**MINERAL METABOLISM**

**Macroelements** are elements needed at high concentrations. Example, Sodium, Potassium, Calcium, Magnesium and Chloride.

**Sodium and Potassium**: They are important in cell physiology, muscle physiology, transmission of messages and other biological processes.

**Sodium** is the principal cation of extra cellular fluid. It is commonly found in all types of foods. Recommended dietary allowance (RDA) is 5-10 gm. It is excreted in the urine. The concentrations are maintained by Aldosterone hormone.

 Serum Sodium normal levels 135-145 Mmol/l

**Potassium** is intracellular cation; daily requirement is 1 gm/day. Its excretion is through kidney, linked to sodium excretion.

Since both are widely distributed, deficiency of the two elements is rarely found.

**Functions**:

• Sodium maintains osmotic pressure of extra cellular fluid (ECF) balance.

• supports the neuro muscular excitability

• Sodium is exchanged with Hydrogen in renal tubules to acidify urine.

• Sodium pump keeps sodium in far higher concentration outside the cell.

 • Sodium and Potassium maintain the degree of hydration of plasma proteins, and there by viscosity of blood.

• Potassium is critically important for the functioning of cardiac muscle.

**Hypernatremia**: It occurs nearly always due to water deficiencies rather than Na+ excess. Increased sodium is found in ECF. It may be due to increased sodium in the body, decreased body water. It is usually seen in patients with dehydration, on steroid therapy or excess sodium intake.

**Hyponatremia**: It is common in patients who are in diuretics or excessive sweating, kidney disease, diarrhea and congestive heart failure.

**Hyperkalemia** is found in patients who are on excess intake orally or given intravenous drip. Other causes are decreased excretion by the kidney, diseases like Anuria, tissue damage or Diabetes Mellitus.

**Hypokalemia**: Low potassium is not due to dietary deficiency but due to conditions like vomiting, diarrhea. Habitual users of laxatives are prone to the condition.

**Calcium and Phosphate:** Major parts (90%) of them are found in the form of crystal lattice in the bone. The rest is found in the soft tissues, teeth and ECF.

**Sources**: Milk, milk products, green leafy vegetables are rich in calcium.

Phosphate is widely distributed in nature.

**Calcium**: RDA 500mg for adults and 1200mg for children, 1500mg for post-menopausal women. People, who get enough sunlight, exercise regularly, on high protein diet, require 300- 400mgs per day.

**Absorption**: It is influenced by

 • Acidic pH solubilizes Calcium salts, promote absorption.

• High protein diet favors absorption

• Certain plant products, high fiber diet, oxalates interfere with absorption.

 • Vitamin D promotes absorption.

• PTH, Calcitonin favors absorption while Glucocorticoids decrease intestinal transport.

 • Normal blood concentration is maintained at 9-11 mg %.

 **Functions**:

• Calcification of bones and teeth. Bone formation requires Calcium continuously.

 • It is important for blood coagulation

• Neuromuscular transmission.

• Muscle contraction

• Acts as secondary messenger in hormone action.

**Clinical conditions:** Hyper- calcemia; may be due to hyper parathyroidism, endocrine causes, renal failure and malignancies.

Hypo- calcemia (below 8.5mg %) due to

• Inadequate dietary intake.

 • Hypoalbuminemia

• Hypo parathyroidism

• Renal disease/ failure

• Vitamin D deficiency

Chronic deficiency leads to loss of bone mass (bone resorption) and osteoporosis, bone fractures

**Phosphorus**:

**Dietary** sources are cheese, milk, nuts. Eggs and organ meats.

Absorption and regulation is similar to that of Calcium.

**Functions**

• Constituent of bone and teeth

• Needed for the synthesis of energy rich molecules like ATP and Creatine phosphate.

 • It forms Phosphate buffer in blood.

 • Constituent of phospholipids, biomolecules and coenzymes.

**Trace elements**

Daily requirements of some elements is very low and such elements are known as trace elements.

**Iron**

Iron In body is found in Haemoglobin, Myoglobin, ferritin, hemosiderin, transferrin and enzymes like cytochromes etc.

**Sources** are meat, fish, eggs, cereals like wheat, green leafy vegetables.

Absorption is through intestinal mucosa.

Requires acidic pH of stomach. Ascorbic acid and Ceruloplasmin promotes absorption.

It combines with intracellular binding protein Apoferritin to form ferritin. Almost 300 ferric ions can bind to one molecule of apoferritin..

For transport, free iron binds to Apo transferrin, in blood to form **transferrin**. It is the major transport form of iron. It also prevents toxicity of free iron.

Excessive binding of iron causes denaturation of ferritin molecule. It undergoes aggregation, to form hemosiderin. Mobilization of iron from hemosiderin is very slow. Thus there is accumulation of hemosiderin and the condition is called **hemosiderosis**.

Massive deposits of hemosiderin in tissues lead to **hemachromatosis**. If this takes place in liver, it causes cirrhosis. In pancreas, it damages β cells, result in Bronze diabetes. The skin of the patient has bronze coloration. Oxidative damage to cardiac muscle is a biggest concern.

Iron is stored in liver, spleen and bone marrow.

**Deficiency**.

Deficiency leads to Iron deficiency anaemia which is a type of hypochromic microcytic anaemia. It is associated with low hemoglobin and low ferritin levels.

**Copper**

Human beings contain around 100 mgs of copper. Liver, brain, kidney and heart are rich in copper. Free copper is 4%, 96 % is bound to Ceruloplasmin in body.

 **Sources**: cereals, legumes, raisins, nuts etc

**Functions**:

• Cofactor of enzymes like cytochrome oxidase, dopamine decarboxylase, tyrosinase, Cytochrome .C oxidase and superoxide dismutase and monoamine oxidases are dependent on copper. Tyrosine oxidase is important for collagen metabolism

**Copper deficiency:**

• Failure of melanin formation because tyrosine oxidase becomes inactive.

**Menke’s** **disease** or **Kinky** hair syndrome: It is a fatal sex linked recessive disorder in which there is cerebral and cerebellar degeneration, connective tissue abnormalities and kinky hair.

• Both serum [Copper] and [Ceruloplasmin] is low.

• Absorption of copper from the intestine is grossly impaired, but treatment with parenteral copper has not proved successful.

 • It is X- linked disorder. Patient has normal absorption of copper but transport across the serosal aspect of mucosal membrane is defective. Patient suffers from mental retardation.

**Wilson’s disease:** It is an Autosomal, recessive disorder. There is a decrease in the biliary excretion of copper. Blood and tissue copper is high in these patients. It leads to retention of copper, followed by hepato-lenticular degeneration. Ceruloplasmin synthesis is incomplete in the liver. Patient suffers from progressive hepatic cirrhosis and finally liver failure.

There is dysfunction of lenticular region of brain

Defective tubular reabsorption in kidney leads to aminoacidurias.

Copper deposition in the eye, as golden brown or green ring around the cornea.

Patients are treated with Pencillamine, which binds to tissue copper and mobilizes it.

**Magnesium:**

It is an intracellular ion, essential for life.

**Sources**: Widely distributed in vegetables, chlorophyll, cereals, beans, potatoes, cheese and animal tissues.

Maximum concentration is found in bones, little in Extra-cellular fluid (ECF) and soft tissues.

2/3 of magnesium in blood is in ionic form, rest is bound to protein.

It is absorbed from the small bowel.

It is excreted through feaces, urine and sweat.

**Functions**:

• Role in enzyme action. It is a cofactor for peptidases, ribonucleases, glycolytic enzymes etc.

 • Its action is similar to that of calcium in neuromuscular irritability.

• High levels depress nerve conduction, low levels may cause Tetany.

 • Major part is found in bones. In teeth, it is present as dentin and enamel.

• Magnesium deficiency occurs rarely in man.

**Fluorine**

It is solely derived from water, tea, and fish. Daily intake should not be more than 3mg. Excess is toxic, lethal dose is 2.5 gm. It is absorbed by diffusion from intestine. Mostly it is found in the bones and teeth. It is eliminated in the urine.

**Functions**:

• Fluorine is important for teeth development and prevention of Dental Caries.

• High consumption, leads to high concentration of Fluorine in enamel and dentine.

 • It decreases calcium deposition.

• Teeth acquires mottling of enamel, teeth develop pits and discoloration.

• Bones contain traces of fluorine. Small quantities of it promotes bone development, increases retention of calcium and phosphate, prevent osteoporosis

 • High level of fluoride in bone causes abnormal rise in calcium deposition, increases bone density Flurosis is due to toxicity of fluoride. Excess can be due to high dietary intake, contaminated water or inhalation of fluorine.

• It damages mitochondria

• Inhibit enzymes which depend on Mg, like Succinic dehydrogenase.

• Protein synthesis decreases in muscle, heart, kidney, lungs, pancreas and spleen.

 • Collagen synthesis is adversely affected.

 **Iodine**

**Sources**: Vegetables, fruits obtained from sea shore, sea fish are rich in iodine. It is absorbed from small intestines and transported as protein complex in plasma.

Deficiency causes goiter

**Zinc**

**Sources** are liver, milk, fish, dairy products, cereals, legumes, pulses, oil seeds, yeast and spinach etc.

It is absorbed in duodenum and ileum.

Absorption of Zinc from the intestine appear to be controlled in a manner similar to Iron. It is transported bound to a protein (α2-macroglobulin and transferrin)

It is excreted in urine and feaces.

Diets rich in calcium, phosphates interfere with Zn absorption.

RDA is 15-20mgs for adult, 3-15mgs for infants and children

It is bound as complex of protein Metallothionein. The sulfur groups of the protein chelate zinc.

The body does not store Zinc to any appreciable extent in any organ, urinary excretion is fairly constant at 10 μmol/day.

**Functions**:

• Zinc is important for the activity of a number of enzymes like

 Carbonic anhydrase, Alkaline phosphatase, Alcohol dehydrogenase Porphobilinogn synthase Leucine aminopeptidase, Carboxy peptidase, Aldolase in glycolysis DNA, RNA polymerases as zinc has crucial role in DNA.

 • Release of vitamin A from liver requires Zinc. Retenene reductase (zinc enzyme) participates in the regeneration of rhodopsin (visual cycle).

• Insulin is secreted, stored as a complex of Zinc

• It is important for wound healing.

**Deficiency of Zinc**: Patients requiring total parenteral nutrition, pregnancy, lactation, old age and alcoholics have been reported as being associated with increased incidence of Zinc deficiency.

It is usually associated with protein energy malnutrition (PEM)

It is caused by diuretics, chelating agents and anti-cancer drug treatment

• Results in dwarfism and hypogonadism

• Delayed sexual development

• It decreases spermatogenesis in males and irregular menstrual cycles in females.

 • It stimulates ribonuclease activity; thereby it affects the synthesis of mononucleotides and nucleic acids.

• Hepatosplenomegaly

• Severe Zinc deficiency can lead to a postular skin rash, loss of body hair, diarrhea and mood change.

**Selenium**

Selenium is rich in liver, kidney, finger nails. Usually plant products are good sources than animal based diet.

It is absorbed from duodenum, transported as selenomethionine. It forms a complex with plasma proteins for transport. In tissues, free selenium is released.

It is excreted in urine.

**Functions**:

• Glutathione peroxidase is a selenium dependent enzyme. The enzyme has a role in oxidative damage by free radicals. The enzyme is critically important for the membrane stability of Red blood cells.

• Selenium has sparing action on vitamin E, by three ways. It promotes digestion, absorption of lipids and vitamin E. It is a part of glutathione peroxidase, prevents peroxidation of PUFA in the membranes. This in turn reduces the requirement of vitamin E. It helps in the retention of vitamin E in the blood.

• It is a cofactor for an enzyme involved in the synthesis of thyroid hormone.

**Deficiency of selenium:**

• Liver cirrhosis

• Pancreatic degeneration

 • Myopathy, infertility

• Failure of growth

Toxicity: - Selenium toxicity is called Selenosis -Toxic dose is 900micro gram/day - It is present in metal polishes and anti-rust compounds

- The Toxicity symptoms are Hair loss, falling of nails, diarrhea, weight loss and gas leaky odor in breath (due to the presence of dimethyl selenide in expired air).

Halogenated aromatic hydrocarbons are useful in the treatment of Selenosis.





