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, and essential trace minerals are those needed in minute quantities (such as selenium) – usually measured in micrograms (one microgram [mcg] equals 1/1,000th of a milligram [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

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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 [μcg] equals 1/1,000th of a milligram [mg]).**

Ca^{++}	1.50 1050
P	1.00 700
K^{+}	0.35 245
Na^{++}	0.15 105
Cl^{-}	0.15 105
Mg^{++}	0.05 035
Fe^{++}	0.004 003
Zn^{++}	0.0033 02

- **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^{++}): 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. 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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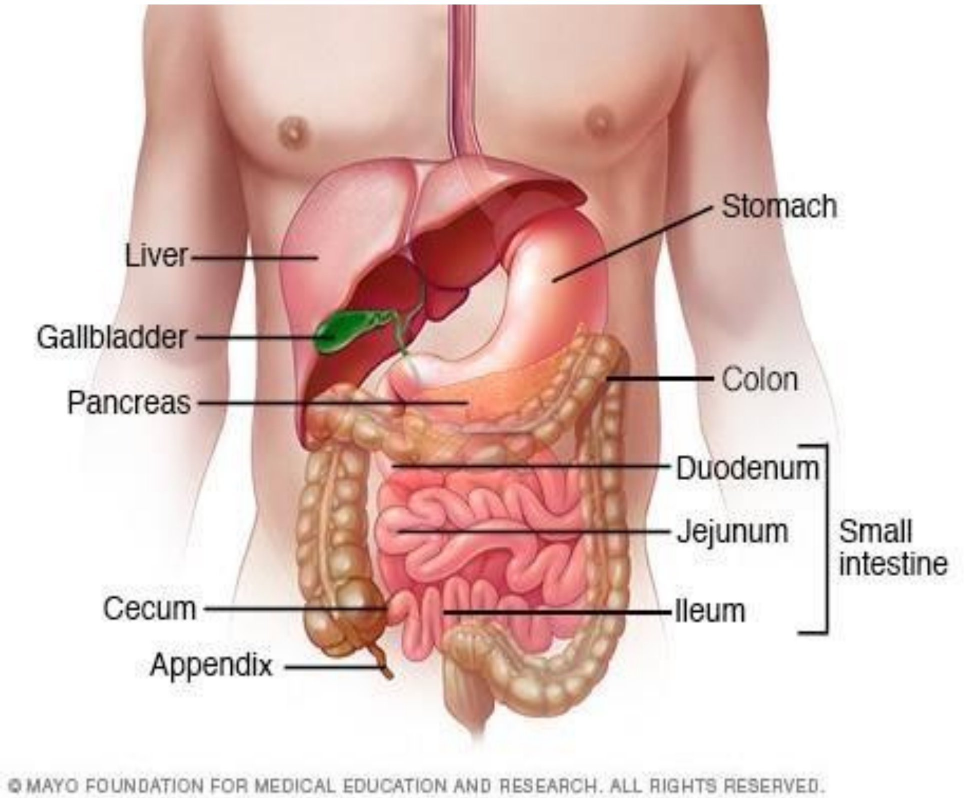
Absorption and availability of sodium

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, neural sympathetic activity increases, and the response comprises vasoconstriction, a redistribution of renal blood flow, reduced glomerular filtration, and increased sodium and water retention. In addition, there are increases in renin production, circulating angiotensin II, noradrenaline, adrenaline, ACTH and ADH.

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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 excretion: **Sodium is filtered from the plasma in the kidneys. The body has potent sodium-retaining mechanisms. Extra sodium is lost from the body by reducing the activity of the renin –angiotensin-aldosterone system (RAAS) that leads to increased sodium loss from the body. Sodium is lost through the kidneys (proximal tubule, loop of Henle and distal tubule), sweat, and feces .**

Sodium depletion **Sodium is lost largely via the urine, with only minimal loss occurring via the faeces 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

-Too high (hypernatremia)

-Too low (hyponatremia)

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.

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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 insipid us , 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+)

Potassium(k^+): **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. 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 (see Na^+/K^+-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/H^+ mechanism. Body stores of potassium most of the potassium is intracellular, i.e., in the cell fluid compartment.

Potassium homoeostasis: the homoeostasis of potassium in the body is controlled by renal glomerular filtration and tubular secretion. Chronic increased dietary potassium intake increases potassium secretion via the kidneys. There is an associated degree of hyperaldosteronism. Increased sodium entering the distal nephron results in an increased, simultaneous urinary loss of potassium. Excretion Potassium is largely lost in the urine, although 10% of the daily loss occurs through the distal ileum and colon. Small amounts are lost in sweat and vomit.

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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

-Too high (hyperkalemia)

-Too low (hypokalemia)

The body can use the large reservoir of potassium stored within cells to help maintain a constant level of potassium in blood. Some potassium is also lost through the digestive tract and in sweat. Healthy kidneys can adjust the excretion of potassium to match changes in consumption. Some drugs and certain conditions affect the movement of potassium into and out of cells, which greatly influences the potassium level in blood.

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 has many causes but usually results from vomiting, diarrhea, adrenal gland disorders, or use of diuretics. 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 (Ca++)

Calcium (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. 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:

-Formation of bone and teeth

-Muscle contraction

-Normal functioning of many enzymes

-Blood clotting

-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

A high calcium level may result from a problem with the parathyroid glands, as well as from diet, cancer, or disorders affecting bone. At first, people have digestive problems, feel thirsty, and may urinate a lot, but if severe, hypercalcemia leads to confusion and eventually coma. If not recognized and treated, the disorder can be life threatening.

Usually, hypercalcemia is detected by routine blood tests. Drinking lots of fluids may be sufficient, but diuretics may increase calcium excretion, and drugs can be used to slow the release of calcium from bone if needed.

Causes

Causes of hypercalcemia include the following:

-Hyperparathyroidism: One or more of the four parathyroid glands secrete too much parathyroid hormone, which helps control the amount of calcium in blood.

-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.

-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.

-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.

-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++)

Magnesium (Mg^{++}): is 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

-Too high (hypermagnesemia)

-Too low (hypomagnesemia)

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

-Muscle weakness

-Low blood pressure

-Impaired breathing

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.

Hypomagnesaemia may also result from the following:

-Consuming large amounts of alcohol (common), which reduces consumption of food (and thus magnesium) and increases excretion of magnesium

-Protracted diarrhea (common), which increases magnesium excretion

-High levels of aldosterone, vasopressin (antidiuretic hormone), or thyroid hormones, which increase magnesium excretion

-**Drugs** that increase magnesium excretion, including diuretics, the antifungal drug amphotericin B, and the chemotherapy drug cisplatin

-**Breastfeeding**, which increases requirements for magnesium

Manganese (Mn)

Manganese (Mn): Manganese content of foods varies greatly. found 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.

Manganese is found in all mammalian tissues with concentrations ranging from 0.3 to 2.9 μg manganese/g. Tissues rich in mitochondria and pigments (e.g., retina, dark skin) tend to have high manganese concentrations. Bone, liver, pancreas, and kidney typically have higher manganese concentrations than other tissues. The largest tissue store of manganese is in the bone. Bone, liver, pancreas, and kidney typically have higher manganese concentrations than other tissues. The largest tissue store of manganese is in the bone.

Some of the enzymes which are present along with magnesium are arginase, diamine oxidase, pyruvate carboxylate, glutamine synthetase. The deficiency cause bleeding disorders due to increased prothrombin time while accumulation over a long period causes anorexia, apathy, headache impotence, leg cramps, speech disturbance, encephalitis like syndrome and parkinsonian like syndrome.

Zinc (Zn)

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 the average body content of zinc is 2-3 g in an average adult. About 99% is intracellular while the rest is in plasma. The average daily requirement is 15-20 mg/day. 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. Plasma zinc levels are decreased in pregnancy, fluid loss, oral contraceptive usage, blood loss, acute myocardial infarction, infections, and malignancies. The function of zinc in cells and tissues is dependent on metalloproteinase and these enzymes are associated with reproductive, neurological, immune, dermatological systems, and GIT. It is essential for normal spermatogenesis and maturation, the genetic disorder related with zinc metabolism is acrodermatitis enteropathica which is an autosomal recessive defect where there is an inability in Zn absorption. Zinc also supports normal growth and development during pregnancy, childhood, and adolescence.

Copper (Cu)

Copper (Cu): **Copper plays a very important role in our metabolism largely because it allows many critical enzymes to function properly. Acidic conditions promotes 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). Rest is excreted via bile and kidney. Copper accumulates in the liver, brain and kidney more than rest of body. Over 90% of plasma copper is associated with ceruloplasmin and 60% of red blood cell (RBC) is bound to superoxide dismutase. In human blood, copper is principally distributed between the erythrocytes and in the plasma. In erythrocytes, 60% of copper occurs as the copper-zinc metalloenzyme superoxide dismutase, the remaining 40% is loosely bound to other proteins and amino acids. Total erythrocytes copper in normal human is around 0.9-1.0 pg/ml of packed red cells. Copper has a selected biochemical function in hemoglobin (Hb) synthesis, connective tissue metabolism, and bone development Excessive Cu either from diet or through any other sources acquired rapidly produces nausea, vomiting, diarrhea, profuse sweating, and renal dysfunction. The symptoms of copper deficiency are hypochromic anemia, neutropenia, hypopigmentation of hair and skin, abnormal bone formation with skeletal fragility and osteoporosis, joint pain, lowered immunity, vascular abnormalities.**

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Iron (Fe)

Iron (Fe): **Iron is an essential constituent of haemoglobin and certain enzymes such as cytochrome oxidase, catalase and peroxidase. It performs two important functions in the body—to transport oxygen to tissues (through Hb) and 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^{+++}) 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 ($Fe^{++)}$ 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 β- globulin, transferring. The normal concentration of protein bound iron in plasma is 50 - 180µ gm/ 100ml. 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, female- 18 mg.

Fluorine (F)

Fluorine (F): **Fluorine is a lightest element; fluorine plays an important role in the hard tissues of the body such as bone and teeth. It helps in producing denser bones and fluoride has been suggested as a therapeutic agent in the treatment of osteoporosis. It is thought that fluoride, in conjunction with calcium, stimulates osteoblastic activity. Fluorine has profound antienzyme properties and prevents dental caries. The increased fluoride utilization could be responsible for the anticariogenic action. Fluoride or fluorine deficiency is a hypothetical disorder, which may cause increased dental caries and possibly osteoporosis due to a lack of fluoride in the diet. High levels of dietary fluoride cause fluorosis (bone disease) and mottling of teeth. High levels of fluoride cause dental lesions. Acute toxicity of fluoride is very rare and can occur due to a single ingestion of a large amount of fluoride and can be fatal. The amount of fluoride considered lethal when taken orally is 35-70 mg F/kg body weight. Symptoms of acute toxicity occur rapidly. There is a diffuse abdominal pain,**

diarrhea, vomiting, excess salivation, and thirst. Chronic toxicity is caused due to long-term ingestion of smaller amounts of fluoride in drinking-water. Excessive fluoride more than 8 ppm in drinking water daily for many years can lead to skeletal and dental fluorosis. Severe cases are normally found only in warm climates where drinking-water contains very high levels of fluoride. Due to chronic toxicity, bone density slowly increases; the joints stiffen and become painful.

Chloride Cl^-

Chloride: is the most abundant free anion in animal cells, and performs or determines fundamental biological functions in all tissues Chloride channels are integral membrane proteins that regulate the movement of chloride ions across cellular membranes. They perform a vital role in physiological processes such as cell volume regulation, epithelial transport, the regulation of nerve and muscle cell membrane excitability and in determining the pH within cytoplasmic membrane-bound organelles Several genetic diseases is the caused by mutations within chloride .channel gene. Chloride ion (Cl-) is the major anion in the extracellular fluid

Main function :-

1- Regulate water balance (osmotic pressure and acid base) as it is the part of NaOH

2- Nerve impulse conduction

3- Hydrochloric acid formation in stomach

4- Plasma level of chloride change might cause abnormal metabolism of Na^+ and Cl^- that might lead to:-

a- Hyperchloremia

b- Hypochloremia

hypochloremia is an electrolyte disturbance in which there is an abnormally low level of the chloride ion in the bloo

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