

Clinical Biochemistry "

$l_3 + l_4$
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Minerals and water in Life Process

Body contain large amount of water 65-90% by weight and smaller amount of inorganic salts (minerals). These minerals regulate distribution of water through out the body and play a vital role in metabolic reaction in the body. Water is powerful solvent for many ionic compound and neutral molecule, because of the polarity and hydrogen bonding of the molecule.

Water balance

Water intake :

An average daily water requirement in adult about 1500 - 2500 ml from :

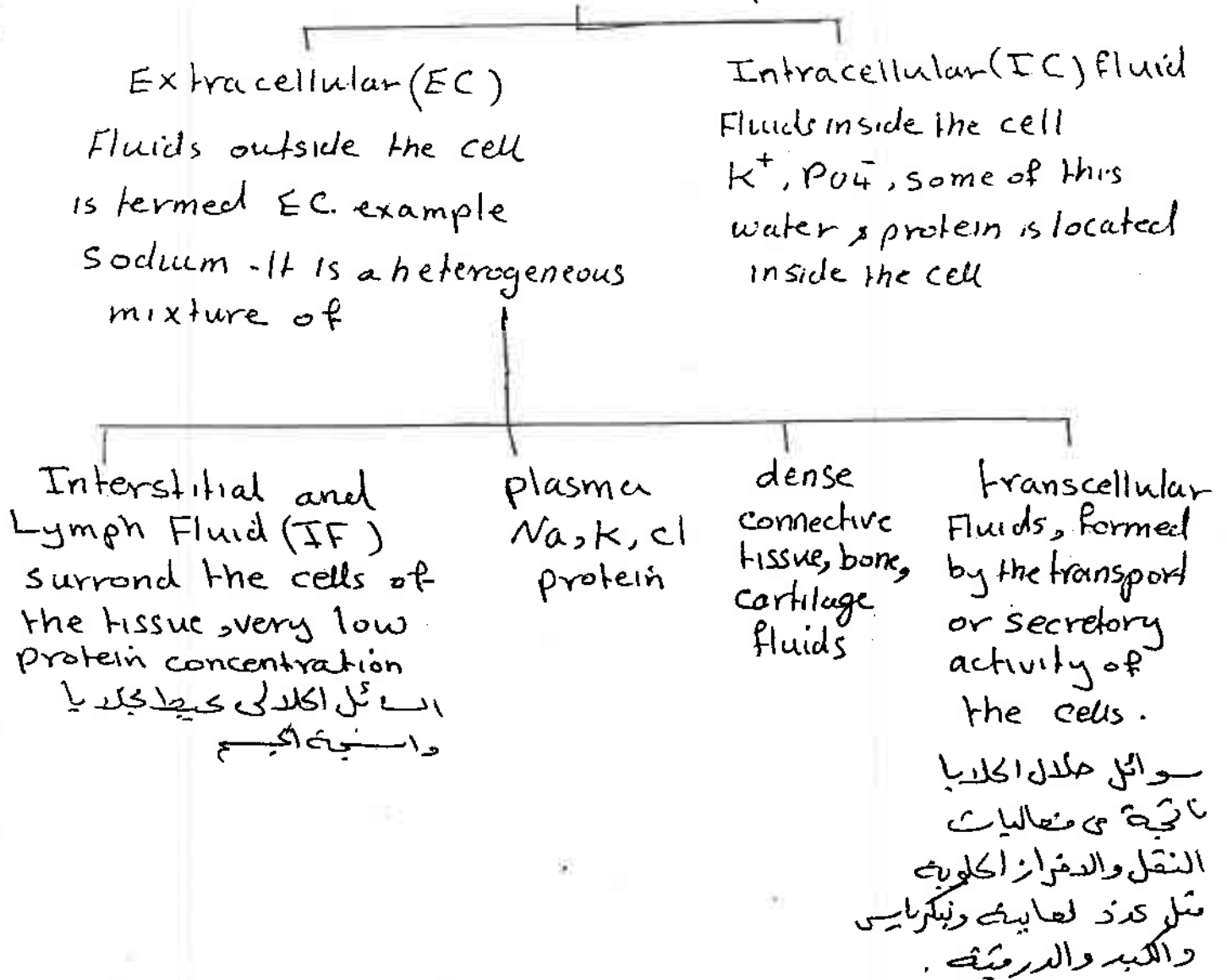
- (a) oral fluids
- (b) water content of food, Melon & Citrus contain 9% H_2O .
- (c) Metabolism, oxidation of food to CO_2 & H_2O provides 300 - 500 ml of water daily.

Water is absorbed in response to the osmotic pressure difference between plasma and intestinal contents.

Water loss:

- (a) Kidneys (urine)
- (b) skin, evaporation occurs from the skin, sweating
- (c) Lungs, water vapour lost into expired air.
- (d) Intestine, Faeces 100-200 ml daily.
- (e) Muscular work & fever produce a marked increase in water loss.
- (f) Salicylate poisoning.

Total body water distributed between 2 main fluid compartment



The important Factors - which effect on distribution of water on the body :

- ① Electrolyte, Na, K (inorganic)
- ② Organic substance with high Mo. wt is protein (albumin).
- ③ Organic substance with low molecular weight, e.g. urea, glucose, amino acids.
- ④ other constituents, these consist of lipids, including triacylglycerols, phospholipids, & cholesterol.

Function of Minerals

- ① Osmotic pressure, the change in osmotic pressure is due to change in sodium ion.
- ② Cell permeability, organic compound of low Mo. wt diffuse freely across cell membrane and aid in retaining H_2O in the body.
- ③ Minerals regulate distribution and retention of H_2O . Minerals are needed to maintain the cellular fluid balance.
- ④ Some minerals act as cofactor for some enzyme activity.
- ⑤ To form bone & blood cells
- ⑥ To provide electrochemical nerve activity and electrical potential.
- ⑦ To regulate muscle activity (including organ muscles like heart, stomach & liver).

(Mineral balance in the body)

It depend upon the following condition:

- ① Amount of mineral present in the food or (nutrients)
- ② Efficiency of absorption from gastrointestinal tract.
- ③ Utilization and storage of minerals by tissue, Minerals are primarily stored in bone & muscle tissue so toxicity is a possibility
- ④ Removal of minerals from the body through the Urine, feces & sweat.

(The minerals present in the body or Element)

The mineral or inorganic substance are called trace metals. They are divided into two groups:

A. major trace metal (macrominerals)

are those needed in relatively large amounts, with requirements expressed as % of the diet, they are:

Ca, P, Na, K, Mg, Cl, S, Li

B. Minor trace metal or mineral

Those are needed in small amount are called minor trace mineral, they are required an activator e.g

Fe, Cu, Zn, F, I, Mn, Co, Mo, Se, Cr

These minerals are important part of physiologic compound such as:

Iodine in thyroxine

Iron in Hb

Zinc in insulin

cobalt in vitamin B₁₂

Sulfur in thiamin, Biotin, CoA, Lipic acid

Calcium (Ca)

Requirement:

400-800 mg, during pregnancy and lactation addition 500 mg is given / day.

The normal level of blood calcium in human from 9-11 mg / 100 ml of serum.

It is present in plasma in three forms:

- 1/ bound to organic acids: example citrate and phosphate about 6% of total calcium.
- 2/ protein bound (to albumin) about 50%, the binding is parallel to increase of blood pH, if increased (pH) binding will increase and if decreased binding will decrease.
- 3/ Ionized and non ^{Free} ionized diffusible state or biologically active calcium.

Function of Calcium (Ca)

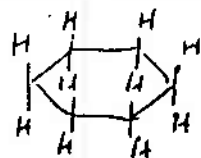
(Composition)

- 1/ It is needed for the formation of a part in bone and teeth (about 90% of the body), Ca is deposited as Ca-P.
- 2/ blood clotting or coagulation.
- 3/ Calcium participates in the protein structuring RNA & DNA.
- 4/ It is essential for the activity of many enzymes e.g. Lipase, succinic dehydrogenase, adenosine triphosphate (ATPase) and certain proteolytic enzyme are activated by Ca.
- 5/ Ca is essential for muscle: contractility & normal neuromuscular activity. In absence of Ca all type of muscle loss their ability to contract.
- 6/ Cell membrane permeability is generally decreased by calcium.

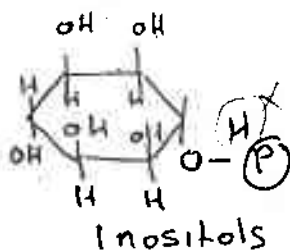
"Factor affecting calcium absorption"

- ① pH : acidic pH favours absorption, increase in gastric acidity increase solubility of Ca-salt.
- ② Ca/P ratio in diet normally 1/1.5 or 1:2
Calcium is very inter-related with phosphorus, so Ca:P ratio is very important. If the ratio outside these limit effect the absorption & excretion.
- ③ presence of phytate, oxalate, fat excess, decrease the absorption of calcium.

e.g. phytate (phytic acid) react with Ca & form insoluble salt of phytic acid, phytic acid is present in some food cereals



Cyclohexane



Inositols

one of the H is replaced by OH called inositol. If OH of all inositol is phosphorylated the compound is called phytic acid

Oxalate precipitate Ca as insoluble Ca-oxalate in the intestine & ↓ absorption

Fat : digestion of fat to glycerol & fatty acid
If free F.A not absorbed in the intestine, it form Ca-salt of fatty acid, ↓ absorption.

④ Iron :

Iron react with phosphate form insoluble Ferric phosphate & ↓ absorption

⑤ protein

high protein intake ↑ the absorption of calcium because certain Ca-salt are much more soluble in aqueous solution of amino acid than in H₂O.

⑥ Lactose increase absorption

Absorption and excretion :

It is poorly absorbed in the intestine according to body need. Absorption is aided by :

- (a) Vitamin D, it is essential for the absorption of Ca from intestine & increase absorption
- (b) parathyroid hormone, corticosteroids, & growth hormone.

Calcium is excreted in feces and urine, Faecal Ca consist of that which has not absorbed & with that secreted into the intestine.

Blood Calcium :

parathyroid gland secretes hormone (PTH), to maintain the constant blood calcium level, or parathyroid hormone are sensitive to the level of Ca.

It draws the Ca from the bones, to raise blood Ca. IF the level of Ca is too high, Calcitonin is secreted from cells in the thyroid gland & control blood serum Ca level, fast & of short duration.

Factor affecting intake of Ca :

The amount of Ca entering the body depend on the amount in the diet which is 1g/day 25-50% absorbed.

Deficiency :

Ricket in young or children
poor growth, Osteomalacia
hyperexcitability, muscle cramps
tooth decay

"phosphorus" P

Requirement : 1.5 g/day adult)

phosphorus is present in every cells 80% in bone & teeth, 10% in combination with carbohydrates, protein and lipid. Remaining 10% in other parts of the body

Functions

- ① plays essential roles in bone and teeth formation.
- ② phosphate is present in high energy phosphate bond such as ATP (adenosine triphosphate)
- ③ It is used in the synthesis of phospholipid & Lecithin & constituent of cell membrane, nervous tissue.
- ④ Various coenzyme are phosphate compound, NAD, NADP, FAD, pyridoxyl phosphat TPP etc.)
- ⑤ Constituent of metabolic intermediates like nucleoproteins,
- ⑥ Constituent of many enzyme
- ⑦ buffer, HPO_4^- & H_2PO_4^- are required for the maintenance or control of acid base balance
- ⑧ it is important in metabolism of R.B.C

phosphate is present in 2 forms in plasma :

a/ Inorganic form

b/ organic form which is phosphate bound to lipid.

Absorption and excretion

It is readily absorbed and excreted by kidney. phosphate is different from calcium at kidney site. The kidney tries to reabsorb calcium and excrete PO_4 in urine this is controlled by parathyroid hormone (PTH). In absence of PTH 90% of PO_4 is reabsorbed in the renal tubule.

Hypophosphataemia

occurs due to excess use of aluminium hydroxide as an antacid.

Uncontrolled metabolic acidosis can lead to excessive phosphate loss in the urine.

Symptom of hypophosphataemia

is muscle weakness & deformity of bones.

Osteomalacia, renal rickets & cardiac arrhythmia

(Sodium, Na)

Requirements:

Normal healthy person 5-15 g/day as NaCl
 patient of hypertension 1 g/day

Metabolic function:

- (1) Na is the major element of extracellular fluid in normal person, it is an important electrolyte.
- (2) Na is essential to maintain the osmotic pressure.
- (3) It protects the body against excessive fluid loss.

- (4) It is associated with Cl^- & HCO_3^- in regulation of acid base balance of the body (buffering action).
It carries an electrical charge when it is dissolved in blood.
- (5) It plays an important role in the permeability of cells CO_2 transport.
- (6) Sodium also plays an important role in nerve & muscle function.

Hyponatremia \downarrow Na

\therefore Low concentration of serum Na, this may develop under the following condition:

- ① In adrenal secretion of cortical hormone may decrease serum Na and increase Na excretion in urine (Addison's disease - adrenocortical insufficiency).
- ② In chronic renal disease, particularly when acidosis exists, Na depletion may occur due to poor tubular reabsorption of Na.
- ③ extreme sweating may cause the loss of Na due to dehydration, acidosis, tissue atrophy.

Symptom of hyponatremia

1. muscular cramps of the extremities and abdomen
2. headaches
3. nausea ~~induced~~, vomiting & diarrhea due to overhydration.

(Hypernatremia \uparrow Na)

Increase in serum Na, this condition is rare but occurs due to:

- ① rapid administration of sodium salt due to hyperactivity of adrenal cortex.
- ② Dehydration associated with diabetic insipidus due to water depletion (rapid loss of H_2O).

Symptoms: excess sodium lead to

1. Hypertension
2. Oedema
3. Anemia

Absorption and excretion of Na

It is readily absorbed, it is excreted in urine & sweat. Aldosterone increases its reabsorption that occurs in renal tubules, concerned in the regulation of Na & K balance.

Potassium K

Source:

drinking water, banana, apricot, dried peach juice orange, pineapple, potatoes

Requirement: 4 gm/day

Function of K

- ① K is the principle cation of the intracellular fluid,
- ② It regulates acid base balance and osmotic pressure.
- ③ It affects muscular activity, cardiac muscle & it is concerned with neuromuscular irritability & nerve function.
- ④ buffering action & CO_2 transport

(5) It is important in retention and distribution of water (water balance).

(6) membrane permeability

Hyperkalemia $\uparrow K$

High serum K :

- (1) Concentration is caused by potassium sparing diuretics.
- (2) High level of K produce cardiac arrest and small bowel ulcers.
- (3) Toxic elevation of serum K in renal failure.
- (4) advanced dehydration or shock, $\uparrow K$
- (5) In adrenal insufficiency, serum K is \uparrow

This elevated serum K is corrected by administration of desoxycorticosterone.

K level is regulated by aldosterone
load in K, increase aldosterone production, while
depletion or \downarrow in K, decrease in aldosterone production.

Symptoms

- (1) Cardia and CNS depression, they are related to elevated of plasma K, and not increase in intracellular K level.
- (2) numbness
- (3) Paralysis of the extremities
- (4) weakness of the respiratory muscle.

Hypokalemia \downarrow K

Low serum K

- ① occur in post operation illness
- ② malnutrition & diarrhoea
- ③ during diuretic therapy e.g. thiazide group - (furosemide) inhibit aldosterone.
- ④ overactivity of adrenal cortex, or injection of excessive quantity of corticosteroid.

Symptom of low K

- ① Muscle weakness, irritability, paralysis
dilatation of heart, hypoxia
- ② prolonged deficiency of K may produce severe damage to kidney, pyelonephritis, kidney inflammation.

Magnesium (Mg)

Requirements: 300-350 mg/day

Functions:

- ① Magnesium is required for the activation of many enzymes involved in the carbohydrate metabolism.
- ② it is also required for the prevention of calcium oxalate stone formation in the kidney.
- (3) It decreases neuro muscular irritability

Deficiency symptoms:

- ① Deficiency symptoms are muscle twitch, convulsion, and cardiac arrhythmia
- ② In diabetes mellitus and acidosis magnesium loss is more from the body.
- ③ Hyperirritability

Iron

Requirement : 10-18 mg/day

Natural sources :

Bananas, black molasses, raisins, Lentils, Walnut oyster shell.

Functions :

- 1) Iron is essential for cellular respiration
- 2) Iron is required for the synthesis of iron containing proteins like hemoglobin, myoglobin, cytochrome, catalase, peroxidase, oxidase, and electron transport system.
3. Remaining iron bound with protein @ transferrin & Ferritin.
The total body contain about 3-4 gm iron.
1/3 of circulating serum iron is transported bound to the protein transferrin and the rest is stored in the liver to the protein ferritin and hemosiderin

Absorption of Iron

Iron in the food is present in the ferric state. In presence of low gastric pH or vitamin C, ferric iron is converted into ferrous state in the stomach. Ferrous form of the iron is absorbed into the mucosal cell.

The absorption of iron is regulated by ferritin protein in the mucosal cell. Iron enters the plasma in ferrous form and combine with glycoprotein called transferrin. While presence of phytate delay iron absorption.

Ferritin protein is stored in liver, spleen, intestine, bone marrow

Transferrin is utilized by various organs like, liver bone marrow, muscle and other tissue for synthesizing iron containing proteins.

Absorption of iron is affected by two factors :

1/ physiological factors :

- a. either state of iron stores
- b. or rate of erythropoiesis e.g thalassemia

2/ Local factor in GIT, chemical state of iron should be in ferrous state, (HCl & vitamin C keep iron in ferrous state).

Deficiency symptoms :

1. anemia (pale skin, fatigue)
2. decreased immunocompetence
3. difficult breathing
4. brittle nails
5. constipation & iron deficiency

Toxic effects of iron :

Excess iron in the body leads to haemochromatosis in which iron deposits are found in abnormally high level in many tissues. This can lead to liver, pancreatic and cardiac dysfunction as well as pigmentation of skin.

Molybdenum (Mo)

Functions :

as component in several enzymes that are involved in alcohol detoxification, uric acid formation, sulfur metabolism e.g xanthine oxidase, important for blood & for enzymes involved in oxidation processes.

Chloride (Cl)

It is responsible for osmotic balance & gastric HCl, acid base balance & chloride shift. It is rapidly absorbed and excreted in urine.

Sulfur (S)

Functions:

- (1) It is elemental component of protein, heparin, thiamine, mucopolysaccharides, biotine, Lipic acid, glutathione, CoA, bile salt, insulin, all containing S.
- (2) It is very important organic molecule present in all cells of the body.
- (3) It is important in connective tissue.
- (4) It is needed for detoxication of hormone and some drugs.

Absorption & excretion.

It is derived from metabolism of S containing amino acid like cysteine, cystine & methionine & excreted in urine.

Deficiency: cystinuria, methioninuria, it is an inherited defect.

Lithium (Li)

It is present in all tissues in extra as well as intracellular fluids or spaces. Human blood contains $0.006 \mu\text{g}$ of Li/ml. It is used in treatment of manic depression, but its level has to be controlled otherwise it will be toxic. It exerts protective effect on heart tissue. Deficiency: nerves, mental disorders.

Copper (Cu)

requirement : 0.05 - 2.5 mg / day

Function :

- (1) Cu function as a cofactor for many enzymes like Cytochrome oxidase, tyrosinase, dopamine, β -hydroxylase, superoxide dismutase and monoamine oxidase.
- (2) It is required for the biosynthesis of hemoglobin.
- (3) In bone formation of myelin within the nervous system
- (4) Oxidation reduction reaction of enzyme activity in tissue.
- (5) It is needed for connective tissue formation (skin) muscle, heart, blood vessels & Lungs.

Ceruloplasmin :

Cu-binding protein globulin in serum or plasma. It is the name applied to protein that carries most of the blood plasma copper.

Hemocyanin : is copper - protein complex act as a carrier of oxygen as Hb

Deficiency Symptoms :

- (1) Fragility of large arteries (damage to wall artery)
- (2) Hypercholesterolemia (high LDL)
- (3) Anemia, poor growth.
- (4) bone disorders & brain disturbances
- (5) Impaired immune function

Iodine (I)

requirement 100-200 μg /day (microgm/day)

Functions :

- (1) Iodine is necessary for the formation of thyroxine & triiodothyronine (T_3) hormones.
- (2) obtained from diet in the form of inorganic iodine.
- (3) The ingested iodine is rapidly absorbed through the digestive tract and taken up by thyroid gland.
- (4) In the thyroid gland iodine is converted to organic iodine containing compound namely thyroxine.
- (5) Thyroid hormone increase the oxygen uptake of all tissues. It is a regulator of cellular oxidations.

Deficiency :

deficiency of iodine affect the development of all tissues, as :

Cretinism : due to iodine deficiency occurs in children and causes swelling of thyroid gland, this is characterized by mental retardation

② slow body development

③ dwarfism

Goiter : deficiency of I cause goiter, this can be prevented by using iodine salt

hypothyroidism is caused by \downarrow in I

hyperthyroidism is caused by \uparrow in I

Iodine is concentrated in the thyroid and transported by protein bound iodine (PBI).

Manganese (Mn)

2.0 — 5.0 mg / day

Function :

- 1) Forms bone, connective tissue, joint cartilage
- 2) Important for brain, thyroid, muscles, & nerves.
- 3) It is a part of glucose metabolism
- 4) Cofactor for metalloenzyme activity such as: carboxylase, hydrolyase, isocitrate dehydrogenase, kinase.
- 5) It is required for the synthesis of mucopolysaccharides.
- 6) needed for normal bone growth

Deficiency :

- ear noises
- ataxia (muscle coordination failure)
- hearing loss
- dizziness

It is stored in bone and in liver & excreted through bile.

Cobalt (Co)

1.1 mg / day, It is present in cyanocobalamin.

Function :

- 1) Form an essential part of vitamin B₁₂
It is also a necessary cofactor for making the thyroid
 - 2) hormone
 - 2) for blood & Hb formation
- It is stored in the liver, limited absorption in the intestine, excreted through bile.

Deficiency : pernicious anemia
excess of Co causes polycythemia

Function,Zinc (Zn)

- (1) It is constituent of insulin, carbonic anhydrase, lactic dehydrogenase, alcohol dehydrogenase, and alkaline phosphatase, RNA, DNA polymerase.
- (2) recently they found that it is associated with memory.
- (3) It is necessary for the functioning of the sense of taste and smell.

Deficiency : causes (1) anemia (2) growth retardation

- (3) hypogonadism and dwarfism
- (4) decrease protein synthesis

Absorption :

It is absorbed in the intestine, it is stored bound to protein.

Selenium (Se)

- (1) It is constituent of glutathione peroxidase
- (2) It inhibits lipid peroxidation
- (3) It is necessary for action of the enzyme glutathione peroxidase which is necessary for conversion of H_2O_2 produced in R.B.E from metabolic process into H_2O & oxidized glutathione.

