peroxidase**.

It performs **two important functions in the body**

1. To transport oxygen to tissues (through Hb)
2. To take part in oxidation-reduction reactions (cytochrome system).

**Sources:** meat, liver, eggs, spinach and fruits.

### *Absorption:*

- ❖ Dietary intake of iron is mainly in **ferric (Fe<sup>+++</sup>)** form as hydroxides or in organic compounds.
- ❖ The action of gastric HCl and of some organic acids liberates free ferric ions, which in turn are **reduced to ferrous ions (Fe<sup>++</sup>)** by reducing substances such as cysteine or ascorbic acid.
- ❖ The **ferrous form** of iron is **more soluble** and thus **easily absorbed**.
- ❖ The absorption of iron occurs in **duodenum and stomach**.

### *Transport and storage:*

- ❖ Iron is transported in plasma in **ferric form**, which remains firmly bound to a specific  $\beta$ - globulin, transferrin.
- ❖ The normal concentration of protein bound iron in plasma is 50-180  $\mu\text{gm}/100\text{ml}$ .
- ❖ **Iron is stored** chiefly in mucosal cells of intestine, liver, spleen and bone marrow as **ferritin**.

### *Daily Requirement:*

- ✚ **Infants:** 6 – 15 mg
- ✚ **Children:** 10 –18 mg
- ✚ **Adult (male):** 10 mg
- ✚ **Adult (Female):** 18 mg.

**Pretest:/** List the basic compounds that iron is an essential component of its formation in the body?